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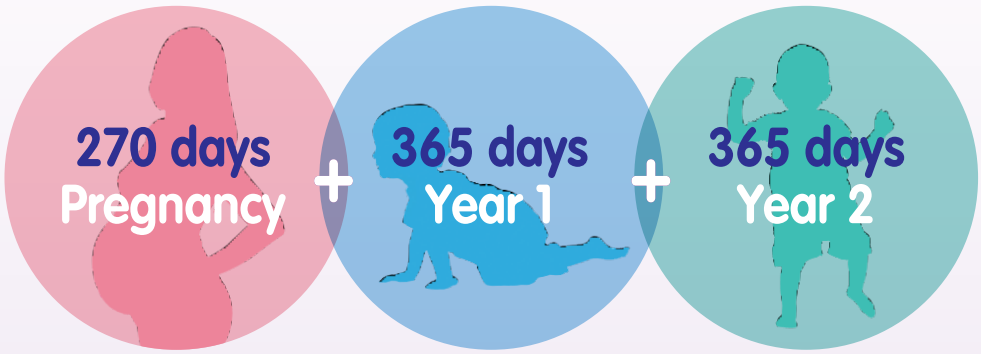

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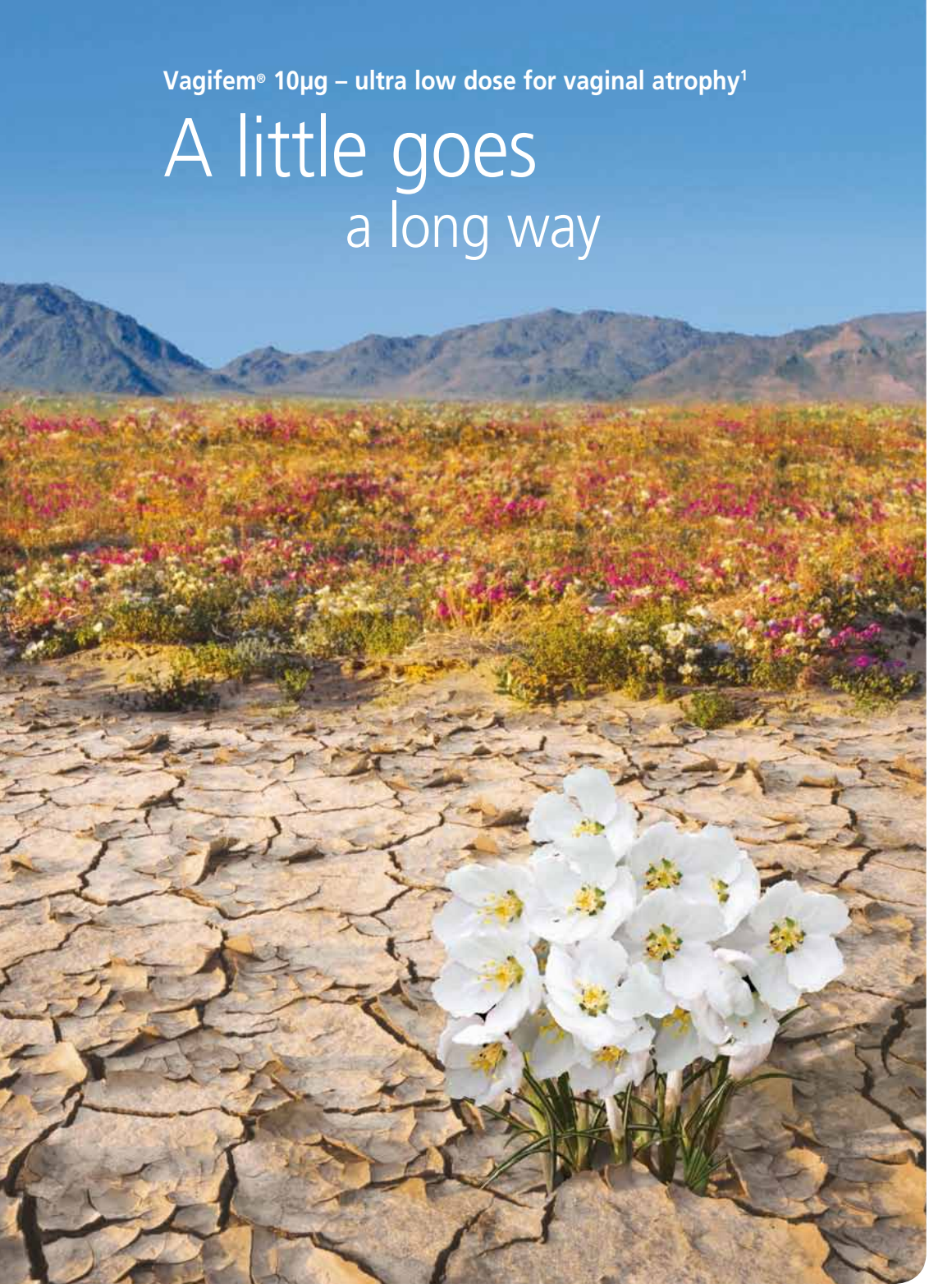

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Editorial
From the Editor-in-Chief

It is my great pleasure and honour to be appointed by our President as the Editor-in-Chief of the *Hong Kong Journal of Gynaecology, Obstetrics and Midwifery*. I am extremely fortunate to follow in the footsteps of Dr Lawrence Tang, who delivered the first issue of the journal in 2000 as the founding Editor-in-Chief, and Dr KY Leung, our second Editor-in-Chief, who has successfully consolidated the recognition of the journal within our specialty and beyond for the past 10 years. My gratitude also goes to Ms Manbo Man, our founding Chief Editor of the Midwifery section, for her dedication and valued contributions over the past 15 years.

You will all be aware of the gradual increase in the number of papers submitted to and published in the journal, with ever increasing levels of research sophistication and noticeable advancements in scientific quality. In order to allow more rapid dissemination of these papers, we have resolved to deliver a half-year online issue of the journal to shorten the acceptance-publication interval of papers. This will be followed by our regular printed annual edition in mid-2015 that will also include the papers released online. With the ever-expanding use of online media, we hope this will be a first step towards publication of more frequent and regular issues of the journal, albeit at a reasonable production cost.

Two new overseas editors have kindly agreed to join our Editorial Board. Dr Kim Hinshaw from Sutherland, United Kingdom, was once a frequent visitor to Hong Kong, and has contributed immensely to our Acute Life Support in Obstetrics courses, as well as to our previous Hospital Authority Commissioned Training programmes and various College academic functions. Dr Hong-Soo Wong, again an old friend and colleague, now settled in Queensland, Australia, is an avid researcher in advanced ultrasound techniques. Given their familiarity with the clinical practices and environment in Hong Kong, their participation in our editorial work will indeed be a great asset to the journal.

In addition, we are most fortunate that many local colleagues have consented to join the board as editors. Ms Irene Lee will succeed Ms Man as Chief Editor of the Midwifery section, and Prof TY Leung and Ms CY Lai will be our new Deputy Editors. Dr Amelia Hui, Dr WL Lau, Dr TK Lo, and Prof WH Tam will join as editors for the Obstetrics & Gynaecology section and Ms L Cheung will join as editor for the Midwifery section. Prof TC Li, previously our overseas editor, has relocated back to Hong Kong, and we are honoured that he will continue to serve as a local editor on our Board.

I hope you agree that the topics presented in this issue encompass most of the 'hot' topics and subspecialties in obstetrics and gynaecology. I believe that every reader, midwife or doctor, trainee or specialist alike will find new information relevant to their daily practice and clinical interest. In the use of array comparative genomic hybridisation techniques for preimplantation diagnosis[1], the accuracy of ultrasound diagnosis of facial and palatal clefts in the fetus[2] could be categorised as fetal medicine. The predictive value of early (≤20 weeks) oral glucose tolerance testing and glycated haemoglobin measurement for subsequent development of gestational diabetes mellitus in high-risk women should be maternal medicine[3]. The impact of the decision-to-delivery interval on maternal and fetal outcomes[4] in extremely urgent Caesarean deliveries, whether intrapartum ultrasound is more accurate than digital vaginal examination in determining fetal head position[5], or a controlled trial of tissue adhesive (2-octylcyanoacrylate) versus interrupted sutures for Caesarean section wounds would suit the label of intrapartum management[6]. In the Gynaecology section, the questionnaire survey to evaluate the knowledge gaps and attitude of our patients who undergo subfertility treatment belongs to reproductive medicine[7]. The retrospective study of the clinical significance of atypical glandular cells in cervical cytology befits gynaecological oncology[8]. The outcome of women having vaginal mesh repair surgery for pelvic organ prolapse, with particular reference to mesh erosion, suits urogynaecology[9]. Finally, in the Midwifery section, there is an excellent discussion of the implementation of mother-friendly workplace policies in Hong Kong[10].

I hope you will continue to enjoy and cherish this journal, and integrate it into your professional life. With your continuing support, this journal will continue to flourish.

William WK TO MBBS, M Phil, MD, Dip Med, FRCOG, FHKCOG, FHKAM (O&G)

Editor-in-Chief, *Hong Kong Journal of Gynaecology, Obstetrics and Midwifery*

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Implementation of Mother-friendly Workplace Policies in Hong Kong

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Department of Obstetrics and Gynaecology, Queen Elizabeth Hospital, Jordan, Hong Kong

Although the Hong Kong Government and health care professionals have made many efforts to implement baby-friendly practices, a recent survey showed that the use of formula milk was still dominant among children in Hong Kong and the exclusively breastfeeding rate remained very low. Only a few Hong Kong women exclusively breastfeed their infants, and most stop breastfeeding within the first few months. Most employed women discontinue breastfeeding after returning to work. Many studies agree that a supportive workplace is crucial for employed women to sustain breastfeeding. It is necessary for the Hospital Authority to act as the pioneer to implement mother-friendly workplace policies. Many studies show that enacting workplace breastfeeding legislation and extension of maternity leave may facilitate employed women to continue breastfeeding after returning to work. It enables women to extend breastfeeding duration to achieve the global aim of exclusive breastfeeding up to 6 months. It is a preventive health policy, which may reduce the long-term cost in health care for child health and maternal health. Furthermore, breastfeeding may help in decreasing the government expenses for environmental protection.
Hong Kong J Gynaecol Obstet Midwifery 2015; 15(1):11-5

Keywords: Breast feeding; Legislation; Workplace

The Importance of Exclusive Breastfeeding for Six Months

According to the World Health Organization (WHO)[1], exclusive breastfeeding for 6 months could prevent 13% of deaths in children who are under 5 years of age, globally. Moreover, breastfed infants are less likely to suffer from acute infections like diarrhoea, pneumonia, otitis media, necrotising enterocolitis, gastroenteritis, meningitis, and urinary tract infection. Many studies show that longer duration of exclusive breastfeeding reduces the risk of obesity, as well as type 1 and type 2 diabetes in later childhood and adolescence[2]. Furthermore, it also promotes mothers' health by reducing the risk of postpartum haemorrhage, osteoporosis, as well as breast and ovarian cancer. Therefore, every mother has a right to exclusively breastfeed her infant for 6 months, and continue breastfeeding up to 24 months[3].

Impact of Suboptimal Breastfeeding Practices

According to Lau[4], breastfeeding is beneficial not only to the health of infants and mothers but also to the socioeconomic status of the society. According to Vickers[5], breastfeeding promotes environmental protection. Therefore, optimal breastfeeding practices may help in decreasing the government expenses for environmental protection. This is because production of formula milk entails the use of plastic and tin for packing, fuel for transportation, and extra land for waste disposal. Bartick and Reinhold[6] estimated that suboptimal breastfeeding amounted to an annual expense of about $US 13 billion in the United States. However, Bartick[7] argues that these costs are likely underestimated and that a more complete economic analysis of all aspects related to infant feeding is warranted. This should include maternal disease, lactation support, costs of maternity leave, costs of formula production, packing, waste disposal, and related feeding equipment, etc, which may provide a more complete picture on the real costs of suboptimal breastfeeding. According to a statement on breastfeeding by the American Academy of Pediatrics[2], breastfeeding may also save costs arising due to parental absenteeism from work or adult deaths from asthma, type 1 diabetes mellitus, or obesity-related disease due to suboptimal breastfeeding during childhood. The huge economic impact of breastfeeding can serve to inform governments about the importance of supporting breastfeeding policies.

Hong Kong Situation

The average breastfeeding rate in Hong Kong has increased over the last decade. Studies show that implementation of baby-friendly practices enables

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more women in Hong Kong to extend the duration of breastfeeding[8,9]. According to a review by Tarrant et al[9], there was a significant improvement in breastfeeding rates from 19% in 1981 to 37% in 1997. According to the annual survey of Baby Friendly Hospital Initiative Hong Kong Association (BFHIHKA), the breastfeeding rate on discharge from Hong Kong hospitals was 85.8% in 2012, which is the highest ever in the past 20 years (Figure[10]). According to Wong[11], the improvement is mainly due to the breastfeeding promotion campaign by the Hong Kong Government, the BFHIHKA, and the effort of health care professionals. However, the range of exclusive breastfeeding rate on discharge varied from 14% to 56% in public hospitals and 0 to 95% in private hospitals for births in 2012, suggesting that there is still much room for improvement in Hong Kong[10].

A recent survey in 2012, including a total of 1272 children (51% boys and 49% girls), shows that the use of formula milk was dominant among children in Hong Kong and the breastfeeding rate at 6 months was very low, with only 6.8% being exclusively breastfed at 6 months of age. About 80.2% of them used formula milk only, and 13% consumed both breast milk and formula milk[12]. Overall, 7.4% of them were given solid food, regularly, before the age of 4 months, and 41.1% between the age of 4 and 6 months[12]. According to Hirani and Premji[13], "inappropriate feeding is a silent killer of children under 5 years of age".

Woo et al[12] found that the average duration of exclusive breastfeeding in Hong Kong was 2 months. One of the most common reasons for stopping breastfeeding was returning to work[14-16]. According to the Census and Statistics Department[17], about 65.1% of Hong Kong women in the childbearing age of 15 to 49 years were employed in 2012.

Factors Affecting Exclusive Breastfeeding Practices

Wong[11] compared exclusive breastfeeding rates at 6 months in different Asian countries; it was 46.4% in India, 32.4% in Indonesia, 24.2% in Taiwan, and 21% in Japan. In China, the exclusive breastfeeding rates at 4 months were 39.2% in Beijing, 28.1% in Shanghai, and 50.5% in Guangzhou (Table[11,18-20]). The exclusive breastfeeding rate at 4 months in Singapore was 7% which is the lowest in Asia. This study also compared the duration of maternity leave and exclusive breastfeeding rates across different countries to conclude that a longer duration of maternity leave may promote continuation of breastfeeding. There are only 8 weeks of maternity leave in Singapore, which may be related with the lowest exclusive breastfeeding rate in the country. However, Wong's study[11] was not based on the 6-month period of time to compare these data. It may not be able to reflect the real updated situation.

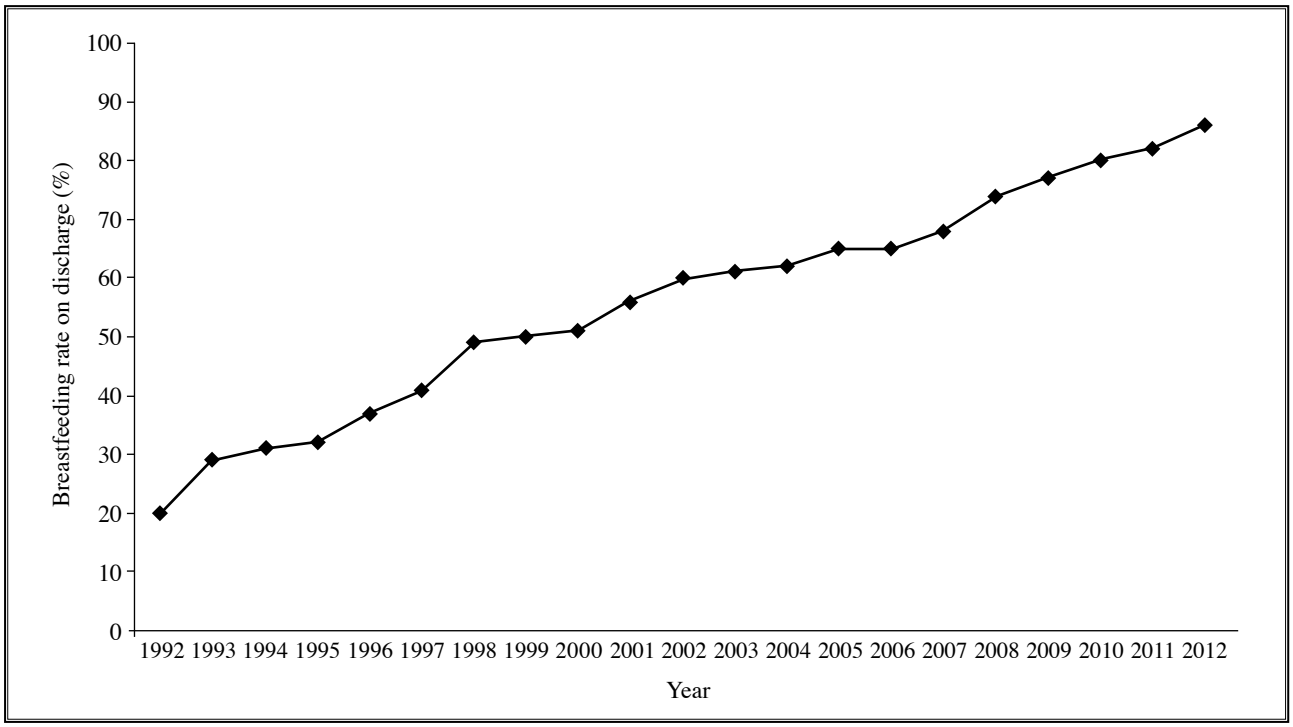

Figure. Data from Baby Friendly Hospital Initiative Hong Kong Association[10]

Table. Rates of ever breastfeeding, and exclusive breastfeeding at 4 and 6 months in different countries[11,18-20]

Countries / regions	Maternity leave	Ever breastfeeding	Breastfeeding at 4 months	Breastfeeding at 6 months
Australia	18 Weeks	87%	57.3%	18.4%
Canada	15 Weeks	72%	51.7%	14.4%
Singapore	8 Weeks	94.0%	7%	
China	98 Days	76-99.9%	22.4-84.2%	
Beijing			39.2%	
Shanghai			28.1%	
Guangzhou			50.5%	
Japan	Paid (14 weeks), unpaid (1 year)	76.7%		21%
India	12 Weeks			46.4%
Indonesia	3 Months	95.2%	40.6%	32.4%
Sweden	13 Months	97.3%	56.2%	12.3%
Taiwan	Full-paid (8 weeks); 60% of salary for 6 more months if she had worked for the employer for more than 1 year	61.8%	39.7%	24.2%
Hong Kong	10 Weeks	85.8%	12.1%	6.8%

According to the Employment Ordinance of Hong Kong[21], pregnant women are entitled to 10 weeks of maternity leave, including 2 weeks before the expected date of confinement, which is one of the shortest maternity leaves in Asia. A study[22] found that most employed mothers considered the 49-day maternity leave to be insufficient for continuation of breastfeeding.

Heymann et al[14] conducted the first analysis that examined the relationships between national labour policies and breastfeeding rates in the 182 member states of the United Nations. In 130 (71%) countries, there are legal breastfeeding breaks with pay and in seven countries, the breastfeeding breaks are without pay. In 45 (25%) countries, there is no policy on breastfeeding breaks. The authors found that a guarantee of paid breastfeeding breaks for at least 6 months was a significant factor associated with increased exclusive breastfeeding rate.

Many studies warn that lack of breastfeeding support in the workplace was a significant barrier for continued breastfeeding among employed women[13,23]. The authors suggest that working mothers should be supported and empowered by offering part-time employment, paid maternity leave, and lactation support at the workplace. The breastfeeding policies and laws in a country may support the working mothers to continue breastfeeding at their workplaces.

Ortiz et al[24] conducted a study on the time spent by working mothers on milk expression. The mothers attended a class on the benefits of breastfeeding, and had access to consultation on lactation. In addition, they had a private room with equipment for pumping breast milk in their workplaces. The authors[24] found that about 77% of women who returned to work would successfully express their milk in their workplaces for a mean of 6.3 months during the study period.

Many studies[22,25,26] agree that support from employers, acceptance towards pumping breast milk by co-workers, and mother-friendly policies are the crucial facilitators for continued breastfeeding among working women.

Hong Kong is one of the countries with no policy for employed women regarding breastfeeding breaks. Guendelman et al[27] found that employed women who have maternity leave of 6 to 12 weeks had a two-fold higher chance of not establishing breastfeeding and increased risk of early cessation of breastfeeding than unemployed women.

Recommendations

Hospitals are the pioneers of breastfeeding promotion. Therefore, hospitals should be the pioneers in protecting, promoting, and supporting employees to sustain

breastfeeding at work. Dodgson et al[28] suggested that employers may provide a supportive working environment to meet the needs of breastfeeding employees including: (1) providing a clean and safe environment such as a designated space or a private room with a door that can be locked for using a breast pump; (2) providing flexibility to allow employees to take breastfeeding breaks as needed to express their milk; (3) providing facilities for expressing and storing breast milk such as a refrigerator for breast milk storage only; (4) allowing the option for part-time employment; and (5) implementing an institutional policy addressing employees' rights to continue breastfeeding after returning to work.

The WHO[3] recommends governments to enact legislation to protect the breastfeeding rights of employed women by providing breastfeeding breaks and extending the period of maternity leave. Lam[8] agrees that government support is crucial in promoting breastfeeding. Hirani and Karmaliani[26] also suggest that policy-makers should extend maternity leave for up to 6 months to achieve optimal exclusive breastfeeding rates to improve child health outcomes.

According to Stewart-Glenn[16], research on breastfeeding should be encouraged as it may reveal benefits such as fewer sick leaves by employees, increased job satisfaction, and decreased loss of skilful staffs. These results may help in obtaining support from employers towards promoting breastfeeding among their female employees. According to the Australian Breastfeeding Association[29], there are many benefits to the employers. It is a simple way to increase the morale and loyalty of their employees. Moreover, it may increase the rate of return to work. Furthermore, it reduces skill loss by retaining valued employees and reducing recruitment and training costs. It may also reduce absenteeism among parents to look after sick children.

According to a statement on breastfeeding published by the American Academy of Pediatrics in 2012[2], employers would benefit from the mother-friendly workplace policies with double to triple return on investment. This is because these policies would reduce employee turnover and increase employee productivity.

Conclusions

There is no legal protection for working mothers to sustain breastfeeding practices after returning to work in Hong Kong. There are many valued employees in the Hospital Authority who are breastfeeding their infants. It would be worthy for the Hospital Authority to act as a pioneer in implementing mother-friendly workplace policies. The return on investment on mother-friendly workplace policies is evidenced by many studies. It is the duty of health care professionals to provide more evidence on it. The WHO[3] advises health sectors to inform decision-makers about the economic burden of suboptimal breastfeeding. It is the duty of health care professionals to conduct research to investigate the impact of suboptimal breastfeeding practices on child health, maternal health, and public health. Government support is a crucial facilitator to protect and promote breastfeeding practices in Hong Kong. It is a cost-saving practice for both the government and the health sector and may serve to decrease the government costs for environmental protection and health care expenses. It is the duty of the health care sector to inform the Hong Kong Government on the importance of addressing these issues and recommend enactment of legislation to protect the breastfeeding rights of employed women by introducing mother-friendly workplace policies, breastfeeding breaks, and extending the period of maternity leave.

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Maternal and Fetal Outcomes in Extremely Urgent Caesarean Delivery in Relation to the Decision-to-delivery Interval

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Objectives: To evaluate whether there were any differences in the maternal and fetal outcomes for extremely urgent Caesarean deliveries having shorter decision-to-delivery interval (DDI) versus those with longer DDI (i.e. >20 minutes), and to explore the reasons for longer DDI.
Methods: Retrospective data were retrieved between 1 January 2011 and 30 June 2013 from all women with singleton pregnancies delivering at >24 weeks of gestation by extremely urgent Caesarean sections for fetal distress. Data including the causes of fetal distress, DDI and the breakdown, perinatal outcomes (Apgar scores, cord blood pH, need for neonatal intensive care unit admission) and maternal outcomes (operative complications, wound infection, need for intensive care unit admission) were collected.
Results: Of 171 extremely urgent Caesarean deliveries, 159 (93%) and 100 (58%) were delivered within 30 and 20 minutes after decision, respectively. Compared with the group with DDI of ≤20 minutes, the antenatal characteristics, gestational age, and birth weight were not significantly different in those with DDI of >20 minutes. No significant differences in the maternal outcomes of fever, endometritis, wound infection, bladder injury, hysterectomy, and the need for special postoperative care were found between these two groups. Besides, the mean cord blood pH was significantly lower in those with DDI of ≤20 minutes (7.19 ± 0.14 vs. 7.23 ± 0.09, p=0.04), however, no significant differences in the Apgar scores at 5 minutes as well as the need for admission to neonatal intensive care unit were noted between these two groups. No hypoxic ischaemic encephalopathy was found in those with DDI of >20 minutes. When compared with those with DDI of ≤20 minutes, more time was required in the preparation and transfer of patient to the operating theatre (15.9 vs. 7.9 mins, p<0.001), induction of anaesthesia (6.9 vs. 6.0 mins, p=0.01), and from skin incision to delivery of the baby (3.4 vs. 2.7 mins, p=0.01) for those with DDI of >20 minutes.
Conclusion: The cord blood pH was lower in the group with DDI of ≤20 minutes than that with DDI of >20 minutes. The reason for delayed DDI was mainly related to the longer time required for preparation and transfer of patient to the operating theatre.
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Keywords: Cesarean section; Decision making; Emergencies; Pregnancy outcome

Introduction

'Crash' Caesarean section (extremely urgent Caesarean delivery) was defined by MacKenzie and Cooke[1] as an abdominal operation to achieve immediate delivery when life-threatening fetal distress occurs. It is regarded as the immediate resort for saving the fetus and/or the mother when instrumental delivery is not achievable or imminent delivery is not expected, with an aim to protect maternal and neonatal well-being. Under the classification system proposed by Lucas et al[2], it is considered as grade 1 emergency Caesarean section. Extremely urgent Caesarean delivery also belongs to the most urgent type of Caesarean section in the continuous spectrum suggested by the Royal College of Obstetricians and Gynaecologists[3]. The global incidence of extremely urgent Caesarean delivery is estimated to be 0.6% to 0.7%[4,5].

Hypoxic ischaemic encephalopathy (HIE), stillbirth or neonatal death may result from delay in delivery, and this has serious implications in litigation. The results of early primate studies demonstrated an increased risk of brain injury with an increased interval of anoxia[6]. In a study of severe placental abruption complicated by fetal bradycardia, a decision-to-delivery interval (DDI) of >20 minutes was associated with substantially increased neonatal morbidity and mortality[7]. Significant neonatal morbidity was also

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observed in uterine rupture with complete fetal extrusion when >18 minutes elapsed between the onset of prolonged deceleration and delivery[8]. Therefore, to obtain the best fetal and maternal outcomes, it seems prudent to achieve a delivery as quickly as possible when severe fetal distress or serious maternal conditions occur.

The guidelines established by several national consensus panels such as the Royal College of Obstetricians and Gynaecologists, American College of Obstetricians and Gynaecologists, as well as Canadian National Consensus Conference recommend that obstetrical services should be capable of performing a Caesarean section within a time interval of 30 minutes[9-11]. The German Society of Gynaecology and Obstetrics advocates a time interval of 20 minutes[4]. However, the literature revealed limited evidence to support this standard, and all these recommendations were established by a consensus of experts.

This study was undertaken to evaluate the maternal and fetal outcomes in extremely urgent Caesarean deliveries with respect to their DDI in the local setting. It aimed to search for evidence concerning the appropriate standard on the time limit for DDI in this locality. The study also explored the reasons for delayed DDI (i.e. >20 minutes) in extremely urgent Caesarean deliveries to estimate the achievability of a shorter DDI.

Methods

Our study comprised women who delivered in Queen Elizabeth Hospital of Hong Kong from 1 January 2011 to 30 June 2013. All singleton births delivered by extremely urgent Caesarean sections at a gestation of >24 weeks were included.

Routine continuous cardiotocograph monitoring was used as standard intrapartum management in the study unit. When there was persistent fetal bradycardia (i.e. <110 beats per minute) for 3 minutes, the use of oxytocin would be routinely discontinued. The decision for extremely urgent Caesarean delivery would be made if the bradycardia showed no sign of recovery, or if it was associated with irreversible causes such as placental abruption or cord prolapse. The woman would be prepared for extremely urgent Caesarean delivery (shaving, insertion of urinary catheter) once the decision was made. On-site emergency anaesthetist support was available for 24 hours. The operating theatre was located in close proximity to the delivery suite, which facilitated the transfer of the patients.

Data were retrieved from the Clinical Data Analysis and Reporting System (CDARS) of the Hospital Authority, supplemented by the hospital's electronic records from the Clinical Management System, the OBSCIS (Obstetric Specialty Clinical Information System), and hospital records. Deliveries by Category A1 emergency Caesarean sections which were formally required to be performed within an hour of decision for Caesarean sections were first selected using CDARS. Those having extremely urgent Caesarean deliveries because of fetal distress were, in turn, selected from the group and included in this study. The definition of extremely urgent Caesarean delivery used in this study was equivalent to the grade 1 emergency Caesarean section under the classification system proposed by the Royal College of Obstetricians and Gynaecologists[3]. Women with multiple pregnancies were excluded.

Medical notes of all eligible cases were retrieved. The causes of fetal distress were reviewed, with the DDI and the corresponding time required in each step collected (preparation and transfer of patient to the operating theatre, induction of anaesthesia, skin incision to delivery of the baby, and uterine incision to delivery of the baby). Demographic data such as age, gravidity, parity, and gestational age were collected. Maternal outcomes including postoperative fever, wound infection, endometritis, injury to bladder, ureter or bowels, hysterectomy and requirements for special care after Caesarean section in addition to routine postoperative care were evaluated. Special care in addition to routine postoperative care included blood transfusion, antihypertensive treatment, use of anticonvulsants in pre-eclampsia, diuretic treatment for renal failure, and surgical management for severe postpartum haemorrhage. Data on neonatal outcomes including Apgar scores at 1 and 5 minutes, cord blood pH, need for intubation or cardiopulmonary resuscitation after birth, need for admission to neonatal intensive care unit, presence of HIE, and neonatal death were retrieved from the neonatal discharge summaries.

The collected data were categorised into two groups: those with DDI ≤20 minutes and those with DDI >20 minutes. Contributory factors for DDI and the corresponding time required as well as the reasons for delayed DDI were analysed. These included: (1) preparation and transfer of the patient to the operating theatre; (2) induction of anaesthesia; (3) skin incision to delivery of the baby; and (4) uterine incision to delivery of the baby.

The collected data were analysed using the IBM Statistical Package for the Social Sciences software, version

22.0 (SPSS Inc., Chicago [IL], US). Baseline characteristics of the study were compared using percentages and a variety of statistical tests. Differences in categorical variables were analysed with Pearson Chi-square test. When the cell counts were less than 5, the differences in categorical variables were analysed with Fisher's exact test. Differences in continuous variables were analysed with independent *t* test. p Values of <0.05 were used as the cutoff point for statistical significance.

The research protocol was approved by the Ethics Committee of the study hospital.

Results

During the study period, extremely urgent Caesarean deliveries accounted for 4.0% of all Caesarean deliveries and 1.1% of all deliveries in the study unit. The subjects' median maternal age was 32 (interquartile range [IQR], 29-36) years. Overall, 123 (72%) women were nulliparous. The median gestational age at delivery was 39 (IQR, 36-40) weeks, and the median birth weight was 3110 g (IQR, 2690-3410g). The median pH of the cord blood was 7.24 (IQR, 7.16-7.29). All the 171 extremely urgent Caesarean deliveries at our hospital were performed under general anaesthesia. A total of 159 (93%) cases were performed within a DDI of 30 minutes. The DDI in our cohort ranged from 11 to 69 minutes, with a median of 19 (mean ± standard deviation, 21 ± 7) minutes.

Identifiable causes for fetal bradycardia included placental abruption (n=16; 9%), cord prolapse (n=15; 9%), and uterine rupture (n=1; 1%). In the remaining 139 (81%) cases, the cause of fetal bradycardia was unknown (Table 1). There was no significant difference in the antenatal characteristics between the two (DDI ≤20 minutes and DDI >20 minutes) groups (Table 2). The proportions of extremely urgent Caesarean deliveries performed after midnight, during weekends or public holidays were similar between the two groups. No significant difference was noted in the experience of surgeons performing Caesarean sections or operative blood loss between the two groups (Table 3).

Regarding neonatal outcome, the birth weight was similar between the two groups. There was no significant difference in the Apgar scores at 5 minutes and the need for admission to the neonatal intensive care unit between the two groups. Also, there were no cases of HIE in the group with DDI >20 minutes (Table 4). The cord blood pH was significantly lower in the group with DDI within 20 minutes (Table 5).

Maternal outcomes including fever, wound infection, endometritis, and bladder injury had similar incidence in the two groups. There was no significant difference in the need for special postoperative care between the two groups. Two cases required hysterectomy, and there were no cases

Table 1. Causes of fetal distress

Cause	DDI ≤20 minutes (n=100)	DDI >20 minutes (n=71)	No. of cases	p Value
				0.39
Unknown cause	79 (79%)	60 (84%)	139 (81%)	
Placental abruption	10 (10%)	6 (9%)	16 (9%)	
Cord prolapse	11 (11%)	4 (6%)	15 (9%)	
Uterine rupture	0	1 (1%)	1 (1%)	

Abbreviation: DDI = decision-to-delivery interval

Table 2. Demographic data of patients who underwent extremely urgent Caesarean delivery

	DDI ≤20 minutes (n=100)	DDI >20 minutes (n=71)	p Value
Mean (± SD) age (years)	31.8 ± 4.7	32.4 ± 5.2	0.47
Median (IQR) gravida	2 (1-2)	1 (1-2)	0.69
Median (IQR) parity	0 (0-1)	0 (0-1)	0.87
No. of previous abdominal operation	9 (9%)	6 (8.5%)	0.56
Mean (± SD) gestational age (weeks)	37.8 ± 3.4	37.4 ± 3.2	0.54

Abbreviations: DDI = decision-to-delivery interval; IQR = interquartile range; SD = standard deviation

Table 3. Details of extremely urgent Caesarean delivery*

	DDI ≤20 minutes (n=100)	DDI >20 minutes (n=71)	p Value
Time of operation			
After midnight	14 (14)	14 (20)	0.40
Weekend / public holiday	36 (36)	17 (24)	0.10
Experience of surgeon (years)	2.8 ± 3.3	2.9 ± 2.7	0.85
Duration of anaesthesia (mins)	51.7 ± 25.9	46.8 ± 10.2	0.13
Operative blood loss (ml)	479.0 ± 642.1	414.1 ± 255.8	0.42

Abbreviation: DDI = decision-to-delivery interval

* Data are shown as No. (%) of subjects or mean ± standard deviation

Table 4. Neonatal outcomes*

	DDI ≤20 minutes (n=100)	DDI >20 minutes (n=71)	p Value
Birth weight (g)	2966 ± 648.1	2964 ± 816.2	0.99
Apgar score			
<4 at 1 min	11 (11)	9 (13)	0.81
<7 at 1 min	38 (38)	37 (52)	0.09
<4 at 5 mins	4 (4)	0	0.14
<7 at 5 mins	13 (13)	6 (9)	0.46
CPR	5 (5)	2 (3)	0.70
Intubation	19 (19)	14 (20)	0.53
NICU admission	34 (34)	27 (38)	0.63
HIE	4 (4)	0	0.14
Neonatal death	1 (1)	1 (1.4)	0.66

Abbreviations: CPR = cardiopulmonary resuscitation; DDI = decision-to-delivery interval; HIE = hypoxic ischaemic encephalopathy; NICU = neonatal intensive care unit

* Data are shown as mean ± standard deviation or No. (%) of subjects

Table 5. Cord blood pH*

	DDI ≤20 minutes (n=90)	DDI >20 minutes (n=67)	p Value
Cord blood pH	7.19 ± 0.14	7.23 ± 0.09	0.04
Cord blood pH <7.20	36 (40)	23 (34)	0.51
Cord blood pH <7.00	6 (7)	1 (1)	0.24

Abbreviation: DDI = decision-to-delivery interval

* Data are shown as mean ± standard deviation or No. (%) of subjects

of ureteric and bowel injury during the study period (Table 6).

In the group with DDI >20 minutes, more time was required for preparation and transfer of patient to the operating theatre (mean difference, 8.0 minutes; p<0.001), induction of anaesthesia (mean difference, 0.9 minutes; p=0.01), and from skin incision to delivery of the baby (mean difference, 0.7 minutes; p=0.01) when compared with the group with DDI within 20 minutes. However, there was no significant difference in the time required from uterine incision to delivery between the two groups (Table 7).

Discussion

The incidence of extremely urgent Caesarean

Table 6. Maternal outcomes*

	DDI ≤20 minutes (n=100)	DDI >20 minutes (n=71)	p Value
Special care	10 (10)	4 (6)	0.40
Fever	7 (7)	6 (9)	0.78
Endometritis	1 (1)	0	0.59
Wound infection	5 (5)	2 (3)	0.70
Bladder injury	0	1 (1)	0.42
Hysterectomy	2 (2)	0	0.51

Abbreviation: DDI = decision-to-delivery interval
* Data are shown as No. (%) of subjects

Table 7. Comparison of the time for preparation in extremely urgent Caesarean deliveries*

	DDI ≤20 minutes (n=100)	DDI >20 minutes (n=71)	p Value
Preparation and transfer to operating theatre (mins)	7.9 ± 2.8	15.9 ± 6.3	<0.001
Induction of anaesthesia (mins)	6.0 ± 1.8	6.9 ± 2.8	0.01
Skin incision to delivery (mins)	2.7 ± 1.3	3.4 ± 2.1	0.01
Uterine incision to delivery (mins)	0.8 ± 0.9	1.1 ± 1.3	0.09

Abbreviation: DDI = decision-to-delivery interval
* Data are shown as mean ± standard deviation

delivery was 1.1% in this study, which was comparable to the rate (0.9%) reported in a local study[12] on extremely urgent Caesarean deliveries. There had been concern on liberal use of extremely urgent Caesarean deliveries in less urgent cases, leading to unjustified maternal and fetal complications. In a study by Bloc et al[13], the indications of 38 extremely urgent Caesarean deliveries were retrospectively reviewed by independent experienced obstetricians and they were confirmed in 12 but rejected in 13 cases (the opinions were discordant for the remaining 13 cases). Since only those cases that underwent extremely urgent Caesarean deliveries for fetal distress were included in this study, it was likely to be a reflection of the actual incidence of these interventions.

In our series, 93% of extremely urgent Caesarean deliveries were performed with a DDI of ≤30 minutes. This encouraging result was probably attributed to adherence to the emergency Caesarean section protocol, good team collaboration, and regular drills in our hospital. In the study by MacKenzie and Cooke[1], fewer than 40% of extremely urgent Caesarean deliveries for intrapartum fetal distress were achieved within a DDI of 30 minutes. Similarly, the 30-minute interval was only obtainable in 63% of emergency Caesarean sections in the case control study by Schauberger et al[14]. On the other hand, in an audit on extremely urgent Caesarean deliveries at a tertiary maternity hospital in Singapore, the mean DDI was 7.7 minutes with 100% of the deliveries accomplished within 17 minutes[15]. The study by Hillemanns et al[4] also showed similar results that all 109 extremely urgent Caesarean deliveries performed within a DDI of 30 minutes (median DDI, 10 mins).

The Royal College of Obstetricians and Gynaecologists, American College of Obstetricians and Gynaecologists, and Canadian National Consensus Conference recommend that extremely urgent Caesarean deliveries be performed within DDI of 30 minutes[9-11]. However, since the majority of extremely urgent Caesarean deliveries in this study were performed in a DDI of ≤30 minutes, the collected data were categorised into two groups using the standard of 20 minutes as recommended by the German Society of Gynaecology and Obstetrics for comparison[4]. Another reason for using the 20-minute cutoff was for a fairer comparison between the two groups.

Although there was no significant difference in the gestational age and birth weight between the two groups, the cord blood pH was lower in the group with DDI within 20 minutes. This finding was consistent with the previous study by Hillemanns et al[4]. In this retrospective

study on 109 extremely urgent Caesarean deliveries, a DDI within 20 minutes was found to be associated with lower cord blood pH[4]. Two possible explanations might account for this paradoxical result. First, clinicians tended to perform Caesarean delivery more promptly in cases with severe fetal distress. Second, a longer DDI may allow the condition to improve spontaneously in cases with reversible causes of fetal distress (e.g. uterine hyperstimulation)[16]. In this study, the causes of fetal distress were unknown in the majority (81%) of cases. There were no cases of fetal distress after regional analgesia. Although extremely urgent Caesarean deliveries were performed because of persistent bradycardia after discontinuation of oxytocin in some cases, the presence of reversible elements could not be totally excluded, as recovery of the fetal heart rate might not occur before making the decision of extremely urgent Caesarean delivery. The possible adverse effects related to prolonged DDI among cases with irreversible causes might be diluted by those cases with reversible elements, leading to this paradoxical result. The fact that the bradycardia-to-delivery interval was not included in the analysis might also affect the result, as fetal hypoxia does not start at the time of decision but around the time of onset of fetal bradycardia. This may give direction to further studies for evaluation.

On the other hand, a longer DDI did not seem to be associated with worse neonatal outcomes, and this finding was consistent with that in a previous study by Thomas et al[17]. In this national cross-sectional survey on emergency Caesarean sections, the odds for Apgar score of <7 at 5 minutes in cases with DDI <15 minutes was not significantly different from those with DDI between 16 and 75 minutes[17]. The odds for Apgar score of <7 at 5 minutes was increased in cases with a DDI of >75 minutes, but this could not be validated in our study because no extremely urgent Caesarean deliveries were performed with a DDI beyond 75 minutes.

In our study, there was no significant difference in complications related to Caesarean section including fever, wound infection, endometritis, bladder injury, hysterectomy, and need for special postoperative care between the two groups. Our findings were consistent with those from a previous study by Hillemanns et al[18] who suggested that extremely urgent Caesarean delivery with a shorter DDI did not have detrimental perioperative effects on the mother or neonate. In our series, 13 (8%) cases developed puerperal fever and two (1%) cases required hysterectomy. The rates were much higher than those reported in a local audit (1.1% and 0.1%, respectively) on the complication rates of Caesarean sections (including both elective and emergency operations)[19]. This finding is consistent with that reported by Pallasmaa et al[20] who opined that maternal morbidity was more frequent in crash than in emergency or elective Caesarean deliveries. Due to the fact that some complications of Caesarean sections are rare (e.g. bowel injury, hysterectomy), a larger-scale study may be able to further explore the relationship between DDI and maternal outcomes, so as to provide more evidence-based recommendations.

In the group with DDI >20 minutes, more time was required for preparation and transfer of patient to the operating theatre (mean difference, 8.0 mins), induction of anaesthesia (mean difference, 0.9 mins), as well as from skin incision to delivery of the baby (mean difference, 0.7 mins) when compared with the group with DDI within 20 minutes. In other words, the most significant contributory factor for the delay was time required for preparation and transfer of patient to the theatre. This was unexpected as the antenatal characteristics were not significantly different between the two groups. A limitation of our study was that data concerning pre-existing medical diseases were not collected. More time would be spent in optimisation of maternal condition in cases with pre-existing medical diseases.

When life-threatening fetal distress occurs, Caesarean sections should be performed swiftly, preferably within 30 minutes, but the well-being of the mother or fetus should not be compromised. In our present study, the most significant contributing factor to a delay in DDI was the time required for preparation and transfer of patients to the operating theatre (mean, 15.9 mins). Preoperative interventions can be carried out smoothly within a shorter period of time if an experienced operating team is available[21]. Earlier preparation in high-risk cases including blood typing and screening, fasting, control of hypertension or optimisation of maternal conditions will shorten the time required for preparation if emergency Caesarean section is needed. Epidural analgesia for pain relief can be considered so that a top-up can be offered if emergency Caesarean section is needed. Having an experienced in-house operating team has the advantage of allowing the intervention to take place within a shorter period of time[22]. The time required for transferring the patient to the operating theatre can be minimised if the operating theatre is located inside or within a short distance from the labour suite.

In our study, general anaesthesia was given to all cases for extremely urgent Caesarean delivery. General

anaesthesia is the method of choice for most anaesthetists in most urgent settings, but it can be more risky than regional anaesthesia[23]. While Dunphy et al[24] suggested that regional blockade was associated with longer DDI than general anaesthesia, Lim et al[15] found that there was no significant difference in the DDI regardless of the type of anaesthesia used.

The limitations of the present study included the retrospective nature and small sample size. A larger-scale prospective study is recommended to further evaluate the relationship between DDI and neonatal and maternal outcomes.

Conclusion

The cord blood pH was lower in the group with DDI within 20 minutes than those with DDI >20 minutes. The major reason for delayed DDI was related to the longer time required for preparation and transfer of patients to the operating theatre.

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Comparison of Digital Vaginal Examination with Intrapartum Transabdominal Ultrasound to Determine Fetal Head Position: a Local Experience

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Objective: To investigate the accuracy of intrapartum digital vaginal examination in assessing fetal head position during active labour, and to compare accuracy of intrapartum digital vaginal examination for fetal head position between specialist trainee doctors and specialist obstetricians.
Methods: A total of 100 patients at term with normal singleton cephalic-presenting fetuses were recruited. Transabdominal ultrasound examination to determine the position of the fetal head was performed by a trained sonographer, followed immediately by digital vaginal examination by attending specialist trainee doctor or specialist obstetrician. Both examiners were blinded to each other's findings. A total of 112 measurements were generated. Statistical analyses included Chi-square test, Kappa test, and logistic regression analysis. p Values of <0.05 were considered statistically significant.
Results: Digital vaginal examinations were completely consistent with ultrasound assessment in 34 (30%) cases. Assuming that the fetal head position was correct provided it was within ± 45 degrees of the ultrasound assessment, digital examination was accurate in 77 (69%) of cases. The respective rate of agreement between the two assessment methods by specialist trainee doctors versus specialist obstetricians was 67% and 75% (p=0.69). There were no significant associations between accuracy of digital vaginal examination and maternal and labour characteristics.
Conclusions: Fetal head position during active labour determined by digital vaginal examination was accurate in about two-thirds of all cases, with only one-third of cases being in complete agreement with that obtained by ultrasound assessment. There was no statistically significant difference in accuracy of digital vaginal examination by specialist trainees compared with that by specialist obstetricians.
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Keywords: Fetus; Labor stage, second; Ultrasonography, prenatal

Introduction

Intrapartum assessment of fetal head position and station is performed by Leopold's manoeuvres followed by transvaginal digital examination[1,2]. The aim is to look for clinical adequacy of the maternal pelvis, cervical position, dilatation, consistency and effacement, and fetal presentation and pelvic (ischial spine) station of the presenting fetal part[3]. Studies on intrapartum ultrasound examinations reported that such clinical assessment is often inaccurate, with clinical examination of the fetal head position being different in 27% to 53% of the cases[4-7].

Accurate assessment of the occipital position during labour is important, especially when operative vaginal delivery is needed, because it is an important determinant of successful and safe use of vacuum and forceps. Placement of the vacuum cup on the flexion point and placement of the forceps blades parallel to the sagittal suture are associated with high success rate and decreased maternal and fetal morbidity[8-10]. Even so, the use of intrapartum ultrasound for determination of fetal head position was not a routine practice in modern obstetrics.

This study aimed to examine the accuracy of digital vaginal assessment of the fetal head position, and also compare the difference in accuracy between specialist trainee doctors and specialist obstetricians.

Methods

At Kwong Wah Hospital, Hong Kong SAR, China, from May 2011 to June 2012, we recruited 100 nulliparous and multiparous women at term (≥37 weeks' gestation) with a singleton pregnancy who were in active labour. Active labour was defined as at least three regular painful

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uterine contractions in 10 minutes and cervical dilatation of ≥3 cm. Women in the second stage with active pushing and prolonged second stage (full cervical dilatation for >1 hour in nulliparous women, >30 minutes in multiparous women) were also included. Women with suspected fetal distress, fetuses with non-cephalic presentation, chorioamnionitis, pre-eclampsia/eclampsia, multiple pregnancies, and previous Caesarean section were not recruited. Informed consent was obtained from all patients at times when they did not have contractions, after approval by our hospital's ethics committee.

A portable 2-dimensional ultrasound machine in the labour ward (MyLab 25; Esaote, Florence, Italy) with frequency of 3.5 MHz was used for all ultrasound examinations in the study. Transabdominal ultrasound was first performed by a trained sonographer with the woman in supine position to determine the fetal head position. Transabdominal ultrasound was used because it is well documented as the gold standard for determination of fetal head position[4-7]. The ultrasound transducer was first placed longitudinally with reference to the abdomen to identify the cervical spine and occipital bone of the fetus, and then transversely, to obtain the position of the spinal column, the midline cerebral echo, and the cerebellum. The landmarks depicting the fetal position were the fetal orbits for occipito-posterior (OP) position, the midline cerebral echo for occipito-transverse (OT) position, and cerebellum or occiput for occipito-anterior (OA) position (Figure 1). The ultrasound findings of fetal occipital position were recorded on a datasheet depicting a circle, like a clock, with 24 divisions, each of 15 degrees (Figure 2).

Immediately after ultrasound examination, digital vaginal examination was randomly performed by either a specialist trainee doctor or specialist obstetrician, after a uterine contraction. The fetal head position was determined by palpation of the sagittal suture and fontanelles, and the

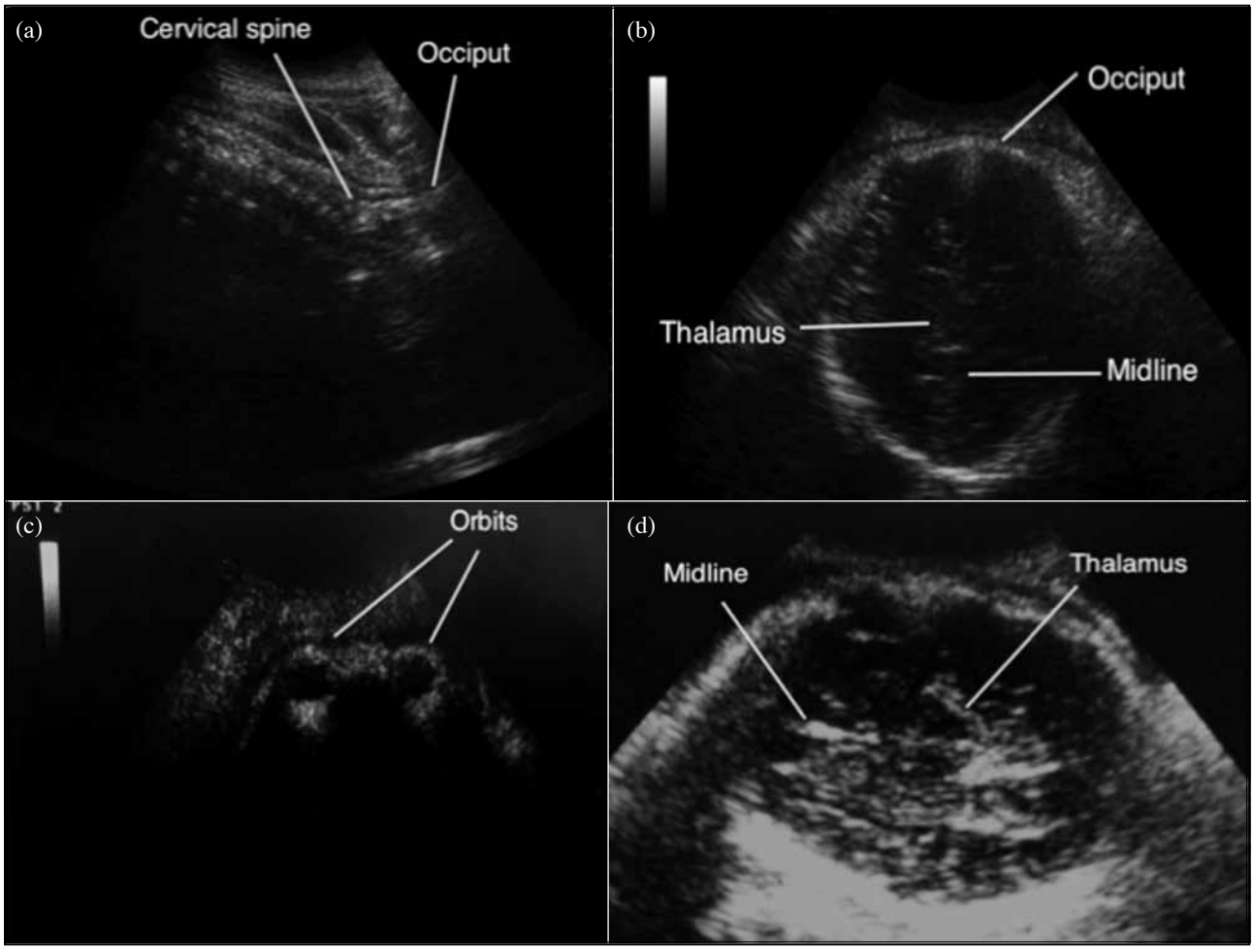

Figure 1. (a) Sagittal view of transabdominal ultrasound in a fetus with occipito-anterior position. (b) Transverse view of transabdominal ultrasound in the same fetus, obtained by turning the probe at 90 degrees. (c) Transverse view of a fetus in occipito-posterior position with both orbits used as landmarks. (d) Transverse view of a fetus in occipito-transverse position with midline cerebral echo, fetal thalami as landmarks

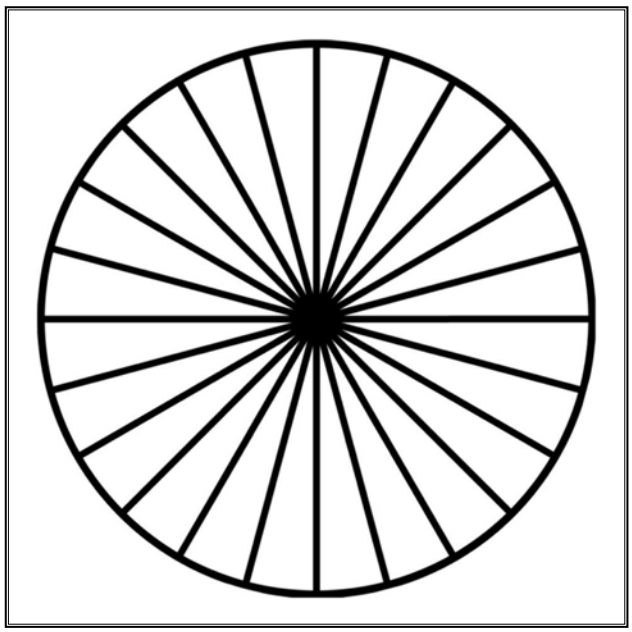

Figure 2. "Clock-face" with 24 divisions (each 15 degrees) used for fetal head position determination

location of these in relation to the maternal pelvis[11]. Both teams were blinded to each other's findings.

Statistical Analysis

Our study is a local pilot study and the sample size was based on that of a study by Sherer et al[4], which had a similar design, as well as primary and secondary outcome measure selection. The degree of agreement between the two examination methods was determined using Kappa test. Logistic regression was used to investigate the association between complete agreement in the fetal occipital position between the two examination methods and maternal and labour characteristics. The continuous numeric variables included maternal age, body mass index, gestational age, birth weight, and cervical dilatation. Presence of caput and presence of moulding were scored as 1 for 'yes' and 0 for 'no'; parity was scored as 1 for multiparous and 0 for nulliparous. Fetal head station at or below the ischial spine was scored as 0, and station +1 or above was scored as 1. Fetal OA was scored as 1 and occipito-lateral or posterior were scored as 2. Trainees were scored as 1 and specialists as 2. Statistical analysis was performed using SPSS version 20 (SPSS Inc., Chicago [IL], US).

Results

A total of 100 women in active labour participated in the study. Their mean (± standard deviation) maternal age was 31 ± 4 years. In all, 86 women were primiparous and 14 were multiparous. Their mean gestational age was 39 ± 1 weeks. Numbers of women recruited (could be repeated) at first stage, second stage and prolonged second stage were 49, 48, and 15, respectively, of which 10 were assessed in two encounters and one was assessed in all three encounters. A total of 112 measurements were generated.

The digital examinations were performed by specialist obstetricians in 18% (n=20) of cases, or by trainee doctors with 1 to 3 years (n=65) or 4 to 6 years (n=27) of experience in obstetrics and gynaecology. The ultrasound-determined fetal head position was OA in 78 (70%), OT in 15 (13%), and OP in 19 (17%) cases. Fetal head position determined by digital vaginal examination was the same as that determined by ultrasound examination in 34 (30%) of cases. Kappa test of concordance indicated a fair concordance of 0.32 (95% confidence interval [CI], 0.21-0.42; $p<0.05$). Assuming that the fetal head position was correct provided it was within ± 45 degrees of the ultrasound assessment, digital examination was accurate in 77 (69%) of cases, with Kappa test of concordance indicating a moderate agreement of 0.57 (95% CI, 0.46-0.67; $p<0.05$). Digital vaginal examination failed to identify the correct fetal head position in 35 (31%) cases, including six cases in which the difference from ultrasound examination was 136 to 180 degrees, two cases with a difference of 91 to 135 degrees, and 27 cases with a difference of 46 to 90 degrees (Table 1).

Table 1. Comparison of accuracy of digital vaginal examination in assessing fetal head position between trainee doctors and specialist obstetricians

Difference between digital vaginal examination and ultrasound examination	Trainees (n=92)	Specialists (n=20)	Trainees + specialists (n=112)
0° (Absolute agreement)	26 (28%)	8 (40%)	34 (30%)
≤45°	36 (39%)	7 (35%)	43 (38%)
46-90°	24 (26%)	3 (15%)	27 (24%)
91-135°	2 (2%)	0	2 (2%)
136-180°	4 (4%)	2 (10%)	6 (5%)

Table 2. Logistic regression analysis on the contribution of independent variables to the accuracy of digital vaginal examination

Variable	Data*	Odds ratio (95% confidence interval)	p Value
Age (years)	32 (19-40)	1.10 (0.96-1.25)	0.16
Body mass index (kg/m^2)	20.3 (15.4-36.7)	0.96 (0.82-1.13)	0.65
Parity		0.54 (0.11-2.60)	0.44
Nulliparous	86		
Multiparous	14		
Gestational age (weeks)	40 (37-41)	1.45 (0.87-2.43)	0.15
Birth weight (kg)	3.3 (2.3-4.4)	1.10 (0.24-4.99)	0.91
Cervical dilatation (cm)	10 (3-10)	0.89 (0.64-1.25)	0.51
Fetal head position	OA: 78 (70) OT+OP: 34 (30)	4.67 (1.61-13.52)	0.004
Fetal head station			
0 or below	35 (31)	2.65 (0.45-15.60)	0.28
1 or above	77 (69)		
Caput			
Yes	74 (66)	0.29 (0.10-0.83)	0.02
No	38 (34)		
Moulding			
Yes	73 (65)	0.79 (0.27-2.31)	0.67
No	39 (35)		
Years of experience			
1-6 (Trainee)	92 (82)	0.69 (0.19-2.45)	0.56
>6 (Specialist)	20 (18)		

Abbreviations: OA = occipito-anterior; OP = occipito-posterior; OT = occipito-transverse

* Data are shown as No. (%) of subjects or median (range)

Table 3. Comparison of characteristics of women who underwent digital vaginal examination by trainees versus specialists*

Characteristic	Trainees (n=92)	Specialists (n=20)
Age (years)	31 (19-40)	32 (24-37)
Body mass index (kg/m^2)	20.3 (15.4-31.3)	20.4 (15.5-36.7)
Parity		
Nulliparous	80 (87)	16 (80)
Multiparous	12 (13)	4 (20)
Gestational age (weeks)	40 (37-41)	39 (37-41)
Cervical dilatation (cm)	10 (3-10)	10 (3-10)
USG (OA)	65 (71)	13 (65)
USG (OT+OP)	27 (29)	7 (35)
Presence of caput	60 (65)	14 (70)
Presence of moulding	59 (64)	14 (70)

Abbreviations: OA = occipito-anterior; OP = occipito-posterior; OT = occipito-transverse; USG = ultrasonography

* Data are shown as No. (%) of subjects or median (range)

Logistic regression analysis revealed that fetal head position and the presence or absence of caput had significant independent contribution in explaining the variance in the accuracy of vaginal examination (Table 2). The odds ratio was 0.29 (95% CI, 0.10-0.83; p=0.02) for the absence of caput, while it was 4.67 (95% CI, 1.61-13.52; p=0.004) for OA fetal head position. The accuracy of digital vaginal examination (within ± 45 degrees of the ultrasound assessment) for specialist trainee doctors versus specialist obstetricians was 67% and 75%, respectively and this difference was not significant (p=0.69). The characteristics of both groups are shown in Table 3. There was no statistically significant difference in accuracy of digital vaginal examination between stage 1 and stage 2 of labour (p=0.31).

Discussion

Our results show that the degree of agreement between fetal head position determined by digital vaginal examination and that by transabdominal ultrasound was within ±45% in around 50% to 70% of patients during the first and second stages of labour; these echo with those from previous studies[4-7]. Although transabdominal ultrasound examination is easy to learn and perform because landmarks such as the fetal orbits, cerebellum, midline echo of the brain, and occiput could be easily identified, a report suggests that exact interobserver agreement only exists in 36.7% of cases[12]. Nevertheless, ultrasound assessment of fetal head position is highly reproducible and accurate as the difference is within 15 degrees in nearly 90% of cases, and within 30 degrees in all cases[12]. It is reasonable to assume a "complete agreement" in fetal head positions determined digitally and sonographically when the difference is within 45 degrees of each other.

Of the 35 (31%) cases in which there was difference of >45 degrees between the two methods of examination, six cases had differences of 136 to 180 degrees. This demonstrates that the examiners had correctly identified the fetal sagittal suture but had incorrectly designated the anterior and posterior fontanelles. The consequence of the incorrect assessment is especially important if instrumental delivery is required, as this could lead to placement of vacuum cups over the wrong flexion point, or underestimation of the difficulty of forceps delivery, especially in a fetus in OP position.

Our study findings suggest that the accuracy of digital vaginal examination is higher with OA fetal head position than OP and lateral positions. This is consistent with the findings by Akmal et al[7]. The accuracy was also increased when caput succedaneum was less. This can be explained by the fact that a large caput succedaneum may prevent differentiation of the various sutures and fontanelles, especially in prolonged labour[11]. It does not impair transabdominal assessment of the fetal head because ultrasound assessment is dependent upon correct identification of midline intracranial structures and/or anterior posterior cranial structures which are not affected by caput succedaneum. While the experience of the examiner was found to be associated with improved accuracy of vaginal examination in one study[7], it was not found to be significant in our study. Nevertheless, our study echoes the findings from previous studies[4] that age, parity, gestational age, cervical dilatation, and birth weight do not affect the accuracy of digital vaginal examination.

In recent years, the use of intrapartum ultrasound has been extended to include transperineal ultrasound for both accurate and reliable assessment of labour progress and outcome[13-20]. Various ultrasound parameters have been described, including head-perineum distance[13,15,20,21], angle of progression[16,17,19,22,23], and recently, head-symphysis distance[24] and pubic arch angle[25]. However, whether or not it is useful to incorporate these ultrasound parameters in the assessment of labour progress remains to be studied.

Intrapartum transabdominal ultrasound assessment of the fetal head position has been shown to be simple and easy to learn, and could overcome the overall high rate of error in fetal head position determination by digital vaginal examination, even in experienced obstetricians. Therefore, ultrasound scanning for the purpose of accurate determination of the fetal head position should be encouraged as part of examination of women in labour, especially before instrumental delivery[7].

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Use of Oral Glucose Tolerance Test and Glycated Haemoglobin at 20 Weeks of Gestation or Less to Predict or Exclude Subsequent Development of Gestational Diabetes Mellitus in the Current Pregnancy in High-risk Patients

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Objective: To determine cutoff values of oral glucose tolerance test (OGTT) and/or glycated haemoglobin at ≤20 weeks of gestation that could predict or exclude subsequent development of gestational diabetes mellitus (GDM) in the current pregnancy in high-risk patients.
Methods: Retrospective review of all non-diabetic pregnant women who had undertaken 75 g OGTT at ≤20 weeks of gestation in Queen Elizabeth Hospital, Hong Kong, from 1 April 2011 to 30 September 2011, was performed. Gestational diabetes mellitus was diagnosed in accordance with the 1999 World Health Organization criteria. If early OGTT results were normal, second OGTT was performed at 24 to 30 weeks. Sensitivity, specificity, positive predictive value, negative predictive value of the cutoff values, and proportion of OGTTs that could be spared at 24 to 30 weeks of gestation were calculated.
Results: In all, 58 (26%) pregnant women were diagnosed to have GDM by the first OGTT; 45 (30%) women with normal first OGTT had GDM diagnosed by the second OGTT, with higher mean 2-hour plasma glucose level than those in the non-GDM group ($p<0.05$). The best cutoff value that excluded GDM was 2-hour plasma glucose level of <4.4 mmol/L, which spared 5.3% of second OGTTs. The sensitivity, specificity, positive predictive value, and negative predictive value were 100%, 92.8%, 32.3% and 100%, respectively.
Conclusion: Approximately 5.3% of OGTTs at 24 to 30 weeks of gestation among women with multiple risk factors for GDM may be omitted using a 2-hour plasma glucose cutoff value of <4.4 mmol/L in early pregnancy, provided that there is no onset of new risk factor(s) after the first OGTT.
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Keywords: Diabetes, gestational/diagnosis; Glucose tolerance test; Hemoglobin A, glycosylated

Introduction

Gestational diabetes mellitus (GDM) is defined as hyperglycaemia with onset of pregnancy or hyperglycaemia if first recognised during pregnancy[1]. It is a common condition with a prevalence of 14.2% in Hong Kong, in contrast to 2% to 7% in the Caucasian population[2,3]. If untreated, it can result in sudden intrauterine fetal death (IUFD), macrosomia and associated birth trauma, preterm delivery, or respiratory distress syndrome. It is also associated with obesity and diabetes mellitus (DM) later in the baby's life[4]. Moreover, pre-GDM or early-onset GDM is associated with an increased risk of development of fetal anomalies and fetal loss[5].

The 1999 World Health Organization (WHO) recommendation of 75 g oral glucose tolerance test (OGTT) is the preferred diagnostic test in Hong Kong. Women are screened for the presence of risk factors at their first visit. If there are two or more risk factors, OGTT is performed shortly after the first visit and then again at 28 to 30 weeks of gestation[5]. Oral glucose tolerance test is inexpensive and has reasonable sensitivity. However, repeated blood taking is inconvenient for patients. Side-effects such as nausea, vomiting, and headache due to administration of glucose solution may also cause discomfort to patients. Some patients may decline a second OGTT because of unpleasant experience during their first OGTT and if that test showed a

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normal result.

Glycated haemoglobin (HbA1c) can be used to reflect glucose control over the previous months because erythrocytes have a constant lifespan and are freely permeable to glucose. The haemoglobin glycation process is non-enzymatic and the rate is directly proportional to the ambient glucose concentration. An expert committee suggested the use of HbA1c value of ≥6.5% to diagnose DM outside pregnancy[6]. Some studies have shown that HbA1c could reduce the need for OGTT in diagnosing GDM[7,8]. The International Association of Diabetes and Pregnancy Study Groups (IADPSG) used HbA1c value of ≥6.5% to diagnose overt DM in pregnancy[9], but other authorities do not recommend its application in pregnant women[10,11].

It is postulated that a normal OGTT with glucose level close to the cutoff value for GDM may reflect cases that may convert to GDM in later stages of pregnancy due to increased insulin resistance. If results of OGTT or HbA1c in early pregnancy could predict or exclude the subsequent development of GDM in the current pregnancy, then subsequent OGTTs may be omitted in selected high-risk women. Moreover, early screening for GDM at the time of Down's screening in the first trimester instead of at 24 to 28 weeks of gestation may allow early commencement of lifestyle modification and treatment before development of diabetic complications, and may reduce the need for repeated blood taking. On the other hand, if the first blood taking predicts a high risk of subsequent development of GDM, a repeated OGTT will be required even if the patient is regarded as low risk by the existing criteria. Therefore, this study aimed to determine whether OGTT and/or HbA1c results at ≤20 weeks of gestation in high-risk group of patients could predict or exclude subsequent development of GDM in the current pregnancy, and to determine the cutoff values of the tests.

Methods

This retrospective observational study included all non-diabetic pregnant women who had undertaken 75 g OGTT at ≤20 weeks of gestation in Queen Elizabeth Hospital, Hong Kong, from 1 April 2011 to 30 September 2011.

The protocol of GDM screening in Queen Elizabeth Hospital was as follows. Women with one risk factor (excluding ethnicity) were routinely screened by 75 g OGTT as close to 28 weeks of gestation as possible (24 to 30 weeks). Those with two or more risk factors were screened by 75 g OGTT in early pregnancy after the initial booking visit and then again at 24 to 30 weeks. Those who had developed new risk factors undertook OGTT as soon as feasible. Risk factors in the departmental protocol were as follows: advanced maternal age (AMA; maternal age ≥35 years), a family history of DM, maternal obesity at booking with body weight of ≥80 kg or body mass index (BMI) of ≥28 kg/m^2, known polycystic ovarian syndrome (PCOS), history of GDM or impaired glucose tolerance (IGT) in previous pregnancy, a history of IUFD or stillbirth, a history of macrosomia ≥4 kg, multiple pregnancy, large for gestational age fetus or polyhydramnios on antenatal ultrasound, maternal use of medications (such as corticosteroids), and excessive weight gain during pregnancy (at the discretion of the managing obstetrician).

Gestational diabetes mellitus was diagnosed in accordance with the 1999 WHO criteria, by fasting plasma glucose (FPG) level of ≥7.0 mmol/L and/or 2-hour plasma glucose (PG) level of ≥7.8 mmol/L after a 75 g OGTT. No further OGTTs were performed when a patient was diagnosed to have GDM. The hospital laboratory used high-performance liquid chromatography for HbA1c quantification with the VARIANT II machine (Bio-Rad, California, US). Glycated haemoglobin level was represented in percentage. Glucose measurement was performed by hexokinase and ultraviolet detection of glucose with the Modular D System (Roche, Indianapolis, US). Both tests were performed in a laboratory with accreditation of the National Association of Testing Authorities/Royal College of Pathologists of Australasia.

Women with pre-existing DM, with incomplete results, and at risk but who did not perform OGTT in the day centre were excluded from the study. Women with second OGTT performed before 24 weeks of gestation were excluded because normal glucose tolerance at that stage might not exclude the subsequent development of GDM. Women with change in risk factor(s) for GDM between two tests were also excluded because it is more appropriate to have repeated OGTT if there is onset of new risk factor(s), regardless of the previous OGTT results. In addition, women with uncertain or known variant haemoglobinopathies such as thalassemia trait were excluded during analysis of HbA1c and cutoff values, as variant haemoglobin patterns might affect the result[12].

Statistical analysis was performed by the SPSS Windows version 19.0. Independent sample *t* test and Chi-square test were used to analyse the parametric and non-parametric data, respectively. Logistic regression test and

receiver operating characteristic (ROC) curve were used to assess the performance of the parameters in predicting GDM. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) of the cutoff values, and proportion of OGTTs that could be omitted at 24 to 30 weeks of gestation were calculated.

Based on a similar study[13], the mean (± standard deviation) FPG values at ≤16 weeks of gestation were 5.4 ± 0.7 mmol/L, 4.9 ± 0.5 mmol/L, and 4.6 ± 0.4 mmol/L for those with GDM diagnosed at 24 to 28 weeks, GDM diagnosed at 32 to 34 weeks, and without GDM, respectively. To detect the smallest potential difference between GDM and non-GDM groups, mean FPG level of 4.9 mmol/L was used to represent the GDM group in order to calculate the sample size. Assuming 5% significance level and 80% power, the number of cases in each group was 36. The mean 2-hour PG values were 7.1 ± 0.4 mmol/L, 6.2 ± 1.2 mmol/L, and 5.5 ± 1.0 mmol/L for those with GDM diagnosed at 24 to 28 weeks, GDM diagnosed at 32 to 34 weeks, and without GDM, respectively. Based on the same rationale, the number of cases in each group was 40.

The study was performed according to the guidelines set forth in the current version of the Declaration of Helsinki. A review of medical records, which were already existing as part of clinical care, posed no physical risks. Therefore, consent from the patients was not obtained. Data were recorded in a manner that did not allow the participants to be identified; a non-recognisable code was assigned to each participant. The study protocol was approved by the Research Ethics Committee (Kowloon Central/Kowloon East).

Results

A total of 223 pregnant women undertook OGTTs at ≤20 weeks of gestation during the study period, accounting for approximately 6.4% of antenatal new case bookings during the same period. Of these, data of 14 women were excluded because of various reasons (Figure 1). Thus, data

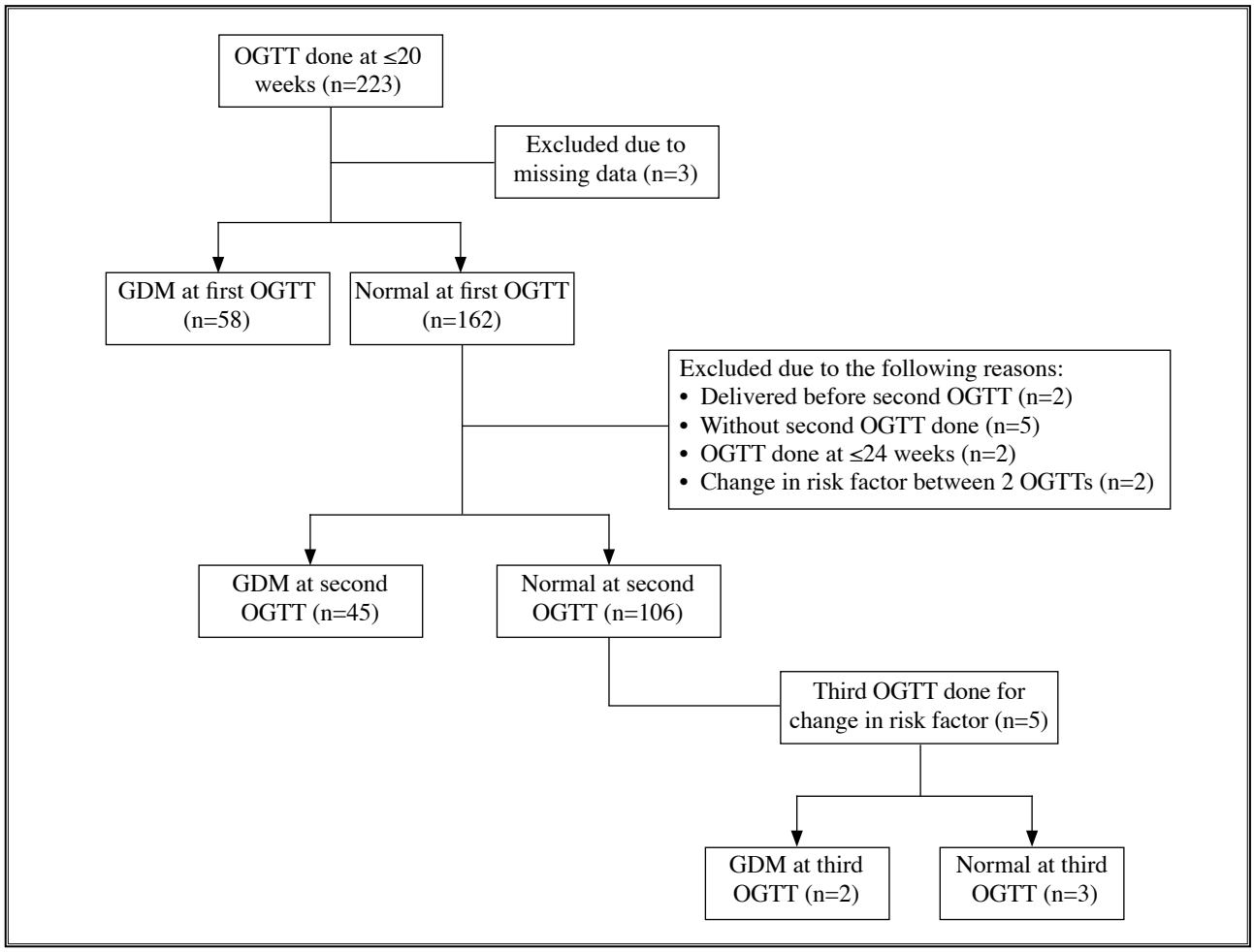

Figure 1. Distribution of study subjects
Abbreviations: GDM = gestational diabetes mellitus; OGTT = oral glucose tolerance test

from the remaining 209 women were analysed. Overall, 105 (50%) women were diagnosed to have GDM at first (n=58), second (n=45), and third (n=2) OGTT. Baseline characteristics of women with and without GDM are compared in Table 1. More women in the GDM group had a history of GDM or IGT in their previous pregnancy, as well as more than two risk factors when compared with those in the non-GDM group. Both the mean FPG and 2-hour PG levels at first OGTT in the GDM group were significantly higher than those in the non-GDM group (4.5 mmol/L vs. 4.4 mmol/L, p=0.01 for FPG; and 7.9 mmol/L vs. 6.0 mmol/L, p<0.001 for 2-hour PG), but not the mean HbA1c level (5.5% vs. 5.4%; p=0.06).

When comparing women with GDM diagnosed by first and second OGTTs (Table 2), no differences in baseline characteristics and risk factors were noted. The mean 2-hour PG at first OGTT was higher in those with GDM diagnosed by first OGTT compared with those diagnosed by second OGTT (9.1 mmol/L vs. 6.4 mmol/L; p<0.001). However, there were no statistically significant differences in the mean FPG and HbA1c values between the two groups (4.6 mmol/L vs. 4.5 mmol/L, p=0.51 for FPG and 5.5% vs. 5.5%, p=0.96 for HbA1c).

Among women with normal first OGTT, the incidence of GDM diagnosed by second OGTT was 30%; more women in this group had more than two risk factors when compared with the non-GDM group. Otherwise, there were no differences in baseline characteristics and timing of performing OGTT between the groups (Table 3). The mean 2-hour PG at first OGTT was higher in the GDM

Table 1. Comparison of demographic data among women with and without GDM

Demographics	With GDM (n = 105)	Without GDM (n = 104)	p Value
Age at delivery (years)	36.3 ± 3.2	36.3 ± 3.0	0.95
Parity			0.28
0	34 (32%)	42 (40%)	
1	62 (59%)	50 (48%)	
≥2	9 (9%)	12 (12%)	
Ethnicity			0.22
Chinese	98 (93%)	92 (89%)	
Asian non-Chinese	7 (7%)	12 (12%)	
Mean (± SD) BMI (kg/m^2)	23.8 ± 4.8	22.9 ± 4.6	0.15
AMA	83 (79%)	92 (89%)	0.07
Obesity	21 (20%)	15 (14%)	0.29
PCOS	2 (2%)	2 (2%)	1.00
Previous GDM / IGT	31 (30%)	17 (16%)	0.02
Family history of DM	80 (76%)	81 (78%)	0.77
Previous big baby	9 (9%)	3 (3%)	0.13
Previous IUFD / SB	2 (2%)	1 (1%)	1.00
Multiple pregnancy	11 (11%)	6 (6%)	0.21
Medication use	1 (1%)	3 (3%)	0.37
Presence of >2 risk factors	30 (29%)	13 (13%)	0.004
Mean (± SD) first OGTT (mmol/L)			
FPG	4.5 ± 0.7	4.4 ± 0.4	0.01
2-Hour PG	7.9 ± 1.9	6.0 ± 1.0	<0.001
Mean (± SD) first HbA1c (%)	5.5 ± 0.4 (n = 94)	5.4 ± 0.3 (n = 97)	0.06

Abbreviations: AMA = advanced maternal age; BMI = body mass index; DM = diabetes mellitus; FPG = fasting plasma glucose; GDM = gestational diabetes mellitus; HbA1c = glycated haemoglobin; IGT = impaired glucose tolerance; IUFD = intrauterine fetal death; OGTT = oral glucose tolerance test; PCOS = polycystic ovarian syndrome; PG = post-glucose; SB = stillbirth; SD = standard deviation

Table 2. Comparison of characteristics among women with GDM diagnosed at first and second OGTT

Characteristic	GDM at first OGTT (n = 58)	GDM at second OGTT (n = 45)	p Value
Age at delivery (years)	35.8 ± 3.4	36.9 ± 2.9	0.11
Parity			1.00
0	18 (31%)	15 (33%)	
1	35 (60%)	27 (60%)	
≥2	5 (9%)	3 (7%)	
Ethnicity			0.13
Chinese	52 (90%)	44 (98%)	
Asian non-Chinese	6 (10%)	1 (2%)	
BMI (kg/m^2)	24.3 ± 4.7	23.1 ± 5.0	0.22
AMA	42 (72%)	39 (87%)	0.08
Obesity	15 (26%)	6 (13%)	0.12
PCOS	2 (3%)	0	0.50
Previous GDM / IGT	20 (35%)	11 (24%)	0.27
Family history of DM	44 (76%)	34 (76%)	0.97
Previous big baby	6 (10%)	3 (7%)	0.73
Previous IUFD / SB	2 (3%)	0	0.50
Multiple pregnancy	4 (7%)	7 (16%)	0.20
Medication use	0	1 (2%)	0.44
Presence of >2 risk factors	18 (31%)	12 (27%)	0.63
Gestation at first OGTT (weeks)	15.4 ± 2.3	15.3 ± 2.2	0.89
Mean (± SD) first OGTT (mmol/L)			
FPG	4.6 ± 0.8	4.5 ± 0.5	0.51
2-Hour PG	9.1 ± 1.5	6.4 ± 1.0	<0.001
Mean (± SD) first HbA1c (%)	5.5 ± 0.4 (n = 49)	5.5 ± 0.3 (n = 43)	0.96

Abbreviations: AMA = advanced maternal age; BMI = body mass index; DM = diabetes mellitus; FPG = fasting plasma glucose; GDM = gestational diabetes mellitus; HbA1c = glycated haemoglobin; IGT = impaired glucose tolerance; IUFD = intrauterine fetal death; OGTT = oral glucose tolerance test; PCOS = polycystic ovarian syndrome; PG = post-glucose; SB = stillbirth; SD = standard deviation

group compared with the non-GDM group (6.4 mmol/L vs. 6.0 mmol/L; p=0.01) [Table 4]. There were no statistically significant differences in mean FPG (4.5 mmol/L vs. 4.4 mmol/L; p=0.05) and HbA1c (5.5% vs. 5.4%; p=0.12) values at first OGTT between the groups.

The ROC curves of the FPG, 2-hour PG, and HbA1c at first OGTT are shown in Figure 2. The area under the curve (AUC) values for FPG, 2-hour PG, and HbA1c were 0.60, 0.66 and 0.57, respectively. Only AUC of FPG was statistically significant. Logistic regression analysis showed that the strongest predictor of GDM among the blood results was 2-hour PG with odds ratio of 1.83 (95% confidence interval, 1.20-2.79; p=0.01), while the others were not statistically significant (Table 5).

In view of potential consequence of missing a case of GDM, cutoff values with high NPV were chosen to exclude a diagnosis of GDM. The cutoff values alone or in combination are shown in Table 6. Second OGTT could be omitted if the results were below the cutoff values. The best cutoff value to exclude GDM was 2-hour PG of 4.4 mmol/L, which spared 5.3% of OGTTs without missing a case of GDM. The sensitivity, specificity, PPV, and NPV were 100%, 92.8%, 32.3% and 100%, respectively.

High PPV and specificity should be used to determine cutoff values that predict GDM, above which the second OGTT could be omitted. The cutoff values derived are shown in Table 7. Additional cutoff values of 5.1 mmol/L for FPG and 6.5% for HbA1c were also analysed,

Table 3. Baseline characteristics of women with normal first OGTT

Characteristic	GDM at second OGTT (n = 45)	Normal at second OGTT* (n = 104)	p Value
Age at delivery (years)	36.9 ± 2.9	36.3 ± 3.0	0.29
Parity			0.37
0	15 (33%)	42 (40%)	
1	27 (60%)	50 (48%)	
≥2	3 (7%)	12 (12%)	
Ethnicity			0.11
Chinese	44 (98%)	92 (89%)	
Asian non-Chinese	1 (2%)	12 (12%)	
Mean (± SD) BMI (kg/m^2)	23.1 ± 5.0	22.9 ± 4.6	0.75
AMA	39 (87%)	92 (89%)	0.76
Obesity	6 (13%)	15 (14%)	0.86
PCOS	0	2 (2%)	1.00
Previous GDM / IGT	11 (24%)	17 (16%)	0.25
Family history of DM	34 (76%)	81 (78%)	0.76
Previous big baby	3 (7%)	3 (3%)	0.37
Previous IUFD / SB	0	1 (1%)	1.00
Multiple pregnancy	7 (16%)	6 (6%)	0.05
Medication use	1 (2%)	3 (3%)	1.00
Presence of >2 risk factors	12 (27%)	13 (13%)	0.03
Mean (± SD) gestation at first OGTT (weeks)	15.3 ± 2.2	15.4 ± 1.7	0.84
Mean (± SD) gestation at second OGTT (weeks)	28.2 ± 1.0	28.0 ± 0.6	0.07
Mean (± SD) duration between 2 tests (weeks)	12.9 ± 2.4	12.6 ± 1.8	0.44

Abbreviations: AMA = advanced maternal age; BMI = body mass index; DM = diabetes mellitus; GDM = gestational diabetes mellitus; IGT = impaired glucose tolerance; IUFD = intrauterine fetal death; OGTT = oral glucose tolerance test; PCOS = polycystic ovarian syndrome; SB = stillbirth; SD = standard deviation

* Two patients with GDM diagnosed at third OGTT were excluded

Table 4. OGTT and HbA1c values in women with normal first oral glucose tolerance test*

	GDM at second OGTT (n = 45)	Normal at second OGTT (n = 104†)	p Value
First OGTT (mmol/L)			
FPG	4.5 ± 0.5	4.4 ± 0.4	0.05
2-Hour PG	6.4 ± 1.0	6.0 ± 1.0	0.01
First HbA1c (%)	5.5 ± 0.3 (n = 43)	5.4 ± 0.3 (n = 97)	0.12
Second OGTT (mmol/L)			
FPG	4.7 ± 0.4	4.4 ± 0.4	<0.001
2-Hour PG	8.7 ± 0.8	6.2 ± 1.1	<0.001
Second HbA1c (%)	5.5 ± 0.3 (n = 43)	5.3 ± 0.3 (n = 97)	0.01

Abbreviations: FPG = fasting plasma glucose; GDM = gestational diabetes mellitus; HbA1c = glycated haemoglobin; OGTT = oral glucose tolerance test; PG = post-glucose

* Data are shown as mean ± standard deviation

† Two patients with GDM diagnosed at third OGTT was excluded

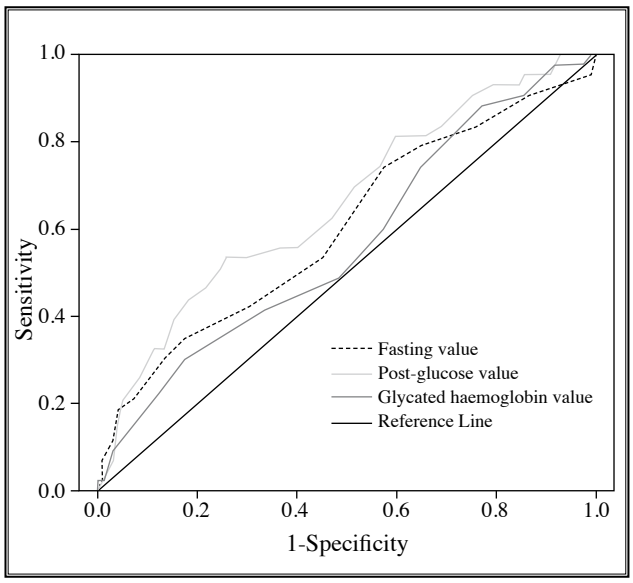

Figure 2. Receiver operating characteristic curves for first fasting plasma glucose, 2-hour post-glucose, and glycated haemoglobin

as these were used to diagnose GDM at the first antenatal visit according to the IADPSG criteria[9]. All the cutoff values were not useful as they spared a limited number of OGTTs while leading to over-treatment of a significant number of women without GDM.

Discussion

This study demonstrated high incidence of GDM in women with two or more risk factors. The mean FPG and 2-hour PG values in early pregnancy were higher in the GDM group compared with the non-GDM group. Among those with normal OGTT in early pregnancy, the mean 2-hour PG values in early pregnancy were higher in the group with GDM diagnosed by second OGTT versus the non-GDM group. However, the 2-hour PG results were of limited use in predicting GDM in the later stage of pregnancy because the AUC value was not high (0.66). We found that 5.3% of second OGTTs could be omitted if

Table 5. Logistic regression analysis of oral glucose tolerance test and glycated haemoglobin values predicting gestational diabetes mellitus

	Coefficient (standard error)	p Value	Odds ratio (95% confidence interval)
FPG	0.80 (0.50)	0.11	2.23 (0.83-5.96)
2-Hour PG	0.60 (0.22)	0.01	1.83 (1.20-2.79)
HbA1c	0.72 (0.62)	0.24	2.06 (0.61-6.93)

Abbreviations: FPG = fasting plasma glucose; HbA1c = glycated haemoglobin; PG = post-glucose

Table 6. Cutoff values at first OGTT that excluded GDM

Cutoff value	Sensitivity	NPV	OGTT spared	GDM missed
FPG (4.2 mmol/L)	79.1%	79.1%	30.7%	20.9%
2-Hour PG (4.4 mmol/L)	100%	100%	5.3%	0%
HbA1c (4.5%)	100%	100%	0.7%	0%
2-Hour PG (6.2 mmol/L) and HbA1c (5.0%)	100%	100%	5.0%	0%

Abbreviations: FPG = fasting plasma glucose; GDM = gestational diabetes mellitus; HbA1c = glycated haemoglobin; NPV = negative predicted value; OGTT = oral glucose tolerance test; PG = post-glucose

Table 7. Cutoff values at first OGTT that predicted gestational diabetes mellitus

Cutoff value	Specificity	PPV	OGTT spared	Over-treated
FPG (≥6.0 mmol/L)	100%	100%	0.7%	0%
2-Hour PG (≥7.5 mmol/L)	95.8%	64.3%	10.0%	5.2%
HbA1c (≥5.9%)	96.9%	57.1%	5.0%	3.1%
FPG (≥5.1 mmol/L)	96.9%	75%	2.9%	1.0%
HbA1c (≥6.5%)	100%	100%	0.7%	0%

Abbreviations: FPG = fasting plasma glucose; HbA1c = glycated haemoglobin; OGTT = oral glucose tolerance test; PG = post-glucose; PPV = positive predicted value

2-hour PG value was <4.4 mmol/L at first OGTT. There was no useful cutoff value to predict development of subsequent GDM in the current pregnancy without over-treating women without GDM.

The prevalence of GDM diagnosed by the WHO criteria was 14.2% according to a local study in 2002[2]. The incidence of GDM in this study was 50%. The high incidence in this study was due to inclusion of women with multiple risk factors for GDM. All the patients were Asians and the majority of patients (93%) were of Chinese ethnicity, which itself was a risk factor for GDM. A study in Hungary also showed incidence of 54% in high-risk women[13].

Among women who had GDM or IGT in their previous pregnancy, the possibility of unrecognised glucose intolerance antedating the current pregnancy could not be excluded, as they might not have undergone postpartum glucose tolerance test in the previous pregnancy. This may explain why more women with GDM had this risk factor. Although a greater proportion of women with GDM diagnosed by the first OGTT had this risk factor compared with those diagnosed by the second OGTT, this did not reach statistical significance.

In this study, only 2-hour PG but not FPG or HbA1c at first OGTT could identify women with pre-GDM or early-onset GDM. Since early diagnosis of GDM allows early commencement of lifestyle modification and treatment before development of adverse pregnancy outcomes and diabetic complications, this finding confirmed that OGTT in early pregnancy could not be omitted based on FPG and HbA1c.

In women without GDM in early pregnancy, first HbA1c was not useful in predicting or excluding GDM in the later stage of pregnancy. This could be explained by the fact that HbA1c in early pregnancy reflects the degree of glycaemia in the preceding few months, which is expected to be normal if the early pregnancy OGTT is normal. The HbA1c results may also be affected by haemoglobinopathies, which are prevalent in our local population. Cost and standardisation of HbA1c testing are also issues for consideration[9].

Fasting plasma glucose is commonly used as a screening test for GDM. There is no consensus on its optimal cutoff value, which varies among different studies[14-16]. In Hong Kong, the optimal value for low-risk populations was suggested to be 4.1 mmol/L[17], which is lower than that in international studies. In a study on high-risk populations in Hungary, the cutoff value of FPG alone in early pregnancy was 5.0 mmol/L, above which a significantly increased risk of subsequent GDM was noted[13]. The cutoff value for FPG in this study was lower and compatible with that in a previous local study[18], but a significant number of GDM patients would be missed if it was used to screen high-risk women. Moreover, both the sensitivity and NPV of the cutoff values in the Hungarian study[13] were more than 90%, which were higher than any cutoff in our study. It is known that FPG has limited use in the Asian population because it identifies only a small proportion of women with GDM even when it is obtained at the time of OGTT[19]. Therefore, it is unlikely that early FPG is useful in predicting GDM, which is consistent with the findings in this study.

A study in non-pregnant population showed that when 2-hour PG fell below FPG, the risk of developing type 2 DM after 8 years of follow-up was lower, when compared with that in patients whose 2-hour PG remained higher than FPG[20]. Although all the women with 2-hour PG lower than FPG at the first OGTT in this study were in non-GDM group at second OGTT, the number was too small to make any reliable conclusion. Further studies investigating the change in glucose level after glucose load in pregnancy may be useful in identifying women who are at risk of progression to GDM in the current pregnancy.

The cutoff value for 2-hour PG was lower in this study compared with that in the Hungarian study (4.4 mmol/L vs. 6.2 mmol/L)[13]. Although it achieved the same sensitivity and NPV, fewer OGTTs were spared, which limited its use in the clinical setting. Given the high incidence of GDM in the high-risk group, small number of OGTTs spared in comparison with all women requiring OGTT, and the minimal risk associated with performing OGTT, the practice of repeating OGTT in the high-risk group should not be abandoned. However, in individual women who decline a repeated OGTT, we may consider omitting the second OGTT if results of the first OGTT do not exceed the cutoff criteria.

New World Health Organization Criteria

The high FPG cutoff value used in the 1999 WHO criteria[21] has been challenged as a majority of women with elevated FPG also had elevated 2-hour PG. Moreover, the criteria were extrapolated from non-pregnant populations and, hence, may not correlate with adverse pregnancy outcomes. The IADPSG proposed new criteria based on continuous graded relationships between higher maternal blood glucose levels and increased frequency of adverse

Table 8. 2013 World Health Organization criteria for diagnosing GDM and DM in pregnancy[22]*

	GDM	DM in pregnancy
75 g OGTT	-	-
FPG	5.1-6.9 mmol/L	≥7.0 mmol/L
1-Hour PG†	≥10.0 mmol/L	-
2-Hour PG	8.5-11.0 mmol/L	≥11.1 mmol/L
Random glucose	-	≥11.1 mmol/L (in the presence of diabetes symptoms)

Abbreviations: DM = diabetes mellitus; FPG = fasting plasma glucose; GDM = gestational diabetes mellitus; OGTT = oral glucose tolerance test; PG = post-glucose

* Diagnosis made if ≥1 glucose value met

† There were no established criteria for the diagnosis of DM based on the 1-hour PG

pregnancy outcomes, based on data predominantly from the HAPO (Hyperglycaemia and Adverse Pregnancy Outcome) study[9]. Because of the emergence of new evidence, the WHO recently published new diagnostic criteria for hyperglycaemia first detected in pregnancy, distinguishing between diabetes and lesser degrees of glucose intolerance in pregnancy (Table 8)[22]. Although the definition of GDM applies at any time during pregnancy, it is uncertain whether early OGTT is beneficial and cost-effective. Moreover, FPG cutoff value of 5.1 mmol/L might lead to overdiagnosis of GDM in non-obese women. Nevertheless, both the WHO and IADPSG recommend a FPG value of ≥5.1 mmol/L at first antenatal visit to diagnose GDM, and performing 75 g OGTT at 24 to 28 weeks if FPG was <5.1 mmol/L[9,22].

It is estimated that the number of cases with DM in pregnancy or GDM will be increased by 50% if the new diagnostic criteria are applied[22]. Since 1-hour PG sample was lacking in this study, direct comparison of the two criteria was not possible. In this study, the number of GDM cases detected by the 2013 WHO criteria[22] was lower than that by the 1999 WHO criteria if only the FPG and 2-hour PG were used. It is likely that 1-hour PG will pick up the remaining cases of GDM. Lowering the FPG cutoff value will increase its sensitivity in detecting GDM, but raising the 2-hour PG cutoff will decrease its sensitivity. Among those with GDM diagnosed by first OGTT in this study, the mean FPG in early pregnancy was <5.1 mmol/L but the mean 2-hour PG was >8.5 mmol/L. Fasting plasma glucose alone was not useful in detecting early-onset GDM. Moreover, it is unlikely that all cases of GDM will be detected by the first OGTT. Therefore, among high-risk women, early OGTT is useful to detect early-onset GDM, and it is likely that second OGTT will be required, even if the 2013 WHO criteria[22] are adopted.

Limitations

Oral glucose tolerance test has been challenged for its reproducibility, as the intra-individual variation may be up to 10% to 30%. The application of the cutoff value in this study is limited to units using the same laboratory assays and similar protocol for screening GDM. Future prospective studies with bigger sample size should be performed to validate the findings. Future studies should also aim at defining cutoff values that address pregnancy outcomes, in particular macrosomia, as it is more important than a laboratory diagnosis of GDM. It is estimated that the prevalence of GDM will be 50% higher if the new WHO criteria are adopted. Future studies with 1-hour PG data are required and the impact of the new criteria on pregnancy outcomes in the local population is yet to be determined.

Conclusion

In the group of patients with two or more risk factors, formal OGTT in early pregnancy cannot be omitted because FPG and/or HbA1c are not useful to screen for GDM. This is valid even if the 2013 WHO criteria[22] are adopted in the local population. An OGTT should replace the use of FPG or HbA1c to screen for GDM at first antenatal visit as suggested by the IADPSG. Although second OGTT might be omitted in up to 5.3% of patients with two or more risk factors, the number was small in comparison with all women requiring OGTT. Therefore, the practice of performing a repeated OGTT in this group should continue. However, in individual women who decline a repeated OGTT, we may consider omitting the second OGTT if the first 2-hour PG is <4.4 mmol/L in the absence of onset of new risk factor(s) after the first OGTT.

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Comparing the Use of Tissue Adhesive (2-Octyl cyanoacrylate) and Interrupted Sutures for Caesarean Section Wound: a Prospective Randomised Controlled Trial

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Objectives: To compare the efficacy of tissue adhesive (2-octyl cyanoacrylate) plus interrupted nylon sutures versus interrupted nylon sutures alone for wound closure in Caesarean section wound in terms of cosmesis, wound complication rates, pain score by patient, and surgeon satisfaction.
Methods: This was a prospective, non-blinded, randomised controlled study involving 80 subjects undergoing elective Caesarean section having transverse suprapubic skin incisions. The subjects were randomised into two groups for wound closure, namely, with interrupted vertical mattress nylon sutures or the tissue adhesive (2-octyl cyanoacrylate, Dermabond) plus nylon sutures. Results were compared using Chi-square test and *t* test where appropriate. Main outcome measures were cosmesis score and wound complication rates in the two arms.
Results: There was no significant difference between the two groups in the Hollander Wound Evaluation Scale as assessed by plastic surgeons (total mean score, 1.3 vs. 1.0; p=0.31). Wound complication rate, pain and cosmesis scores given by patients using visual analogue scale were comparable between the two groups.
Conclusion: Use of 2-octyl cyanoacrylate in addition to interrupted nylon sutures showed an insignificant favourable trend towards lower cumulative wound complication rate with no significant differences in cosmesis or pain score.
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Keywords: Cesarean section; Nylons; octyl 2-Cyanoacrylate; Tissue adhesives; Wound closure techniques

Introduction

Caesarean section wounds are most commonly closed with suture materials. This method of wound closure carries a risk of needle stick injury, the need for suture removal, and possibility of leaving permanent suture tracks. The lack of tensile strength after suture removal will also put the patients at increased risk of wound dehiscence or widened scar if adequate healing has not occurred before the removal.

Tissue adhesives for closure of surgical wounds are developed to overcome these problems[1]. A Cochrane review[1] shows the presence of significant difference in the surgeons' assessment of cosmetic appearance with higher mean rating for tissue adhesives. Early use of tissue adhesive with butyl cyanoacrylate was limited mainly to areas with low tension because of its physical properties by which it becomes brittle and fractures over longer scars and skin creases[2]. The octyl cyanoacrylate tissue adhesive (Dermabond), on the other hand, is a long-chain cyanoacrylate derivative that is stronger and more pliable than the butyl derivative. In addition to the reduction in needle stick injury[3], it also provides a barrier for the wound against bacterial infection[4]. Featured as monomers in a liquor form, it polymerises on contact with tissue anions and forms a strong bound to hold the edges of the wound together. The application skill can be easily acquired[5]. Removal is not required as it will usually slough off when wound re-epithelialisation occurs within 5 to 10 days.

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The use of Dermabond has been studied in wound closure for laparoscopic surgery, long surgical incisions[6], breast surgery[7], thyroid surgery[8,9], paediatric laceration repair, and hand surgery[10] with satisfactory results[11]. Studies on its use in Caesarean section are limited. A report in Italy showed no substantial differences in the strength of wound closure or cosmetic outcomes between closure with intradermal suture with non-absorbable thread, metallic clips, and 2-octyl cyanoacrylate. However, greater patient compliance was found in the group using the adhesive[12]. Another retrospective study in Virginia comparing methods of skin closure of Pfannenstiel incision included Dermabond, staples, and subcuticular absorbable sutures[13]. Results were not significant when the three groups were compared on wound complications (p=0.65) and surgical site infection (p=0.10).

Therefore, this study aimed to compare the efficacy of using additional tissue adhesive (2-octyl cyanoacrylate) with interrupted nylon sutures versus nylon sutures alone for wound closure in Caesarean section wound in terms of cosmesis, wound complication rates, pain score by patient, and surgeon satisfaction.

Methods

This prospective randomised controlled study was carried out at the Department of Obstetrics and Gynaecology, Queen Mary Hospital, The University of Hong Kong, where vertical mattress sutures using nylon was the standard method of skin closure in Caesarean section. The study was conducted between August 2008 and March 2011. With reference to previous studies[14], patient's preference towards tissue adhesive as the method of choice for wound closure in breast surgery was 73% at 6 weeks postoperation, while it was 20% towards interrupted prolene sutures (p<0.01). With a sample size of 64 patients, this study had a 99% power to detect a statistically significant difference at the 5% level. Eighty patients were recruited in this study to allow for a dropout rate of 20%.

Patients aged 18 years or above undergoing elective Caesarean section at Queen Mary Hospital were eligible for the study. Patients were not eligible if they were allergic to cyanoacrylate, required vertical skin incisions, and had a temperature of >37°C on the day of operation. Patients who were on systemic steroids or had diabetes requiring insulin injections were also excluded.

Patients were invited to participate in the study a day prior to the scheduled elective Caesarean section if the above criteria were met. Written informed consent was obtained from subjects who were willing to participate in the study. After that, a full medical, obstetrical and gynaecological history was undertaken, and physical examination was performed. By computer-generated randomisation, patients were assigned to one of two methods of wound closure: using nylon sutures alone (nylon group) and using Dermabond in addition to nylon sutures (Dermabond group). In the nylon group, five vertical mattress sutures with nylon were applied as a conventional method in our centre. One patient in the nylon group had three vertical mattress sutures and another patient had seven vertical mattress sutures due to individual surgeon's preference. In Dermabond group, Caesarean section wounds were first closed by three stitches of interrupted nylon with application of 2-octyl cyanoacrylate in between the stitches.

The randomisation was performed at the time of Caesarean section in a 1:1 ratio, and the allocation was placed in a sealed envelope, which was only opened at the start of operation. Operating surgeons were instructed to attend a briefing on application of Dermabond to skin wound. All skin wounds were positioned at two fingers above the pubis. For patients with previous Caesarean sections with suprapubic transverse incisions, the same skin incision would be used. The skin edges were closed with either method, depending on randomisation. The length of the incision and the time needed for wound closure were recorded. The surgeons were asked about the ease of application at the end of the operation. This was reflected by the surgeon satisfaction score, with the highest satisfaction score being 10. The nylon sutures were removed on day 5 for patients having first operation and on day 6 for patients having previous laparotomy.

During the hospital stay, patients were examined on postoperative day 1 and day 3. The patients were reviewed again at postoperative 5, 14, and 28 days and any wound complications were documented. Patient's satisfaction on pain and cosmesis using visual analogue scale (VAS) were also recorded. Photos of the wound were taken on day 28, and were shown to a plastic surgeon who was blinded to the method of wound closure for assessment of the wound using the Hollander Wound Evaluation Scale (HWES).

The basic demographics of the patients were compared. The associations between clinical variables and treatment assignments were assessed by Chi-square test or *t* test, as appropriate. Statistical significance was set at p<0.05. The study was approved by the Institutional Review Board of the University of Hong Kong / Hospital Authority Hong Kong West Cluster Committee. The

primary outcome of the study was the cosmesis score using HWES by plastic surgeon, and wound complication rates between the two arms at intervals until postoperative day 28. The secondary outcomes included cosmesis and pain scores using VAS, surgeon's satisfaction on the ease of application, and time of application.

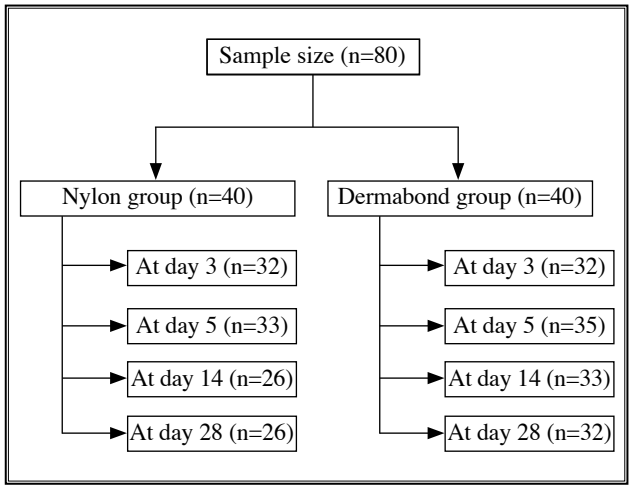

Figure. Number of patients attending follow-up

Results

Recruitment period was initially planned for 8 months only, but with the low recruitment rate and high dropout rate at follow-up, we had to extend our recruitment period. A total of 80 patients were included in this study from August 2008 to March 2011. The randomisation was performed in a 1:1 ratio, with 40 patients randomised to each arm. Informed consent was obtained from all patients and criteria were met in all of them. None of the patients withdrew from the study. Some data were missing because of loss to follow-up and incomplete documentation. The trial profile is shown in the Figure. All patients recruited in our study were Chinese.

As shown in Tables 1 and 2, the basic demographics and indications for Caesarean section were similar among the two groups. In most patients, Caesarean section was performed due to a history of Caesarean delivery. The number of patients with previous wound complications, such as keloid formation, as well as the lengths of Caesarean section skin wound, were similar in the two groups. Acetaminophen-phenyltoloxamine (dologesic) 325 mg/tablet or paracetamol 500 mg/tablet was used as routine

Table 1. Basic demographics in the two groups*

	Nylon group (n=40)	Dermabond group (n=40)	p Value
Age (years)	34.7	34.6	0.19
Body mass index (kg/m^2)	27.6	28.6	0.07
Weeks of gestation	38.8	38.6	0.31
Length of incision (cm)	15.2	15.3	0.14
Experience of surgeon (years)	2.7	2.1	0.08
History of laparotomy	68% (n=27)	68% (n=27)	1.0
History of keloid	23% (n=9)	18% (n=7)	0.62
History of gestational diabetes	20% (n=8)	18% (n=7)	0.73
Use of dologesic / panadol after operation (no. of tablets/patient)	5	4.7	0.63

* Data are shown as mean, unless otherwise specified

Table 2. Indications for Caesarean section

Indication	Nylon group (n=40)	Dermabond group (n=40)
Previous Caesarean section	65% (n=26)	65% (n=26)
Breech presentation	13% (n=5)	13% (n=5)
Multiple pregnancy	3% (n=1)	13% (n=5)
Placenta praevia	10% (n=4)	8% (n=3)
Others	10% (n=4)	3% (n=1)

prescription for postoperative analgesia in our department. There was no significant difference in terms of usage of analgesics between nylon and Dermabond groups.

Photos were taken on day 28 of follow-up, and scores were given by one experienced plastic surgeon who was blinded to the method of wound closure, using HWES. There were 24 photos from the nylon group and 33 photos from Dermabond group as some patients defaulted the follow-up on day 28. Two photos were excluded from analysis as the labelling of patient identity was not clear. The HWES score comprises of six parameters: presence of step-off border, irregular contour, widening of scar of >2 mm, presence of inversion, presence of inflammation, and overall cosmesis. Score 0 was given if none of the above parameters was present. A score of 1 was given for each parameter that was present or when there was suboptimal overall cosmesis, and a total HWES score was calculated (Table 3). Total mean score did not show any statistical difference between the two groups, although it was slightly higher in the nylon group, representing less favourable wound cosmesis (1.3 vs. 1.0; p=0.31).

Complications including wound dehiscence, infection, haematoma, overlapping, and hernia were assessed on postoperative days 3, 5, 14, and 28. Although

Table 3. Wound evaluation by Hollander Wound Evaluation Scale

	No. (%)		p Value
	Nylon group (n=24)	Dermabond group (n=33)	
Step-off borders			0.21
Nil	19 (79%)	30 (91%)	
Present	5 (21%)	3 (9%)	
Irregular contour			0.38
Nil	14 (58%)	23 (70%)	
Present	10 (42%)	10 (30%)	
Widening of scar			0.88
Nil	17 (71%)	24 (73%)	
Present	7 (29%)	9 (27%)	
Presence of inversion			1.0
Nil	24 (100%)	33 (100%)	
Present	0	0	
Presence of inflammation			0.88
Nil	20 (83%)	28 (85%)	
Present	4 (17%)	5 (15%)	
Overall cosmesis			0.64
Optimal	18 (75%)	28 (85%)	
Suboptimal	6 (25%)	5 (15%)	
Total mean score	1.3	1.0	0.31

Table 4. Postoperative cumulative complication rates

No. of days post-surgery	Nylon group (n=40)	Dermabond group (n=40)	p Value
Day 3	2.5% (n=1)	0	1.00
Day 5	30% (n=12)	10% (n=4)	0.05
Day 14	30% (n=12)	13% (n=5)	0.10
Day 28	30% (n=12)	15% (n=6)	0.18

the difference in cumulative complication rates on day 28 between the two groups was not significant, it showed a trend of higher complication rate in the Nylon group (30% vs. 15%; p=0.18). Subgroup analysis also showed that the cumulative complication rate was significantly higher in the Nylon group on postoperative day 5 compared with Dermabond group (30% vs. 10%; p=0.05) [Table 4]. In the nylon group, a total of 12 patients had complications, and one of them had infection, wound dehiscence and overlapping of wound. In Dermabond group, six patients had complications, and one of them had both overlapping of wound and haematoma formation. In subgroup analysis, patients in the nylon group had a trend towards an increased frequency of wound infection (2 vs. 0; p=0.53) and overlapping wounds (7 vs. 2; p=0.64), though the differences were not statistically different (Table 5).

Secondary outcome measures included patient's satisfaction on pain and cosmesis scores using VAS (Table 6). The pain and cosmesis scores showed an insignificant trend of being in favour of Dermabond group, especially on postoperative day 14 (2.6 vs. 1.7; p=0.06 for pain score and 6.2 vs. 6.1; p=0.08 for cosmesis score). Understandably, application of Dermabond added extra time for skin closure and, in general, surgeons preferred to use nylon alone without addition of Dermabond (Table 7).

Discussion

Different methods of wound closure in Caesarean section are used in different centres. Each of them has its benefits and disadvantages. The Cochrane review on techniques and materials for skin closure in Caesarean section[15] included studies on closure with staples versus

Table 5. Frequencies of complications

Complication	Nylon group (n=14)	Dermabond group (n=7)	p Value
Wound dehiscence	3	3	0.35
Haematoma formation	2	2	0.57
Wound infection	2	0	0.53
Overlapping wound	7	2	0.64

Table 6. Mean pain and cosmesis scores using visual analogue scale

Postoperative score	Nylon group	Derbamond group	p Value
Pain score			
At day 1	1.1	1.0	0.92
At day 3	4.9	4.8	0.45
At day 5	3.9	3.5	0.55
At day 14	2.6	1.7	0.06
At day 28	1.3	0.9	0.19
Cosmesis score			
At day 3	5.8	5.5	0.33
At day 5	5.5	5.1	0.74
At day 14	6.2	6.1	0.08
At day 28	7.2	7.5	0.46

Table 7. Time required for wound closure and surgeon satisfaction score

	Nylon group	Dermabond group	p Value
Mean time required for application (mins)	03:51	05:50	0.02
Mean surgeon satisfaction score	8.3	6.8	0.001

subcuticular absorbable sutures, which showed faster operating time but higher pain score in patients using staples. However, there are no (or limited if there is any) studies on the use of interrupted non-absorbable sutures for closure of Caesarean section. Another Cochrane review[16] addressing the use of tissue adhesives versus sutures for closure of surgical wounds showed a lower complication rate including wound dehiscence when sutures were used. Dermabond would, theoretically, decrease wound infection rate as it forms a waterproof layer above the surgical wound and acts as a barrier to bacterial invasion.

To our best knowledge, this is the first randomised controlled trial comparing the use of Dermabond and interrupted nylon sutures versus nylon sutures alone for wound closure in Caesarean sections. An insignificant favourable trend was seen towards Dermabond in terms of overall pain and cosmesis. This was similar to the finding in a previous study[14] comparing interrupted prolene with Dermabond for wound closure in mammoplasty, suggesting an overall preference towards the use of Dermabond, with the panelists noting a significantly better HWES score in patients with Dermabond ($p<0.02$) and a better cosmesis score using VAS by patients ($p<0.05$). A previous study[17] comparing the use of Dermabond, sutures, and staples in laparotomy wounds showed similar infection rate. From our study, though overall complication rates were comparable in the two groups after 4 weeks of operation, there was a favourable trend of fewer overlapping wounds and low rate of infection in Dermabond group, which reached statistical significance on day 5 after operation.

Use of Dermabond could represent a reasonable alternative closure method. We acknowledge the fact that significant results were obtained in previous studies[1,7] using Dermabond over conventional suture methods. One of the postulated reasons is that these studies were mainly on laparoscopic wounds and wounds that were not in the abdominal area where they were subject to movements due to breathing and coughing.

The relatively high dropout rate and missing data could be one of the limitations of this study. This was due to non-compliance of the patients with the relatively frequent and prolonged postoperative evaluations in the postnatal period. It was technically not feasible to blind the patients and surgeons to the method of suture, which could cause bias in developing the pain and cosmesis scores as well as the surgeon satisfaction score. However, the potential bias was minimised by an independent assessment on day 28 by plastic surgeons who were blinded to the method of skin closure. Although the photos were not taken by the same assessors and the distance of the camera from wound was not standardised, results of tele-assessment of wounds have been proven to be similar to those of real-time assessment[18].

We used VAS and HWES in our study as these assessment tools have been proven to be highly reproducible and to minimise inter-observer errors[19,20]. The pain and cosmesis scores ranked by patients showed favourable trends toward the use of Dermabond; by increasing the sample size in future studies, the result may reach statistical significance. In our study, the majority of surgeons applied five stitches of nylon in the nylon group; there was only one case with application of three stitches and one with seven stitches of nylon due to the respective surgeon's personal preference. The use of nylon has been the traditionally advocated method of closure in our unit. Surgeons in this study had a mean of 2 years of experience; thus, they were already accustomed to using nylon for wound closure. It is, therefore, not surprising to note that closure with Dermabond was less popular compared with nylon sutures given that they needed to learn a new method for skin closure. One may expect that if Dermabond is applied without the three Nylon stitches, the surgeons may get more accustomed to using Dermabond for wound closure. The operating time and surgeon satisfaction rate may eventually become comparable between these two methods.

In conclusion, this is the first randomised controlled trial comparing the efficacy of tissue adhesive (Dermabond) in addition to interrupted nylon sutures with interrupted nylon sutures alone for wound closure in Caesarean section. Dermabond in addition to nylon sutures showed a trend, though insignificant, towards lower cumulative wound complication rates with similar cosmesis and pain scores.

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Declarations

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Evaluation of the Accuracy of Prenatal Ultrasound Assessment of Facial Clefts

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Objective: To evaluate the accuracy of two-dimensional and three-dimensional ultrasound in the diagnosis of facial clefts, and particularly in predicting the presence or absence of associated alveolar cleft / cleft palate in the presence of cleft lip.
Methods: All cases of facial clefts diagnosed before 24 weeks over a 5-year period from 2009 to 2013 in a single obstetric unit were reviewed. The findings from conventional two-dimensional ultrasound scanning and three-dimensional ultrasound imaging, using the reverse face view, oblique face view, or other modified techniques were compared with the findings at postnatal examination of the babies or at pathological examination of the fetuses after termination of pregnancy. The degree of accuracy of prenatal diagnosis of cleft lip alone, or cleft lip with alveolar cleft / cleft palate was determined.
Results: A total of 42 cases were analysed. There were 35 unilateral, six bilateral, and one median cleft lips. Three cases involved a fetus of a monochorionic twin pair, and one case involved a fetus of a dichorionic twin pair. Associated structural abnormalities were detected by antenatal ultrasound in five cases, and significant karyotype abnormalities were detected in four cases. Termination of pregnancy was performed in 13 cases. There were 12 cases with cleft lip only, six cases with cleft lip with associated alveolar cleft, and 24 cases with cleft lip and palate. There were five cases where antenatal ultrasound overdiagnosed the severity of the cleft, while in three cases the extent of the cleft was underdiagnosed, giving an overall accuracy of 81%. The most common discrepancy was in the overdiagnosis or underdiagnosis of alveolar clefts, whereas there were no errors concerning the side of the cleft. When only the antenatal diagnostic accuracy of presence or absence of palate clefts was calculated, the overall accuracy was 95% (40/42; Phi value, 0.91).
Conclusion: The accuracy of prediction of the presence or absence of cleft palate in the presence of cleft lip was high, but the prediction of alveolar clefts was most prone to error. The limitations of such ultrasound predictions should be explained to parents at the time of antenatal counselling.
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Keywords: Cleft lip; Cleft palate; Imaging, three-dimensional; Ultrasonography

Introduction

Facial clefts are among the most common congenital fetal abnormalities. The overall prevalence of facial clefts has been reported to be between 1:500 and 1:1000 live births in various studies[1,2]. Facial clefts, or orofacial clefts, refer to cleft lip (CL), cleft lip with associated alveolar cleft (CLA), cleft lip and palate (CLP), and cleft palate (CP). The prevalence of these different types of clefts has been reported to be 0.29/1000 (CL), 0.48/1000 (CLP), and 0.31/1000 (CP)[3,4]. Mid-trimester ultrasound (USG) screening for facial clefts has been instituted in many different countries, and different authorities have also established guidelines for fetal morphology USG to detect these abnormalities[5,6]. However, screening of isolated CP has not been included in such protocols and the assessment of CP or alveolar clefts in the presence of other facial clefts is not detailed in such guidance.

Antenatal USG imaging of the fetal palate has improved in recent years with the use of advanced techniques using two-dimensional (2D) or three- or four-dimensional (3D / 4D) USG[7-12]. The improved detection and assessment of CP is mainly focused on those fetuses with associated CL, while in general, the detection of isolated CP without CL is still a rare event[13,14]. In addition, errors of varying degrees in the reporting of these facial clefts are not uncommon[15,16] and may influence the counselling given to the prospective parents.

This retrospective study in a local regional obstetric unit aimed to determine accuracy in predicting clefting of the alveolar bone or hard palate in the presence of CL

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using current 2D and 3D / 4D USG techniques, as well as to assess performance against that reported in the literature.

Methods

A retrospective review of all cases of facial clefts diagnosed before 24 weeks' gestation over a 5-year period from 2009 to 2013 in a single obstetric unit were reviewed, based on the prenatal diagnosis registry of the department and a comprehensive obstetric database currently in use in all public obstetric units in Hong Kong. Within the study period, all patients detected to have facial clefts were referred to the prenatal diagnosis clinic for assessment by an accredited maternal-fetal-medicine subspecialist. The subspecialist routinely performed detailed USG to look for associated structural abnormalities, and also used conventional 2D USG and other 3D USG techniques, such as the reverse face view[7], flipped face view[8], oblique face view[9,10], or other modified views as appropriate or feasible, in an attempt to verify the extent and type of facial cleft. All USG examinations were carried out using either the Voluson 730 Expert or the Voluson E6 system (GE Healthcare, Wisconsin, US) and image volumes were obtained with a 4-8 MHz RealTime 4D curved array abdominal probe (GE Healthcare, Wisconsin, US), via a parasagittal section of the fetal head. Multi-slice techniques were not used in this series. Stored image volumes were processed with 4D View PC software (GE Healthcare, Wisconsin, US). The patient was counselled on the need for karyotyping by amniocentesis according to the findings, and in regard to their decisions on the subsequent management of the pregnancy. A joint 'cleft clinic' consultation, with the presence of the obstetric team, the neonatal team, the paediatric surgical team, and the maxillofacial and dental team was available for patients who wished to have more information and discussion on postnatal management plans and the long-term outcome for these babies.

The case notes, USG reports and stored images and volumes, if any, of each of the identified cases were reviewed in detail. The antenatal findings and provisional diagnosis that was given to the patient / couple at that stage for counselling were compared with the findings at the postnatal examination after birth, or at pathological examination of the fetus after termination of pregnancy. The degree of accuracy of antenatal predictions was determined, and the original diagnoses were then classified into either correct diagnosis, underdiagnosis, or overdiagnosis.

Results

Within the study period, there were a total of 24,978 deliveries. The overall incidence of facial clefts was 0.2% (n = 50). Of these cases, two did not have antenatal USG assessment and the clefts were diagnosed only after birth, while for one case, the antenatal routine morphology scan failed to detect a left CL, which was subsequently only detected on a repeat scan in the third trimester. Another two cases underwent antenatal assessment by their own obstetricians and were referred to our unit for delivery care only after 24 weeks. In addition, three had isolated CP without associated CL and were not diagnosed during the antenatal period; of these, one had associated congenital cardiac malformation and another had gastroschisis. The six undetected cases and the two referred cases were excluded from our analysis. The overall antenatal detection rate of facial clefts before 24 weeks in this cohort, including the two referred cases, was 88% (44/50).

The final cohort for analysis consisted of 42 cases, including 35 unilateral and six bilateral CLs as well as one median cleft. Three cases involved a fetus of a monochorionic-diamniotic twin pair, and one case involved a fetus of a dichorionic-diamniotic twin pair. Associated structural abnormalities were detected by antenatal USG in five cases, and significant karyotype abnormalities were detected in four cases. Termination of pregnancy was performed in 13 (31%) of the cases, and there was one case of stillbirth at around 35 weeks (case 14). There were 12 (29%) cases with CL only, six (14%) with CLA, and 24 (57%) with CLP (Tables 1 and 2). There were five cases where antenatal USG overdiagnosed the severity of the cleft, while three cases were underdiagnosed, giving an overall accuracy of 81% (34/42) [Table 2]. The most common discrepancy was in the overdiagnosis or underdiagnosis of CLA, with four of eight errors in diagnosis having a final diagnosis of cleft alveolar bone. There were no errors in diagnosing the side of the cleft. While all true palatal clefts were diagnosed on antenatal assessment, there were two false-positive diagnoses (cases 25 and 30). In a fetus with a unilateral CLP, the initial USG assessment showed an obvious left CL with associated CLP and a suspicious dimple CL on the right side (case 36). However, repeat USG at the time of amniocentesis within 1 week was able to exclude bilateral clefts, and so the USG diagnosis was considered correct. When only the antenatal diagnostic accuracy of presence or absence of CP was calculated, the overall accuracy was 95% (40/42, Phi, 0.91), giving a specificity of 88.8% and a sensitivity of 100% for the detection of CPs in the presence of CLs in this cohort (Table 3[13]).

Table 1. Clinical characteristics of the cohort (n=42)

	Antenatal diagnosis	Definitive diagnosis	Associated abnormalities	Karyotype abnormalities	Outcome	Diagnostic accuracy
1	Right CL	Right CL	Partial absence of corpus callosum	46,XY,del7q31.3-q34	TOP	
2	Left CLP	Left CLP	One of DCDA twins	Normal	LB	
3	Right CLP	Right CLP		Normal	LB	
4	Right CLP	Right CLP		Normal	LB	
5	Left CLP	Left CLP		Normal	LB	
6	Left CLA	Left CL		Normal	LB	Overdiagnosis
7	Right CLP	Right CLP		Normal	LB	
8	Left CL	Left CLA		Normal	LB	Underdiagnosis
9	Bilateral CLP	Bilateral CLP	One of MCDA twins; stillbirth of co-twin	Normal	LB	
10	Left CLP	Left CLP		Normal	LB	
11	Left CLP	Left CLP		Normal	TOP	
12	Left CLP	Left CLP		Normal	LB	
13	Left CL	Left CLA		Normal	LB	Underdiagnosis
14	Left CLP	Left CLP	One of MCDA twins	Normal	SB	
15	Left CL	Left CL		Normal	LB	
16	Left CLP	Left CLP		Normal	TOP	
17	Right CLP	Right CLP		Normal	LB	
18	Left CLA	Left CLA		Normal	TOP	
19	Right CL	Right CL		Normal	LB	
20	Right CLP	Right CLP		Normal	TOP	
21	Right CL	Right CL		Normal	LB	
22	Left CLA	Left CLA		Normal	LB	
23	Bilateral CLP	Bilateral CLP	Multiple malformations	46,XX,18q-	TOP	
24	Bilateral CLP	Bilateral CLP		Normal	LB	
25	Left CLP	Left CL		Normal	TOP	Overdiagnosis
26	Bilateral CLP	Bilateral CLP		Normal	LB	
27	Right CLA	Right CL		Normal	LB	Overdiagnosis
28	Right CL	Right CL		Normal	LB	
29	Left CLP	Left CLP		Normal	LB	
30	Left CLP	Left CL	Tetralogy of Fallot	Normal	TOP	Overdiagnosis
31	Left CL	Left CL		Normal	TOP	
32	Median CLP	Median CLP	Omphalocoele, limb deformities	Trisomy 18	TOP	
33	Right CLP	Right CLP	One of MCDA twins; hydropic co-twin	Normal	LB	
34	Right CL	Right CL		Normal	LB	
35	Left CLP	Left CLA		Normal	LB	Overdiagnosis
36	Left CLP	Left CLP		Normal	LB	
37	Left CLP	Left CLP		Normal	TOP	
38	Left CL	Left CLA		Normal	LB	Underdiagnosis
39	Bilateral CLP	Bilateral CLP		Normal	TOP	
40	Left CL	Left CL		Normal	LB	
41	Left CLP	Left CLP		Normal	LB	
42	Bilateral CLP	Bilateral CLP	Overlapping fingers, CPC	Trisomy 18	TOP	

Abbreviations: CL = cleft lip; CLA = cleft lip with associated alveolar cleft; CLP = cleft lip and palate; CPC = choroid plexus cyst; DCDA = dichorionic-diamniotic; LB = live birth; MCDA = monochorionic-diamniotic; SB = stillbirth; TOP = termination of pregnancy

Table 2. Characteristics of facial clefts and antenatal ultrasound prediction

Characteristic	Cleft lip (n=12)	Cleft lip with associated alveolar cleft (n=6)	Cleft lip and palate (n=24)
Type of cleft			
Unilateral	12	6	17
Bilateral	0	0	6
Median	0	0	1
Outcome of pregnancy			
Termination of pregnancy	4	1	8
Stillbirth	0	0	1
Live birth	8	5	15
Twin pregnancy	0	0	4
Associated structural abnormalities	2	0	3
Chromosomal abnormalities	1	0	3
Antenatal ultrasound diagnosis			
Lip cleft	8	3	0
Lip cleft with alveolus	2	2	0
Lip cleft with palate	2	1	24
Accuracy of antenatal ultrasound diagnosis			
Correct	8	2	24
Overdiagnosis	4	1	0
Underdiagnosis	0	3	0

Table 3. Antenatal ultrasound prediction of presence or absence of associated palate clefts*

	Antenatal ultrasound diagnosis		
	CLP	No palate cleft (CL and CLA)	Total
CLP	24[a]	0[b]	24
No palate cleft (CL and CLA)	2[c]	16[d]	18
Total	26	16	42

Abbreviations: CL = cleft lip; CLA = cleft lip with associated alveolar cleft; CLP = cleft lip and palate

* Degree of association (Phi) between antenatal and postnatal diagnosis of CLP versus no CLP[13]: (ad–bc) / √(a+b)(a+c)(d+b)(d+c), i.e. (24 x 16 – 0) / √(24 x 26 x 16 x 18) = 384 / 423.9 = 90.5%, p<0.001

Discussion

The overall detection rate of facial clefts by mid-trimester USG in this series was comparable to that reported in the literature[1,2,13]. There were apparently no false-positives and the specificity for detection of cleft lip approached 100%. The accuracy of detection of CP in the presence of CL was also comparable to results reported in the literature[13,15,17], with an overall accuracy of around 95%. Half of the cases of underdiagnosis or overdiagnosis related to the diagnosis of alveolar ridge clefts.

The performance of screening USG in the detection of facial clefts has been observed to progressively improve over the years in several studies. This improvement has been associated with improvements in USG techniques and training of sonographers. In a survey of all orofacial clefts referred to a specialist centre in Glasgow, it was reported that the antenatal detection rate had increased from 11% in 1999 to over 50% in 2008. The increased use of routine USG for anomaly screening was shown to significantly improve the detection rates when compared with scanning high-risk pregnancies only[18]. In another Norwegian study, the detection rate was observed to increase from 34% in 1987-1995, to 58% in 1996-2004[13]. In a recent prospective

screening study of 35,000 low-risk women and 2800 high-risk women in the Netherlands, the overall detection rate of facial clefts was 88%[19]. Our calculated detection rate of facial clefts of 88% in this retrospective cohort was in line with the high detection rates reported in the literature[17,19,20]. However, where the fetal lip is normal, midline CP is almost never diagnosed on antenatal assessment unless there is clinical suspicion arising from the family history, and expert USG is carried out specifically to look for hard and soft palate clefts. Our experience concurs with various studies that have reported very low or zero detection rates of isolated CPs in the absence of lip clefts, even in the presence of other structural abnormalities[19,21].

The accuracy of diagnosing the presence or absence of CP when CL is detected is important for counselling parents. The existence of CP would imply additional surgical procedures to repair the CP in addition to the CL[21,22], as well as a higher rate requiring further surgery, and audiology and orthodontic services well into the teenage years[22]. Therefore, various 3D USG techniques have been advocated for the evaluation of facial clefts. In this study, when CL was diagnosed, our team commonly used a 2D transverse view starting at the level just below the nasal septum[23] to directly visualise the integrity of the alveolar ridge and the maxilla. This was commonly supplemented by the use of 3D volumes, which employ the flipped face[8] or angulated views[9] approach to visualise the alveolar ridge and hard palate (Figure). However, there was no preset protocol and the sonographer was free to

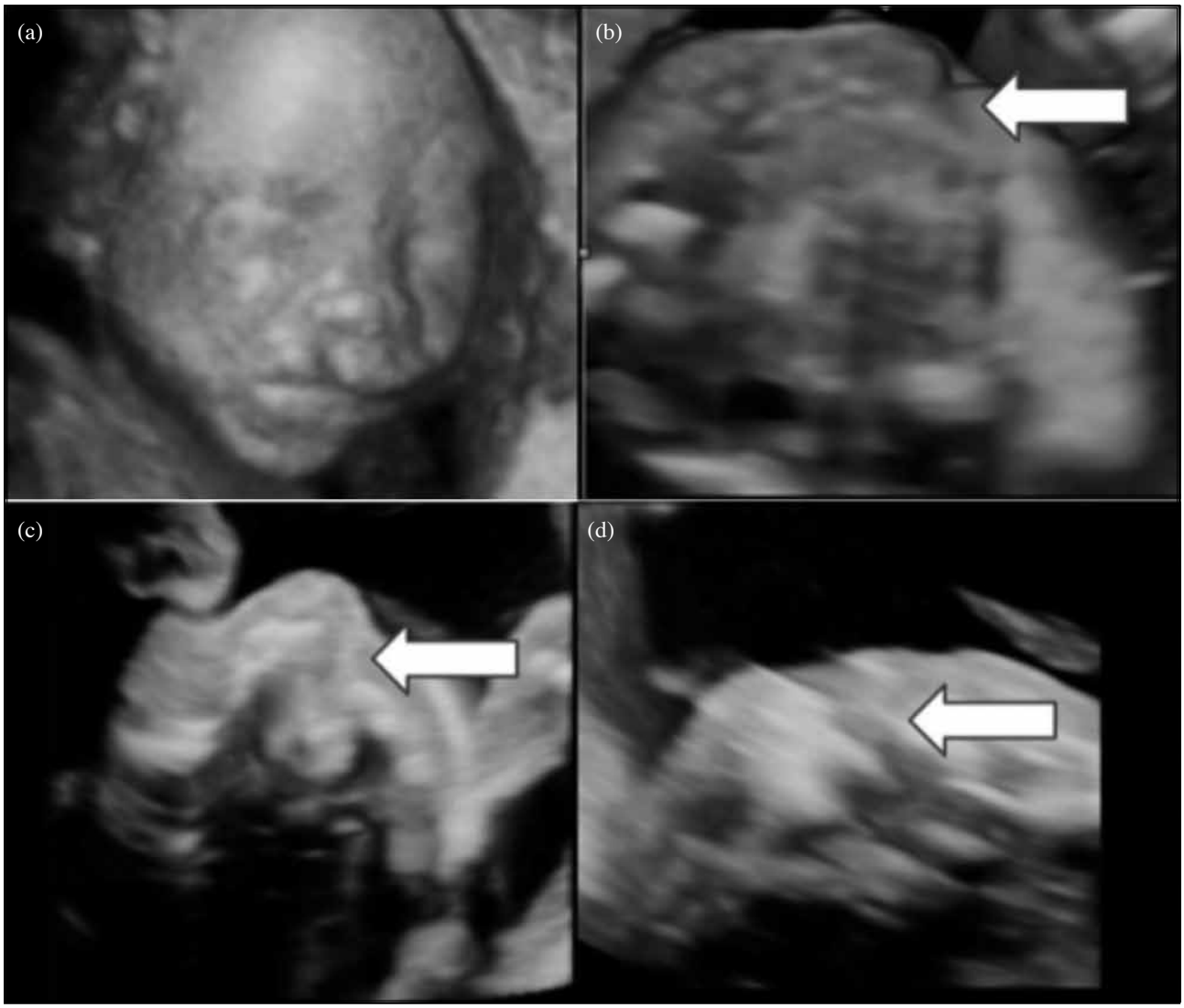

Figure. Cleft lip, alveolar cleft, and cleft palate as visualised by 3-dimensional (3D) ultrasound (USG) surface-rendered images: (a) facial cleft as seen by 3D USG; (b) cleft lip with intact alveolar ridge (arrow); (c) associated alveolar cleft as visualised by rotational 3D views (arrow); and (d) associated cleft palate as visualised by rotational 3D views (arrow)

choose the technique of preference, or a combination of techniques[10-12,16], depending on the sonographer's training and experience, fetal position, precise gestation, presence or absence of associated abnormalities, until the sonographer was satisfied as to the probable extent of the cleft. In this series, as diagnoses were only made after the completion of both 2D and 3D imaging, we were unable to compare the performance of 2D USG alone versus 2D / 3D USG assessment.

One major reason why our team would not want to restrict our protocol to one standard or routine 3D USG technique for the assessment of facial clefts is the lack of evidence on the actual precision, sensitivity or specificity of these various methods. Most of the studies describing new 3D USG techniques were primarily concerned with the practical methodology and sonographic approach for providing images of palatal structures in largely normal fetuses, and the number of pathologies described in these studies was surprisingly small[24]. For instance, the technique described by Faure et al[11] and Wong et al[25] included no abnormal cases, and even the well-known papers by Platt et al[8] and Pilu and Segata[9] described only one abnormal case as an example. Other studies, including Campbell et al[7], Martínez Tens et al,[10] and Wang et al[26] described small case series of eight, 10, and 22 abnormal cases, respectively. Thus, no precise sensitivity or specificity figures can be reliably calculated from these studies. Nevertheless, whatever the technique employed, the diagnostic accuracy is anticipated to be high in skilled hands. In a series of 79 cases of facial clefts, it was reported that 77 (97%) of the associated CPs were diagnosed accurately and the sensitivity of detection of CP was 100% and specificity was 90% in this high-risk population[13]. In a meta-analysis, it was estimated that when CL is detected, careful 2D USG, supplemented with various 3D USG techniques, should detect a cleft of the hard palate in around 86% to 90% of cases[23]. Our reported accuracy in this cohort of around 95% is in line with this reported performance.

There are also limited data in the literature comparing the accuracy of different 3D USG techniques in delineating associated CP. In one of the only such studies that included 50 normal and 10 abnormal fetuses (gestation of 23-33 weeks), it was found that the upper lip and alveolar ridge were well visualised by either the reverse face, flipped face, or oblique face methods. Involvement of the hard palate was accurately diagnosed in 71% of cases with the reverse face view, in 86% with the flipped face view, and in 100% with the oblique face view[10]. Involvement of the soft palate was diagnosed correctly in only one in seven of the fetuses with secondary palate defects in the flipped face and oblique face views[10]. The authors favoured using these latter two views, which could allow visualisation of the soft palate in selected cases[10]. In our experience, actual visualisation of the soft palate requires fluid between the tongue and soft palate, and a curving plane to follow the structure of the palate, which is not possible practically with the reverse face view. We thus also prefer the flipped face or oblique face view because of the higher chance of satisfactory visualisation. Another possible source of error in the visualisation of CLA or CP could be motion artefacts that frequently occur in the rendered images obtained from rotational views. The use of multi-slice views was suggested to reduce such artefacts. In a series of 22 CLs, oblique views detected only eight of the nine associated CPs while multi-slice views detected all of them[26]. The value of using multi-slice views, together with rotational views, should be further explored.

Our results showed that the diagnostic precision was greater when there was CP. All of the true CPs were detected in this cohort. However, overdiagnosis was common when there were clefts in the alveolar ridge and some were misdiagnosed as CP. This could be expected when visualisation by manoeuvring of the 3D volume was suboptimal, and artefacts would easily be taken as palatal clefts. This was particularly true in high-risk cases, for example those with bilateral clefts, when the sonographer was more likely to overdiagnose due to expecting to see more serious pathology, often quoted as 'context bias'. In addition, this was a retrospective case series, and the results were compiled based on the diagnosis reported by the sonographer at the time of assessment, rather than by reviewing the stored images or volumes. Therefore, we have not excluded possible inter-observer discrepancies in the diagnosis if the actual images were reviewed by the investigators.

We conclude that with our current practice of a combination of 2D and 3D USG techniques, our prediction of the presence or absence of CP in those diagnosed with CL was good and the results were on a par with those reported in the literature. However, overdiagnosis and underdiagnosis did occur in some cases, particularly when associated with assessment of alveolar ridge clefts. The limitations of such USG predictions should be explained to parents at the time of counselling.

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Clinically Significant Lesions in Women with Atypical Glandular Cells on Cervical Cytology: A Nine-year Retrospective Study

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Objectives: To determine the incidence of clinically significant lesions in patients with cytologically atypical glandular cells (AGC) in Hong Kong; and to study the association between clinical characteristics and risks of developing clinically significant lesions as well as the long-term impact of cytologically AGC in a patient cohort to make appropriate recommendations for managing these patients.
Methods: A retrospective study in 261 women with cytologically AGC, who were first referred to the colposcopy clinics of the New Territories West Cluster, Hospital Authority, was conducted. Follow-up records, as well as cytological and histological reports, were analysed. Clinically significant lesions were defined as cervical intraepithelial neoplasia 2 or 3, severe glandular dysplasia, atypical endometrial hyperplasia, adenocarcinoma in situ, or invasive carcinoma.
Results: Significant lesions were diagnosed in 77 (30%) patients after referral for cytologically AGC. Twenty-nine (11%) patients had gynaecological cancer. Forty-eight (18%) patients had severe premalignant conditions of the gynaecological tract. Fifty-eight patients (75%) had lesions diagnosed within the first year of referral. Of 229 patients referred for AGC not otherwise specified, 58 (25%) had significant lesions. Of 32 patients referred for AGC-favour neoplasia, 19 (59%) had significant lesions. Presence of concurrent atypical squamous cells of unknown significance (ASCUS) at referral was significantly associated with the diagnosis of genital tract cancer (p=0.02). Concurrent ASCUS at referral was also significantly associated with delayed diagnosis of clinically significant lesions (p=0.01).
Conclusions: Incidence of clinically significant lesions in women with cytologically AGC was high. In particular, concurrent ASCUS at referral conferred an increased risk of clinically significant lesions.
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Keywords: Neoplasms, squamous cell; Papanicolaou test; Uterine cervical neoplasms

Introduction

Interpreting abnormal cervical smears is one of the most commonly encountered tasks by gynaecologists. Management of smears with glandular abnormalities remains a challenging problem. A significant number of lesions are associated with glandular abnormalities[1]. Atypical glandular cells (AGC) are defined as cells showing either endometrial or endocervical differentiation displaying nuclear atypia that exceeds obvious reactive or reparative changes but without the unequivocal features of invasive adenocarcinoma[1].

In order to improve the clinical relevance of the categories and to further define 'atypical', atypical glandular cells of undetermined significance (AGUS) was reclassified by Bethesda System Workshop in 2001[2]. Atypical glandular cells are now classified into subcategories of 'favour neoplasia' and 'not otherwise specified' (NOS).

A diagnosis of AGC on Pap smear has been shown to have a high correlation with clinically significant histology, ranging from 0% to 83% in various studies[3-5]. Aggressive approach is needed for the evaluation of patients with AGC on Pap smear as many of them have underlying premalignant or malignant changes.

Although algorithms for management vary, the consensus in literature suggests that these patients require colposcopically directed cervical biopsy and endocervical curettage (ECC)[5-7]. Cervical conisation should be done in patients with persistent AGC. Endometrial sampling (ES) is commonly recommended for patients >35 years and in the presence of abnormal uterovaginal bleeding[4,6,7].

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This study aimed to determine the local incidence of clinically significant lesions in patients with cytologically AGC in a local region in Hong Kong. The risk factors for developing clinically significant lesions were also studied. We also examined the long-term impact of cytologically AGC in a patient cohort in order to make appropriate recommendations for management of these women.

Methods

Data were extracted from the electronic endoscopic record systems (ERS) of Tuen Mun Hospital and Pok Oi Hospital. Patients who were referred to the colposcopy clinics of these two hospitals between 1 January 2004 and 31 December 2012 were analysed. The hard copies of the medical records of these patients were traced and reviewed. For the purpose of this study, patient data were examined up to 31 December 2013, allowing for at least 1 year of follow-up for all patients.

Clinically significant lesions were defined by a histological result of high-grade cervical intraepithelial neoplasia (CIN) 2 or 3, severe glandular dysplasia, atypical endometrial hyperplasia, adenocarcinoma in situ (AIS), or invasive carcinoma.

The database (including ERS and hard copies of medical records) was reviewed for patient age, sub-classification of Pap smear, AGC subtypes, the most significant histological result, patient characteristics, follow-up smears, and colposcopy.

Patients were excluded from the study if they had a history of genital tract cancer or hysterectomy. Statistical analysis was performed using IBM SPSS Statistics version 21. Chi-square test, Fisher's exact test, and Mann-Whitney *U* test were employed for statistical analyses, with a value of $p<0.05$ considered statistically significant. Binary logistic regression was used to study the correlation between patient characteristics and presence of clinically significant lesions. Odds ratios with their respective 95% confidence intervals were used to evaluate the magnitude of association.

Results

From the ERS, 287 patients had their first referral to our colposcopy clinics for cytologically AGC in the 9-year study period. Review of the hard copies of the medical records showed that 19 patients who were referred for high-grade squamous intraepithelial lesions (HGSIL) only were wrongly recorded as having AGC cytology in the ERS. In total, 268 patients were truly referred to us for cytological AGC within the study period. Among these 268 patients, seven (3%) who had a history of genital tract cancer were excluded from the subsequent analysis (Table 1).

There were 229 (88%) referrals for AGC NOS and 32 (12%) for AGC-favour neoplasia. The mean age at referral for all patients was 45.4 (range, 22-84) years. The mean age for patients with AGC NOS was 44.9 (range, 22-84) years whereas that for patients with AGC-favour neoplasia was 48.5 (range, 28-79) years. There was no significant difference between the mean age of patients with AGC NOS and that with AGC-favour neoplasia ($p=0.13$, Mann-Whitney *U* test).

The original smear reports were traced to verify the origins of AGC and to examine whether there were concurrent squamous abnormalities. The original smear reports were lost in 16 (6%) patients. These were arbitrarily classified as AGC subtypes not specified and without

Table 1. Patients excluded from the study

Patient No. with previous gynaecological cancer	Previous cancer diagnoses	Previous hysterectomy	Referral smear	Diagnosis after cytological AGC identified
1	Cervical cancer stage 1b1 and vaginal intraepithelial neoplasia 3	Yes	AGC NOS	Vaginal cancer
2	Cancer of corpus uteri	Yes	AGC NOS	No lesion
3	Cancer of corpus uteri	Yes	AGC NOS	Vaginal HPV
4	Cancer of corpus uteri	Yes	AGC NOS	No lesion
5	Cervical cancer stage 1a1	No	AGC NOS	CIN 1, HPV
6	Cancer of corpus uteri	Yes	AGC NOS	No lesion
7	Cancer of corpus uteri	Yes	AGC NOS	Vaginal recurrence

Abbreviations: AGC NOS = atypical glandular cells not otherwise specified; CIN 1 = cervical intraepithelial neoplasia 1; HPV = human papillomavirus

concurrent squamous abnormalities. The subtypes of AGC are shown in Table 2.

The number of patients having concurrent squamous abnormalities was 50 (19%), including 32 (64%), 13 (26%) and five (10%) with atypical squamous cells of unknown significance (ASCUS), low-grade squamous intraepithelial lesions (LGSIL) and HGSIL, respectively.

All 261 patients were followed up in our colposcopy clinics for at least 1 year. They were evaluated by means of colposcopy with or without biopsies, ECC, and ES according to their age and clinical history. One patient had a history of cytologically AGC NOS 3 years before referral to our clinic. Only cervical human papillomavirus (HPV) infection was diagnosed at her first presentation with cytologically AGC. Thirty (12%) patients had repeat AGC smears in the follow-up period. Two (0.8%) patients had repeat AGC diagnosed for more than twice on their follow-up smears.

Endometrial sampling was done in 226 (87%) patients. Significant lesions were detected in 19 (8%) patients. Endometrial cancer was diagnosed in nine (4%) patients. The mean age of patients without ES was 38 years whereas those diagnosed with endometrial cancer on ES was 54 years. For patients with ES done but insufficient quantity of tissue for diagnosis, their mean age was 61 years.

Colposcopy was performed in all 261 patients. The numbers of colposcopic diagnoses made for CIN 2/3, AIS, and cervical cancer were 25, 2, and 7, respectively. Thirty-six (14%) patients had significant lesions detected on colposcopically guided cervical biopsies, by means of punch biopsies or loop electrosurgical excisional procedure. Among them, the numbers with CIN 2/3, AIS, cervical cancer, and severe glandular dysplasia were 19, 3, 8 and 6, respectively. The sensitivity of colposcopy for detecting clinically significant lesions was 94.4%. The mean age of patients diagnosed with cervical cancer on colposcopy was 38 years for squamous carcinoma and 50 years for adenocarcinoma. The mean age of patients with CIN 2/3 was 43 years.

Endocervical curettage was done in 232 (89%) patients. Among them, 10 (4%) patients were diagnosed with significant lesions. The numbers of adenocarcinoma, AIS, glandular dysplasia, and CIN 2/3 were 2, 1, 6 and 1, respectively. The mean age of patients with and without ECC was 46 years and 44 years, respectively. The mean age of patients with malignant lesions on ECC was 51 years.

In all, 77 (30%) patients had significant lesions diagnosed after referral for cytologically AGC. Among them, 29 (38%) patients suffered from gynaecological cancer; 48 (62%) patients suffered from premalignant conditions of the gynaecological tract. Distribution of the significant lesions is shown in Table 3.

Table 2. Subtypes of atypical glandular cells versus final diagnosis

Subtype	Data
Endocervical (n=75; 29%)	
Cancer	6 (8%)
Severe preneoplastic	15 (20%)
Endometrial (n=34; 13%)	
Cancer	2 (6%)
Severe preneoplastic	3 (9%)
Not specified (n=152; 58%)	
Cancer	21 (14%)
Severe preneoplastic	30 (20%)

Table 3. Final histological diagnoses after referral for cytological atypical glandular cells

Diagnosis	No.
Non-cervical significant lesions	
Cancer of fallopian tube	1
Cancer of corpus uteri	12
Atypical endometrial hyperplasia	11
Cervical cancer	
Poorly differentiated carcinoma	1
Adenocarcinoma	9
Squamous cell carcinoma	6
Cervical pre-cancer	
Severe glandular dysplasia	7
Adenocarcinoma in situ	9
Cervical intraepithelial neoplasia 2/3	21
Insignificant lesions	
HPV infection/CIN 1	152
Benign	32

Abbreviations: CIN 1 = cervical intraepithelial neoplasia 1; HPV = human papillomavirus

Among the 77 patients with significant lesions, 53 (69%) suffered from cervical lesions, while 23 (30%) had uterine lesions; one patient suffered from cancer of the fallopian tube. The mean age of patients with cervical lesions was 43 years, and that of patients with non-cervical lesions was 52 years. There was significant difference between the mean ages of these two groups of patients ($p<0.001$, Mann-Whitney *U* test).

Forty-nine (64%) patients had glandular cell lesions while 27 (35%) patients had squamous cell lesions. One patient suffered from poorly differentiated carcinoma of the cervix. The mean age of patients with glandular cell lesions was 48 years, and that of patients with squamous lesions was 42 years. The difference between the mean ages of these two groups of patients was statistically significant ($p=0.02$, Mann-Whitney *U* test).

In all, 58 (75%) patients had lesions diagnosed within the first year of referral; the remaining 19 (25%) patients had lesions diagnosed after more than 1 year of follow-up (Table 4).

At initial evaluation within the first year of follow-up, about one-fifth of women (58/261) with AGC on Pap smear had significant lesions diagnosed. In the remaining women, 9% (19/203) had delayed diagnoses of significant lesions in the 9-year study period. The mean follow-up duration of women with negative initial evaluation in the first year but delayed diagnoses of significant lesions was 3.1 years. Among the 203 women with negative diagnoses in the first year, nine (4%) had CIN 2/3 or AIS diagnosed in the subsequent follow-up. Six patients had cancer diagnosed later, including four patients with cervical cancer and two patients with cancer of the corpus uteri; four patients suffered from atypical endometrial hyperplasia later. The percentage for significant cervical lesions and uterine lesions, diagnosed within second year and after follow-up for 2 years, was 6.4% (13/203) and 3% (6/203), respectively.

The follow-up of each subject (in person-years) was calculated from the date of referral to the date of diagnosis of the most significant lesion, date of death, or date of hysterectomy, whichever came first until 31 December 2013. The total follow-up duration was 1247 person-years and so the respective mean and median duration of follow-up was 4.78 and 4 years (range, 1-10 years). Incidence rates were calculated by dividing the number of cervical or uterine corpus malignancies by the number of person-years of follow-up. The incidence rate of cervical malignancies in these patients with cytologically AGC was 0.013 (16/1247), whereas that of uterine corpus malignancies was 0.010 (12/1247). The crude rate of cervical cancer and uterine cancer was 1283 and 962 per 100,000, respectively. The rates were 123-fold and 52.8-fold of those in the general Hong Kong population (according to the Hong Kong Cancer Registry of Hospital Authority in November 2013, the respective crude rate of cervical cancer and uterine corpus cancer in 2011 was 10.4/100,000 and 18.2/100,000[8]).

Of 229 patients referred for AGC NOS, 58 (25%) had significant lesions. Of 32 patients referred for AGC-favour neoplasia, 19 (59%) had significant lesions. Besides, 21/229 (9%) patients with AGC NOS and 8/32 (25%) patients with AGC-favour neoplasia suffered from genital tract cancer (Table 5).

Table 4. Years of follow-up till diagnosis of clinically significant lesions (n=77)

Follow-up	Data
Within the first year	58 (75%)
Cancer	23
Pre-cancer	35
Within the second year	13 (17%)
Cancer	6
Pre-cancer	7
After follow-up for 2 years	6 (8%)*
Cancer	0
Pre-cancer	6

* No. of patients with lesions diagnosed at the 4th, 5th, 6th, and 8th year of follow-up were 1, 3, 1, and 1, respectively

Table 5. Categories of atypical glandular cells versus distribution of lesions

Category	No. of patients
AGC-favour neoplasia (n=32)	
Clinically significant lesions	19
Genital tract cancer	8
Severe preneoplastic conditions	11
No lesions	13
AGC not otherwise specified (n=229)	
Clinically significant lesions	58
Genital tract cancer	21
Severe preneoplastic conditions	37
No lesions	171

Abbreviation: AGC = atypical glandular cells

Concurrent ASCUS alone was both a significant predictor of cancer (p=0.02, logistic regression) and presence of significant lesions (p=0.001, logistic regression). Concurrent HGSIL alone was not a significant predictor of cancer (p=0.45, Fisher's exact test). Concurrent LGSIL was not a significant predictor of the presence of significant lesions (p=0.47, Chi-square) or cancer (p=0.57, Fisher's exact test).

The distribution of lesions according to the subtypes of AGC is shown in Table 6. There was no significant difference in the presence of significant lesions among patients with AGC NOS or atypical endocervical cells (p=0.40, Mann-Whitney *U* test). There was also no significant difference in the presence of cancer lesions or significant cervical lesions among patients with AGC NOS or atypical endocervical cells (p=0.20 and p=0.87, respectively, Mann-Whitney *U* test). Presence of atypical endometrial cells was not significantly associated with the presence of significant uterine lesions, compared with other AGC subtypes (p=0.20, Fisher's exact test).

Table 6. Subtypes of atypical glandular cells versus lesion sites or cell types

	Not specified	Endocervical	Endometrial
Lesion site			
Non-cervical	16	3	5
Cervical	35	18	0
Lesion cell type			
Others	1	0	0
Squamous	20	7	0
Glandular	30	14	5

The magnitude of association between various factors and disease by binary logistic regression is shown in Table 7. Concurrent ASCUS at referral was associated with the presence of significant lesion (p=0.001), genital tract cancer (p=0.02), or cervical lesions (p=0.003). Diagnosis of AGC-favour neoplasia was associated with the presence of significant lesions (p<0.001), cancer (p=0.02), or cervical lesion (p<0.001). Having multiple sexual partners was associated with the presence of cervical lesions (p=0.02).

The mean number of follow-up smears was 4.77. The mean number of follow-up colposcopies was 0.71 (range, 0-4).

Among patients who did not have any significant lesions detected within the first year of follow-up, repeat AGC on follow-up smear was significantly associated with future disease (p=0.002). Of 25 patients with repeat AGC during follow-up, eight (32%) had significant disease later. Among patients without any significant lesion detected within the first year, AGC-favour neoplasia, as compared with AGC NOS, was not significantly associated with future disease (p=0.59) or cancer (p=0.39). Concurrent ASCUS at referral was significantly associated with future

Table 7. Risk factors associated with clinically significant lesions in women with cytological AGC by binary logistic regression

Factor	Significant lesions		Cancer		Cervical lesions	
	Odds ratio (95% CI)	p Value	Odds ratio (95% CI)	p Value	Odds ratio (95% CI)	p Value
Age	0.98 (0.94-1.03)	0.40	1.04 (0.98-1.10)	0.23	0.95 (0.90-1.00)	0.06
Menopause	2.01 (0.76-5.37)	0.16	1.03 (0.26-4.13)	0.97	1.39 (0.40-4.79)	0.60
Smoker	0.94 (0.35-2.49)	0.90	0.61 (0.13-3.00)	0.55	1.41 (0.52-3.83)	0.50
Multiple sexual partners	1.74 (0.81-3.69)	0.15	2.22 (0.80-6.13)	0.12	2.65 (1.18-5.94)	0.02
History of sexually transmitted diseases	1.53 (0.40-5.80)	0.53	1.08 (0.13-9.29)	0.94	2.22 (0.56-8.77)	0.26
Concurrent ASCUS	3.81 (1.71-8.49)	0.001	3.35 (1.22-9.19)	0.02	3.57 (1.53-8.35)	0.003
Non-barrier contraception	0.80 (0.41-1.58)	0.52	0.80 (0.30-2.17)	0.67	0.97 (0.46-2.03)	0.93
Multi-parity	0.96 (0.72-1.29)	0.81	0.74 (0.14-3.89)	0.73	0.52 (0.13-2.06)	0.35
AGC-favour neoplasia	5.43 (2.41-12.24)	<0.001	3.45 (1.27-9.33)	0.02	6.43 (2.68-15.40)	<0.001

Abbreviations: AGC = atypical glandular cells; ASCUS = atypical squamous cells of undetermined significance; CI = confidence interval

disease (p=0.01). The association between various factors and delayed diagnosis of clinically significant disease is shown in Table 8. Repeat AGC (p=0.001) and concurrent ASCUS at referral (p=0.01) were significantly associated with the presence of cervical lesions after the first year of evaluation.

Discussion

The results of this study strongly suggest that the presence of AGC in a routine cytological specimen is often associated with a pathological condition and warrants investigations and appropriate management.

In our study in predominantly southern Chinese population, 30% of women had significant lesions diagnosed after referral for cytologically AGC, including 11% rate of gynaecological cancer. This is similar to the rate published in the review by Schnatz et al[8], which included 24 studies in predominantly western populations. Their review showed that 29.0% of AGUS Pap tests had findings requiring follow-up or therapeutic intervention, including a 5.2% rate of malignancy.

While the majority of patients may have benign histological follow-up, a significant proportion of patients with precancerous or malignant disease will harbour lesions in difficult-to-sample areas such as the endocervical canal, fallopian tubes, ovaries, or, very rarely, even in extragenital sites. This diversity in follow-up outcomes creates significant challenges for optimal clinical follow-up. One patient in our study suffered from cancer of the fallopian tube, but she was completely asymptomatic and the diagnosis was made only after hysterectomy.

The rate of delayed diagnoses of cervical lesions of CIN 2 or above in this cohort of 203 women was 7.4% (glandular dysplasia in one, CIN 2/3 in five, AIS in four, and cervical cancer in five patients). This was higher than the rate of 4.3% in a cohort of 117 women as reported by Valdini et al[9]. This may be related to the fact that the mean age of women in our cohort was higher (45 years) than that in their study (42 years). Age seems to be a risk factor for delayed diagnoses in patients with AGC, although our study did not demonstrate any statistically significant association.

Among patients with significant lesions, 35% had lesions of squamous cell type only. The possible explanation for the relative absence of glandular pathology might be that the cells were so badly deformed that they appeared to be glandular to the cytopathologists.

Comparing with the 2-year study by Chan et al published in 2003[10] performed in the same regional hospital, the rate of clinically significant lesions on 2 years of follow-up was lower with AGC diagnosis (27%; n=71/261) than with AGUS diagnosis (43%; n=31/72). However, the study by Chan et al[10] regarded patients with CIN 1 (exact number of patients with CIN 1 was not published) and one patient with metastatic tumour from the breast as clinically significant diseases, while our study did not. Also, some patients did not have complete follow-up of 2 years in our study. Judging from these, the rate of significant lesions might well be similar over the years. This was reflected by the fact that the frequency of genital tract cancer in AGC patients in our study in the first 2 years of follow-up was 11% (n=29/261), while the frequency of genital tract malignancy in AGUS patients in the study by Chan et al[10]

Table 8. Risk factors associated with delayed diagnosis of clinically significant lesions in women with normal initial evaluation in the first year by binary logistic regression

Factor	Significant lesions		Cancer		Cervical lesions	
	Odds ratio (95% CI)	p Value	Odds ratio (95% CI)	p Value	Odds ratio (95% CI)	p Value
Age	0.96 (0.89-1.04)	0.31	1.03 (0.92-1.16)	0.59	0.92 (0.83-1.02)	0.11
AGC-favour neoplasia	1.61 (0.29-9.04)	0.59	2.92 (0.25-33.53)	0.39	3.75 (0.56-25.24)	0.18
Repeat AGC	5.91 (1.93-18.07)	0.002	3.31 (0.50-21.84)	0.21	9.62 (2.54-36.47)	0.001
Menopause	1.20 (0.16-9.08)	0.86	0.61 (0.02-19.28)	0.78	1.76 (0.34-8.92)	0.69
Smoker	1.11 (0.25-4.93)	0.90	1.37 (0.14-13.80)	0.79	1.75 (0.34-8.92)	0.50
Multiple sexual partners	1.00 (0.25-4.05)	1.00	3.66 (0.58-23.33)	0.17	1.97 (0.42-9.29)	0.39
Concurrent ASCUS at referral	4.42 (1.36-15.74)	0.01	4.95 (0.74-32.96)	0.01	7.09 (1.64-30.64)	0.01

Abbreviations: AGC = atypical glandular cells; ASCUS = atypical squamous cells of undetermined significance; CI = confidence interval

was 14% (n=10/72).

This was in contrast with the results in previous studies that showed improved sensitivity and specificity in detecting diseases after revision of The Bethesda System (TBS) in 2001. A study in Geneva[11] showed that, when AGUS smears using TBS 1991 were reclassified using AGC subcategories of TBS 2001, the frequency of clinically significant lesions on follow-up was higher with AGC diagnosis (51%; n=21/41) than AGUS diagnosis (36%; n=37/103). In another study by Gurbuz et al[12], when AGUS smears were reclassified according to TBS 2001, a significant difference (p=0.04) between the rates of the malignant pathologies in the AGUS (25%) and in the AGC (43%) was identified. This discrepancy in results between our study and that of the study by Chan et al[10] may be explained by the decreasing cervical cancer incidence rate in the past 10 years (according to the Hong Kong Cancer Registry, the crude rates of cervical cancer in 1998 and 2008 were 14.9 and 9.8 per 100,000, respectively[13]).

In our study, among women with a diagnosis of AGC-favour endometrial cells in origin, 15% (n=5/34) had a significant uterine lesion. This was lower than the rate of 24% of significant uterine lesions (n=11/45) in women with AGUS-favour endometrial origin, as reported by Chhieng et al[14] in 2001. The rate of significant uterine lesions was 33% (n=18/55) in another study on women with AGC-favour endometrial origin in 2006 by Saad et al[15]. The lower rate of significant uterine lesions in our study might be explained by the lower incidence of uterine cancer in Hong Kong (18.2 per 100,000 from the Hong Kong Cancer Registry 2011[13]) than in the western white population (30.9 per 100,000 from Pennsylvania Cancer Incidence and Mortality 2001[16]).

Our study was limited by its retrospective nature. Future study on a greater number of patients may help to identify the risk factors for predicting significant disease, as cytologically AGC is not a common entity. A multicentre prospective study will meet this purpose. A recent literature review[17] suggested that HPV DNA testing may be useful in differentiating between the risk of cervical and endometrial cancer, based on an analysis of 661 women with AGC cytology and HPV DNA testing. In 2006, consensus guidelines for managing AGC released by the American Society for Colposcopy and Cervical Pathology[18] recommended the combined use of colposcopy and endocervical sampling along with high-risk HPV testing for women with AGC-graded Pap test results. Hence, the role of HPV DNA testing will also be the focus of future studies.

The number of significant lesions in the group we studied is big enough to suggest the need for complete evaluation (colposcopy with cervical biopsies, ECC, and diagnostic conisation when needed) of all women with an AGC smear. An endometrial biopsy is warranted in the absence of abnormal cervical findings for persistent AGC. For women with unexplained AGC in the first year of follow-up, the percentage of future uterine lesions was 3% (6/203) in this study. There may be a role for the use of ultrasound or hysteroscopy in helping to exclude uterine lesions, and this needs further studies. The proportion of patients having cancer after negative initial evaluation in the first year was only 3.0% in this study. Hence, aggressive management like hysterectomy is not warranted for these women. If the patient has AGC that favour a neoplastic process, a concurrent ASCUS, or persistent AGC, or a cone biopsy should be performed. In our study, none of the women suffered from cancer outside the genital tract during follow-up. But if all the above-mentioned evaluations are normal, it should be confirmed that the woman has received other age-appropriate screening modalities, including for breast or colon cancer. If all comprehensive evaluations are normal, follow-up Pap tests should be performed because of a high rate of delayed significant diagnoses.

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Women's Perception on Subfertility Service in Hong Kong

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Objectives: To assess the knowledge, attitude, and practice among women in Hong Kong on subfertility service and treatment.
Methods: This cross-sectional survey was conducted in Department of Obstetrics and Gynaecology of Pamela Youde Nethersole Eastern Hospital, a local regional hospital in Hong Kong. Women aged from 20 to 50 years attending gynaecological clinic and subfertility clinic from June 2013 to October 2013 were invited to complete an anonymous questionnaire.
Results: During the study period, 503 questionnaires collected at the gynaecology outpatient clinic and subfertility clinic were considered valid for analysis. Overall, 113 (22.5%) women had sought advice from subfertility service before while 36 (7%) had undergone subfertility treatment before. Nearly half of the women did not know that fertility was affected by age. Although two-thirds of the participants were aware that the success rate of subfertility treatment dropped with advancing female age, two-thirds of them thought that assisted reproductive technology such as in-vitro fertilisation could overcome the effect of ageing.
Conclusion: This study showed that women in Hong Kong were not aware of the significance and prevalence of subfertility, the subfertility service available, and the importance of the effect of age on fertility and the success rate of assisted reproduction. Early and comprehensive counselling on complications and success rate of subfertility treatments is necessary, so as to allow an informed choice when couples decide to postpone their parenthood.
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Keywords: Hong Kong; Infertility, female

Introduction

Subfertility is defined as the failure to conceive after regular unprotected sexual intercourse for 1 year in the absence of known reproductive pathology[1]. It is estimated that subfertility affects one in six couples in the United Kingdom[1]. Assisted reproductive technology (ART) are methods used to achieve pregnancy by artificial or partially artificial means and comprise of ovarian stimulation, intrauterine insemination, in-vitro fertilisation (IVF), donor insemination, and cryopreservation of gametes or embryo.

Delaying childbearing is common nowadays; however, women may not be aware of the implication of this decision such as potential impact of age on their fertility and pregnancy complications at advanced age. Hong Kong's fertility showed a declining trend over the past 30 years, according to a feature article issued in the Hong Kong Monthly Digest of Statistics[2]. The crude birth rate, defined as the number of live births in a calendar year to the mid-year population, declined from 16.8 live births per 1000 population in 1981 to 7.0 in 2003 and then rebounded to 13.5 in 2011[2].

In the Hong Kong society, postponement of marriage and childbearing are considered a major cause of subfertility[3]. With higher education and better professional development, women play an increasingly important role in society. Many women chose to delay their marriage and childbearing till later part of their reproductive age[2,4], without full understanding that postponing their parenthood till mid-30s could have irreversible effect on their chances of getting pregnant, and the potential complications associated with advanced maternal age. A retrospective study conducted in Hong Kong showed that women aged ≥36 years had a significantly lower clinical pregnancy rate per initiated cycle of IVF versus younger women. It

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concluded that ageing has a significant deleterious effect on women's reproductive capability and that women should be encouraged to seek early medical advice and treatment for subfertility[5-7].

Women are encouraged to seek subfertility service early in order to improve their outcomes. According to the guideline issued by the National Institute for Health and Care Excellence[1], couples who do not conceive after 1 year of regular unprotected sexual intercourse should be offered specialist advice and counselling, and receive treatment from a specialist team as this is likely to improve the effectiveness of treatment as well as patient satisfaction. The guideline also suggested that people who are concerned about their fertility should be informed that female fertility declines with age and that the chance of live birth following IVF varies with female age, with the optimal age for IVF treatment ranging from 23 to 39 years[1].

A study exploring women's awareness and perceptions of delay in childbearing conducted by Maheshwari et al[4] showed that almost all participants in the study believed that women should be informed about the implications of delaying childbearing at an early age and that there was a need to provide accurate information to women in the childbearing age.

In Hong Kong, to our knowledge, no studies have been conducted to investigate the readiness of women to seek subfertility service and their awareness of services such as IVF and the associated outcomes. This is important as it would form a basis to direct future health education and promotion, and raise awareness among health care professionals about the needs of subfertile women, and enable them to provide more timely and comprehensive information to those in need of subfertility service[4,6].

The Hong Kong Government had proposed the population policy for public consultation while this study was being conducted. The Hong Kong statistics show that our total fertility rate remains low despite the encouraging rise from the trough of 0.9 child per woman in 2003 to 1.3 children per woman in 2012; however, this rate is hardly adequate to achieve the natural replacement level of 2.1 children per woman[2]. In view of the ageing population, the government wishes to provide a supportive environment for families to raise children, and ART has been proposed as one of the ways to promote childbearing in the subfertility group.

The objective of this study was to assess the knowledge, attitude, and practice among women in Hong Kong on subfertility service and treatment. Primary outcomes included knowledge on significance of subfertility, effect of age on fertility, knowledge on subfertility service and treatment available with the associated outcomes and complications, as well as factors affecting the women's decision to seek subfertility service.

Methods

This cross-sectional questionnaire study was conducted in a local regional hospital in Hong Kong. Women aged from 20 to 50 years attending gynaecology clinic and subfertility clinic from June 2013 to October 2013 in Department of Obstetrics and Gynaecology of Pamela Youde Nethersole Eastern Hospital (PYNEH) and who could read Chinese and English were invited to participate. Eligible women were recruited in the gynaecology and subfertility clinics by nurses at their first visit or subsequent follow-up. Written consent was obtained from these women. This study was approved by the Hong Kong East Cluster Ethics Committee and was conducted in full conformance with the International Conference on Harmonisation E6 guideline for Good Clinical Practice and the principles of the Declaration of Helsinki.

Participants in the study were asked to complete a self-administered questionnaire comprising 33 items (Appendices 1 and 2). This questionnaire was developed, piloted among women attending gynaecology clinic and subfertility clinic, and amended to facilitate data collection and improving the effectiveness. Written information including the objective and details of the study was provided to the participants before completing the questionnaire.

Sample size calculation was based on the formula comprising confidence level, prevalence rate of subfertility, and population prevalence rate. Assuming 95% confidence interval (CI), estimated prevalence rate of 0.15 (1 out of 6-7 couples), and margin of error as 0.05, the sample size was 196. Assuming a dropout rate of 20%, the final sample size deemed sufficient to identify those who would seek subfertility service was 245.

Demographic data of the participants were obtained from both the questionnaire and medical record of the participants. Primary outcome measures included knowledge of participants on subfertility service in Hong Kong, perception of the need for subfertility service, factors affecting their decision to seek advice and some overview of ART. As the participants' perception depended on their individual situations and need for future fertility,

this was also explored in the questionnaire. Significantly incomplete questionnaires and duplicated questionnaires were excluded from the analysis.

The data collected in this study were kept confidential. Only the researcher and designated staff of the Department of Obstetrics and Gynaecology of PYNEH were permitted access to the research materials.

All statistical analyses of data were done with PASW Statistics 18, Release Version 18.0.0 (SPSS, Inc., 2009, Chicago [IL], US). For categorical data, the Chi-square test and Fisher's exact test were used according to the data pattern. For continuous data with a highly skewed distribution, a non-parametric test (i.e. Mann-Whitney *U* test) was used. The critical level of statistical significance was set at 0.05. Statistically significant variables were adopted as potential predictors and entered into logistic regression to look for significant factors for willingness to seek subfertility service. The multiple logistic regression analysis (backward elimination procedure) was performed by including variables found to be significant at the level of $p<0.2$ by univariate analysis.

In order to investigate the structure of factors deterring subjects from seeking subfertility service, an exploratory factor analysis (i.e. principal component analysis) with varimax rotation was performed. An exploratory factor analysis was chosen (instead of a confirmatory factor analysis) because the factor structure of the instrument was still rather uncertain; hence, such factor analysis seemed more appropriate. The number of factors to be extracted was based on the results from the scree plots, and the Kaiser eigenvalue criterion (eigenvalues >1). Missing values were excluded listwise. The quality of the factor analysis models was assessed using Bartlett's test for sphericity and the Kaiser-Meyer-Olkin test.

Results

A total of 580 questionnaires were collected at the gynaecology outpatient clinic as well as subfertility assessment clinic during the study period. Two questionnaires were excluded because those were answered by participants not in the prescribed age range. Overall, 578 questionnaires which fulfilled the inclusion criteria were included, of which 75 were excluded due to significantly incomplete data (Figure). The response rate, defined as the number of completed questionnaires (n=503) divided by the number of eligible participants who fulfilled the inclusion criteria, was 87%. Thus, 503 questionnaires were available for analysis.

Of the 503 questionnaires available for analysis, 454 (90.3%) participants came from the gynaecology outpatient clinic whereas 49 (9.7%) were from the subfertility clinic. Their median age was 38 years. Overall, 189 (37.6%) participants wished to have children in future. The median age of those who wished to have children in future was 32 (range, 21-47) years. With regard to education, 188 (37.4%) had received tertiary education or above. A majority (84.3%) of the participants earned a monthly income of <HK$30,000 (Table 1). A monthly income of HK$30,000 was chosen as a cutoff for analysis because the median monthly domestic household income

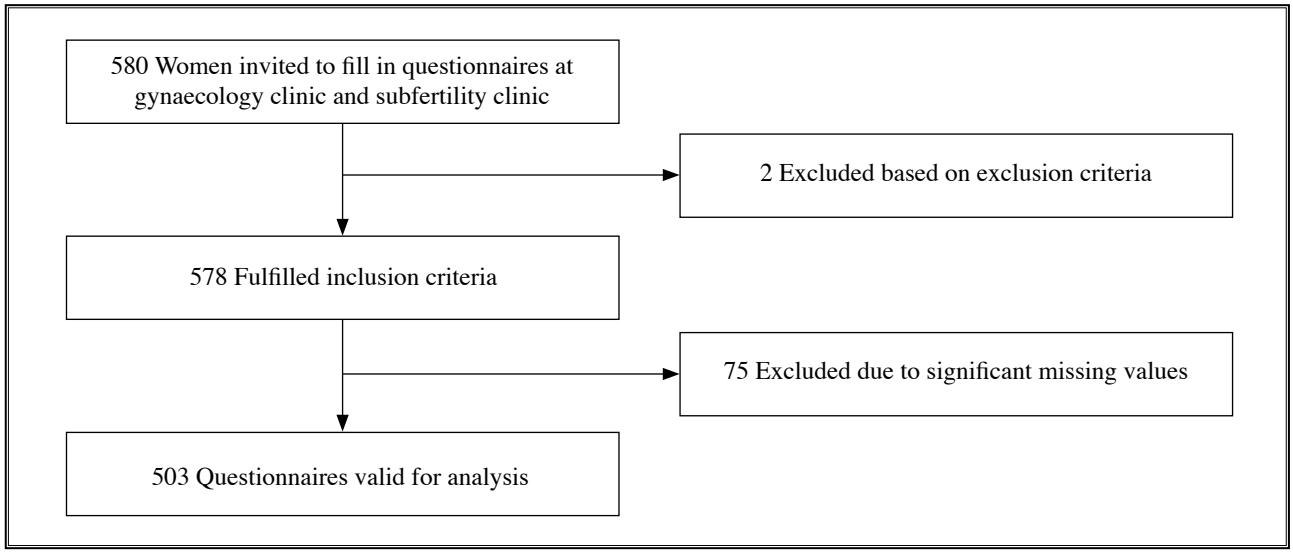

Figure. Flowchart illustrating the recruitment of women in the study

Table 1. Demographic data of study participants (n=503)

	Data
Mean age (years)	37.79
Median (range) age (years)	38 (32-44)
Place of recruitment	
Gynaecology outpatient clinic	454 (90.3%)
Subfertility clinic	49 (9.7%)
Marital status	
Married	362 (72.0%)
Single	135 (26.8%)
Others (e.g. divorced)	6 (1.2%)
Previous pregnancies	
Yes (can choose more than one answer)	307 (61.0%)
Live birth	258 (51.3%)
Miscarriage	86 (17.1%)
Termination of pregnancy	86 (17.1%)
Ectopic pregnancy	7 (1.4%)
No	196 (39.0%)
Plan for future pregnancy	
Yes	189 (37.6%)
No	291 (57.9%)
Missing data	23 (4.6%)
Education level	
No formal education	4 (0.8%)
Primary school	13 (2.6%)
Secondary school	294 (58.4%)
Tertiary level	158 (31.4%)
Master / Doctorate degrees	30 (6.0%)
Missing data	4 (0.8%)
Occupation	
Managers and administrators	15 (3.0%)
Professionals	62 (12.3%)
Associate professionals	50 (9.9%)
Clerks	125 (24.9%)
Service workers and shop sales	78 (15.5%)
Skilled agricultural and fishery	5 (1.0%)
Elementary occupations	14 (2.8%)
Students	5 (1.0%)
Housewives	93 (18.5%)
Unemployed / retired	14 (2.8%)
Missing data	42 (8.3%)
Monthly income (HK$)	
No income	62 (12.3%)
<10,000	125 (24.9%)
10,000-29,999	237 (47.1%)
30,000-50,000	42 (8.3%)
>50,000	12 (2.4%)
Missing data	25 (5.0%)
Religious belief	
None	303 (60.2%)
Buddhism	58 (11.5%)
Christianity	29 (5.8%)
Catholic	90 (17.9%)
Islam	3 (0.6%)
Others	2 (0.4%)
Missing data	18 (3.6%)
Method(s) of contraception used	
None	219 (43.5%)
Withdrawal method	28 (5.6%)
Calendar method	10 (2.0%)
Barrier method	173 (34.4%)
Hormonal contraception	22 (4.4%)
Intrauterine device	17 (3.4%)
Male or female sterilisation	15 (3.0%)
Others	7 (1.4%)
Missing data	12 (2.4%)
Attended or sought advice from subfertility service in Hong Kong before	
Yes (can choose more than one answer)	113 (22.5%)
Family Planning Association	35 (7.0%)
Public hospital	49 (9.7%)
Private doctor	47 (9.3%)
No	388 (77.1%)
Missing data	2 (0.4%)

in 2013 was around that amount according to government statistics[8].

Women who had had previous pregnancies were more willing to seek subfertility service than those who had not been pregnant before (55% vs. 45%; p<0.01) [Table 2]. This result was also consistent with the natural understanding that people who had family planning were more likely to consider ART than those who had no such plans (74% vs. 43%; p<0.001) [Table 3]. Those with tertiary or higher level of education were more likely to seek ART advice and consider ART than those with secondary or lower education level (32% vs. 16% for subfertility service, and 66% vs. 49% for ART consideration; both p<0.001) [Table 4]. It was also found that those with monthly income of ≥HK$30,000 were more likely to seek subfertility service and consider ART than those lower monthly income (43% vs. 20% for subfertility service [p<0.001], and 78% vs. 53% for ART service [p=0.02]) [Table 5].

Previous Experience with Subfertility Service

In our study, 113 (22.5%) women had sought advice from subfertility service in Hong Kong before (Table 1). These women were more likely to consider subfertility treatment in future than those who had never sought advice from subfertility service (80% vs. 48%; p<0.001) and those who wished to have children in future (89% vs. 67%; p<0.001) [Table 6]. Women who had plans of starting a family (odds ratio [OR], 3.33; 95% CI=2.20-5.05) and those who had consulted subfertility service before (OR, 2.93; 95% CI=1.73-5.00) were more willing to seek subfertility service than those who had not have immediate plans of starting a family and those who had never consulted subfertility service, respectively (Table 7).

Overall, 36 (7%) women had undergone a subfertility procedure or ART before. Among those women who had undergone ART before, the majority (58%) had obtained their information about ART via counselling with gynaecology specialists (Table 8). Women who had had subfertility treatment before were more likely than their counterparts to consider the same treatment (100% vs. 52%; p<0.001). This was true both for the whole study cohort as well as for the subgroup analysis among those who wished to have children in future (100% vs. 70%; p<0.001) [Table 9].

Readiness for Subfertility Service

As for the perception on subfertility service in Hong Kong, more than half of the participants (55.1%) thought

Table 2. Association between demographics and willingness to seek subfertility service (assuming that patients had not been able to conceive after trying for a certain period of time)*

Demographics	Not willing / not known to seek advice (n=226)	Willing to seek advice (n=277)	p Value
Median (range) age (years)	41 (35-45)	36 (32-42)	0.001
Place of recruitment			<0.001
Gynaecology outpatient clinic	226 (100%)	228 (82.3%)	
Subfertility clinic	0	49 (17.7%)	
Marital status			1
Married	162 (71.7%)	200 (72.2%)	
Single	61 (27.0%)	74 (26.7%)	
Others (e.g. divorced)	3 (1.3%)	3 (1.1%)	
Previous pregnancies			0.01
Yes	152 (67.3%)	155 (56.0%)	
No	74 (32.7%)	122 (44.0%)	
Education level†			<0.001
No formal education	1 (0.4%)	3 (1.1%)	
Primary school	10 (4.5%)	3 (1.1%)	
Secondary school	149 (66.8%)	145 (52.5%)	
Tertiary level	56 (25.1%)	102 (37.0%)	
Master / Doctorate degrees	7 (3.1%)	23 (8.3%)	
Missing data	3	1	
Monthly income (HK$)†			0.001
<10,000	68 (31.8%)	57 (21.6%)	
10,000-29,999	101 (47.2%)	136 (51.5%)	
30,000-49,999	10 (4.7%)	32 (12.1%)	
>50,000	2 (0.9%)	10 (3.8%)	
No income	33 (15.4%)	29 (11.0%)	
Missing data	12	13	
Religious belief†			0.67
None	136 (62.1%)	167 (62.8%)	
Buddhism	31 (14.2%)	27 (10.2%)	
Christianity	11 (5.0%)	18 (6.8%)	
Catholic	38 (17.4%)	52 (19.5%)	
Islam	2 (0.9%)	1 (0.4%)	
Others	1 (0.5%)	1 (0.4%)	
Missing data	7	11	

* Categorical data were analysed by Chi-square test or Fisher's exact test. Continuous data were analysed by Mann-Whitney *U* test

† Missing data were excluded from the calculation of percentages

Table 3. Effect of women's family planning on their willingness to consider assisted reproductive technology (n=480)

Willingness to consider assisted reproductive technology	Family planning		p Value
	Yes (n=189)	No (n=291)	
Yes	141 (74%)	125 (43%)	<0.001*
No	47 (25%)	163 (56%)	
Unknown	1 (1%)	3 (1%)	

* Fisher's exact test

Table 4. Effect of education level on women's readiness to seek subfertility service and willingness to consider assisted reproductive technology (n=497)

	Secondary education or below	Tertiary education or above	p Value
Readiness to seek subfertility service (n=497)			
Yes	51 (16%)	61 (32%)	<0.001*
No	258 (84%)	127 (68%)	
Willingness to consider assisted reproductive technology (n=499)			
Yes	151 (49%)	125 (66%)	<0.001†
No	157 (50%)	62 (33%)	
Unknown	3 (1%)	1 (1%)	

* Pearson Chi-square test
† Fisher's exact test

Table 5. Effect of monthly income on women's readiness to seek subfertility service and willingness to consider assisted reproductive technology (n=416)

	Monthly income		p Value
	<HK$30,000	≥HK$30,000	
Readiness to seek subfertility service (n=414)			
Yes	72 (20%)	23 (43%)	<0.001*
No	288 (80%)	31 (57%)	
Willingness to consider assisted reproductive technology (n=415)			
Yes	192 (53%)	42 (78%)	0.02†
No	167 (46%)	12 (22%)	
Unknown	2 (1%)	0	

* Pearson Chi-square test
† Fisher's exact test

Table 6. Effect of women's experience about seeking subfertility service on their likelihood of considering subfertility treatment in future

Group	Sought subfertility service before		p Value
	Yes	No	
Whole group (n=501)			
Will consider ART in future	90 (80%)	186 (48%)	<0.001*
Will not consider ART in future	22 (19%)	199 (51%)	
Unknown	1 (1%)	3 (1%)	
Those with family planning (n=187)			
Will consider ART in future	59 (89%)	81 (67%)	<0.001*
Will not consider ART in future	7 (11%)	39 (32%)	
Unknown	0	1 (1%)	

Abbreviation: ART = assisted reproductive technology
* Fisher's exact test

Table 7. Unadjusted and age-adjusted odds ratios for women's willingness to seek subfertility service

	Unadjusted odds ratio (95% confidence interval)	Age-adjusted odds ratio (95% confidence interval)	p Value
Had family planning	3.33 (2.20-5.05)	3.09 (1.87-5.11)	<0.001
Consulted subfertility service before	2.93 (1.73-5.00)	2.99 (1.76-5.06)	<0.001

Table 8. Attempted assisted reproductive technology and source of information

	Data
Attempted subfertility treatment or assisted reproductive technology before?	
Yes (can choose more than one answer)	36 (7%)
Ovarian stimulation (oral or injections)	28 (6%)
Intrauterine insemination	13 (3%)
In-vitro fertilisation with / without embryo cryopreservation	9 (2%)
Egg cryopreservation	1 (0.2%)
Sperm cryopreservation	0
Recipient of egg or sperm donation	0
Others	0
No	467 (93%)
How did they obtain information on subfertility service (can choose more than one answer)?	
Friends or peers	9 (25%)
Television / newspaper / websites	3 (8%)
Counselling by general practitioner or family doctor	5 (14%)
Counselling by gynaecology specialists	21 (58%)
Counselling by Family Planning Association	4 (11%)
Others	0

Table 9. Effect of women's experience of having subfertility treatment on their likelihood of considering subfertility treatment in future

Group	Had ART before		p Value
	Yes	No	
Whole group (n=503)			
Will consider ART in future	36 (100%)	241 (52%)	<0.001*
Will not consider ART in future	0	222 (47%)	
Unknown	0	4 (1%)	
Those with family planning (n=189)			
Will consider ART in future	27 (100%)	114 (70%)	<0.001*
Will not consider ART in future	0	47 (29%)	
Unknown	0	1 (1%)	

Abbreviation: ART = assisted reproductive technology

* Fisher's exact test

that the incidence of subfertility was less than one in six couples and 211 (42.9%) women agreed that couples should seek subfertility service if they did not conceive after 1 year of regular, unprotected sexual intercourse (Table 10).

When asked about factors that affected their decision to seek subfertility service, the most important factor was "failure to conceive naturally after trying for some years" (70.4%). Other factors included advanced maternal age

Table 10. Perception of need for subfertility service (n=503)*

	Data
Incidence of subfertility in heterosexual couples	
1 In 4	68 (13.5%)
1 In 5	48 (9.5%)
1 In 6	**77 (15.3%)**
1 In 8	68 (13.5%)
1 In 10	209 (41.6%)
Do not know	33 (6.6%)
Number of year(s) should wait before consulting subfertility service, when no pregnancy occurred after regular unprotected sexual intercourse (2-3 times per week) [n=492]	
1 Year	**211 (42.9%)**
2 Years	168 (34.1%)
3 Years	93 (18.9%)
4 Years	10 (2.0%)
5 Years	10 (2.0%)
Consider seeking subfertility service assuming that you have not been able to conceive after trying for the above period of time	
Yes	277 (55.1%)
No	222 (44.1%)
Unknown	4 (0.8%)
Factor(s) leading to the decision of seeking subfertility service (n=277)	
Advanced maternal age	166 (59.9%)
Advanced paternal age	47 (17.0%)
Failure to conceive naturally after trying for some years	195 (70.4%)
Family or peer pressure	50 (18.1%)
Recommendation by health care professional	48 (17.3%)
Advice or experience from friends who have had subfertility service before	21 (7.6%)
Previous tubal surgery / previous endometriosis or abnormal investigations results such as blocked tube	33 (11.9%)
History of miscarriage	26 (9.4%)
Others	7 (2.5%)
Statement(s) related to assisted reproductive technology you think is / are true concerning effect of age on pregnancy:	
Subfertility and age are not related (n=486)	
True	203 (41.8%)
False	**249 (51.2%)**
Do not know	34 (7.0%)
Delaying childbearing is associated with increased chance of miscarriage (n=490)	
True	**359 (73.3%)**
False	74 (15.1%)
Do not know	57 (11.6%)
Egg quality decreases with age (n=493)	
True	**404 (81.9%)**
False	31 (6.3%)
Do not know	58 (11.8%)
Risk of chromosomal abnormalities increases with age (n=485)	
True	**325 (67.0%)**
False	40 (8.2%)
Do not know	120 (24.7%)
Success rate of assisted reproductive technology drops as the age of female partner increases (n=487)	
True	**327 (67.1%)**
False	53 (10.9%)
Do not know	107 (22.0%)
Fertility is even lower at age >40 years, even with in-vitro fertilisation (n=490)	
True	**298 (60.8%)**
False	73 (14.9%)
Do not know	119 (24.3%)
Do you agree that assisted reproductive technology such as in-vitro fertilisation could overcome the effect of ageing? (n=495)	
Yes	335 (67.7%)
No	**160 (32.3%)**

* Rows in bold denote correct or recommended options

(59.9%), family or peer pressure (18.1%), recommendation by health care professional (17.3%), and advanced paternal age (17.0%) [Table 10].

Table 11 illustrates the factors that deterred women from seeking subfertility service. The most important deterrent factors were "personal belief that nature should take its course" (59%) and "lack of support from partner or partner's refusal to seek advice" (47%). When we grouped the deterrent factors into two main categories: "personal perception factors" and "resource factors" for further analysis, we found that "personal belief that nature should take its course" was the most important 'personal perception' factor while "cost involved in undergoing subfertility treatment" was the most important 'resource' factor.

Knowledge and Perception on Assisted Reproductive Technology

Concerning the perception about ARTs, more than half of the participants were correct in identifying that subfertility was affected by age, the fact that delaying childbearing would increase the risk of miscarriage and chromosomal abnormalities, and that fertility rate was even lower at age above 40 years, even with IVF. Overall, 327 (67.1%) women were aware that success rate of ART drops with advancing female age, and the majority (81.9%) of women knew that egg quality decreases with age. However, only 160 (32.3%) women were aware that ARTs such as IVF could not overcome the effect of ageing (Table 10).

Within our study, when asked about the knowledge on subfertility service and ART in Hong Kong, more than 60% of women reported that they had heard about the various ARTs. However, only 20% to 55% were aware of the potential complications associated with ARTs such as ovarian hyperstimulation syndrome, multiple pregnancy, miscarriage, and ectopic pregnancy. When compared with the counterparts, a significantly higher proportion of those who had attended or sought advice from subfertility service before knew that female aged over 40 years would affect pregnancy rate of IVF and were aware that ovarian hyperstimulation syndrome and multiple pregnancies were potential complications of ART. Only around 40% of the participants knew that there was an age limit for publicly funded subfertility treatment in Hong Kong (Table 12).

As for the opinion about the resources and provision of ART service, only 11 (2%) women were happy with the 30-to-36-month waiting time from referral to first IVF cycle. A majority of them (85%) thought that 24 months was the maximum waiting time they could accept. The maximum charge that the majority of women (74%) could accept for one cycle of IVF was below HK$20,000 (Table 13).

In all, 463 (94%) women agreed that couples should be seen together during subfertility counselling and treatment. Among those who had undertaken ART before, "doctors in charge of their subfertility service" (72%) and "specialised subfertility nurses" (72%) were both equally important in providing support to the couple, followed by family members (58%), support groups who had undertaken ART before (53%), friends (36%), clinical psychologist (22%), and social worker (8%) [Table 14].

We found that more than 80% of the participants in this study would like to have further information on subfertility service. Among these, 64% with fertility plan wished to have more counselling from their gynaecology specialists; 56% suggested acquiring more information

Table 11. Factors deterring women from seeking subfertility service

Factor	Data
Personal belief that nature should take its course (n=344)	204 (59%)
Lack of support from partner or partner's refusal to seek advice (n=340)	158 (47%)
Lack of information and source for referral (n=341)	35 (10%)
Long waiting time (n=340)	35 (10%)
Cultural difficulty in discussion on fertility issue (n=336)	29 (9%)
Cost involved in undergoing subfertility treatment (n=342)	25 (7%)
Religious reason (n=333)	22 (7%)
Social stigmatisation (n=337)	22 (7%)
Ethical concerns (n=336)	22 (7%)

Table 12. Knowledge on subfertility service and ART in Hong Kong*

	Data
Have you heard of the types of subfertility service or ART services available in Hong Kong, either in public or private sector?	
Ovarian stimulation (oral or injections) [n=474]	
Yes	301 (63.5%)
No	173 (36.5%)
IUI (n=479)	
Yes	397 (82.9%)
No	82 (17.1%)
IVF with embryo cryopreservation (n=481)	
Yes	403 (83.8%)
No	78 (16.2%)
Eggs cryopreservation (n=462)	
Yes	320 (69.3%)
No	142 (30.7%)
Sperm cryopreservation (n=462)	
Yes	336 (72.7%)
No	126 (27.3%)
Egg donation (n=458)	
Yes	291 (63.5%)
No	167 (36.5%)
Sperm donation (n=461)	
Yes	347 (75.3%)
No	114 (24.7%)
For women aged between 35 and 40 years, what do you think is the approximate pregnancy rate for each IVF-ET cycle in Hong Kong? (n=475)	
0-20%	75 (15.8%)
21-40%	**181 (38.1%)**
41-60%	170 (35.8%)
61-80%	46 (9.7%)
81-100%	3 (0.6%)
In your opinion, do you think that the following is / are factor(s) affecting the pregnancy outcome in IVF?	
Female age >40 years (n=486)	
Yes	**323 (66.5%)**
No	75 (15.4%)
Do not know	88 (18.1%)
Male age >40 years (n=476)	
Yes	146 (30.7%)
No	**230 (48.3%)**
Do not know	100 (21.0%)
Maternal smoking (n=485)	
Yes	**378 (77.9%)**
No	31 (6.4%)
Do not know	76 (15.7%)
Passive smoking (n=478)	
Yes	**328 (68.6%)**
No	43 (9.0%)
Do not know	107 (22.4%)
Body mass index of women >30 kg/m^2 (n=480)	
Yes	**224 (46.7%)**
No	47 (9.8%)
Do not know	209 (43.5%)

Abbreviations: ART = assisted reproductive technology; ET = embryo transfer; ICSI = intracytoplasmic sperm injection; IUI = intrauterine insemination; IVF = in-vitro fertilisation

* Rows highlighted in bold denote correct or recommended options

Table 12. (cont'd)

	Data
Duration of subfertility (n=481)	
Yes	**270 (56.1%)**
No	61 (12.7%)
Do not know	150 (31.2%)
Previous ovarian surgery (n=485)	
Yes	**274 (56.5%)**
No	49 (10.1%)
Do not know	162 (33.4%)
Do you think the following is / are potential complication(s) associated with ART?	
Ovarian hyperstimulation syndrome (n=487)	
Yes	**194 (39.8%)**
No	37 (7.6%)
Do not know	256 (52.6%)
Multiple pregnancy (n=488)	
Yes	**269 (55.1%)**
No	47 (9.6%)
Do not know	172 (35.2%)
Spontaneous miscarriage (n=488)	
Yes	**239 (49.0%)**
No	57 (11.7%)
Do not know	192 (39.3%)
Ectopic pregnancy (n=486)	
Yes	**177 (36.4%)**
No	88 (18.1%)
Do not know	221 (45.5%)
Breast cancer (n=486)	
Yes	70 (14.4%)
No	**136 (28.0%)**
Do not know	280 (57.6%)
Ovarian cancer (n=483)	
Yes	104 (21.5%)
No	**101 (20.9%)**
Do not know	278 (57.6%)
Structural congenital abnormality (n=482)	
Yes	**91 (18.9%)**
No	105 (21.8%)
Do not know	286 (59.3%)
Chromosomal abnormality with ICSI (n=482)	
Yes	**92 (19.1%)**
No	105 (21.8%)
Do not know	285 (59.1%)
Premature menopause (n=486)	
Yes	77 (15.8%)
No	**115 (23.7%)**
Do not know	294 (60.5%)
Are you aware of any age limit for publicly funded subfertility treatment in Hong Kong? (n=462)	
Yes	181 (39.2%)
No	281 (60.8%)
Are you aware of the following patient selection criteria for publicly funded IVF services in public hospital in Hong Kong?	
Couple needs to be legally married (n=492)	
Yes	**326 (66.3%)**
No	166 (33.7%)
There is no living child for the current marriage (n=484)	
Yes	**197 (40.7%)**
No	287 (59.3%)
Woman must not be more than 40 years old at the time the procedure is initiated (n=489)	
Yes	**130 (26.6%)**
No	359 (73.4%)

Table 13. Resources for and opinions about assisted reproductive technology services

Item	Data
Maximum waiting time (from referral to first IVF cycle) that you could accept (n=482)	
<12 Months	163 (34%)
12 To <18 months	140 (29%)
18 To <24 months	106 (22%)
24 To <30 months	25 (5%)
30 To 36 months	11 (2%)
>36 Months	37 (78%)
Will seek IVF service from private if the waiting time is longer than you accept (n=491)	
Yes	259 (53%)
No	232 (47%)
The maximum charge (HK$) you could accept for one cycle of IVF (n=483)	
<10,000	201 (41%)
10,000-20,000	158 (33%)
20,001-30,000	72 (15%)
30,001-40,000	18 (4%)
40,001-50,000	21 (4%)
>50,000	13 (3%)
Do you think couples should be seen together during subfertility counselling and treatment? (n=491)	
Yes	463 (94%)
No	28 (6%)
Studies showed that undergoing subfertility counselling and treatment could be stressful for couples, whom / where do you think the couple would like to have support from (can choose more than one answer)? (n=503)	
Family members	322 (64%)
Friends	174 (35%)
Support groups and peers	245 (49%)
Doctors in charge of their subfertility service	315 (63%)
Specialised subfertility nurses	228 (45%)
Clinical psychologist	166 (33%)
Social worker	80 (16%)
Do you think family planning and fertility counselling service should be given early routinely, such as during premarital counselling? (n=496)	
Yes	433 (87%)
No	63 (13%)
Do you wish to obtain more information on subfertility service in Hong Kong? (n=494)	
Yes (can choose more than one answer)	323 (65%)
Television / newspaper / websites	221 (45%)
Educational talks	108 (22%)
General practitioner or family doctor	92 (19%)
Gynaecology specialists	186 (38%)
Family Planning Association	161 (33%)
Others	8 (2%)
No	171 (35%)

Abbreviation: IVF = in-vitro fertilisation

Table 14. From where and whom women who had subfertility treatment wanted support (n=36)

	Data
Family members	21 (58%)
Friends	13 (36%)
Support groups and peers who had assisted reproductive technology treatment before	19 (53%)
Doctors in charge of their subfertility service	26 (72%)
Specialised subfertility nurses	26 (72%)
Clinical psychologist	8 (22%)
Social worker	3 (8%)

Table 15. Readiness to obtain more information on subfertility service for women who had family planning and their preferred method of communication of information (n=139)

	Data
Wish to obtain more information on subfertility service in Hong Kong	
Yes (can choose more than one answer)	121 (87%)
Television / newspaper / websites	78 (56%)
Educational talks	46 (33%)
General practitioner or family doctor	47 (34%)
Gynaecology specialists	89 (64%)
Family Planning Association	62 (45%)
Others	5 (4%)
No	18 (13%)

about ART via television, newspapers, and websites; 45% wished for more information on ART from the Family Planning Association; and around 33% for each hoped to obtain relevant information via both educational talks and their general practitioner (Table 15). Overall, 87% of women agreed that family planning and fertility counselling services should be routinely provided early, such as during premarital counselling (Table 13).

Discussion

To our knowledge, this is the first study in Hong Kong to investigate the knowledge and attitude of women on subfertility service in Hong Kong. The response rate in our study was 87%, which was acceptable as subfertility did not seem to be a common problem among our study participants. Overall, 55% of the women did not believe that subfertility affected one out of six couples, as reported by the Family Planning Association of Hong Kong[5]. More than 20% of women had sought advice from subfertility service before, while around 7% had experience in subfertility treatment. These results align with the report from the Centers for Disease Control and Prevention that approximately 10% of women (6.1 million) in the United States, aged 15 to 44 years, had difficulty getting pregnant[9].

Nearly 40% of participants in our study wished to have children in future, and the median age of these women was 32 years. This result was consistent with that from a cross-sectional study by Maheshwari et al[4] who investigated the awareness and perception of issues surrounding delay in childbearing; they suggested that subfertile women were more likely to have tried for their first pregnancy after the age of 30 years. The above study also showed that 85% of the women in the subfertile group were overly optimistic about the ability of IVF to overcome the effect of age on fertility[4,7]. This was also reflected in our study with more than two-thirds of participants having the misconception that ARTs such as IVF could overcome the effect of ageing, although 67.1% of the women knew that the success rate of fertility treatment dropped with advancing female age.

Epidemiological data have consistently shown

that fertility declines as early as in the middle of the third decade[10,11], and female age remains the most important determinant of success in an IVF programme[12,13]. In our study, only around 38% of women were aware that success rate for each IVF cycle was around 30% for age between 35 and 40 years; 46% of women overestimated the pregnancy rate with each IVF cycle. According to the statistics of the subfertility centre in Queen Mary Hospital, Hong Kong, in 2009, just over half of the patients undergoing subfertility treatment were aged between 36 and 40 years, while 5.5% were over the age of 40 years[14]. Lack of education and the misconception that IVF could overcome the effect of ageing are possible reasons for the lack of awareness among women in Hong Kong about the effect of age on fertility and success rate of IVF treatment.

In Hong Kong, there were three publicly funded IVF centres, with the waiting time from referral to first IVF cycle being a mean of 36 months[14,15]. Recruitment guideline in the Hospital Authority for IVF also limits public ART to those under the age of 40 years at the time of treatment[14], making many of those referred ineligible by the time they receive an appointment for their first IVF cycle. According to reports by the Council on Human Reproductive Technology[16], 4025 women had undergone IVF in 2011 and 4924 treatment cycles had been initiated. The number of people who had undergone ART increased from 4968 in the year 2009 to 8668 in the year 2010 and to 10,436 in the year 2011. Ongoing pregnancy rate was around 33% for those aged between 31 and 35 years; nearly 25% for those aged between 36 and 40 years; and even lower for those aged between 41 and 45 years, at only about 15%.

The majority of women in our study were unaware of the potential complications associated with ART[13,17]. In fact, complications of subfertility treatment were relatively uncommon. Report from Queen Mary Hospital[14] showed that 1.3% of women developed moderate-to-severe ovarian hyperstimulation syndrome among the 396 oocyte retrieval cycles in 2009, and 0.3% developed infections. The rate of multiple pregnancy was 23.8%[14]. Most of the women thought that the waiting time of 30 to 36 months from referral to first IVF cycle as in publicly funded IVG was not acceptable. While the option of fertility treatment in the private sector is available, this cannot be utilised by a majority of women as the cost (around HK$70,000 per cycle of IVF) far exceeds what most couples can afford.

Although one out of six couples would be in need of subfertility service[18], there are many barriers for obtaining subfertility service and undergoing subfertility treatment. Women with tertiary or higher level of education are more likely to seek ART advice and consider ART than those with secondary or lower education level. It was also found that those with monthly income of ≥HK$30,000 were more likely to seek subfertility service and consider ART than those with monthly income <HK$30,000. These data were consistent with the common belief in women that ART is expensive.

In fact, on investigating factors which acted as deterrents against seeking subfertility service, we found that many believed in "let nature takes its course". Although having children and whether to choose to seek subfertility counselling was the couples' choice, those who might still have a strong wish to start a family may be deterred by the lack of understanding about subfertility service and treatment. In reality, limitations exist in the provision of publicly funded subfertility service, including "cost involved in undergoing subfertility treatment", "lack of referral", and "long waiting time". Other social factors include cultural difficulty in discussing the fertility issue, social stigmatisation, ethical concerns, and religious considerations.

Married couples who fail to bear children are commonly stigmatised[19]. Social impact of subfertility cannot be underestimated. Many women perceive subfertility as a personal failure, a sign of incompleteness as a woman; it can even affect their marital relationship. While traditional Chinese culture is in favour of letting nature takes its course, many have ignored the importance of the irreversible factor on fertility, which is age.

A study by Loke et al[20] involving interviews of seven women and four men in Hong Kong showed that couples in subfertility treatment reported feelings of incompleteness, guilt, shame, and isolation from those with children. These couples regretted not having earlier treatment. A few were resentful that no one had ever mentioned about subfertility services to them. The study, thus, recommended that family planning be incorporated into premarital screening, and emphasised timely provision of support and counselling. This was concordant with our finding that support from the team involved in subfertility care, including from "doctors in charge of their subfertility service" and "specialised subfertility nurse", was of great importance to those who had undergone ART. Besides, family members, support groups, friends, clinical psychologist, and social worker also play a crucial role in providing psychosocial support for the couples. These findings underscore the importance of raising public awareness on subfertility.

Increasing the government subsidy for publicly funded subfertility service can be helpful. However, it is also important that doctors in primary care and gynaecologists to identify couples in need and provide timely referrals and treatment[6]. Our study found that, for those who had attended subfertility service or had undertaken subfertility treatment before, the majority had obtained information about ART from their gynaecologists.

More than 60% of participants in our study would like to have more information on subfertility service. The most preferred channel of communication for ART service was during consultation with their gynaecologists and health care professionals, followed by media publicity of subfertility service on television. Hence, the attitude of gynaecologists or primary care doctors towards promoting ART is important. A study by Bonetti et al[21] investigating the awareness and attitudes of professionals towards assisted reproduction found that almost all the 70 ART professionals would willingly undergo IVF if they were faced with a diagnosis of infertility. Gynaecologists or primary care doctors have an invaluable opportunity to discuss about family planning during consultation with their patients so as to allow timely referral and treatment for age-related subfertility problems[22].

There were some limitations in our study. Firstly, this cross-sectional study included a heterogeneous group of women recruited from both the gynaecology as well as subfertility clinics. Although women from the gynaecology clinic could provide a fair representation of the general population, there could be a bias when assessing their knowledge and attitudes on subfertility service as these are on a "need-to-know" basis. Those women who had naturally conceived before, those who had completed a family or who had no wish to have children in future would understandably have less knowledge and readiness to seek subfertility service. Since around 60% of participants had no wish to have children in future, this could affect the incentive for these women of completing the questionnaire and their perception on subfertility treatment.

On the other hand, subgroup analysis of those who wished to have children in future helped to demonstrate significant findings such as differences in the attitude and knowledge between those who had had ART before and those who had not. Moreover, one could argue that subfertility service, although serving only around one out of six couples, should be publicised by the government and be known to all Hong Kong citizens, as this could, in turn, help to raise the acceptance and understanding of ART among the public, and minimise social stigmatisation for those receiving fertility treatments.

Secondly, the view of the male counterparts on subfertility service was not addressed in this study. Male partners are equally important in making a decision on the issue of family planning and seeking subfertility service[20]. Our study demonstrated that "lack of support from partner or partner's refusal to seek advice" was one of the deterrent factors[20] and, thus, future studies could be performed to investigate the view of male partners on subfertility treatment. Furthermore, the view of health care providers on subfertility service was not explored in this study.

Thirdly, most of the participants in our study were of Chinese origin; there could be cultural bias by which Chinese women less readily accept ART as an alternative way of fulfilling their natural responsibility of passing on the family genes versus women from other ethnicities[20,23].

Conclusion

It is of no doubt that the success rate of subfertility treatment declines with age[16] and early advice and treatment bring better outcomes. Many subfertile couples wish they were told earlier of the availability of subfertility service[20]. Most of the participants in our study agreed that fertility counselling service should be routinely given early, for instance, at the time of premarital counselling. Therefore, it is not only the duty of the government to provide public education with regard to the optimal time for childbearing, but also, more importantly, the responsibility of health care professionals who might already have rapport with these women. During their consultations, gynaecologists could play an important role in exploring the fertility issue, which might be culturally sensitive and personally awkward for many couples, while respecting their decisions towards the subfertility service[6]. Early and comprehensive counselling on complications and success rates of subfertility treatments is also important, as this allows informed choice when couples decide to postpone their fertility plan. This, at the same time, would avoid giving couples a false sense of hope towards treatment outcomes.

To our knowledge, no study has been conducted to explore the perception and readiness of health care professionals in Hong Kong in promoting subfertility service. This is an important issue as it affects the accessibility of ART for couples in need. Education of health care professionals and encouraging gynaecologists to bring up the issue of subfertility during patient consultations could help to encourage open discussion and make timely,

informed choice. Future work is needed to determine the best way forward to provide education to the public and effective information of ART to couples in need. To that end, it is worth considering the use of public media, as well as exploring the cost-effectiveness of publicly funded subfertility treatment.

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Appendix 1. Questionnaire of women's perception on subfertility service in Hong Kong (Chinese version)

香港婦女對輔助生育服務的認知及接受程度問卷	
姓名：_____ 年齡：_____	**Participant's label**
(A) **背景資料**	
1. **婚姻狀況：**	已婚 ☐　　未婚 ☐
2. **你以前有否懷孕？**	有 ☐　　沒有 ☐ 如有，多少次懷孕？ _____ 次 結果 _____ 次成功生產 _____ 次小產 _____ 次終止懷孕 _____ 次宮外孕
3. **你第一次懷孕的年齡是（不論成功與否）：**	_____ 歲
4. **你將來會生育嗎？**	會 ☐　　不會 ☐
5. **教育程度：**	沒有正式教育 ☐　　小學程度 ☐ 中學程度 ☐　　大專 / 大學程度 ☐ 碩士或博士 ☐
6. **職業：**	_____
7. **每月收入（港幣）：**	少於$10,000 ☐　　$10,000-$29,999 ☐ $30,000-$50,000 ☐　　多於$50,000 ☐
8. **宗教信仰：**	沒有 ☐　　佛教 ☐ 天主教 ☐　　基督教 ☐ 伊斯蘭教 ☐　　其他，請註明：_____
9. **現在使用的避孕方法：**	沒有 ☐　　體外射精 ☐ 安全期 ☐　　男 / 女性避孕套 ☐ 避孕丸 / 避孕針 ☐　　避孕環 ☐ 男 / 女性絕育手術 ☐　　其他，請註明：_____
10. **你有否徵詢過醫護人員有關輔助生育服務的問題？**	有 ☐　　沒有 ☐ 如有，你從哪裏得到相關答覆或建議？ 香港家庭計劃指導會 ☐ 公立醫院 ☐ 私人醫生 / 診所 ☐
輔助生殖技術（Assisted reproductive technology [ART]）是指採用醫療輔助手段幫助不育夫婦妊娠的技術，包括人工授精（IUI）和體外授精（IVF）、胚胎移植等技術。	
11. **你有否試過有關輔助生育程序或輔助生育技術？**	有 ☐　　沒有（請跳到第13條）☐ 如有，請問是哪一類服務（可選多項）？ 口服排卵藥 / 注射排卵針 ☐ 子宮內人工授精（IUI）☐ 體外授精（俗稱試管嬰兒 / 人工受孕 / IVF）及冷凍儲存胚胎 ☐ 冷凍儲存卵子 ☐ 冷凍儲存精子 ☐ 接受卵子 / 精子捐贈 ☐ 其他，請註明：_____
12. **你從甚麼途徑得知有關輔助生育服務的資訊？**	朋友 ☐ 電視 / 電台 / 報紙 / 網頁 ☐ 私家普通科醫生 / 家庭醫生 ☐ 婦產科專科醫生 ☐ 香港家庭計劃指導會 ☐ 其他，請註明：_____

Appendix 1. (cont'd)

(B) 關於輔助生育服務需要的認知	
13. 你認為不育情況在異姓夫妻中的發生率是多少？	每四對夫婦有一對 ☐ 每五對夫婦有一對 ☐ 每六對夫婦有一對 ☐ 每八對夫婦有一對 ☐ 每十對夫婦有一對 ☐
14. 你認為當夫婦在沒有避孕而有定期行房後未能懷孕，應等多少年才尋求輔助生育服務？	一年 ☐　二年 ☐　三年☐　四年 ☐　五年 ☐
15 在上述的情況下，你自己是否會考慮尋求輔助生育的意見？	是（請回答第16條問題）☐　否（請回答第17條問題）☐
16. 你決定尋求輔助生育服務的原因是什麼？（可選擇多於一項）	女性年齡漸長 ☐ 男性年齡漸長 ☐ 多年未能自然懷孕 ☐ 朋輩或家庭壓力 ☐ 醫護人員建議 ☐ 曾接受輔助生育服務的朋友經驗分享 ☐ 曾接受輸卵管手術，或曾有子宮內膜移位，或不正常的檢查報告（如輸卵管阻塞）☐ 過去曾小產 ☐ 其他，請註明：_____
17. 你不會尋求輔助生育服務的原因是什麼？（請填1-9：1為最重要，9最不重要）	(a) ____ 我選擇順其自然 (b) ____ 我擔心會被標籤或歧視 (c) ____ 我沒有有關輔助生育服務的足夠資料 (d) ____ 在傳統文化上難以與別人討論關於生育的問題 (e) ____ 沒有配偶支持，或配偶拒絕尋求協助 (f) ____ 我擔心會很昂貴 (g) ____ 基於個人宗教理由，我不接受輔助生育服務 (h) ____ 我認為輔助生育服務有違個人的道德標準 (i) ____ 過長的輪候時間 (j) ____ 其他，請註明：_____
18. 你認為下列哪一些有關女性年齡對懷孕及輔助生育的影響是對的？	對　不對　不知道
(a) 不育與年齡沒有關係	☐　☐　☐
(b) 年紀愈大，小產機會愈高	☐　☐　☐
(c) 卵子的質素會因年齡漸長而下降	☐　☐　☐
(d) 胎兒染色體有問題的機會，會隨着年齡增加	☐　☐　☐
(e) 輔助生育的成功率會因年紀漸大而下降	☐　☐　☐
(f) 如女性年齡大於四十歲，就算是經輔助生育協助，懷孕機會率會是相對低的	☐　☐　☐
19 你同意現今的輔助生育技術可以取代年紀漸大所產生對生育的影響嗎？	同意 ☐　不同意 ☐
20. 你認為自己現在自然懷孕的機會率有多少（0-100%）？	_____ %

Appendix 1. (cont'd)

(C) 對輔助生育服務及輔助生育技術的認識			
21. 你有沒有聽過以下各種在香港公營或私家診所 / 醫院的輔助生育技術？	有		沒有
(a) 口服排卵藥 / 注射排卵針	☐		☐
(b) 子宮內人工授精（IUI）	☐		☐
(c) 試管嬰兒 / 人工受孕（IVF），冷凍儲存胚胎	☐		☐
(d) 冷凍儲存卵子	☐		☐
(e) 冷凍儲存精子	☐		☐
(f) 卵子捐贈	☐		☐
(g) 精子捐贈	☐		☐
22. 你認為在香港，35-40歲婦女一次體外授精（IVF）及胚胎轉移的治療週期的妊娠率大概有多少？	0%-20% ☐ 61%-80% ☐	21%-40% ☐ 81%-100% ☐	41%-60% ☐
23. 你認為以下哪些因素會影響人工受孕IVF（俗稱試管嬰兒）的妊娠率？	會	不會	不知道
(a) 女性年齡 >40歲	☐	☐	☐
(b) 男性年齡 >40歲	☐	☐	☐
(c) 女性是吸煙者	☐	☐	☐
(d) 長期吸入二手煙	☐	☐	☐
(e) 女性的身體質量指數（BMI）多於 30 kg/m^2	☐	☐	☐
(f) 不育的年數	☐	☐	☐
(g) 之前曾接受卵巢手	☐	☐	☐
24. 你認為以下這些是輔助生育技術的潛在併發症嗎？	會	不會	不知道
(a) 卵巢過度刺激	☐	☐	☐
(b) 多胞胎	☐	☐	☐
(c) 流產	☐	☐	☐
(d) 宮外孕	☐	☐	☐
(e) 乳癌	☐	☐	☐
(f) 卵巢癌	☐	☐	☐
(g) 胎兒先天性結構異常	☐	☐	☐
(h) 胎兒染色體異常	☐	☐	☐
(i) 過早停經	☐	☐	☐
25. 你知道政府資助的輔助生育服務的公家症有年齡上限嗎？	有 ☐　　沒有 ☐ 如有，是什麼年齡：_____ 歲		
26. 根據醫院管理局有關選擇體外授精 / 人工受孕（IVF）病人的指引，你知道政府資助的公家（publicly funded IVF service）病人的選擇有以下各項標準嗎？	知道		不知道
(a) 夫婦必須有合法婚姻	☐		☐
(b) 當前的婚姻未有健在的孩子	☐		☐
(c) 接受治療時，婦人的年齡必須不超過四十歲	☐		☐

Appendix 1. (cont'd)

由於體外授精 / 人工受孕（IVF）是一項昂貴的療程，加上資源有限，故接受人工受孕（IVF）的公家病人需有一段輪候時間。	
27. **你認為由轉介到第一次體外授精 / 人工受孕（IVF）最長可接受的輪候時間是多少？**	<12個月 ☐ 12-18個月 ☐ 18 - 24個月 ☐ 24-30個月 ☐ 30-36個月 ☐ >36個月 ☐
28. **如果實際的輪候時間較你能接受的為長，你會考慮轉為私家病人嗎？**	會 ☐ 不會 ☐
雖然公家症病人獲得醫院管理局的部份資助，但因應醫療成本不斷上升的情況下，公家症病人仍須自行繳付在療程期間的部份費用。	
29. **你認為一週期的體外授精 / 人工受孕（IVF）治療最高可接受的費用（公家症）是多少（港幣）？**	<$10,000 ☐ $10,000-$20,000 ☐ $20,001-$30,000 ☐ $30,001-$40,000 ☐ $40,001-$50,000 ☐ >$50,000 ☐
30. **你認為夫婦二人是否需要一同接受輔助生育服務及治療的輔導和講解？**	是 ☐ 否 ☐
31. **研究發現接受輔助生育技術治療的夫婦會面對一定程度的壓力，你認為夫婦會想從哪裏獲得支援？**	(a) 家人 ☐ (b) 朋友 ☐ (c) 有輔助生育經驗的夫婦組成的支援小組 ☐ (d) 負責他們輔助生育服務的醫生 ☐ (e) 輔助生育服務的專科護士 ☐ (f) 心理科醫生 ☐ (g) 社工 ☐
32. **有關家庭計劃及生育服務的輔導，你認為是否應涵括在常規的婚前輔導當中？**	是 ☐ 否 ☐
33. **你希望獲得更多有關香港輔助生育服務的資訊嗎？**	是 ☐ 否 ☐ 如是，希望從哪裏獲得？（可選擇多於一項） (a) 電視 / 報紙 / 網頁 ☐ (b) 講座 ☐ (c) 私人 / 家庭醫生 ☐ (d) 婦產科專科醫生 ☐ (e) 香港家庭計劃指導會 ☐ (f) 其他，請註明：_____
感謝你的參與！	

Appendix 2. Questionnaire of women's perception on subfertility service in Hong Kong (English version)

Name: _____
Age: _____
Please tick the appropriate boxes

Label

A. Background information

1. Marital status	Married ☐ Single ☐
2. Previous pregnancies	Yes ☐ → How many? _____ No ☐ (Please go to Question 4) If Yes → What is the outcome? And how many? _____ Live birth _____ Miscarriage _____ Termination of pregnancy _____ Ectopic pregnancy
3. At what age did you have your first pregnancy, regardless of outcome?	_____ years old
4. Do you have any plan for future pregnancy?	Yes ☐ No ☐

5. Education level
No formal education ☐ Primary school ☐ Secondary school ☐ Tertiary level ☐
Master / Doctor degrees ☐

6. Occupation
Business ☐ Clerk / sales / service industry ☐ Health care professional ☐ Professional ☐
Manager / administrative ☐ Skilled / non-skilled worker ☐ Teacher ☐ Housewife ☐
Others (e.g. student / retired), please state: _____

7. Monthly income (HK$)
<$10,000 ☐ $10,000-$29,999 ☐ $30,000-$50,000 ☐ >$50,000 ☐

8. Religious belief
None ☐ Buddhism ☐ Christianity ☐ Catholic ☐ Islam ☐
Others, please state _____

9. Which method(s) of contraception are you using?
☐ None
☐ Withdrawal method / coitus interruptus / extracorporeal ejaculation
☐ Calendar method / periodic abstinence
☐ Barrier method (including male and female condom, diaphragm, etc)
☐ Hormonal contraceptive pills / injectables
☐ Intrauterine device / intrauterine system
☐ Male or female sterilisation
☐ Others, please state _____

10. Have you attended or sought advice from subfertility service in Hong Kong before?
Yes ☐ No ☐
If yes, from where? ☐ Family Planning Association ☐ Public hospital ☐ Private doctor

Appendix 2. (cont'd)

Assisted reproductive technology (ART) involves surgically removing eggs from a woman's ovaries, combining them with sperm in the laboratory, and returning them to the woman's body or donating them to another woman.

11. Have you ever had or attempted subfertility procedure or ART before?

Yes ☐ No ☐ (please proceed to Question No. 13)

If yes, what type of service? (Tick one or more than one)

☐ Ovarian stimulation (oral or injections)
☐ Intrauterine insemination
☐ In-vitro fertilisation (IVF) with / without embryo cryopreservation
☐ Egg cryopreservation
☐ Sperm cryopreservation
☐ Recipient of egg or sperm donation
☐ Others, please state: _____

12. How did you obtain information on subfertility service? (Please tick one or more items)

☐ Friends or peers ☐ Television, newspaper or websites
☐ Counselling by general practitioner or family doctor ☐ Counselling by gynaecology specialists
☐ Counselling by Family Planning Association
☐ Others, please state: _____

B. Perception on need for subfertility service

13. What do you think is the incidence of subfertility in heterosexual couples?

☐ 1 ln 4 ☐ 1 ln 5 ☐ 1 ln 6 ☐ 1 ln 8 ☐ 1 ln 10

14. What do you think is the number of years one should wait before consulting subfertility service, when no pregnancy occurred after regular unprotected sexual intercourse (2-3 times per week)?

☐ 1 Year ☐ 2 Years ☐ 3 Years ☐ 4 Years ☐ 5 Years

15. In your opinion, would you consider seeking advice from subfertility service, assumed that you have not been able to conceive after trying for the above period of time?

☐ Yes (Proceed to Question No. 16) ☐ No (Proceed to Question No. 17)

16. Based on what factors would you decide on seeking advice from subfertility service? (Please tick one or more items)

☐ Advanced maternal age
☐ Advanced paternal age
☐ Failed number of years of trying to conceive
☐ Family or peer pressure
☐ Recommendation by health care professional
☐ Advice or experience from friends who have had subfertility service before
☐ Previous tubal surgery / previous endometriosis or abnormal investigations results such as blocked tube
☐ History of miscarriage
☐ Others, please state: _____

17. In your opinion, what are the deterrent factors for one from seeking advice from subfertility service? (Please rank 1 as most important factor and 9 as least important)

_____ Personal belief that let nature takes its course
_____ Social stigmatisation
_____ Lack of information and source for referral
_____ Cultural difficulty in discussion on fertility issue
_____ Lack of support from partner or partner refusal to seek advice
_____ Cost involved in undergoing subfertility treatment
_____ Religious reason
_____ Ethical concerns
_____ Long waiting time
_____ Other reasons, please state: _____

Appendix 2. (cont'd)

18. Which of the followings concerning effect of age on pregnancy and ART do you think is true?	**True**	**False**	**Do not know**
(a) Subfertility and age are not related	☐	☐	☐
(b) Delaying childbearing is associated with increased chance of miscarriage	☐	☐	☐
(c) Egg quality decreased with age	☐	☐	☐
(d) Risk of chromosomal abnormalities increased with age	☐	☐	☐
(e) Success rate of ART drops as the age of female partner increases	☐	☐	☐
(f) Fertility is even lower at age 40 years or above, even with IVF	☐	☐	☐

19. Do you agree that ART such as IVF could overcome the effect of ageing?
Yes ☐ No ☐

20. What do you think your chance of spontaneous pregnancy now is (0-100%)? _____ %

C. Knowledge on subfertility service and ART in Hong Kong

21. Have you heard of the following types of subfertility service or ART services available in Hong Kong, either in public or private sector?	**Yes**	**No**
(a) Ovarian stimulation (oral or injections)	☐	☐
(b) Intrauterine insemination	☐	☐
(c) IVF with embryo cryopreservation	☐	☐
(d) Eggs cryopreservation	☐	☐
(e) Sperm cryopreservation	☐	☐
(f) Egg donation	☐	☐
(g) Sperm donation	☐	☐

22. For women aged between 35 and 40 years, what do you think is the approximate pregnancy rate for each cycle of IVF and embryo transfer in Hong Kong?
☐ 0%-20% ☐ 21%-40% ☐ 41%-60% ☐ 61%-80% ☐ 81%-100%

23. In your opinion, do you think that the followings are factors affecting the pregnancy outcome in IVF?	**Yes**	**No**	**Do not know**
(a) Female age >40 years	☐	☐	☐
(b) Male age >40 years	☐	☐	☐
(c) Maternal smoking	☐	☐	☐
(d) Passive smoking	☐	☐	☐
(e) Body mass index of women >30 kg/m^2	☐	☐	☐
(f) Duration of subfertility	☐	☐	☐
(g) Previous ovarian surgery	☐	☐	☐

24. Do you think the followings are potential complications associated with ART?	**Yes**	**No**	**Do not know**
(a) Ovarian hyperstimulation syndrome	☐	☐	☐
(b) Multiple pregnancy	☐	☐	☐
(c) Spontaneous miscarriage	☐	☐	☐
(d) Ectopic pregnancy	☐	☐	☐
(e) Breast cancer	☐	☐	☐
(f) Ovarian cancer	☐	☐	☐
(g) Structural congenital abnormality	☐	☐	☐
(h) Chromosomal abnormality with intracytoplasmic sperm injection	☐	☐	☐
(i) Premature menopause	☐	☐	☐

Appendix 2. (cont'd)

25. Are you aware of any age limit for publicly funded subfertility treatment in Hong Kong?

Yes ☐ No ☐

If yes, at what age do you think it is? _____ years

26. Are you aware of the following patient selection criteria for publicly funded IVF services in public hospital in Hong Kong?	**Yes**	**No**
(a) Couple needs to be legally married	☐	☐
(b) There is no living child for the current marriage	☐	☐
(c) Woman must not be more than 40 years old at the time the procedure is initiated	☐	☐

Due to the limited resources in public hospitals, there is a waiting time for the first cycle of IVF.

27. What is the maximum waiting time (from referral to first IVF cycle) that you could accept?

☐ <12 Months ☐ 12-18 Months ☐ 18-24 Months ☐ 24-30 Months

☐ 30-36 Months ☐ >36 Months

28. Will you seek IVF service from private if the waiting time is longer than what you can accept?

Yes ☐ No ☐

Although public ART cycles are still heavily subsidised by the Hospital Authority, partial cost recovery is required to cope with the increase in cost of drugs and consumables and maintenance of the ART services.

29. In your opinion, what is the maximum charge (HK$) you could accept for one cycle of IVF?

☐ <$10,000 ☐ $10,000-$20,000 ☐ $20,001-$30,000

☐ $30,001-$40,000 ☐ $40,001-$50,000 ☐ >$50,000

30. Do you think couples should be seen together during subfertility counselling and treatment?

Yes ☐ No ☐

31. Studies showed that undergoing subfertility counselling and treatment could be stressful for a couple, whom / where do you think the couple would like to have support from? (Please tick one or more items)

☐ Family members
☐ Friends
☐ Support groups and peers who had experience of undergoing ART treatment before
☐ Doctors in charge of their subfertility service
☐ Specialised subfertility nurses
☐ Clinical psychologist
☐ Social worker

32. Do you think family planning and fertility counselling service should be given early routinely, such as during premarital counselling?

Yes ☐ No ☐

33. Do you wish to obtain more information on subfertility service in Hong Kong?

Yes ☐ No ☐

If yes, from where / whom? (Please tick one or more items)

☐ Television / newspaper / websites
☐ Educational talks
☐ General practitioner or family doctor
☐ Gynaecology specialists
☐ Family Planning Association
☐ Others, please state: _____

Thank you very much for your participation

Outcomes for Hong Kong Women Following Vaginal Mesh Repair Surgery for Pelvic Organ Prolapse

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Objective: To assess outcomes for pelvic organ prolapse and operative complications in women having vaginal mesh repair at a tertiary referral centre in Hong Kong.
Methods: A retrospective study design was used to collect both preoperative and postoperative data including the Pelvic Organ Prolapse–Quantification (POP-Q) score and complication rates. The primary outcome was improvement in POP-Q score. Secondary outcomes included perioperative and postoperative complications.
Results: A total of 65 women had vaginal mesh repair completed during the period of interest (1 January 2005 to 31 December 2012). In all, 34 women had total vaginal mesh repair while 24 and seven patients had anterior vaginal mesh repair and posterior vaginal mesh repair, respectively. One patient had anterior vaginal mesh repair and cervical amputation. There was significant elevation of the prolapsed part in both the anterior and posterior mesh repair groups. The 26 women in the total vaginal mesh repair group had significant elevation of the anterior and posterior vaginal wall and cervix. There was good preservation of vaginal length and no significant lengthening of the perineal body. Four (7.4%) patients were found to have mesh erosion. Three of the patients were asymptomatic and managed conservatively. One patient required partial excision of the mesh. There was one case of buttock abscess. No reported bowel or bladder injury was reported.
Conclusions: The study showed significant improvements on the POP-Q score in the corresponding compartment of the vaginal mesh repairs postoperatively.
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Keywords: Pelvic floor; Pelvic organ prolapse; Surgical mesh; Uterine prolapse

Introduction

Pelvic organ prolapse (POP) is a common clinical condition affecting parous women as they age. The prevalence of POP in the United States has been reported as up to 40%[1]. A territory-wide audit in Hong Kong demonstrated that the prevalence of POP has been consistently increasing over the last decade[2]. Pelvic organ prolapse causes symptoms such as vaginal bleeding, dragging discomfort, vaginal ulcers, and infection. In severe cases, patients may even present with complications such as acute urinary retention, hydronephrosis, and recurrent urinary tract infection[3]. These complications may be associated with an adverse effect on quality of life. Use of a vaginal pessary as conservative management was adopted by more than 85% of gynaecologists as initial treatment of POP[4]. However, use of a vaginal pessary is not the definitive treatment and complications including vaginal discharge, vaginal ulcer, discomfort, and abstinence from sexual activity are commonly reported[5]. Many patients may therefore prefer definitive surgical treatment. However, the quoted recurrence rate is up to 30% to 40% for traditional pelvic floor reconstruction surgery[6,7]. This rate is even higher in obese women with POP[8].

The concept of using polypropylene mesh for pelvic floor reconstruction aimed at reducing recurrence by reforming the defective pelvic floor with the new material[9]. It has been reported that vaginal mesh repair surgery produces better results in recurrent prolapse or for women with uterine procidentia when compared with traditional pelvic floor reconstruction surgery[9].

The history of vaginal mesh repair for POP began with abdominal sacrocolpopexy followed by laparoscopic sacrocolpopexy. However, the recurrence rate was high and

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was reported as up to 17.8% in a Swiss study[10]. Vaginal mesh repair has been used clinically since 2004[11]. The mesh is introduced via a specially designed trocar system, through a few small incisions. According to a Cochrane review, the mesh exposure rate is around 10% post-surgery[12]. Other commonly encountered complications included bladder or rectal perforation intra-operatively[9].

This study aimed to compare preoperative and postoperative POP-Q scores and to assess perioperative complications in local Chinese women having vaginal mesh repair for POP from 2005 to 2012, in a tertiary referral centre in Hong Kong.

Methods

This study was designed as a retrospective study. Information was retrieved from the Urogynaecology Team, Queen Elizabeth Hospital, Hong Kong, for all patients having vaginal mesh repair as treatment for POP in the period from 1 January 2005 to 31 December 2012. Demographic data including age, parity, number of vaginal deliveries, weight of heaviest baby delivered vaginally, and a history of POP surgery were retrieved and analysed. The results of preoperative urodynamic study performed for existing urinary symptoms were also reviewed. Operation details including types of procedure, duration of operation, mean blood loss, perioperative complications (bladder and bowel perforation, vaginal haematoma, deep vein thrombosis, buttock abscess, urinary tract infection, and mesh erosion) were all retrieved and analysed. Quantification of the POP outcome measurements was based on clinical assessment using the International Continence Society Pelvic Organ Prolapse–Quantification (POP-Q) scoring system[13].

All cases were recruited from the Urogynaecology Clinic, Department of Obstetrics and Gynaecology, Queen Elizabeth Hospital, Hong Kong. All women presented with symptoms of POP and were offered the following surgical options: vaginal mesh / sacrocolpopexy / sacrospinous fixation or traditional pelvic floor repair, with or without hysterectomy. All patients gave signed written consent before vaginal mesh surgery. Urodynamic studies were performed for women who complained of lower urinary tract symptoms, such as urgency, frequency, and urinary incontinence. If a diagnosis of urodynamic stress incontinence was made, the option of concomitant transobturator tension-free vaginal tape (TVT-O) was discussed and performed at the same time, if the patient gave consent.

Preoperatively, bowel preparation was given on the day before vaginal mesh repair. Preoperative vaginal examination was performed to assess the severity of POP using the POP-Q scoring system. If the patient had only anterior or posterior compartment prolapse, then only anterior or posterior mesh repair was completed. If the prolapse affected both compartments, total vaginal mesh repair surgery was performed. There were three types of mesh kit used in 65 women, namely GYNECARE PROLIFT (Ethicon, US) in 37 cases, Apogee / Perigee (AMS, US) in nine cases, and DynaMesh (FEG Textiltechnik Forschungs- und Entwicklungsgesellschoft mbH, Germany) in 19 cases. All operations were performed by an experienced urogynaecology subspecialist or a urogynaecology trainee under supervision. All procedures were completed according to the original technique reported[14].

A single dose of prophylactic antibiotics was given to all women preoperatively. Further intravenous and oral antibiotics were given postoperatively. Patients were discharged after bowel opening and passing urine without problem.

After discharge from hospital, all patients were assessed at 1 year post-surgery according to the follow-up protocol of this study. This included assessment on the POP-Q scoring system by vaginal examination, and assessment of peri- and post-operative complications by questionnaire. Details of the operation record were also collected for this study from the patient's medical record, with informed consent obtained.

The primary outcome measures of this study were improvement of POP-Q score and POP-Q staging of prolapse at 1 year post-surgery. Secondary outcome measurements included duration of operation, mean blood loss, bladder and bowel perforation, buttock abscess, urinary tract infection, and mesh erosion.

All collected data were grouped into tables accordingly. Statistical analyses were performed using the Statistical Package for the Social Sciences (Windows version 15.0; SPSS Inc, Chicago [IL], US). The preoperative and 1-year follow-up POP-Q scores were compared using the Student's *t* test and a p value of <0.05 was considered statistically significant. This study was approved by the Kowloon Central Cluster / Kowloon East Cluster Research Ethics Committee of the Hospital Authority (Reference No.: KC/KE-13-0614/ER-1).

Results

There were 65 women who had vaginal mesh repair

completed between 1 January 2005 and 31 December 2012. Their mean age (± standard deviation) was 65 ± 11 years and their mean duration of delay (i.e. from POP symptoms to first medical attendance) was 5 ± 4 years. In all, 26 (40%) women had a trial of a vaginal ring pessary as conservative treatment before the surgical intervention; 18 (28%) women had utero-vaginal prolapse. The mean parity was 3.6 ± 1.7 and the mean number of vaginal deliveries was 3.6 ± 1.7. The mean weight of baby delivered vaginally was 3.4 ± 0.4 kg. In addition, seven (11%) of the women had previous POP surgery.

Overall, 64 women had urodynamic studies performed preoperatively; among these, 40 (63%) had normal findings and 24 (38%) had a diagnosis of urodynamic stress incontinence. Of these 24 women, 22 (92%) had concomitant TVT-O completed during surgery.

All women had preoperative prolapse assessment by POP-Q score. The results are listed in Table 1. If the reported score was positive, it indicated the leading point of prolapse was out of the vaginal hymen and a negative value indicated the contrary.

Details on the types and number of operations performed are shown in Table 2. In all, 34 (52%) women had total vaginal mesh repair performed; among these, 23 (68%) and 11 (32%) women presented with vault and utero-vaginal prolapse, respectively. In addition to vaginal mesh repair, one woman presented with anterior compartment prolapse and a long cervix (4 cm) and she underwent anterior mesh repair and cervical amputation.

Table 1. Preoperative Pelvic Organ Prolapse–Quantification scores at different points/landmarks for measurement

Point/landmark	Frequency	Mean ± standard deviation score	Range
Aa	65	0.4 ± 2.0	-3 to 3
Ba	65	0.9 ± 2.9	-3 to 3
C	65	-1.3 ± 4.7	-8 to 10
gh	65	5.4 ± 0.8	4-6
pb	65	2.1 ± 0.4	1-3
tvl	65	8.2 ± 1.1	6-10
Ap	65	-1.3 ± 1.9	-3 to 3
Bp	65	-0.9 ± 2.9	-3 to 3
D	18	-2.9 ± 4.9	-8 to 8

Abbreviations: Aa, Ba = anterior compartment; Ap, Bp: posterior compartment; C = middle compartment; D = posterior vaginal fornix; gh = genital hiatus; pb = perineal body length; tvl = total vaginal length

Table 2. Details of surgery performed for all patients who underwent vaginal mesh repair surgery

	Overall (n = 65)	Vault prolapse (n = 47)	Utero-vaginal prolapse (n = 18)	
			Mesh-only group ± TVT-O (n = 11)	Mesh + vaginal hysterectomy group ± TVT-O (n = 7)
Total (i.e. anterior + posterior) vaginal mesh repair	34	23	6	5
Anterior mesh only	24	19	3	2
Posterior mesh only	7	5	2	0
Concomitant continence surgery	19	17	2	0
Mean ± SD operating time (mins)	88.9 ± 33.3	80.4 ± 26.1	89.7 ± 32.8	146.3 ± 23.3
Mean ± SD blood loss (ml)	221.5 ± 225.3	183.1 ± 229.5	125.0 ± 82.2	460.0 ± 181.7
Mean ± SD hospital stay (days)	6.3 ± 2.2	6.5 ± 2.4	5.6 ± 1.3	6.7 ± 1.4

Abbreviations: SD = standard deviation; TVT-O = transobturator tension-free vaginal tape

The mean operating time was similar for vault prolapse and utero-vaginal prolapse (80.4 mins vs. 89.7 mins). For concomitant vaginal hysterectomy and mesh repair, the mean operative time was 146.3 minutes, indicating additional time needed for vaginal hysterectomy. The overall mean blood loss was 221.5 ml, with higher mean blood loss for concomitant vaginal hysterectomy and mesh repair (460.0 ml). The overall mean hospital stay was 6.3 days.

Details of intra-operative and immediate postoperative complications are shown in Table 3. There were no reported incidences of bowel or bladder injury, or postoperative urinary tract infection. However, one woman had a buttock abscess that required incision and drainage. The mesh implant was left in situ and the infection was resolved after drainage and antibiotics. The patient had no further complications afterwards.

Of the 65 women, four (7.4%) were found to have mesh erosion at 1-year follow-up. Three were asymptomatic and adopted conservative management. One woman presented with on-and-off vaginal spotting and so partial excision of the vaginal mesh (3 x 2 cm) was performed. There was no case of postoperative chronic pelvic pain at 1-year follow-up.

Details of the pre- and post-operative POP-Q score according to the type of vaginal mesh repair (anterior, posterior, or total) are listed in Table 4. The comparison of POP-Q scoring was stratified into the respective type of surgeries performed with data from 54 women (21 with anterior, 7 with posterior, and 26 with total vaginal mesh repair). The remaining cases had undergone surgery within the previous year.

For the anterior vaginal mesh repair group, there were significant changes in points Aa ($p<0.001$), Ba ($p<0.001$), and C ($p=0.001$). This reflected that the anterior mesh repair was successfully targeted at correction of the anatomical defect and addressed the corresponding POP region. For the seven women who had posterior vaginal mesh repair performed, the changes at point Ap and Bp at 1-year post-surgery were statistically significant (p values of <0.001 and 0.001, respectively), which was similar to the effect of anterior vaginal mesh repair. Regarding those having total vaginal mesh repair, the corresponding POP-Q scoring for anterior and posterior wall and cervix (i.e. point Aa, Ba, Ap, Bp and C) demonstrated statistically significant change at 1-year post-surgery (all $p<0.001$), which reflected the effectiveness of total vaginal mesh repair for repairing both anterior and posterior POP.

Table 5 shows the results of postoperative changes in total vaginal length, genital hiatus, and perineal body. There was no significant shortening of vagina or lengthening of perineal body, but significant shortening of genital hiatus by 0.5 cm ($p = 0.001$). The shorter the parameters of genital hiatus, the less the chance of having a recurrence of prolapse. The preservation of vaginal length is important to maintain quality of sexual function postoperatively. The respective mean preoperative and postoperative vaginal length was 8.2 cm and 7.8 cm, with mean vaginal shortening of 0.4 cm ($p = 0.72$). This represented good preservation of vaginal length postoperatively.

In addition to comparison of the POP-Q scoring, the leading points of POP interpreted by stages are also commonly used for comparison of postoperative outcome. Usually the value of stage 2 or earlier vaginal vault prolapse / utero-vaginal prolapse postoperatively was used to define an objective cure of POP post-surgery. In this study, 51/54 (95%) women had stage 0 POP and 3/54 (6%) women had stage 2 POP at 1-year post-surgery. The overall mean improvement of POP-Q staging was 2.7 at 1-year post-surgery. Thus, according to the above definition, the objective cure rate was 100% for all 54 women.

The data were further stratified into three groups according to the type of mesh kit used (Prolift, Apogee /

Table 3. Details of intra-operative and postoperative complications

Complication	Overall (n = 65)	Vault prolapse (n = 47)	Utero-vaginal prolapse (n = 18)
Bowel injury	0	0	0
Bladder injury	0	0	0
Urinary tract infection	0	0	0
Mesh erosion	4	3	1
Buttock abscess	1	1	0
Chronic pelvic pain	0	0	0

Table 4. POP-Q scores of women undergoing anterior, posterior, or total vaginal mesh repair at 1-year follow-up

Point/landmark	No. of patients assessed	Mean preoperative POP-Q score	Mean POP-Q score at 1-year follow-up	Mean improvement	p Value
Anterior					
Aa	21	0.9	-2.8	-3.7	<0.001
Ba	21	1.1	-2.9	-4.0	<0.001
C	21	-3.6	-6.5	-2.9	0.001
gh	21	5.4	4.7	-0.7	0.004
pb	21	2.3	2.6	0.3	0.04
tvl	21	7.9	7.3	-0.6	0.15
Ap	21	-2.9	-2.7	0.2	0.21
Bp	21	-2.9	-2.7	0.2	0.21
D	3	-6.7	-7.7	-1.0	0.23
Posterior					
Aa	7	-2.6	-2.7	-0.1	0.36
Ba	7	-2.6	-2.7	-0.1	0.36
C	7	-5.7	-7.9	-2.2	0.04
gh	7	5.1	4.7	-0.4	0.48
pb	7	2.2	2.9	0.7	0.01
tvl	7	7.9	8.1	0.2	0.65
Ap	7	0.0	-2.9	-2.9	<0.001
Bp	7	0.0	-2.4	-2.4	0.001
D	7	-6.0	-8.5	-2.5	0.13
Total					
Aa	26	0.6	-2.3	-2.9	<0.001
Ba	26	1.6	-2.0	-3.6	<0.001
C	26	1.2	-5.7	-6.9	<0.001
gh	26	5.4	5.1	-0.3	0.43
pb	26	2.0	2.6	0.6	<0.001
tvl	26	8.5	8.1	-0.4	0.12
Ap	26	-0.3	-2.5	-2.2	<0.001
Bp	26	0.5	-2.1	-2.6	<0.001
D	3	-4.0	-4.0	0.0	1.00

Abbreviations: Aa, Ba = anterior compartment; Ap, Bp: posterior compartment; C = middle compartment; D = posterior vaginal fornix; gh = genital hiatus; pb = perineal body length; POP-Q = Pelvic Organ Prolapse–Quantification; tvl = total vaginal length

Table 5. Postoperative change in perineum and vaginal length

Point/landmark	No. of patients assessed	Mean preoperative POP-Q score	Mean POP-Q score at 1-year follow-up	Mean improvement	p Value
gh	54	5.4	4.9	-0.5	0.001
pb	54	2.1	2.7	0.5	0.80
tvl	54	8.2	7.8	-0.4	0.72

Abbreviations: gh = genital hiatus; pb = perineal body length; POP-Q = Pelvic Organ Prolapse–Quantification; tvl = total vaginal length

Perigee, and Dynamesh) and the respective preoperative and postoperative POP-Q scores were compared. No significant differences in all the POP-Q scores were found among these three mesh kit sets (Table 6).

Discussion

The usually quoted objective cure rate for POP in the literature is between 92.4% and 100%, and 97.6% at the 1-year postoperative period[15,16]. In this study, the objective cure rate for 54 women at 1-year post-surgery was 100%, according to the definition of the International Continence Society POP-Q scoring system[13]. However, it could be argued that the commonly used POP-Q scoring system is too crude to reveal the entire clinical picture and anatomical improvement postoperatively. This study provides this additional information by using individual mean POP-Q score improvement for the corresponding anatomical defect and measured the outcome on these scores postoperatively. The results of this study demonstrate the significant improvement in anterior and posterior vaginal compartment prolapse after anterior and posterior vaginal mesh repair, respectively. This cannot be shown if only the overall POP-Q score is used as it measures the leading point alone.

One of the main criticisms of use of the POP-Q score is the subjectivity of clinician assessment which may be a cause of bias. A literature report from the US addressed this argument specifically[16]. When comparing objective and 'eyeballing' measurement results in experienced hands, the POP-Q scores were highly associated[16]. In our study, we endeavoured to improve the objectivity of assessment by using a disposable ruler in the measurement of the individual POP-Q reference points in order to minimise bias.

Table 6. Significance of postoperative POP-Q scores among the three different mesh kit sets (Prolift, Apogee/Perigee, and Dynamesh)

Point/landmark for measurement	p Value
Aa	0.18
Ba	0.22
C	0.32
gh	0.09
pb	0.38
tvl	0.62
Ap	0.07
Bp	0.12
D	0.09

Abbreviations: Aa, Ba = anterior compartment; Ap, Bp: posterior compartment; C = middle compartment; D = posterior vaginal fornix; gh = genital hiatus; pb = perineal body length; POP-Q = Pelvic Organ Prolapse–Quantification; tvl = total vaginal length

The other important yet interesting finding in this study was the success in preservation of vaginal length postoperatively. This is important for sexual function and quality of life. In this study, the preoperative and postoperative total vaginal length was similar (8.2 cm vs. 7.8 cm) with no significant shortening ($p = 0.72$). This involved the technique involving avoidance of trimming of excessive vaginal skin, and preservation of vaginal tissue during wound closure. Appropriate insertion of the trocar has also been found to be important to avoid excessive shrinkage of mesh[17].

The mean hospital stay for the women in this study was 6.3 ± 2.2 days. This duration was longer than the usually quoted duration of hospital stay of around 4 to 5 days[18]. This finding could be explained by the extra postoperative observation during the early phase of vaginal mesh surgery development in our centre, extending the overall length of hospital stay in this study.

No intra-operative bladder or bowel injury was reported in this study. According to the literature, the bladder injury rate ranges from 0% to 4.26%[19-21]. Our low complication rate may be explained by the restriction of surgery to only a very experienced urogynaecologist in our unit, and strict control of operation quality by following the guided surgical procedure. There was one case of postoperative buttock abscess, with the patient presenting with fever and pain in the peri-anal area. The patient was effectively treated by incision and drainage and a course of antibiotic treatment. Mesh removal was not required. It could be argued as to whether removal of foreign body material from this patient was essential during infection. However, the rate of mesh removal after such surgery has been lowered by the design of type 1 polypropylene mesh, which allows macrophages to pass through and thus combat bacterial infection[22]. The final outcome for this patient was encouraging. There were no delayed complications seen in this study, such as chronic pelvic pain on further assessment.

The mesh erosion rate in our case series was 7.4% (4/54) and the re-operation rate for mesh erosion was 1.9% (1/54). The reported mesh erosion rate from Cochrane review was around 10% from 40 randomised controlled

trials[12]. Overall, the mesh erosion rate in our study was comparable with other international unit. Although we tried to minimise mesh erosion by double-layer vaginal closure, the evidence shows that this may not help in avoiding mesh erosion. One woman had mesh excision for symptomatic vaginal spotting. Other patients were asymptomatic and refused further surgical intervention.

No patient complained of chronic pelvic pain at 1-year post-operation. However, pelvic pain or dyspareunia has been reported in the literature after vaginal mesh surgery[23]. One of the possible explanations for absence of pelvic pain in our series is the adjustment of mesh size before insertion. As we found that the female pelvic floor area is variable in different patients but that the vaginal mesh only comes in a standard size, we cut the mesh according to the size of the pelvic floor area of individual patients to avoid excess implant material being introduced. The excess foreign body material may lead to extensive scarring and contracture and hence chronic pelvic pain. However, as the sample size is small in this case series, further study in this area is encouraged to provide more information on this modified aspect of vaginal mesh surgery.

Furthermore, the data from this study demonstrated the importance of precise and concise preoperative counselling before vaginal mesh surgery. The risk of mesh erosion is important to discuss in detail with the patient before surgery to avoid the possibility of medico-legal consequences; one of the patients in this study required re-operation for symptomatic mesh erosion. Although there was no reported intra-operative bowel or bladder injury in this study, it is also recommended to discuss these potential risks in detail, as consequences such as a stoma or prolonged catheterisation may not be anticipated by a patient having vaginal mesh surgery for POP.

Although different mesh kits were used in this study due to the supply limitations in the publicly funded hospital setting, the overall design of the mesh kits and anatomical placement of the mesh were very similar. There was also no significant difference demonstrated on the postoperative POP-Q score when comparing the three different groups of patients using the respective mesh kit sets (Prolift, Apogee / Perigee, Dynamesh).

The limitation of this study was the absence of subjective assessment and quality of life assessment, as there were no data available from the case records. The suggested solution is to perform a prospective study in future, including assessment on subjective improvement of symptoms and quality of life assessment using a validated questionnaire. Furthermore, the long-term success rate of POP repair is important to determine the efficacy of this treatment option. Prospective follow-up assessment of patients is essential to provide further information in this area.

In conclusion, in comparison to most reports in the literature, this study provides stratified POP-Q score data for women having vaginal mesh repair for POP. This can help to illustrate the true anatomical improvement after specific types of vaginal mesh repair, rather than simply a comment of objective cure when the POP-Q score is used alone. Furthermore, this case series supports the view that stringent surgeon training and selection may help to reduce commonly reported intra-operative bladder and rectal injuries. However, the long-term results following vaginal mesh repair for POP for the patients in this study are still awaited.

Declaration

No conflicts of interest were declared by the authors.

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The First Live Birth in Hong Kong Following Preimplantation Genetic Diagnosis for Robertsonian Translocation Using Array Comparative Genomic Hybridisation

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The use of preimplantation genetic diagnosis has been available in Hong Kong for more than 10 years. In the past, fluorescence in-situ hybridisation technique was used for preimplantation genetic diagnosis for translocation carriers. Array comparative genomic hybridisation was developed with the advantages of testing all 24 chromosomes and being a user-friendly technique. We report the first live birth in Hong Kong after preimplantation genetic diagnosis for Robertsonian translocation using array comparative genomic hybridisation.
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Keywords: Comparative genomic hybridization; Preimplantation diagnosis; Translocation, genetic

Introduction

We would like to report the first live birth in Hong Kong following preimplantation genetic diagnosis (PGD) for Robertsonian translocation using array comparative genomic hybridisation (aCGH).

Case Report

A 34-year-old patient was referred to our subfertility clinic in 2009 for primary severe male factor subfertility. Repeated semen analysis of her husband revealed severe oligozoospermia, with sperm concentration of <1 million/ml. Thus, the couple was advised to undergo in-vitro fertilisation (IVF) and intracytoplasmic sperm injection (ICSI) treatment. Karyotyping of the husband showed 45,XY,rob(14;15)(q10;q10) and no Y chromosome microdeletion. In view of the balanced translocation, PGD using fluorescence in-situ hybridisation (FISH) was offered after extensive counselling.

The first IVF/PGD cycle was performed in July 2010. After 9 days of ovarian stimulation, eight oocytes were retrieved and four were fertilised after ICSI of seven mature oocytes. Embryo biopsy done on four day-3 embryos showed one embryo with normal FISH signals. On day 5, the embryo was of fair quality at morula stage and was transferred. However, the patient failed to conceive.

The second IVF/PGD cycle was performed in December 2010. After 9 days of ovarian stimulation, 18 oocytes were retrieved and 13 were fertilised after ICSI of 17 mature oocytes. Embryo biopsy of 10 day-3 embryos showed four embryos with normal FISH signals. One morula and one early blastocyst of fair quality were transferred on day 5. The patient became pregnant but this ended up in a biochemical pregnancy.

The third IVF/PGD cycle was performed in July 2011. After 8 days of ovarian stimulation, 18 oocytes were retrieved and 16 were fertilised after ICSI for 16 oocytes. Eleven day-3 embryos were available for embryo biopsy. It showed three embryos with normal FISH signals. Two embryos were of good quality on day 5 and were transferred. The patient became pregnant but the pregnancy ended again as an early spontaneous miscarriage.

After further extensive counselling, she decided to

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proceed to the fourth IVF/PGD cycle in May 2012. After 8 days of ovarian stimulation, 25 oocytes were retrieved and 16 were fertilised after ICSI of 24 oocytes. Embryo biopsy was done on 13 day-3 embryos. In April 2012, we acquired the platform of aCGH for translocation. As only nine sets of FISH probes were available, the couple was counselled to use aCGH for the remaining four embryos. We found three embryos with normal FISH signals (Figure 1) and three embryos with no aneuploidy on aCGH (Figure 2). One morula and one blastocyst of grade 4BB, both after aCGH, were transferred on day 5 and the patient became pregnant with a singleton pregnancy. One blastocyst of grade 5BB, after aCGH, was vitrified on day 6. She declined invasive prenatal diagnosis testing because of the associated risk of miscarriage. She delivered a healthy and phenotypically normal baby boy in February 2013. Cord blood analysis revealed the karyotype of the baby boy to be 46,XY, which was compatible with our PGD results; no uniparental disomy was detected.

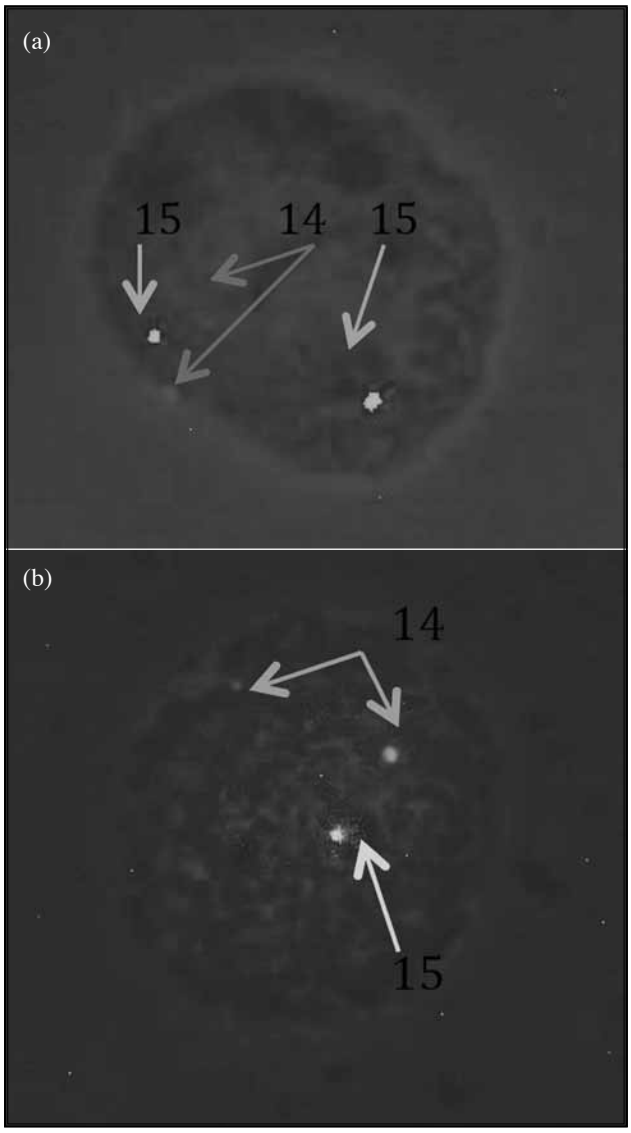

Figure 1. An embryo with (a) normal and (b) abnormal fluorescence in-situ hybridisation signals

Embryo Biopsy and Preimplantation Genetic Diagnosis Treatment Cycles

One blastomere was biopsied from each good-quality day-3 embryo. The blastomere was either fixed for FISH analysis or underwent aCGH according to the manufacturer's protocol (BlueGnome, UK). For FISH analysis, Cytocell (UK) 14qter (red) and Cytocell 15qter (green) probes were used. Two laboratory staffs independently interpreted the FISH results.

Discussion

The use of PGD for sex-linked disease in the first-born baby in the world was reported in 1990[1], followed by another baby born after PGD of cystic fibrosis 2 years later[2]. Embryo biopsy is usually performed on day 3 after oocyte retrieval and one or two blastomere biopsies were used for the genetic testing. Subsequently, there was increasing use of the technique for both monogenetic diseases using polymerase chain reaction (PCR) and translocation carriers using FISH. Aneuploidy screening (preimplantation genetic screening [PGS]) for embryos before transferring back to the uterus in some at-risk groups of women, such as those with advanced maternal age and recurrent pregnancy loss, was advocated to increase the pregnancy rate and reduce miscarriage rate. In our unit, we have been offering PGD treatment for more than 10 years and reported the first case of PGD using FISH[3]. We use blastomere biopsy together with PCR and FISH for monogenetic diseases and translocation carriers, respectively. An increasing number of PGD cycles have been performed in this decade.

Fluorescence in-situ hybridisation has been used for translocation and aneuploidy screening but it can only test for five to nine chromosomes, at most 15 chromosomes, in repeated rounds, as there is a limited number of spectrally distinct fluorochromes (colours) available for labelling of DNA probes. However, the accuracy of FISH analysis decreases with each additional round of hybridisation[4]. Moreover, as shown by evidence using an array-based approach on the remaining blastomeres from embryos after PGD, aneuploidies and chromosomal rearrangements, including chromosome breakage leading to segmental aberrations, were not picked up by the traditional FISH technique[5-7]. Moreover, there is technical difficulty with FISH technique itself[4] and an error rate of 7% to 10% has been estimated[8,9]. In translocation carriers, there is evidence that interchromosomal effect may increase

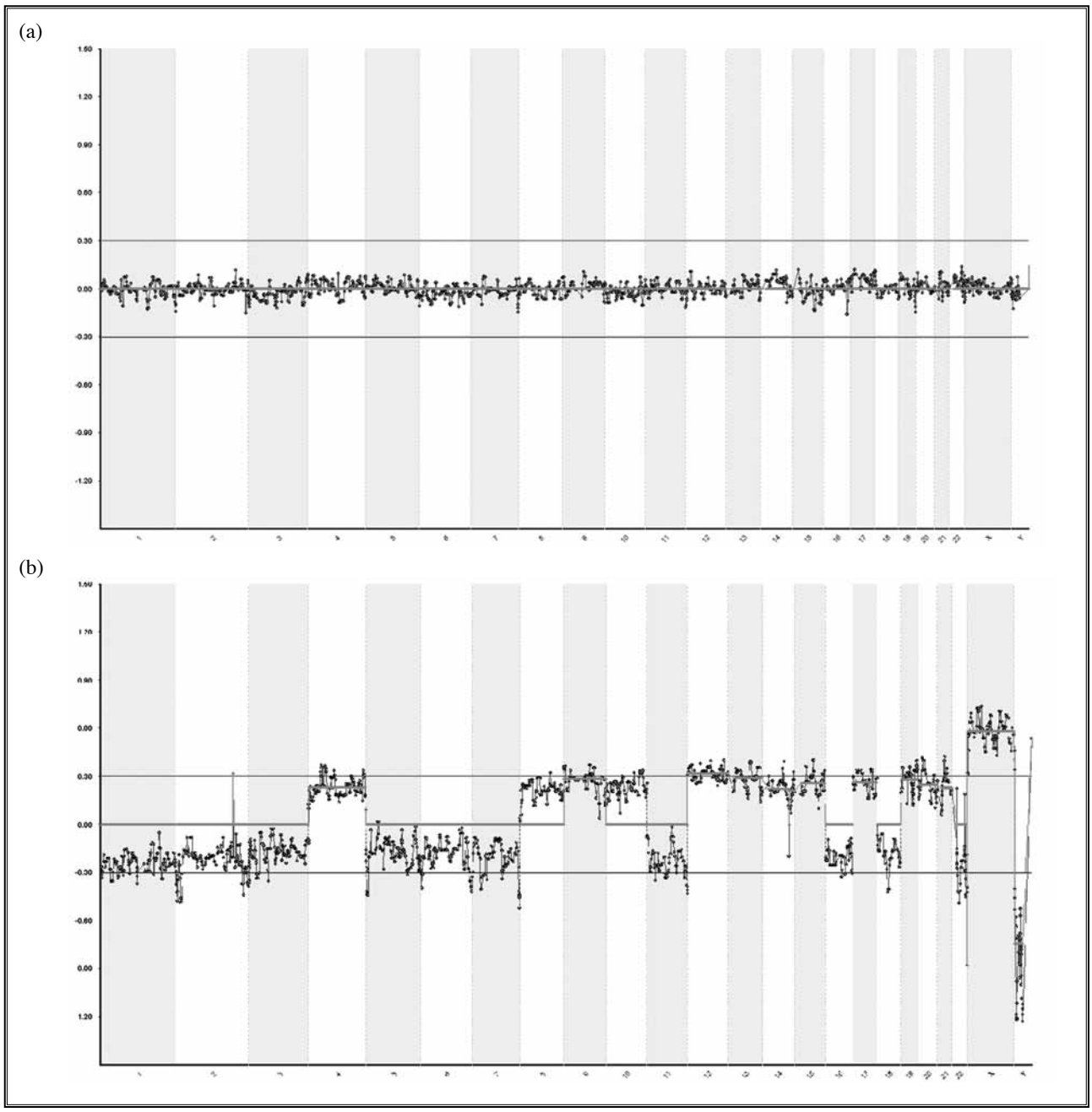

Figure 2. (a) Array comparative genomic hybridisation (aCGH) result of an embryo which resulted in a singleton live birth after transfer. (b) aCGH result of an abnormal embryo

aneuploidy other than in the involved chromosomes in the sperms and embryos, which may be missed by FISH[10,11]. Undiagnosed aneuploidies may be able to explain the two early miscarriages in our patient when FISH was used for PGD.

A systematic review on the reproductive outcome in couples with translocation with recurrent pregnancy loss showed that the pregnancy rate was not improved after the use of PGD[12]. However, it was criticised that all studies in this review were using the FISH technique, with its known disadvantages as mentioned above. The negative results associated with FISH are confined not only to PGD for translocation carriers, but also extend to PGS. To date, there are 11 randomised controlled trials on the use of FISH for aneuploidy screening in early human embryos, showing no benefit in the pregnancy rate in specific groups of women, mostly those with advanced maternal age[13]. A position statement published by the European Society of Human Reproduction and Embryology[13] concluded that there was no evidence showing the beneficial effect with routine use of PGS for patients with advanced maternal age, and that

conclusive data on recurrent pregnancy loss, implantation failure, and severe male factor were missing.

There has been emerging evidence regarding the use of aCGH in both translocation carriers and preimplantation aneuploidy screening since 2008[4,7,14]. This technique is able to provide information on all 24 chromosomes for the detection of aneuploidy and translocation[7]. The use of aCGH combined with single blastocyst transfer was shown to produce promising results in patients with good prognosis and, in general, subfertile patients with improved pregnancy rates and reduced miscarriage rates[14,15]. It has largely replaced the role of FISH in both translocation and preimplantation aneuploidy screening. The protocol of using aCGH for single cell testing was launched in our unit in 2012, and now we have used this technique in 15 subjects for diagnosing both translocation carriers and PGS, with an ongoing pregnancy rate of 38.5% per transfer.

Conclusion

We report the first live birth in Hong Kong following PGD for translocation using aCGH. It reveals the feasibility and practicability of using aCGH in a single cell of PGD. Starting from 2013, we have replaced FISH-based PGD with the aCGH platform in our unit, which is also an emerging trend all over the world.

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Editorial
Changes to Professional Indemnity

Obstetricians in Hong Kong remember that Christmas 2014 felt chilly, despite normal winter temperatures. In that month, the Medical Protection Society (MPS) unilaterally directed that Hong Kong obstetric professional indemnity would change from an occurrence basis to a claim-made basis. Care of pregnancy beyond 24 weeks is considered obstetrics, and the gynaecological work of an obstetrician is also treated as claim made based indemnity by the MPS. The Hong Kong College of Obstetricians and Gynaecologists (HKCOG), Obstetric and Gynaecological Society of Hong Kong, and even the Hong Kong SAR Government made huge efforts to communicate and suggest logical amendments. We received firm NOs at all levels. The MPS declared that it was an important BUSINESS decision that should be implemented immediately in synchrony around the world, in contradiction of its own declaration that each region holds independent books. Doctors had to make a quick decision on whether to continue childbirth services, and patients were of necessity sometimes referred at very short notice to another obstetrician when their current obstetrician made the difficult decision to stop performing deliveries. Responses were in stark contrast to what we had expected based on a member-for-member institutional character. This article will not discuss the MPS, but rather analyse reasons and offer solutions.

Occurrence-based indemnity means that a doctor is insured for costs arising from a medico-legal dispute and covers both legal fees and any financial compensation that may be awarded. Claim made based indemnity protects the doctor only if the doctor was covered by the protection scheme both when the event being disputed happened and when the claim arises, or the case was reported and accepted by the insurer while the doctor was covered. It may look complicated. To clarify, with occurrence-based indemnity the doctor need not be concerned about future claims. With a claim-made basis, he must continue his indemnity indefinitely to guard against future litigation.

The root of the problem lies in huge amounts of compensation paid for problems that arise as a direct result of the delivery process, for example, asphyxia and birth trauma. These events are considered to be attributable to actions or inactivity of the attendant obstetrician. The problem is further aggravated by the length of time that may pass before a claim is filed. This delay may result in financial inflation, and changes to social norms, including the basis on which the court awards compensation. Doctors may not like the present judicial approach to compensation but we have to submit to society norms. In addition, the image of a powerful and unjust doctor against a suffering baby is not favourable. Obstetricians have had particularly bad publicity profile in 2015: an obstetrician in private practice who was recently disciplined by the Medical Council, and the long list of allegations against private obstetricians during the mainland obstetric saga, are still fresh in the public's mind.

It is true that occurrence basis to professional indemnity, and unlimited compensation are difficult to sustain, despite historic declarations by the MPS that these two features are their 'core values' that distinguish them from other providers. In 2015, the MPS removed both aspects from the protection it provided. Current practitioners may be envious of their predecessors who paid relatively small premiums, were not sued, and enjoyed virtually limitless immunity. We must acknowledge that 'the world has changed, and we have to change as well'.

Private delivery suites are not going to close overnight, but frost followed snow in Hong Kong with the mainland obstetrics event and then the indemnity problem. Readers should nonetheless not despair: the future is NOT fixed, but rather lies in our own hands.

The problem is not MPS, which is merely a provider, but the rapidly escalating indemnity costs. This in turn is due to escalation in the number of claims.

A doctor may face legal action after retirement and after he / she has stopped paying for indemnity. In claim-made indemnity, subscription amounts may continue to increase: a retired practitioner may not be able to afford such costs, despite claims by the MPS that subscriptions would remain affordable. No one knows, least of all the MPS, what will happen in future. Data informally released from the MPS indicated that up to 2% to 3% of claims occur 5 years after the index case. Thereafter the chance drops a lot, and it allows us to have a feeling of costs for the second and subsequent 5-yearly intervals of 'extended

reporting' for coverage. Compensation amounts are also likely to continue increasing. The obstetrician faces the prospect of losing everything he has worked for because of one bad case, if he cannot afford to pay for indemnity or if he lacks protection by the MPS.

When private obstetric indemnity is not protective, private practice ceases to be an attractive option. This may deter young doctors from entering the specialty. In terms of obstetrics and gynaecology, our specialty enters menopause — the specialty looking after reproduction will cease producing offspring.

Although the private sector will bear the brunt of these changes, the government is not unaffected. After two decades of experiment, Hong Kong has learnt that her health care system needs to be two-tiered with private practice running alongside public. Although the public-private overall admission rates now stand at about 88:12, in obstetrics it is about 60:40. With stabilisation of the private obstetric sector, private paediatrics and anaesthesiology also grow. A fatal attack on the private obstetric sector has serious implications for society and the government.

In an effort to continue providing services, adaptations may be required. Some patients return to the public sector for deliveries when supply in the private sector recedes. This is a further insult to public units that are already short-staffed and have difficulty in recruitment. Some trained doctors may transfer to the private sector despite taking apparently more risks, because they cannot tolerate the ever-increasing public sector workload. In the next decade, retirement will become a theme in human resource management of the Hospital Authority (HA), and the early departure of experienced doctors will add more pressure to the frail human resource backbone. The HA in theory may increase its headcount by assigning new and unwilling doctors. We have witnessed backlashes in many other historic events: it is hoped that the HA will have learnt the hard way that doctors may not be compliant when personal safety is at risk. We have also learnt from overseas experience that when claims escalate, obstetric compensation, even in the public sector, consumes a lot of resources to the extent that the sustainability of the health care system is jeopardised.

Labour ward risk management will be emphasised, whether doctors like it or not. In the private sector, it may infringe the autonomy that many doctors take for granted. It may be worth reminding readers that part of the reality of claims-made indemnity is that one generation of private doctors funds their own claims, instead of leaving it to the next generation when he retires. Therefore the long-held approach that we are not interested in what is happening next door may now be seen as harmful to our own wallets. Each doctor actually contributes to compensation paid for mishaps next door. It speaks strongly for open peer review and collective prevention of problems whenever possible. When annual indemnity premiums rise to unaffordable levels despite self-regulation, doctors will need to be attached to private hospitals in order to continue private practice. Obstetrics could then be institutionalised, meaning that private hospitals dictate the actions of doctors, whether or not they agree. If even private institutionalisation is not successful, and private teams cannot afford indemnity coverage, obstetrics will further be institutionalised under public organisations. Colleagues who wish to retain control of their own practice must now realise that self-discipline is an important tool, and make immediate changes while it may still work.

The author has stated earlier that the future is not yet determined. It is time for us to take a united stand and look for a solution. The MPS advises us that claims in Hong Kong are not out of control, although the rate of their increase is worrying. Hong Kong may be unique in that there exists no alternative provider of professional indemnity. A logical and important aspect of management is competition. The HKCOG has formed a subcommittee to examine this aspect, and we are open to all parties who may be interested in provision of such a service in Hong Kong.

The HKCOG is encouraging the focus to be on labour ward risk management, and is prepared to do everything possible in this respect. The author has explained that it is not a nosy exercise. Instead, it could be the difference between collective survival and extinction. Furthermore, unless we do everything seen as appropriate in self-regulation, it is difficult to lobby for social support from other areas of management, such as capping of claims and the maximum period for bringing a claim.

A most important part in the overall solution is tail coverage that will enable doctors to retire in peace. It may be difficult to estimate the total amount required for each doctor, as changes occur over time. Nevertheless some calculations may be feasible and some mechanisms to pool subscriptions may help each doctor significantly. The bare minimum may be coverage of legal fees and a modestly capped compensation. Nonetheless adequate cover is necessary to protect the doctor, as well as provide a valid

alternative to specialties for whom MPS indemnity remains occurrence-based.

Conceptually, any single indemnity provider may be liquidated. We have been given to understand that the MPS is financially stable, but we have witnessed the recent fall of so-called financial giants, and history is prone to repeat itself. In the 21st century with the half-life of everything shortening, it may be safer to seek indemnity support for the whole of Hong Kong on a year-by-year claim-made basis, in order to prevent liquidation of the insurer that would leave doctors unprotected. Furthermore, insurers are regulated by governments, but the MPS is not controlled by jurisdiction.

It may be an opportunity to review our existing mechanisms for resolving conflict. The MPS relies heavily on support from lawyers, and it may be fair to describe MPS as a financial facilitator with little other capacities. The future system may start with an individual service unit for conflict resolution, of which the author has experience. Each private delivery suite may set up such a mechanism. The importance of mediation might increase, as it is far more cost-effective than legal proceedings. Another way forward may be to install centralised clinical case handlers, who may advise early settlement of claims without recourse to lengthy and costly legal work. Legal support becomes part, instead of all, of the mechanism.

The College is doing everything possible to handle the matter, and a subcommittee has been established under the Professional Development Committee for this purpose. We are not able to produce regular announcements because changes frequently occur during negotiation, and any solution must be deliberated until it is deemed definitely sustainable. Colleagues please kindly accept our apologies that we are unable to rapidly produce sustainable, safe fixes. We welcome advice and communications. The author is also prepared to continue serving the fraternity on the matter after stepping down from present appointments.

Obstetrics and gynaecology is not as small as our membership number reflects. We have a huge stake in private medicine, and our high compensations make us high in the subscription / claim profile. We do not belittle ourselves when we try to find alternative(s). We shall be humble to every other stakeholder in Hong Kong and overseas. We need support. We need friends and allies, more now than ever, regardless of how we were treated (or shall be) at any time. We already have strong indicators from MPS membership electronic application forms that may next face similar treatment: orthopaedics, cosmetic surgery, and ophthalmology. Neurosurgery is close behind us in terms of subscription levels. The logic of the MPS that occurrence basis is difficult to maintain for minors applies to paediatrics and related fields, anaesthesiology and psychiatry. In the long run even general practitioners may not be immune. We shall tell 100% truth, and not conceal or exaggerate the truth, to enable our colleagues in other specialties to understand THEIR own problems.

This matter is not unique to obstetricians. It is a blight on medicine in Hong Kong. It may simply leave a scar on the dignity of doctors in Hong Kong, and change obstetrics and gynaecology for the worse. We may live to tell our story that private obstetrics in Hong Kong ended when we were active. Alternatively, we may tell our profession grandchildren that we oldies fought to provide them chances to serve. It may actually provide us an opportunity to review our system and find a proud solution, so that even our mother country may benefit. The outcome depends on ourselves, no one else.

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Abnormal First Trimester Maternal Serum Biochemical Markers and Prediction of Adverse Pregnancy Outcomes

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Objective: To review the obstetric outcomes associated with abnormal first trimester maternal serum markers, including pregnancy-associated plasma protein A and beta-human chorionic gonadotrophin.
Methods: A retrospective review of all singleton pregnancies with first trimester Down syndrome screening by a combination of fetal nuchal translucency thickness, and maternal serum pregnancy-associated plasma protein A and beta-human chorionic gonadotropin done at 11+0 to 13+6 weeks of gestation in a public hospital from 1 July 2010 to 31 December 2011 was conducted. The biochemical markers were converted to multiples of the expected normal median for a pregnancy of the same gestation. The associations between abnormal biochemical markers and adverse pregnancy outcomes, including small for gestational age, preterm delivery, low Apgar score, neonatal intensive care unit admission rate, miscarriage, and stillbirth were studied.
Results: A total of 4367 women were included in the study. Low pregnancy-associated plasma protein A level (<0.4 multiples of the expected normal median) was significantly associated with an increased rate (adjusted odds ratios) of small-for-gestational-age infants (4.8; 95% confidence interval, 2.8-8.2), preterm deliveries (2.0; 1.3-3.2), neonatal intensive care unit admissions (3.1; 1.8-5.3), and stillbirths (7.7; 2.0-29.1), but not low Apgar scores (2.6; 0.8-8.6) or miscarriages (1.3; 0.7-2.6). A low beta-human chorionic gonadotrophin level (<0.4 multiples of the expected normal median) was not associated with any of these adverse outcomes, except in a subgroup analysis of low Apgar score in gestation at or after 37 weeks.
Conclusion: Low pregnancy-associated plasma protein A level was significantly associated with increased rates of small-for-gestational-age infants, preterm deliveries, neonatal intensive care unit admissions, and stillbirths. These results may help in counselling women and consideration of increased fetal surveillance in such cases.
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Keywords: Apgar score; Chorionic gonadotropin, beta subunit, human; Infant, small for gestational age; Intensive care units, neonatal; Pregnancy-associated plasma protein-A

Introduction

In the first trimester of pregnancy the placentally derived biochemical markers, pregnancy-associated plasma protein A (PAPP-A) and beta-human chorionic gonadotropin (beta-hCG), are increasingly being used in conjunction with ultrasound measurement of nuchal translucency (NT) thickness as part of screening programmes for trisomy 21 and other aneuploidies.

Independent of the presence of aneuploidy, women undergoing biochemical screening and are found to have markedly reduced PAPP-A levels in the first trimester are increasingly recognised as being at increased risk for other pregnancy complications. Such adverse outcomes include miscarriage, preterm delivery, small-for-gestational-age (SGA) infant, low Apgar score of <7 at 5 minutes, neonatal intensive care unit (NICU) admission, and stillbirth[1-16]. The results for low beta-hCG levels and other pregnancy complications are more controversial[1-5].

The association between PAPP-A or beta-hCG levels and various adverse obstetric outcomes has been explained by the fact that both hormones are produced in

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the placenta soon after implantation, and low levels could possibly reflect abnormal placentation. This may, in turn, account for or be associated with adverse obstetric and neonatal outcomes[3-7].

Most studies addressing this issue have concentrated on outcomes of pregnancies where PAPP-A and beta-hCG levels are less than the fifth centile of a normal population (approximately 0.41 multiples of the expected normal median [MoM])[1-8]. However, similar studies have not been reported within the Chinese population, which is especially relevant as it is well known that the normal range of serum markers varies among different populations[1-11,13-16].

This study aimed to assess whether low levels of PAPP-A or beta-hCG, measured as part of first trimester screening for chromosomal aneuploidies, were related to increased risk of SGA infants, preterm deliveries, low Apgar scores, NICU admissions, and stillbirths in a Chinese population.

Methods

This was a retrospective cohort study of all singleton pregnant women who had undergone first trimester Down syndrome screening by a combination of fetal NT thickness, and maternal serum PAPP-A and beta-hCG levels. Screening was performed between 11+0 and 13+6 weeks of gestation in a public hospital from 1 July 2010 to 31 December 2011.

This study included only women for whom there was complete information on serum markers and primary outcome measures, including fetal loss (miscarriage or stillbirth), birth weight, maturity at delivery, Apgar score, and NICU admission. Women with pregnancies with abnormal karyotype, multiple pregnancies, blood sample taken before 11+0 weeks or after 13+6 weeks of gestation, type 1 or 2 diabetes, and non-Chinese ethnicity were excluded from the final analysis.

Miscarriage was defined as fetal loss before 24 completed weeks of gestation, and stillbirth as delivery of a fetus with no cardiac activity after 24 weeks. Fetal loss included all miscarriages and stillbirths. Small for gestational age was defined as birth weight of less than the 10th centile for gestational age. The study was reviewed and approved by the local research ethics committee.

All pregnant women who accepted first trimester screening test had a blood sample taken between 11+0 and 13+6 weeks. All the serum samples were analysed at a single laboratory (Tsan Yuk Hospital), and levels of PAPP-A and beta-hCG were measured using the Kryptor analyser (Thermo Fisher Scientific, Waltham [MA], US). The levels of the biochemical markers were converted into MoMs by expressing the absolute concentration relative to the median value of the gestational age on the day of blood sampling. The MoM values were not calculated until the gestational age was determined by crown-rump length (CRL) at the first trimester scan. Furthermore, the MoM values were corrected for maternal weight, as high maternal weight is known to be associated with low PAPP-A and beta-hCG levels. In the analyses, PAPP-A and beta-hCG MoM values were both included as continuous variables and dichotomised by a cut-off at 0.4 MoM (corresponding to the fifth percentile). Data regarding the analyses of PAPP-A and beta-hCG levels were obtained from the Tsan Yuk Hospital Down syndrome screening database. An ultrasound examination was performed during 11+0 to 13+6 weeks of gestation and, at this time, the gestational age of the fetus was estimated by means of the CRL using the formula of Robinson and Fleming[17]. The gestational age determined at this scan was used to calculate the expected date of delivery and thereby the gestational age at delivery.

Outcome information was obtained through the Obstetrics Clinical Information System, which is part of the Clinical Data Analysis and Reporting System, where all obstetric patients' data are recorded. This system is used in all hospitals under the Hospital Authority in Hong Kong for recording, data retrieval, statistics, and audit. Women were considered lost to follow-up when they delivered in other private hospitals and details of the pregnancy outcome were not known.

Information for other potential explanatory variables (maternal age, weight, parity, and maternal lifestyle factors such as smoking and alcohol consumption) was obtained from questionnaires completed by the pregnant women.

Dichotomised data were analysed by linear logistic regression. Results for PAPP-A and beta-hCG levels in relation to SGA, preterm delivery, low Apgar scores, NICU admission rate, miscarriage, and stillbirth were presented as adjusted odds ratios (adjusted ORs) with 95% confidence interval (95% CI).

To investigate whether a potential association between the placental hormones and neonatal outcomes could be due to the newborns being born preterm, we performed all the analyses for the entire study population

and then only for newborns with gestational ages of more than 37 weeks at birth. The prevalences of various adverse outcomes, including spontaneous miscarriage, stillbirth, SGA, prematurity, low Apgar scores, and NICU admission were determined from the available data.

Results

A total of 5979 women were recruited into the first trimester Down syndrome screening programme during the study period. Of them, six were confirmed to have abnormal karyotypes, 11 had multiple pregnancies, 12 had pre-existing type 1 or type 2 diabetes, 514 were of non-Chinese ethnic origin, 971 had incomplete obstetric outcome information, and 98 were subsequently noted to have date problem with gestation not eligible for first trimester Down's screening. After all the exclusions, 4367 pregnancies were investigated.

Of these 4367 pregnancies, 204 (4.7%) had low PAPP-A level, and 190 (4.4%) had low beta-hCG level. There were 128 (2.9%) infants requiring NICU admission, 27 (0.6%) with low Apgar scores, 265 (6.1%) preterm deliveries, 100 (2.3%) SGA infants, 148 (3.4%) miscarriages, and 11 (0.3%) stillbirths. Of the 971 women with incomplete data, five had low PAPP-A levels and six had low beta-hCG levels.

All miscarriages and stillbirths were excluded during subgroup analysis of NICU admission, low Apgar scores, and preterm delivery as these did not provide clinical outcomes. Only miscarriages were excluded from the stillbirth data and vice versa for the miscarriage data.

Neonatal Intensive Care Unit Admission

There were 128 (2.9%) NICU admissions. An increased rate of NICU admissions was associated with low PAPP-A level (adjusted OR, 3.1; 95% CI, 1.8-5.3) [Table 1], but not with low beta-hCG level. The difference in PAPP-A level was also significant when applied only to those delivered at gestational week 37 or later (adjusted OR, 3.5; 95% CI, 1.6-7.9).

Low Apgar Score

A total of 27 (0.6%) infants had low Apgar scores. A significant increased rate of low Apgar score was associated with low beta-hCG level when applied to infants delivered at or after 37 weeks of gestation (adjusted OR, 8.8; 95% CI, 1.7-45.8). Low PAPP-A level was not found to be associated with a low Apgar score of <7 at 5 minutes (adjusted OR, 2.6; 95% CI, 0.8-8.6) [Table 1].

Small for Gestational Age

Using the 10th centile as a cut-off measurement, there were 100 (2.3%) SGA newborns. A significant increased rate of SGA newborns was associated with low PAPP-A level (adjusted OR, 4.8; 95% CI, 2.8-8.2)

Table 1. Neonatal intensive care unit admissions, low Apgar scores, and small-for-gestational-age infants after delivery of women with different levels of PAPP-A and beta-hCG*

	PAPP-A				beta-hCG			
	All deliveries (n=4367)		≥37 Weeks (n=4108)		All deliveries (n=4367)		≥37 Weeks (n=4108)	
	<0.4 MoM (n=204)	≥0.4 MoM (n=4163)	<0.4 MoM (n=182)	≥0.4 MoM (n=3926)	<0.4 MoM (n=190)	≥0.4 MoM (n=4177)	<0.4 MoM (n=180)	≥ 0.4 MoM (n=3928)
NICU admissions	16 (7.8%); 3.1 (1.8-5.3) p<0.001	112 (2.7%)	7 (3.8%); 3.5 (1.6-7.9) p=0.002	44 (1.1%)	7 (3.7%); 1.3 (0.6-2.8) p=0.53	121 (2.9%)	4 (2.2%); 1.9 (0.7-5.3) p=0.23	47 (1.2%)
Low Apgar scores	3 (1.5%); 2.6 (0.8-8.6) p=0.13	24 (0.6%)	1 (0.5%); 2.8 (0.4-30.1) p=0.24	6 (0.2%)	3 (1.6%); 2.8 (0.8-9.3) p=0.10	24 (0.6%)	2 (1.1%); 8.8 (1.7-45.8) p=0.01	5 (0.1%)
SGA infants	18 (8.8%); 4.8 (2.8-8.2) p<0.001	82 (2.0%)	14 (7.7%); 4.7 (2.6-8.6) p<0.001	68 (1.7%)	7 (3.7%); 1.7 (0.8-3.7) p=0.19	93 (2.2%)	7 (3.9%); 2.1 (0.9-4.6) p=0.07	75 (1.9%)
Preterm deliveries	22 (10.8%); 2.0 (1.3-3.2) p=0.003	243 (5.8%)	-	-	10 (5.3%); 0.9 (0.5-1.7) p=0.69	255 (6.1%)	-	-

Abbreviations: beta-hCG = beta-human chorionic gonadotrophin; MoM = multiples of the expected normal median; NICU = neonatal intensive care unit; PAPP-A = pregnancy-associated plasma protein A; SGA = small for gestational age

* Data are shown as No. (%), odds ratios (interquartile range), and p values

[Table 1]. The beta-hCG level was not shown to have any statistical correlation with SGA newborns.

Preterm Delivery

A total of 265 (6.1%) preterm deliveries was found. Significant increased rate of preterm deliveries was associated with low PAPP-A level (adjusted OR, 2.0; 95% CI, 1.3-3.2), but not with low beta-hCG level (Table 1).

On further analysis of these 265 individual case notes, eight (3.0%) had intrauterine growth restriction (IUGR), of which only one was born by iatrogenic preterm delivery, i.e. induction of labour at 34 weeks for a fetus with IUGR with abnormal Doppler ultrasound results. The other seven deliveries were due to spontaneous preterm labour or preterm premature rupture of membrane.

Miscarriage

A total of 148 (out of 4515; 3.3%) deliveries were due to miscarriage. Low PAPP-A (adjusted OR, 1.3; 95% CI, 0.7-2.6) or beta-hCG levels (adjusted OR, 0.8; 95% CI, 0.3-1.9) were not associated with increased risk of miscarriage [Table 2].

Stillbirth

There were 11 (out of 4378; 0.3%) stillbirths. A significant increased rate of stillbirth was associated with low PAPP-A level (adjusted OR, 7.7, 95% CI, 2.0-29.1) [Table 2]. The beta-hCG level was not statistically correlated with stillbirth.

Discussion

In this retrospective study of 4367 pregnancies, we found that low PAPP-A level was significantly associated with an increased rate (adjusted OR) of SGA infants (4.8), preterm deliveries (2.0), NICU admissions (3.1), and stillbirths (7.7), but not with low Apgar scores or miscarriages. Low beta-hCG level was not associated with any of these adverse outcomes except in a small subgroup of infants with low Apgar scores delivered after 37 weeks of gestation (8.8).

Our study results regarding PAPP-A level are comparable to studies in western populations[1-15]. However, the non-significant results for low Apgar scores and miscarriage might be due to the small number of cases with abnormal outcomes in this study causing statistical inadequacy. A larger study with more participants might help in eliminating this error.

It was found that the risk of newborns being admitted to the NICU was increased if the placental biochemical marker PAPP-A level was <0.4 MoM. The same association was established in deliveries at or after 37 weeks of gestation, which could further support that the increased rate of NICU admissions was not solely due to the effects of prematurity. On reviewing individual case records, it was noted that only one of the 265 preterm deliveries was iatrogenic due to intervention for IUGR, and all the others were due to spontaneous preterm labour.

In contrast to the results for PAPP-A level, beta-HCG level was not shown to be significantly associated with adverse pregnancy outcomes in our study, except in a small subgroup analysis of infants with low Apgar scores delivered at or after 37 weeks of gestation. Indeed, the same observation has been made in other reports, and hypotheses have been postulated to explain these discrepancies[1-5].

Both PAPP-A and beta-hCG are produced by syncytiotrophoblasts. It seems likely that these

Table 2. Miscarriages and stillbirths in women with different levels of PAPP-A and beta-hCG*

Variable†	PAPP-A		beta-hCG	
	<0.4 MoM	≥0.4 MoM	<0.4 MoM	≥0.4 MoM
Miscarriage	9/213 (4.2%); 1.3 (0.7-2.6) p=0.43	139/4302 (3.2%)	5/195 (2.6%); 0.8 (0.3-1.9) p=0.57	143/4320 (3.3%)
Stillbirth	3/207 (1.4%); 7.7 (2.0-29.1) p=0.003	8/4171 (0.2%)	0/190 Odds ratio NA p=1.0	11/4188 (0.3%)

Abbreviations: beta-hCG = beta-human chorionic gonadotrophin; MoM = multiples of the expected normal median; NA = not applicable; PAPP-A = pregnancy-associated plasma protein A

* Data are shown as No. (%), odds ratios (interquartile range), and p values

† Stillbirth data were excluded from the miscarriage data and miscarriage data were excluded from the stillbirth data

different patterns of association may reflect different pathophysiological mechanisms relating to first trimester trophoblast function and later adverse pregnancy outcomes. The fact that the strength and pattern of the associations differed for the two trophoblast-derived proteins suggests that PAPP-A is not acting as a simple marker of the volume of the trophoblast, but that the association reflects a specific property of PAPP-A in the physiological regulation of trophoblastic function. Pregnancy-associated plasma protein A has been identified as a glycoprotein protease that acts on insulin-like growth factor (IGF)–binding protein (IGFBP), specifically IGFBP-4. Once IGF-1 and IGF-2 are released from their IGFBPs, they promote fetal growth and development through metabolic and differentiation pathways. This provides a biological rationale for PAPP-A influencing fetal-placental growth and development, particularly for an association between low PAPP-A level and poor pregnancy outcome[1-16].

The strength of our study lies in the fact that our prenatal screening programme covers approximately 90% of the population booked at our unit and is free of charge. Accordingly, our study population is highly representative without an oversampling of high-risk pregnancies. However, this is a retrospective study and like all retrospective reviews, it could be subjected to collection and interpretation errors, and bias. The size of our study population made it difficult to study rare, but important, neonatal outcomes such as neonatal death or hypoxic ischaemic encephalopathy. We chose a cut-off of 0.4 MoM for PAPP-A and free beta-hCG levels because this corresponds roughly to the fifth centile, and this cut-off has most often been used in previous studies[1-8]. A lower cut-off could have been relevant, and more clinically applicable, because of a lower screen-positive rate, but the size of our population did not allow us to investigate this cut-off properly.

From previous studies[1-16] and this present study, an unexplained low PAPP-A level (<0.4 MoM) in the first trimester is associated with an increased frequency of adverse obstetrical outcomes but, at present, no specific protocols for monitoring and intervention are available. In our department, we have been performing universal first trimester combined screening for Down syndrome. The proportion of women with low PAPP-A or beta-hCG levels was around 9.0% (394/4367). At present, if the PAPP-A or beta-hCG level is very low (<0.2 MoM), a mid-trimester detailed scan followed by fetal assessment (growth scan plus Doppler ultrasound studies of the umbilical artery and middle cerebral artery) at 28 to 30 weeks will be scheduled after counselling the women. These measures might help in detecting intrauterine growth restriction in the at-risk population.

Conclusion

Low PAPP-A level was significantly associated with adverse neonatal outcomes. These results may be crucial in counselling women and consideration of increased fetal surveillance in such cases.

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Perception of Chinese Pregnant Women of Weight, Obesity and Exercise, and Their Exercise Habits during Pregnancy

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Objective: Obesity is known to be associated with adverse maternal and fetal outcomes. Published guidelines suggest that moderate exercise for up to 30 minutes daily is safe and beneficial during pregnancy. There are nonetheless limited data for a Chinese population. This study examined the perception of pregnant women of weight, obesity and exercise during pregnancy, and their exercise habits before and during pregnancy.
Methods: This was a cross-sectional study conducted at a regional hospital in Hong Kong. Chinese pregnant women who attended an antenatal clinic for an oral glucose tolerance test during their third trimester were asked to complete a questionnaire that covered several domains, including demographic data, perception of weight and obesity in pregnancy, exercise pattern before and during pregnancy, and the perceived safety of exercise during pregnancy. Questionnaires were collected and analysed.
Results: Questionnaires were completed by 712 pregnant women. In all, 23.8% of the study population were diagnosed to have gestational diabetes. Overweight women were more likely to perceive themselves as being of normal weight ($p<0.001$). Although 47.9% of women were aware of the increased risks associated with obesity in pregnancy, only 14.1% of women knew all of the risks listed. Those who exercised before pregnancy and those who were given advice on exercise during pregnancy were more likely to exercise during pregnancy ($p<0.001$). Nonetheless only 4.5% of women who exercised before pregnancy exercised at the recommended level during pregnancy. In addition, 82.3% of women were interested in receiving more information on exercise during pregnancy. Moderate-intensity exercise once or twice per week was considered safe by 69.4% of women, but only 31% considered the same to be so for exercise more than 5 times per week.
Conclusion: Overweight pregnant women were more likely to consider their weight as normal. Awareness of pregnancy complications associated with obesity was generally lacking. Although the majority of pregnant women exercised during pregnancy, only a minor proportion exercised at the recommended level. Most women were keen to have more information about exercise in pregnancy.
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Keywords: Exercise; Obesity; Pregnancy

Introduction

In 2000, the World Health Organization (WHO) defined obesity in the Asian population as a body mass index (BMI) of > 25 kg/m^2 [1]. The reported age-standardised prevalence of obesity in Hong Kong Chinese women was 18.8% in 2005, making it one of the Chinese communities with the highest prevalence of obesity. At the same time, the prevalence of obesity among women in mainland China was 15.4%[2].

Obesity is known to be associated with adverse maternal and fetal outcomes[3], including gestational diabetes, pre-eclampsia, and preterm delivery. A study published in 2008 in Hong Kong confirmed these associations[4], and concluded that a high BMI may have a stronger impact in Chinese pregnant women than in their Caucasian counterparts — the prevalence of women in this study[4] with a BMI of >25 kg/m^2 was 15.8%, comparable to that of the general population.

Moderate exercise is considered beneficial in pregnancy. On the Borg scale of perceived exertion, moderate exercise was rated at 12 to 14 on a scale of 6 to 20[5]. In descriptive terms, moderate exercise was characterised as quickened breathing, but not shortness of breath, light

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sweating, and the ability to continue a conversation but not sing[6]. The prevalence of exercise at the recommended level in pregnancy was 15.8% in the United States[7] and 21.5% in Ireland[8]. In the UK, 42% of women exercised during pregnancy[5].

Excessive weight gain during pregnancy has been reported to be an established predictor of long-term obesity[9]. It also increased deprivation and adverse infant, childhood, and maternal outcomes[9-12]. A national study in the UK[13] suggested focusing on a healthy diet. Level of physical activity, instead of body weight, in management interventions during pregnancy was useful and less stigmatising.

Most studies of weight, obesity, and exercise in pregnancy have involved a Caucasian population and data on Asian populations are limited. Our study aimed to examine the perception of Chinese pregnant women of weight, obesity, and exercise during pregnancy and their exercise habits during pregnancy.

Methods

This was a cross-sectional study performed over a 14-week period between May and August 2013 in the obstetrics department of a regional public hospital in Hong Kong. A universal screening oral glucose tolerance test (OGTT) between 28 and 30 weeks of gestation is offered to all pregnant women who are registered at the hospital for antenatal care. All Chinese women who attended this OGTT and could read Chinese were included. Participants were given written information regarding the objective and details of the study. Written consent for the study was obtained.

Participants were asked to complete on-site a Chinese questionnaire (Appendix) that had been pilot-tested. Demographic data were collected and included parity, education level, occupation, past medical health, current obstetric problems, smoking and drinking habits, and income. Additional data on current height, weight and gestational age as well as that at booking visit were retrieved from the computerised antenatal records system. Body mass index was calculated. Given the small change in body weight during early pregnancy and to avoid recall error in pre-pregnancy weight, body weight at the booking visit was used for BMI calculation. Oral glucose tolerance test results were also retrieved from the system.

Participants were questioned about their perception of their current weight and their weight during the first 3 months of the pregnancy, and whether they perceived themselves to be underweight, normal weight, overweight, or obese. They were also assessed on their knowledge about pregnancy outcomes associated with obesity. Pregnancy complications including gestational diabetes, hypertension and pre-eclampsia, miscarriage, preterm delivery, intrauterine death, venous thromboembolism, fetal intrauterine growth restriction, congenital abnormality, Caesarean section rates, instrumental delivery rates, postpartum sepsis, postpartum haemorrhage, and neonatal death were listed. Participants were also asked whether they considered each complication likely to be increased, decreased or remain unchanged, or if they were uncertain.

Data on exercise habits before pregnancy and during the recent 2 weeks of pregnancy were collected. Exercise pattern was defined by duration of exercise per episode, frequency of exercise per week, and intensity of exercise. Intensity was defined as the magnitude of effort required to perform an activity or exercise. Low intensity exercise was defined as no noticeable change in breathing and the ability to continue full conversation or even sing, for example, a light walk, or household chores such as vacuuming and mopping. Moderate intensity was defined as quickened breathing, but not out of breath, light sweating, and the ability to continue conversation but not sing. Examples were brisk walking and light jogging. High intensity was defined as deep and rapid breathing, the ability to talk only in short phrases, and sweating after 3 to 5 minutes, for example, running. Participants were asked to rate exercise intensity according to the Borg scale of perceived exertion. Participants were also questioned about what advice they were given regarding exercise in pregnancy.

Beliefs about safety of exercise in pregnancy were also assessed. Five exercise intensities were used for safety rating: low intensity, moderate intensity, high intensity, scuba diving, and high impact exercise. Each was subdivided into three categories according to frequency of exercise. Participants were asked to rate safety as very safe, somewhat safe, neutral, somewhat unsafe, or very unsafe.

Gestational diabetes was defined according to the WHO recommendation[14]: fasting plasma glucose level of ≥7 mmol/l or plasma 2-hour OGTT value of ≥11.1 mmol/l, or fasting plasma glucose level of <6.1 mmol/l and plasma 2-hour OGTT value of ≥7.8 but <11.1 mmol/l. Body mass index was categorised according to the WHO criteria[1]: <18.5 kg/m^2 as underweight; 18.5 to 24.9 kg/m^2 as normal weight, 25.0 to 29.9 kg/m^2 as overweight, and ≥30 kg/m^2 as obese.

Ethical Considerations and Statistical Analysis

This study was approved by the Institutional Review Board of the hospital (Ref: HKEC-2013-030). Statistical analysis was performed using PASW Statistics 18, Release Version 18.0.0 (SPSS, Inc., Chicago [IL], US). Categorical data were analysed by Chi-square and Fisher's exact tests. Continuous data with normal distribution were analysed by independent samples *t* test. Highly skewed data were analysed by Mann-Whitney *U* test. The McNemar test was used for dichotomous variables and the McNemar-Bower test was used to compare categorical variables of higher levels. A p value of <0.05 was considered statistically significant.

Results

During the study period, a total of 756 women were approached and 726 questionnaires were collected. The response rate was 96.0%. Of the questionnaires collected, 14 were incomplete and were excluded from analysis. Missing data were also subtracted from the total number as denominators to calculate the percentages.

Demographic Statistics

The mean ± standard deviation age of pregnant women in the study group was 31.6 ± 4.59 years. The median (interquartile range) gestational age at booking visit was 12.4 (12.0-13.4) weeks and at the time of study it was 28.7 (28.4-29) weeks. The mean BMI at booking visit was 21.64 ± 2.93 kg/m^2. Among the study population (i.e. 712 women), 168 (23.8%; after excluding 6 women who failed to complete OGTT) were subsequently diagnosed to have gestational diabetes mellitus. Based on the WHO criteria for BMI grouping, 553 of 705 (78.4%) women had normal weight, 77 (10.9%) were underweight, and 75 (10.6%) were overweight or obese with BMI of ≥25 kg/m^2. There were 442 (62.1%) nulliparous women. Most women (98.7%) had been educated to secondary level or above.

Weight, Obesity, and Pregnancy

Around half of pregnant women (53%; 375/705) were concerned about gaining too much weight in pregnancy. A consultation with doctors regarding weight control in pregnancy was considered the most useful source (54.4%) of information, followed by specific dietary advice (48.9%) and specific physical activity advice (33.9%).

Of those 75 overweight / obese women, about three-quarters (n=55) perceived themselves to be of normal weight during the first 3 months of pregnancy. Nonetheless, at the time of study in the third trimester, only 38 (50%) of women considered their weight normal. Overweight and obese women were more likely to consider themselves to be of normal weight, regardless of whether or not they were concerned about gaining too much weight during pregnancy. There was a significant difference between self-categorised BMI and BMI by WHO criteria (p<0.001; Table 1). Perceived change in weight between the first 3 months of pregnancy and in the third trimester (at the time of study) was also statistically significant (p<0.001; Table 2). In other words, pregnant women considered themselves heavier than they were supposed to be during pregnancy.

With regard to obesity and pregnancy (Table 3), 339 out of 708 (47.9%) women knew that obesity increases the risks in pregnancy. Overall, there was no significant difference in the knowledge of women with BMI of <25 kg/m^2 and those with BMI of ≥25 kg/m^2 (p=0.60).

Regarding knowledge of risk for specific obstetric complications, only 40 (14.1%) women knew that the risk

Table 1. Comparison of self-categorised body mass index in the first 3 months of pregnancy and that according to the WHO criteria (n=705)*

Self-categorisation of body mass index in the first 3 months of pregnancy	Body mass index according to the WHO criteria						p Value
	Underweight (n=77)		Normal weight (n=553)		Overweight / obese (n=75)		
	C	NC	C	NC	C	NC	
Underweight (n=59)	3 (15.8%)	15 (25.9%)	15 (5.0%)	24 (9.5%)	2 (3.8%)	0	<0.001
Normal (n=603)	16 (84.2%)	43 (74.1%)	263 (87.4%)	225 (89.3%)	36 (69.2%)	20 (87.0%)	
Overweight (n=31)	0	0	18 (6.0%)	2 (0.8%)	9 (17.3%)	2 (8.7%)	
Obese (n=12)	0	0	5 (1.7%)	1 (0.4%)	5 (9.6%)	1 (4.3%)	

Abbreviations: C / NC = concerned / not concerned on gaining too much weight in pregnancy; WHO = World Health Organization

* Data are shown as No. (%) and analysed by Fisher's exact test. Missing data were excluded from the calculation of percentages

Table 2. Perception of weight in the first 3 months of pregnancy and current weight at third trimester (n=701)*

Current weight	Weight in the first 3 months of pregnancy				p Value
	Underweight (n=57)	Normal (n=601)	Overweight (n=31)	Obese (n=12)	
Underweight (n=17)	8 (14.0%)	9 (1.5%)	0	0	<0.001
Normal (n=565)	45 (78.9%)	513 (85.4%)	7 (22.6%)	0	
Overweight (n=94)	4 (7.0%)	64 (10.6%)	22 (71.0%)	4 (33.3%)	
Obese (n=25)	0	15 (2.5%)	2 (6.5%)	8 (66.7%)	

* Data are shown as No. (%) and analysed by McNemar-Bowker test (Chi-square statistics=89.427). Missing data were excluded from the calculation of percentages

of all listed items was increased in obese women, even though 42.8% claimed to have received information on obesity and pregnancy. The risks associated with obesity and about which women knew least were neonatal death (22.7%), postpartum haemorrhage (21.4%), and infection after delivery (20%) [Table 3].

Exercise and Pregnancy

Those women with obstetric or medical contra-indications to exercise in pregnancy, according to the guidelines of American College of Obstetricians and Gynaecologists (ACOG[15]), were excluded. Those with previous operations were individually checked for contra-indications and subsequently included. At the time of study, 590 out of 705 (83.7%) women reported no obstetric complications, and among them, 530 (89.8%) had no medical diseases that would exclude exercise in pregnancy. They were then included in this subgroup analysis.

Expression of concern about gaining too much weight in pregnancy did not differ between those who exercised before or during pregnancy. The distribution of self-categorisation of BMI among this subgroup was similar to that of the overall study population.

With regard to knowledge about obesity and pregnancy (Table 3), those who exercised before or during pregnancy were more likely to know there were increased risks than those who did not ($p \leq 0.01$). Of the individuals in this subgroup who got all the items correct, half (n=10) exercised before and during pregnancy, and 26.4% (n=10) exercised either before or during pregnancy.

Around half of the participants (266/527, 50.5%) in this subgroup exercised before pregnancy, similar to those who exercised during the most recent 2 weeks of pregnancy (247/527, 46.9%). The exercise pattern before and during pregnancy is summarised in Table 4. There was no significant difference in BMI distribution between those who exercised before pregnancy and those who did not — significantly more overweight or obese women did not exercise before pregnancy. Also, there was no significant difference in doing exercise before or in the past 2 weeks of pregnancy between those with BMI <25 kg/m^2 and >25 kg/m^2, or any significant difference between those with and without gestational diabetes (Table 4). Those who exercised before pregnancy were more likely to have exercised in the most recent 2 weeks of pregnancy (p=0.01). Women who were nulliparous and who had a higher education level were more likely to exercise before and during their pregnancies (Table 5).

With regard to perception of weight gain during pregnancy (Table 6), a significantly higher proportion of those who did not exercise before or during pregnancy considered the maximal weight gain to be >20 kg. Nonetheless there was a significant difference in the perceived minimal weight gain among the groups with different exercise pattern.

A third of this subgroup population (n=176, 33.3%) were given advice on exercise in pregnancy. Most were advised to perform low-intensity exercise (70.5%) for 15 to 30 minutes (63.1%). The advice on frequency of exercise varied: 36.9% were advised to exercise 3 to 4 times per week and 29.5% were advised 1 to 2 times per week. Women who were given advice on exercise in pregnancy were more likely to exercise during pregnancy (p<0.001; Table 7).

Overall, among those who exercised during pregnancy, the majority (67.5%, n=179) were at a low intensity. Among women who exercised before pregnancy, only 12 (4.5%) performed the recommended moderate exercise, 30 minutes per day and more than 3 times a week during pregnancy (p=0.001; Table 7).

Table 3. Knowledge about obesity and pregnancy (n=712)*

	BMI <25 kg/m²	BMI ≥25 kg/m²	p Value	NEBP	EBP	p Value	NEDP	EDP	p Value
Knowledge about overweight / obesity and pregnancy			0.60			0.01			0.001
There are no risks (n=11)	9 (1.4)	2 (2.7)		5 (1.9)	2 (0.8)		5 (1.9)	2 (0.7)	
There may be risks (n=265)	231 (36.7)	32 (42.7)		86 (33.0)	106 (39.8)		87 (33.3)	107 (39.8)	
There are risks (n=339)	306 (48.6)	32 (42.7)		121 (46.4)	133 (50.0)		117 (44.8)	137 (50.9)	
Do not know (n=93)	84 (13.3)	9 (12.0)		49 (18.8)	25 (9.4)		52 (19.9)	23 (8.6)	
Missing data (n = 4)	Missing data (n = 7)			Missing data (n = 3)					
Birth defect			0.02			0.02			0.01
Increased risk (n=210)	191 (31.4)	19 (26.8)		63 (24.7)	89 (35.5)		59 (23.6)	94 (36.3)	
Decreased risk (n=2)	0	2 (2.8)		1 (0.4)	1 (0.4)		1 (0.4)	1 (0.4)	
No change in risk (n=219)	197 (32.4)	20 (28.2)		84 (32.9)	83 (33.1)		85 (34.0)	82 (31.7)	
Not sure (n=251)	220 (36.2)	30 (42.3)		107 (42.0)	78 (31.1)		105 (42.0)	82 (31.7)	
Missing data (n = 30)	Missing data (n = 33)			Missing data (n = 24)			Missing data (n = 21)		
Diabetes			0.21			0.02			0.02
Increased risk (n=617)	550 (88.1)	64 (87.7)		215 (84.0)	240 (92.0)		214 (83.9)	243 (91.7)	
Decreased risk (n=5)	3 (0.5)	2 (2.7)		3 (1.2)	0		3 (1.2)	0	
No change in risk (n=13)	12 (1.9)	1 (1.4)		6 (2.3)	3 (1.1)		6 (2.4)	3 (1.1)	
Not sure (n=65)	59 (9.5)	6 (8.2)		32 (12.5)	18 (6.9)		32 (12.5)	19 (7.2)	
Missing data (n = 12)	Missing data (n = 15)			Missing data (n = 13)			Missing data (n = 10)		
High blood pressure / pre-eclampsia			0.07			0.03			0.55
Increased risk (n=545)	489 (79.0)	53 (74.6)		189 (73.8)	214 (83.6)		194 (77.0)	211 (80.2)	
Decreased risk (n=4)	2 (0.3)	2 (2.8)		2 (0.8)	0		2 (0.8)	0	
No change in risk (n=24)	20 (3.2)	4 (5.6)		12 (4.7)	6 (2.3)		9 (3.6)	9 (3.4)	
Not sure (n=120)	108 (17.4)	12 (16.9)		53 (20.7)	36 (14.1)		47 (18.7)	43 (16.3)	
Missing data (n = 19)	Missing data (n = 22)			Missing data (n = 18)			Missing data (n = 15)		
Preterm labour			0.22			0.004			0.003
Increased risk (n=407)	368 (59.5)	37 (50.7)		127 (49.4)	165 (64.0)		128 (50.4)	165 (62.5)	
Decreased risk (n=0)	0	0		0	0		0	0	
No change in risk (n=83)	74 (12.0)	8 (11.0)		42 (16.3)	31 (12.0)		48 (18.9)	25 (9.5)	
Not sure (n=205)	177 (28.6)	28 (38.4)		88 (34.2)	62 (24.0)		78 (30.7)	74 (28.0)	
Missing data (n = 17)	Missing data (n = 20)			Missing data (n = 15)			Missing data (n = 12)		
Miscarriage			0.72			0.02			0.12
Increased risk (n=217)	193 (31.6)	22 (31.4)		62 (24.6)	91 (35.8)		64 (25.8)	91 (34.9)	
Decreased risk (n=4)	4 (0.7)	0		2 (0.8)	1 (0.4)		2 (0.8)	1 (0.4)	
No change in risk (n=167)	153 (25.1)	14 (20.0)		67 (26.6)	68 (26.8)		72 (29.0)	63 (24.1)	
Not sure (n=295)	260 (42.6)	34 (48.6)		121 (48.0)	94 (37.0)		110 (44.4)	106 (40.6)	
Missing data (n = 29)	Missing data (n = 32)			Missing data (n = 24)			Missing data (n = 21)		
Stillbirth			0.60			0.03			0.12
Increased risk (n=234)	211 (34.4)	22 (30.6)		70 (27.5)	95 (37.4)		70 (27.8)	96 (36.9)	
Decreased risk (n=2)	2 (0.3)	0		1 (0.4)	1 (0.4)		1 (0.4)	1 (0.4)	
No change in risk (n=156)	141 (23.0)	14 (19.4)		62 (24.3)	66 (26.0)		70 (27.8)	59 (22.7)	
Not sure (n=296)	259 (42.3)	36 (50.0)		122 (47.8)	92 (36.2)		111 (44.0)	104 (40.0)	
Missing data (n = 24)	Missing data (n = 27)			Missing data (n = 21)			Missing data (n = 18)		

Abbreviations: BMI = body mass index; EBP / NEBP = exercise / no exercise before pregnancy; EDP / NEDP = exercise / no exercise during pregnancy

* Data are shown as No. (%) and analysed by Pearson Chi-square test or Fisher's exact test

Table 3. (cont'd)

	BMI <25 kg/m²	BMI ≥25 kg/m²	p Value	NEBP	EBP	p Value	NEDP	EDP	p Value
Thrombosis			0.76			0.06			0.31
Increased risk (n=376)	337 (55.1)	37 (52.1)		129 (51.2)	154 (60.6)		128 (51.8)	156 (59.5)	
Decreased risk (n=7)	7 (1.1)	0		3 (1.2)	3 (1.2)		3 (1.2)	3 (1.1)	
No change in risk (n=55)	49 (8.0)	6 (8.5)		20 (7.9)	25 (9.8)		22 (8.9)	23 (8.8)	
Not sure (n=248)	219 (35.8)	28 (39.4)		100 (39.7)	72 (28.3)		94 (38.1)	80 (30.5)	
Missing data (n = 26)	Missing data (n = 29)			Missing data (n = 24)			Missing data (n = 21)		
Fetal growth retardation			0.48			0.14			0.22
Increased risk (n=194)	175 (28.6)	18 (25.7)		61 (24.1)	76 (30.0)		59 (23.7)	79 (30.4)	
Decreased risk (n=20)	18 (2.9)	2 (2.9)		5 (2.0)	9 (3.6)		5 (2.0)	9 (3.5)	
No change in risk (n=155)	143 (23.4)	12 (17.1)		61 (24.1)	66 (26.1)		64 (25.7)	63 (24.2)	
Not sure (n=315)	275 (45.0)	38 (54.3)		126 (49.8)	102 (40.3)		121 (48.6)	109 (41.9)	
Missing data (n = 28)	Missing data (n = 31)			Missing data (n = 24)			Missing data (n = 21)		
Caesarean delivery			1.00			0.49			0.63
Increased risk (n=482)	431 (69.5)	50 (68.5)		168 (65.6)	180 (70.0)		164 (65.1)	185 (70.1)	
Decreased risk (n=9)	8 (1.3)	1 (1.4)		3 (1.2)	2 (0.8)		3 (1.2)	2 (0.8)	
No change in risk (n=62)	55 (8.9)	7 (9.6)		26 (10.2)	29 (11.3)		28 (11.1)	28 (10.6)	
Not sure (n=143)	126 (20.3)	15 (20.5)		59 (23.0)	46 (17.9)		57 (22.6)	49 (18.6)	
Missing data (n = 16)	Missing data (n = 19)			Missing data (n = 17)			Missing data (n = 14)		
Instrumental delivery			1.00			0.06			0.47
Increased risk (n=403)	360 (58.7)	42 (59.2)		138 (54.8)	157 (61.3)		138 (55.4)	158 (60.3)	
Decreased risk (n=9)	8 (1.3)	1 (1.4)		3 (1.2)	2 (0.8)		3 (1.2)	2 (0.8)	
No change in risk (n=93)	84 (13.7)	9 (12.7)		34 (13.5)	44 (17.2)		37 (14.9)	42 (16.0)	
Not sure (n=182)	161 (26.3)	19 (26.8)		77 (30.6)	53 (20.7)		71 (28.5)	60 (22.9)	
Missing data (n = 25)	Missing data (n = 28)			Missing data (n = 22)			Missing data (n = 19)		
Infection after delivery			0.43			<0.001			0.19
Increased risk (n=137)	121 (19.8)	16 (22.5)		40 (15.7)	63 (24.7)		46 (18.3)	58 (22.2)	
Decreased risk (n=7)	7 (1.1)	0		2 (0.8)	2 (0.8)		3 (1.2)	1 (0.4)	
No change in risk (n=211)	194 (31.7)	17 (23.9)		73 (28.7)	96 (37.6)		77 (30.7)	93 (35.6)	
Not sure (n=331)	290 (47.4)	38 (53.5)		139 (54.7)	94 (36.9)		125 (49.8)	109 (41.8)	
Missing data (n = 26)	Missing data (n = 29)			Missing data (n = 21)			Missing data (n = 18)		
Bleeding after birth			0.99			<0.001			0.31
Increased risk (n=147)	131 (21.4)	15 (21.1)		44 (17.3)	61 (24.1)		46 (18.4)	60 (23.0)	
Decreased risk (n=8)	7 (1.1)	1 (1.4)		2 (0.8)	2 (0.8)		3 (1.2)	1 (0.4)	
No change in risk (n=173)	155 (25.3)	17 (23.9)		57 (22.4)	85 (33.6)		66 (26.4)	76 (29.1)	
Not sure (n=359)	320 (52.2)	38 (53.5)		152 (59.6)	105 (41.5)		135 (54.0)	124 (47.5)	
Missing data (n = 25)	Missing data (n = 28)			Missing data (n = 22)			Missing data (n = 19)		
Neonatal death			0.58			0.57			0.69
Increased risk (n=156)	142 (23.2)	14 (19.7)		57 (22.4)	60 (23.7)		54 (21.6)	64 (24.5)	
Decreased risk (n=3)	3 (0.5)	0		1 (0.4)	0		1 (0.4)	0	
No change in risk (n=146)	133 (21.7)	12 (16.9)		57 (22.4)	65 (25.7)		59 (23.6)	63 (24.1)	
Not sure (n=382)	335 (54.6)	45 (63.4)		140 (54.9)	128 (50.6)		136 (54.4)	134 (51.3)	
Missing data (n = 25)	Missing data (n = 28)			Missing data (n = 22)			Missing data (n = 19)		

Table 4. Exercise pattern before and during pregnancy*

Exercise pattern	BMI <25 kg/m² (n=466)	BMI ≥25 kg/m² (n=61)	p Value	GDM (n=134)	Non-GDM (n=393)	p Value
No exercise before and during pregnancy	180 (39%)	19 (31%)	0.53	54 (40%)	145 (37%)	0.73
No exercise before pregnancy, but exercise during pregnancy	55 (12%)	7 (12%)		14 (10%)	48 (12%)	
Exercise before and during pregnancy	180 (39%)	25 (41%)		52 (39%)	153 (39%)	
Exercise before but not during pregnancy	51 (11%)	10 (16%)		14 (10%)	47 (12%)	

Abbreviations: BMI = body mass index; GDM = gestational diabetes mellitus

* Missing data were excluded from the calculation of percentages

Table 5. Demographic characteristics and exercise pattern*

Characteristic	No exercise in the past 2 weeks	Exercise in the past 2 weeks	p Value
Parity (n=530)			0.003
No	148 (57%)	186 (69%)	
Yes	113 (43%)	83 (31%)	
Education level (n=529)			0.04
Primary or below	3 (1%)	5 (2%)	
Secondary school	143 (55%)	118 (44%)	
Tertiary or above	115 (44%)	145 (54%)	

* Categorical data were analysed by Pearson Chi-square test or Fisher's exact test

Table 6. Perceived maximal weight gain in pregnancy (n=516)*

Exercise pattern	Maximal weight gain (kg)					p Value
	0-4	5-10	11-16	17-20	>20	
No exercise before and during pregnancy	7 (3.6)	50 (25.3)	68 (34.7)	49 (25.0)	22 (11.2)	0.01
No exercise before pregnancy, but exercise during pregnancy	3 (4.8)	7 (11.3)	31 (50.0)	19 (30.6)	2 (3.2)	
Exercise before pregnancy and during pregnancy	4 (2.0)	38 (19.0)	98 (49.0)	53 (26.5)	7 (3.5)	
Exercise before but not during pregnancy	1 (1.7)	8 (13.8)	29 (50.0)	17 (29.3)	3 (5.2)	

* Data are shown as No. (%) of women. Missing data were excluded from the calculation of percentages

Among women who did exercise before pregnancy, the frequency of exercise changed during pregnancy although the duration and intensity was significantly reduced (Table 8). Median (interquartile range) rating by the Borg Scale of perceived exertion during exercise before pregnancy was 13 (11-13) and that during the past 2 weeks of pregnancy was 11 (9-13); this reduction in Borg Scale scoring was statistically significant ($p \leq 0.001$). The main reason given for not exercising during the past 2 weeks of pregnancy was 'never had a habit of doing exercise' (23.6%), followed by 'too tired' (19.2%) and 'no time' (17.2%). Moreover, 11.9% perceived that exercising in pregnancy in general might be or is unsafe.

Overall, 580/705 (82.3%) women were interested in receiving information about exercise during pregnancy. Information leaflets (46.8%) and consultation with doctors (38.9%) were the two most preferred information sources.

Table 9 illustrates the views about safety of exercise during pregnancy, in terms of intensity, frequency, as well as certain types of activities. Over 70% of pregnant women

Table 7. Exercise and pregnancy

	No exercise in the past 2 weeks	Exercise in the past 2 weeks	p Value
Advice on exercise in pregnancy (n=529)*			<0.001
No	212 (81.5%)	141 (52.4%)	
Yes	48 (18.5%)	128 (47.6%)	
Exercise before pregnancy (n=527)*			<0.001
No	199 (76.5%)	62 (23.2%)	
Yes	61 (23.5%)	205 (76.8%)	
Exercise in past 2 weeks (recommended by guidelines)			0.001
Yes	0	12 (4.5%)	
No	261 (100%)	254 (95.5%)	
Missing data (n=3)			

* Data were analysed by McNemar test

Table 8. Change in frequency, duration, and intensity of exercise among pregnant women who exercise before and during pregnancy*

	Before pregnancy				p Value
Frequency during pregnancy/week (n=198)	**<1 Time/week**	**1-2 Times/week**	**3-4 Times/week**	**>4 Times/week**	
<1 Time	15 (40.5)	8 (9.5)	3 (6.3)	0	0.14
1-2 Times	14 (37.8)	61 (72.6)	9 (18.8)	1 (3.4)	
3-4 Times	4 (10.8)	9 (10.7)	30 (62.5)	4 (13.8)	
>4 Times	4 (10.8)	6 (7.1)	6 (12.5)	24 (82.8)	
Duration during pregnancy (n=200)	**<15 Minutes**	**15-30 Minutes**	**31-60 Minutes**	**>60 Minutes**	
<15 Minutes	22 (84.6)	13 (14.3)	4 (6.5)	3 (14.3)	<0.001
15-30 Minutes	4 (15.4)	71 (78.0)	19 (30.6)	7 (33.3)	
31-60 Minutes	0	7 (7.7)	36 (58.1)	3 (14.3)	
>60 Minutes	0	0	3 (4.8)	8 (38.1)	
Intensity during pregnancy (n=201)	**Low**	**Moderate**	**High**		
Low	87 (92.6)	31 (42.5)	18 (52.9)		<0.001
Moderate	5 (5.3)	40 (54.8)	16 (47.1)		
High	2 (2.1)	2 (2.7)	0		

* Data are shown as No. (%) of women and analysed by McNemar-Bower test

considered low intensity exercise to be safe regardless of frequency. Consideration of the safety of moderate-intensity exercise decreased with increasing exercise frequency. While 69.4% of women considered moderate-intensity exercise 1 to 2 times per week to be safe, only 31% women considered it safe when the frequency increased to more than 5 times a week. In general, women regarded high-intensity exercise during pregnancy to be unsafe. Most women considered high impact exercise (95.9%) such as skiing and horse-riding, and scuba diving (92.7%) unsafe.

Discussion

Both ACOG[15] and Royal College of Obstetricians and Gynaecologists (RCOG)[5] have published guidelines about exercise in pregnancy. Both Colleges recommend 30 minutes of moderate exercise per day up to daily in the absence of obstetric and medical contra-indications. Exercise improves health and wellbeing and is considered safe and beneficial in pregnancy. A sedentary lifestyle during pregnancy contributes to excessive weight gain, frequent physical complaints, and increased risks of

Table 9. Safety of different types of exercise in pregnancy*

Item	Very safe	Somewhat safe	Neither safe or unsafe	Somewhat unsafe	Very unsafe
Low intensity					
(1-2 times per week) [n=668]	527 (78.9)	91 (13.6)	46 (6.9)	2 (0.3)	2 (0.3)
(3-5 times per week) [n=674]	402 (59.6)	176 (26.1)	80 (11.9)	14 (2.1)	2 (0.3)
(>5 times per week) [n=664]	315 (47.4)	152 (22.9)	143 (21.5)	42 (6.3)	12 (1.8)
Moderate intensity					
(1-2 times per week) [n=672]	225 (33.5)	241 (35.9)	164 (24.4)	35 (5.2)	7 (1.0)
(3-5 times per week) [n=666]	97 (14.6)	232 (34.8)	235 (35.3)	91 (13.7)	11 (1.7)
(>5 times per week) [n=653]	41 (6.3)	161 (24.7)	275 (42.1)	138 (21.1)	38 (5.8)
High intensity					
(1-2 times per week) [n=679]	26 (3.8)	78 (11.5)	189 (27.8)	242 (35.6)	144 (21.2)
(3-5 times per week) [n=654]	5 (0.8)	26 (4.0)	148 (22.6)	276 (42.2)	199 (30.4)
(>5 times per week) [n=656]	4 (0.6)	16 (2.4)	107 (16.3)	262 (39.9)	267 (40.7)
Scuba diving (n=679)	3 (0.4)	9 (1.3)	38 (5.6)	141 (20.8)	488 (71.9)
High impact exercise (e.g. skiing, horse-riding) [n=678]	2 (0.3)	3 (0.4)	23 (3.4)	46 (6.8)	604 (89.1)

* Data are shown as No. (%) of women

gestational diabetes and pre-eclampsia. Exercise benefited pregnant women both physically and psychologically. Common complaints in pregnancy such as fatigue and varicosities were reduced. Active women experienced less insomnia, stress, anxiety, or depression. Weight-bearing exercise reduced the length of labour and lessened delivery complications[16-19].

Our study population had a similar age distribution to the general obstetric population and compared with the Hong Kong Territory-wide Audit in 2004[20]. A previous study[4] estimated the prevalence of pregnant women with a BMI of ≥25 kg/m^2 at booking visit to be 16.8%: the prevalence in our study was 10.5%. We performed our study at the time of routine OGTT in pregnancy, around 28 weeks. A small proportion of women with risk factors such as obesity and a history of gestational diabetes had already undergone OGTT at 16 to 18 weeks. Those who were diagnosed at this time to have gestational diabetes did not undergo the 28-week gestation OGTT. This might have contributed to the slightly lower incidence of women with BMI of ≥25 kg/m^2 in this study population, although the number of women who did not undergo 28-week OGTT was small.

The prevalence of gestational diabetes in our study was 23.8%, much higher than the reported 6.3% in the 2004 Territory-wide Audit[20]. Although this may be due to differences in diagnostic criteria, there has been a notable increase in the incidence of gestational diabetes in more recent years. Previous audit revealed that the incidence doubled between 1994 and 2004[20]. Leung et al[4] determined that 22.9% and 15.2% of women with BMI of ≥30 kg/m^2 and BMI between ≥25 and <27 kg/m^2 had gestational diabetes, respectively. Furthermore, universal screening is likely to detect more women with gestational diabetes in the low-risk population. The prevalence of gestational diabetes in our unit was 25.8%[21]. Although our study showed no significant difference in exercise pattern between those with and without gestational diabetes, it demonstrates that the prevalence of gestational diabetes may be greater than previous statistics. This further emphasises the need to raise awareness of gestational diabetes that is more common in obese pregnant women[22].

Just over 50% of women were concerned about gaining too much weight in pregnancy. Our study revealed that they generally perceived themselves to be heavier than they were supposed to be at the time of study. This might reflect their false perception of gaining too much weight during the course of pregnancy, although this might not be a concern to the pregnant women themselves. Contrary to this, overweight women were more likely to consider themselves to be normal in weight; this reflects a need for

better education about weight change during pregnancy.

Current public health education emphasises the association of obesity with hypertension and diabetes in the general population and therefore, not surprisingly, more than 75% of women in our study were aware that obesity increases the risk of hypertension and diabetes in pregnancy. A study in the US revealed that only a small proportion of pregnant women were counselled about the risks associated with obesity[23]. While 42.8% of women in our study claimed to have received information on risks related to obesity in pregnancy, only 14.1% knew about the increased risk for all listed items. Knowledge of specific obesity-associated obstetric complications, such as neonatal death, postpartum haemorrhage, and infection after delivery was poor. These results indicate a need for enhanced public education about the adverse effects of obesity in pregnancy specifically.

The Institute of Medicine and the National Research Council in the US has issued guidelines for gestational weight gain[9], whereby women who are underweight, normal weight, overweight, or obese should gain 12.5 to 18 kg, 11.5 to 16 kg, 7 to 11.5 kg and 5 to 9 kg, respectively. Those who did not exercise before and during pregnancy are clearly the target group of higher priority for education and intervention, especially when they perceive exercise weight gain as appropriate.

Exercise pattern in the 2 weeks prior to the study was used to indicate exercise pattern in pregnancy. This assumption was valid according to a prospective cohort in the UK[24]. In that study, the prevalence of physical activity, with sweating for 3 hours or more a week, was similar at 18 weeks and 32 weeks of gestation. Although 46.9% of pregnant women exercised during pregnancy in our study, only 4.5% exercised at the recommended level. In contrast, the prevalence was higher than other overseas studies (15.8% in the US[7], 48.8% in the UK[25], and 21.5% in Ireland[8]). Women who habitually exercised before pregnancy and who had not delivered previously were more likely to exercise during pregnancy. Women with higher education level were likely to be more health conscious and aware of the benefits and safety of exercise — these findings have also been illustrated in other studies[25,26] Demographic characteristics should be taken into consideration when distributing realistic advice about exercise in pregnancy.

Our study shows that the availability of advice about exercise significantly altered the attitudes to exercising in pregnancy: women who were given advice were more likely to exercise. Nonetheless despite the recommendation for moderate exercise 30 minutes per day, more than 3 times a week for previously active women, they were commonly advised to perform only low-intensity exercise for 15 to 30 minutes. Irrespective of their health status, most (82.3%) women were eager to receive information about physical activities and exercising in pregnancy. The perceived most effective sources of information were information leaflets, specific advice on physical activity, and consultation with doctors during antenatal visits. This illustrates the important role of health care professionals in encouraging exercise and physical activity during pregnancy, and in being proactive in disseminating appropriate advice. Although exercise alone does not prevent excessive weight gain or obesity in pregnancy, it has been shown that physically active women are more likely to continue exercising after delivery. This was, in general, an important public health issue in weight management.

It is not surprising to find that pregnant women who did not exercise before pregnancy did not exercise during pregnancy either. Nonetheless, sedentary women were advised to commence exercising for 15 minutes, 3 times a week, increasing gradually to 30-minute sessions, 4 times a week[5].

Our study examined the exercise pattern at two time-points, pre-pregnancy and at around 28 weeks of gestation. Although we did not examine when women started exercising during pregnancy or demonstrate the change in exercise patterns across gestations, our study does illustrate that exercise duration and intensity are significantly lower during pregnancy than before.

Among women who did not exercise in pregnancy, 11.9% perceived that exercising in pregnancy in general might be or is unsafe. Over 70% of pregnant women considered low-intensity exercise to be safe regardless of frequency. In contrast, the perception of safety of moderate-intensity exercise decreased with increasing frequency. This shows that safety is one of the perceived barriers to exercising during pregnancy.

Further study of the perceived benefits of exercise may provide insight into the potential motivation to exercise during pregnancy. Views of health care professionals on exercise in pregnancy may also be explored. This may provide guidance on effective means of information dissemination and can also improve antenatal counselling as well as general public health education.

Conclusion

In this study, overweight women generally perceived their weight to be normal and an awareness of the pregnancy complications associated with obesity was generally lacking. Although about half of the study pregnant women exercised during pregnancy, only a small proportion exercised at the recommended level. Public education to enhance awareness of obesity and its associated risks in pregnancy is needed. Promotion of exercise among pregnant women is beneficial.

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Appendix. Questionnaire for this study

臨床調查同意書

臨床調查之題目：香港孕婦對於懷孕期間體重和運動的看法

主要調查者：東區尤德夫人那打素醫院婦產科駐院醫生羅欣珮醫生

聯絡電話：2595 6111

這項調查是本人在本院婦產科的覆診孕婦中進行的一項問卷調查。

這項問卷需時約5分鐘，而且是全自願性質的。您可隨時終止參與。終止參與不會影響您現有或日後接受的醫療護理服務。

這調查的目的是調查香港孕婦對懷孕期間的體重、體重增加和運動各方面的意見。

本調查希望提升孕婦對懷孕期間體重之重要性的認知，以及院方於將來之資源分配，及提供有關上述主題的資訊予孕婦時作參考之用。

如果你曾經填寫過這份問卷，請不用再次填寫。

私隱保障：你所填寫的資料將被視為機密，只有主要調查者及指定東區尤德夫人那打素醫院婦產科負責人員才可檢視你的資料。這份問卷所收集的個人資料將會於完成研究五年後被銷毀。

如果你同意參與這項問卷調查，請簽署及完成所附問卷，以及保留這頁同意書作參考。

多謝你的參與

參與者簽署：

日期：

Appendix. (cont'd)

東區尤德夫人那打素醫院婦產科
臨床調查：香港孕婦對於懷孕期間體重和運動的看法

Official use only
Gestation at OGTT: _____
Weight at OGTT: _____ (kg)

Label

Gestation at first visit: _____
Height: _____ (cm)
Weight at FIRST visit: _____ (kg)
BMI at FIRST visit: _____

Addition notes: _____

請✓適當的方格

背景資料

1. **您有沒有生過小孩子?**
   - ☐ 沒有—請到第2題
   - ☐ 有:
     - (a) 多少個? _____
     - (b) 對上一次生小孩子是什麼時候? (月份/年份) _____
     - (c) 對上一次分娩週數是: 懷孕 _____ 週
     - (d) 上一次生小孩子和這次懷孕之間, 您的體重:
       - ☐ 返回到上一次懷孕前的體重
       - ☐ 增加了1-3公斤
       - ☐ 增加了3-5公斤
       - ☐ 增加了多於 5公斤
       - ☐ 不清楚
       - ☐ 比上一次懷孕前的體重減輕了
2. **教育程度**
   - ☐ 小學
   - ☐ 中學
   - ☐ 大學/大專或以上
3. **職業**
   - ☐ 文職/秘書
   - ☐ 教育專業人士/老師
   - ☐ 行政人員
   - ☐ 學生
   - ☐ 商業/會計/建築師/律師
   - ☐ 家庭主婦
   - ☐ 飲食/美容/其他服務行業
   - ☐ 醫護人員
   - ☐ I.T./廣告電視行業
   - ☐ 其他，請列明: _____

Appendix. (cont'd)

4. **請問您有沒有以下病歷?**
   - ☐ 糖尿病（不包括妊娠糖尿病）
   - ☐ 高血壓
   - ☐ 心臟病，請列明: _____
   - ☐ 哮喘/呼吸系統疾病，請列明: _____
   - ☐ 自體免疫性疾病，請列明: _____
   - ☐ 肌肉與骨骼的疾病，請列明: _____
   - ☐ 接受手術：(不包括剖腹產子)
     請列明: _____
   - ☐ 其他，請列明: _____
   - ☐ 沒有以上情況

5. **您有沒有吸煙的習慣?** 有 ☐ 沒有 ☐ 已戒煙 ☐
   如有，你每天抽多少支煙: _____

6. **您有沒有喝酒的習慣?** 有 ☐ 沒有 ☐ 已戒酒 ☐
   如有，你每天喝多少? _____

7. **您有沒有濫用藥物?** 有 ☐ 沒有 ☐ 已戒 ☐
   如有：(a) 哪種藥物? _____
   (b) 多久一次? 1個月 _____次

8. **家庭每月收入**
   - ☐ <$10,000
   - ☐ >$10,000-30,000
   - ☐ >$30,000-50,000
   - ☐ >$50,000

9. **到目前為止，您懷孕期間 曾否有以下情況?**
   - ☐ 持續陰道出血
   - ☐ 低位胎盤
   - ☐ 多胎妊娠
   - ☐ 穿羊水/羊水過少
   - ☐ 先兆早產
   - ☐ 胎兒生長遲緩
   - ☐ 沒有以上情況

關於體重和懷孕期間的體重增長

10. **您曾否接收或閱讀有關懷孕期間過重/肥胖的資訊?**
    - ☐ 沒有
    - ☐ 有 →資訊來源:
      - ☐ 醫護人員
      - ☐ 互聯網
      - ☐ 資訊單張
      - ☐ 講座
      - ☐ 其他, 請列明: _____

11. **您認為:**
    (a) 您懷孕首3個月的體重是：
    - ☐ 過輕
    - ☐ 正常
    - ☐ 過重
    - ☐ 肥胖

    (b) 您現時的體重是：
    - ☐ 過輕
    - ☐ 正常
    - ☐ 過重
    - ☐ 肥胖

Appendix. (cont'd)

12. 您認為在整個懷孕期間, 您的體重應該:

(a) 最少增長多少?

☐ 0-4公斤
☐ 5-10公斤
☐ 11-16公斤
☐ 17-20公斤
☐ >20公斤

(b) 最多增長多少?

☐ 0-4公斤
☐ 5-10公斤
☐ 11-16公斤
☐ 17-20公斤
☐ >20公斤

13. 您曾否擔心懷孕期間體重增長過多?

☐ 擔心
☐ 不擔心

14. 您認為以下哪項最能夠協助您在懷孕期間維持理想體重? (可選多項)

☐ 資訊單張
☐ 關於妊娠期的飲食講座
☐ 關於妊娠期的運動講座
☐ 產前檢查期間與醫生討論
☐ 互聯網/電郵
☐ 其他，請列明: _____

<u>關於過重 / 肥胖和懷孕的認知</u>

15. 孕婦如有肥胖的情況：

☐ 不會增加懷孕風險
☐ 可能增加懷孕風險
☐ 會增加懷孕風險
☐ 我不知道會否增加懷孕風險

16. 懷孕期間, 肥胖和以下情況有什麼的關係?

請✓適當的方格

	增加風險	減少風險	沒有關係	不知道
(a) 嬰兒先天缺陷	☐	☐	☐	☐
(b) 糖尿病	☐	☐	☐	☐
(c) 血壓高/先兆子癇	☐	☐	☐	☐
(d) 早產	☐	☐	☐	☐
(e) 小產	☐	☐	☐	☐
(f) 胎死腹中	☐	☐	☐	☐
(g) 血管栓塞	☐	☐	☐	☐
(h) 胎兒生長遲緩	☐	☐	☐	☐
(i) 需要剖腹生產	☐	☐	☐	☐
(j) 需要助產	☐	☐	☐	☐
(k) 產後感染	☐	☐	☐	☐
(l) 產後出血	☐	☐	☐	☐
(m) 新生兒死亡	☐	☐	☐	☐

Appendix. (cont'd)

關於運動與妊娠

運動的強度可以分為3個程度:

- 輕度運動：運動時呼吸沒有明顯變化，可以如常的交談，甚至唱歌，例如：散步，做家務（如吸塵，拖地）
- 中度運動：運動時呼吸加快，輕微出汗，可以交談，但不能唱歌，如急步行走，慢步跑
- 強度運動：運動時-呼吸急促，只能說短語，3-5分鐘內已出汗，如快步跑

17. 產前檢查以來，您曾否接收或閱讀有關懷孕期間運動的建議?

☐ 沒有 -> 請到第18題

☐ 有 -> 得到的建議是：

(a) 運動的頻率 / 次數：

☐ 少於一星期一次
☐ 一星期一至兩次
☐ 一星期三至四次
☐ 多於一星期四次
☐ 沒有提及

(b) 每次運動的時間：

☐ <15分鐘
☐ 15-30分鐘
☐ 31-60分鐘
☐ 多於60分鐘
☐ 沒有提及

(c) 運動的強度：

☐ 輕度運動：運動時呼吸沒有明顯變化，可以如常的交談，甚至唱歌，例如：散步，做家務（如吸塵，拖地）
☐ 中度運動：運動時呼吸加快，輕微出汗，可以交談，但不能唱歌，如急步行走，慢步跑
☐ 強度運動：運動時呼吸急促，只能說短語，3-5分鐘內已出汗，如快步跑
☐ 沒有提及

18. 您會否想知道更多關於運動與妊娠的資訊?

☐ 不會 -> 請到第19題

☐ 會，以什麼形式?(可選最多3項)

☐ 資訊單張
☐ 關於妊娠期的飲食講座
☐ 關於妊娠期的運動講座
☐ 產前檢查期間與醫生討論
☐ 互聯網/電郵
☐ 其他，請列明: _____

Appendix. (cont'd)

19. **在這次懷孕前，您有沒有運動的習慣?**
    - ☐ 沒有 -> 請到第20題
    - ☐ 有 -> 如有：
      - (a) 運動的頻率/次數：
        - ☐ 少於一星期一次
        - ☐ 一星期一至兩次
        - ☐ 一星期三至四次
        - ☐ 多於一星期四次
      - (b) 每次運動的時間：
        - ☐ <15分鐘
        - ☐ 15-30分鐘
        - ☐ 31-60分鐘
        - ☐ 多於60分鐘
      - (c) 運動的強度:
        - ☐ 輕度運動：運動時呼吸沒有明顯變化，可以如常的交談，甚至唱歌，例如: 散步，做家務（如吸塵，拖地）
        - ☐ 中度運動：運動時呼吸加快，輕微出汗，可以交談，但不能唱歌，如急步行走，慢步跑
        - ☐ 強度運動：運動時呼吸急促，只能説短語，3-5分鐘內已出汗，如快步跑
20. **在過去兩星期間，您有沒有做運動?**
    - ☐ 沒有 -> 請到第21題
    - ☐ 有 -> 請到第22題
21. **在過去兩星期間沒有做運動的原因是 (可選多項)：**
    - ☐ 沒有做運動的習慣
    - ☐ 不喜歡做運動
    - ☐ 過於勞累
    - ☐ 身體不適
    - ☐ 沒有時間
    - ☐ 認為懷孕期間做運動不安全
    - ☐ 不清楚懷孕期間做運動是否安全
    - ☐ 醫護人員建議不應做運動
    - ☐ 家人和朋友建議不應做運動
    - ☐ 其他，請列明：_____

→請到第23題

22. **在過去兩星期間，您做運動的**
    - (a) 頻率 / 次數：
      - ☐ 少於一星期一次
      - ☐ 一星期一至兩次
      - ☐ 一星期三至四次
      - ☐ 多於一星期四次
    - (b) 每次運動的時間：
      - ☐ <15分鐘
      - ☐ 15-30分鐘
      - ☐ 31-60分鐘
      - ☐ 多於60分鐘
    - (c) 運動的強度
      - ☐ 輕度運動：運動時呼吸沒有明顯變化，可以如常的交談，甚至唱歌，例如：散步，做家務（如吸塵，拖地）
      - ☐ 中度運動：運動時呼吸加快，輕微出汗，可以交談，但不能唱歌，如急步行走，慢步跑
      - ☐ 強度運動：運動時呼吸急促，只能説短語，3-5分鐘內已出汗，如快步跑

Appendix. (cont'd)

23. 運動的強度

另一個量度或決定運動時強度的方法，就是採用由瑞典心理學家 Gunnar Borg（1970，1985，1994，1998）發展出來的〈感覺盡力程度評級表〉。< Rate of Perceived Exertion >(RPE) 評級表讓參與者藉著運動時的自身感覺（心跳、呼吸、排汗、肌肉疲勞等），來估計運動時的強度。評級表的數值範圍是由 6 至 20（見下表）。

6 是指"完全沒有用力的感覺，而20是指"竭盡能力，必須停止"。

評級	評級描述	例子
6	完全沒有用力的感覺	
7	極之輕鬆	
8		
9	非常輕鬆	按自己的步調慢慢走
10		
11	輕鬆	
12		
13	有點辛苦	可以繼續
14		
15	辛苦	
16		
17	非常辛苦	非常費勁，需要很努力很才可繼續
18		
19	極之辛苦	對於大多數人來說，這是他們曾經做過的最劇烈的運動
20	竭盡能力	虛脫，必須停止

如果以以上的評級來描述您的運動的強度, 您會怎樣評級:

i. 您在這次懷孕前每次運動的強度：_____

(如果你懷孕前沒有做運動，請不用填寫，請到第24題)

ii. 您在過去兩星期間每次運動的強度：_____

(如果你過去兩星期間沒有做運動，請不用填寫，請到第24題)

<u>關於在懷孕期間運動的安全</u>

24. 您對懷孕期間運動的安全性的看法

運動的頻率/強度	非常安全	偏於安全	中立	偏於不安全	非常不安全
(a) 輕度運動					
(i) 一星期1至2次	☐	☐	☐	☐	☐
(ii) 一星期3至5次	☐	☐	☐	☐	☐
(iii) 一星期多於5次	☐	☐	☐	☐	☐
(b) 中度運動					
(i) 一星期1至2次	☐	☐	☐	☐	☐
(ii) 一星期3至5次	☐	☐	☐	☐	☐
(iii) 一星期多於5次	☐	☐	☐	☐	☐
(c) 強度運動					
(i) 一星期1至2次	☐	☐	☐	☐	☐
(ii) 一星期3至5次	☐	☐	☐	☐	☐
(iii) 一星期多於5次	☐	☐	☐	☐	☐
(d) 潛水	☐	☐	☐	☐	☐
(e) 高衝擊力的運動，例如騎馬，滑雪	☐	☐	☐	☐	☐

輕度運動：運動時呼吸沒有明顯變化，可以如常的交談，甚至唱歌，例如：散步，做家務（如吸塵，拖地）

中度運動：運動時呼吸加快，輕微出汗，可以交談，但不能唱歌，如急步行走，慢步跑

強度運動：運動時呼吸急促，只能說短語，3-5分鐘內已出汗，如快步跑

謝謝您的參與

Companionship during Labour: Attitudes and Expectations of Hong Kong Chinese

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Objectives: To assess the attitudes and expectations of Hong Kong women and their partners toward companionship during labour.
Methods: A prospective questionnaire survey was conducted from February to July 2013 in a regional obstetric unit. A total of 450 Hong Kong Chinese women carrying a singleton pregnancy in cephalic presentation at term, and their partners were enrolled. Questionnaires were distributed to the women and their partners when they attended the out-patient clinic or when they were admitted to the antenatal ward.
Results: A total of 315 women and 197 partners completed the self-administered questionnaires, of whom 96% of women and 93% of partners considered emotional support as the major element of companionship during labour. There were significantly more partners than women who considered taking photographs / videos to be one of the elements of companionship during labour. Around 78% of women wished for companionship, while 83% of partners planned to accompany the labour. Among the women who planned for companionship, they were significantly more educated, and a higher proportion were either born in Hong Kong or had been resident for more than 7 years compared with those who did not.
Conclusion: Companionship during labour was highly acceptable among women and partners.
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Keywords: Attitude; Friends; Labor, obstetric; Parturition; Social support

Introduction

Childbirth is a stressful physical and psychological experience in a woman's life, requiring optimal coping strategies. According to a Cochrane review[1], women who received continuous psychological support from companionship during labour were more likely to give birth naturally. These women were less likely to use analgesics, more likely to be satisfied with their labour experience, and had slightly shorter duration of labour. Their babies were less likely to have a low 5-minute Apgar score. As no adverse effects were identified from such companionship, continuous support during labour was recommended for all women.

In actual clinical practice, there are a wide range of cultural and societal differences in childbirth support systems. In developed countries, the main social supporters are usually the partners or close relatives[2,3]. In contrast, in many developing countries like South America and Africa, companionship during labour (CDL) is not routine[4,5]. In Hong Kong, CDL has been advocated for several decades[6].

This study aimed to assess the attitudes and expectations of Hong Kong Chinese women and their partners regarding CDL.

Methods

Participants

The present study was conducted at the United Christian Hospital, Hong Kong, from February to July 2013. Hong Kong Chinese women carrying a singleton pregnancy in cephalic presentation at 37 weeks or more were recruited either from the antenatal clinic or ward. Both the women and their partners were invited to complete a self-administered questionnaire written in Chinese. Subjects

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who were recruited in the clinic were recorded to avoid duplication of questionnaire distribution when they were subsequently admitted to the ward. Women with a fetus in non-cephalic presentation, with multiple gestations, and those scheduled for elective Caesarean section or of non-Chinese ethnic origin were excluded from recruitment.

Questionnaire

The assessment was carried out by a self-administered questionnaire. There were two sets of slightly different questionnaires distributed for the women and their partners. They were advised to complete the questionnaires separately without any discussion among themselves. Each of them was asked specific questions about their opinion of CDL. Information about the expectations of CDL, views on suitability of CDL in different clinical situations, desire for CDL, and the reasons were collected. In addition, their views on the need for antenatal childbirth education classes and their feelings about the attitudes of staff towards CDL were explored. Finally, demographic data were collected and correlated with the data obtained from the questionnaires.

Ethical Consideration

The study was approved by the hospital research ethics committee prior to recruitment of participants. Written informed consent was obtained.

Sample Size

Assuming the population from which samples were drawn was 900 for 3 months, with an expected prevalence of preference for CDL at around 50%, and allowing a 95% confidence level, the sample size for this study would be 269.

Data Analysis

Statistical analysis was performed with the Statistical Package for the Social Sciences Windows version 15.0 (SPSS Inc., Chicago [IL], US). Means and standard deviations were calculated for continuous variables, while Student's *t* test was used to assess means between groups. Chi-square test or Fisher's exact test were used for proportions. Significance was established at p values of <0.05.

Results

A total of 450 eligible women and their partners were invited to participate in this study: 315 women and 197 partners returned their questionnaire during the 6-month period with an overall response rate of 70% and 44%, respectively.

A great majority (99% of women and 98% of their partners) were aware of the meaning of CDL. With reference to their precise understanding of the meaning, women and their partners largely shared the same view. Within this cohort, 96% of women and 93% of partners considered emotional support as the major element of CDL (p=0.15). Other elements of CDL included making decisions together (52% of women vs. 48% of partners; p=0.40), physical support (31% of women vs. 35% of partners; p=0.42), and cutting the umbilical cord (21% of women vs. 21% of partners; p=0.86). There were significantly more partners than women who considered taking photographs / videos as one of the elements of CDL (1% of women vs. 20% of partners, $p<0.001$).

With regard to the expectations of the effects of CDL, the majority of women and their partners expected CDL to have positive effects on the progress of labour, to reduce labour pain, increase chance of spontaneous vaginal delivery, increase labour satisfaction, and decrease postnatal depression. Paradoxically, more women than partners believed CDL could reduce blood loss during delivery (23.6% vs. 14.2%, p=0.03) while more partners believed CDL would reduce episiotomy rates (19.3% vs. 12.1%, p=0.04). In contrast, most women and their partners considered CDL had no major effects on use of oxytocin, as well as the health of newborn or breastfeeding rates (Table 1).

When understanding suitability of CDL, while 98% of both women and partners agreed that CDL was appropriate for spontaneous vaginal delivery, around half suggested that it could also be continued when assisted vaginal delivery or emergency Caesarean section was required (Table 2).

Regarding the nature of the supporters during labour, most women recommended their partner (97%). Other suitable persons included mother (30%), sisters (13%), and friends (4%). If women were allowed to choose only one individual to accompany them, 95% would choose their partners, 4% their mothers, and less than 1% their sisters or friends.

Around 78% of women wished for CDL while 83% of their partners planned to accompany the labour. The top three supporting reasons were to provide support to the women, provide emotional security to the women, and witness the birth of the newborn. Of those women who did not prefer CDL, the top three reservations were distraction due to CDL, embarrassment, and their partners being busy

Table 1. Expectations of effects of companionship during labour*

	Women (n=313†)			Partners (n=197)			p Value
	Positive effects	Negative effects	No effects	Positive effects	Negative effects	No effects	
Progress of labour	170 (54.3)	2 (0.6)	141 (45.0)	117 (59.4)	3 (1.5)	77 (39.1)	0.28
Reduce pain	186 (59.4)	3 (1.0)	124 (39.6)	118 (59.9)	1 (0.5)	78 (39.6)	0.85
Reduce blood loss	74 (23.6)	1 (0.3)	238 (76.0)	28 (14.2)	1 (0.5)	168 (85.3)	0.03
Reduce use of oxytocin	91 (29.1)	0	222 (70.9)	70 (35.5)	0	127 (64.5)	0.13
Less episiotomy	38 (12.1)	0	275 (87.9)	38 (19.3)	0	159 (80.7)	0.04
Increase chance of spontaneous vaginal delivery	200 (63.9)	1 (0.3)	112 (35.8)	135 (68.5)	0	62 (31.5)	0.43
Improve health of newborn	108 (34.5)	2 (0.6)	203 (64.9)	74 (37.6)	1 (0.5)	122 (61.9)	0.77
Increase satisfaction	234 (74.8)	0	79 (25.2)	142 (72.1)	0	55 (27.9)	0.50
Decrease postnatal depression	236 (75.4)	3 (1.0)	74 (23.6)	150 (76.1)	0	47 (23.9)	0.39
Increase breastfeeding rate	54 (17.3)	1 (0.3)	258 (82.4)	36 (18.3)	0	161 (81.7)	0.70

* Data are shown as No. (%) of subjects
† 2 Subjects did not complete this part of questions

Table 2. Attitudes on suitability of companionship during labour*

	Women (n=312†)		Partners (n=197)		p Value
	Suitable	Not suitable	Suitable	Not suitable	
Spontaneous vaginal delivery	305 (97.8)	7 (2.2)	193 (98.0)	4 (2.0)	0.86
Assisted delivery	174 (55.8)	138 (44.2)	102 (51.8)	95 (48.2)	0.38
Elective Caesarean section	153 (49.0)	159 (51.0)	84 (42.6)	113 (57.4)	0.16
Emergency Caesarean section	89 (28.5)	223 (71.5)	49 (24.9)	148 (75.1)	0.37
First stage	258 (82.7)	54 (17.3)	148 (75.1)	49 (24.9)	0.06
Second stage	265 (84.9)	47 (15.1)	160 (81.2)	37 (18.8)	0.27
Third stage	243 (77.9)	69 (22.1)	148 (75.1)	49 (24.9)	0.47

* Data are shown as No. (%) of subjects
† 3 Subjects did not complete this part of questions

at work. For the partners, the top three reservations were distraction, being afraid of blood, and witnessing the pain of the woman in labour (Table 3).

Those who opted for CDL were significantly more likely to have received tertiary education, be born in Hong Kong, and have stayed in Hong Kong for more than 7 years, compared with those who opted not to have CDL (Table 4). Similarly, there were also significantly more partners who had stayed in Hong Kong for more than 7 years among those opting for CDL. There were no differences between the two groups in age, marital status, occupational categories, or household income.

About half of the women and their partners considered antenatal childbirth education classes essential. Women and their partners were also asked to rate their feeling about attitudes of staff in supporting CDL on a visual analogue scale from 0 to 10. The score given by women who opted for CDL was significantly higher than that given by those refused (7.9 vs. 7.0, p=0.01). There was a similar but non-significant trend among partners (7.6 vs. 7.0, p=0.09).

Discussion

Based on the data from this survey, there was a high overall understanding by pregnant women and their

Table 3. Acceptability of companionship during childbirth*

	Data†	
Noted benefit(s) of companionship	**Women (n=246)**	**Partners (n=164)**
CDL has positive effect on delivery	94 (38.2)	62 (37.8)
CDL is the responsibility of partner	29 (11.8)	48 (29.2)
Support the mother	150 (61.0)	127 (77.4)
Reduce stress	87 (35.4)	63 (38.4)
Provide emotional security to mother	149 (60.6)	77 (47.0)
Witness the birth of newborn	138 (56.1)	68 (41.5)
Increase the intimacy with partner	55 (22.3)	31 (18.9)
Increase bonding with the newborn	35 (14.2)	11 (6.7)
A good experience to witness the process	1 (0.4)	1 (0.6)
Improve medical knowledge	NA	4 (2.4)
Reservation(s) against companionship	**Women (n=28)**	**Partners (n=15)**
No partner	0	NA
Not in Hong Kong	3 (10.7)	1 (6.6)
Busy at work	9 (32.1)	1 (6.6)
Embarrassment	14 (50.0)	2 (13.3)
Affect sexuality	7 (25.0)	NA
Partner refused CDL	7 (25.0)	NA
Distract mothers	17 (60.7)	7 (46.7)
Fear of blood	NA	7 (46.7)
Annoyed by crying of newborn	NA	1 (6.6)
Fear of crying of the labouring mother	NA	3 (20.0)
Long labour time predicted	NA	1 (6.6)

Abbreviations: CDL = companionship during labour; NA = not available

* Data are shown as No. (%) of subjects

† Women and their partners were requested to list the noted benefit(s) of companionship if they planned for CDL; the reservation(s) against companionship if they planned not for CDL; and to list both if they were indecisive. Some women and their partners did not fill in this part of questions

partners of CDL. Nearly all subjects were aware of its existence. Companionship during labour was apparently also highly acceptable among women and partners.

According to the recently updated Cochrane review in July 2013[1], common elements of CDL include emotional support, information about labour progress and advice regarding coping techniques, comfort measures, and advocacy. Similarly, the majority of our subjects considered emotional support to be the major element although only one-third considered physical support to be a role of the companion. This might be explained by the fact that they were not aware of the importance and methods of providing this kind of support, particularly concerning pain control. This could be improved by attending antenatal childbirth education classes, and also dual participation in a birth ball programme that has been considered an alternative means of relieving labour pain and decreasing pethidine consumption[7,8]. Its use may nonetheless require some adaptations to current midwifery practice in Hong Kong wherein patient mobility is usually limited by the common use of continuous electronic fetal heart monitoring.

Interestingly, around one-fifth of the women and their partners considered cutting the umbilical cord an important element of CDL, and significantly more partners considered taking photographs or videos as one of the elements of CDL. This practice might be fuelled by media coverage of celebrity couples who share their birth experience, emphasising the ritual cutting of the

Table 4. Baseline demographics of women and their partners*

Demographics	Women†			Partners†		
	Planned CDL (n=244)	Planned no CDL / indecisive (n=53)	p Value	Planned CDL (n=158)	Planned no CDL / indecisive (n=30)	p Value
Age (years)			0.47			0.99
≤25	34 ± 14	9 ± 17		10 ± 6.3	2 ± 6.7	
26-30	86 ± 35.2	14 ± 26.4		39 ± 24.7	8 ± 26.7	
31-34	71 ± 29	20 ± 37.8		52 ± 32.9	9 ± 30	
≥35	53 ± 21.8	10 ± 18.8		57 ± 36.1	11 ± 36.6	
Marital status			0.63			
Married	229 (93.9)	52 (98.1)		–	–	
Never married	10 (4.1)	1 (1.9)				
Divorced / separated	1 (0.4)	0				
Cohabitation	4 (1.6)	0				
Education level			0.02			0.59
Primary	4 (1.6)	3 (5.7)		3 (1.9)	1 (3.3)	
Secondary	163 (66.8)	42 (79.2)		93 (58.9)	20 (66.7)	
Tertiary	77 (31.6)	8 (15.1)		62 (39.2)	9 (30)	
Place of birth			0.003			0.54
Hong Kong	129 (52.9)	16 (30.2)		99 (62.7)	17 (56.7)	
Mainland China	115 (47.1)	37 (69.8)		59 (37.3)	13 (43.3)	
Residency			<0.001			0.05
>7 Years	197 (80.7)	30 (56.6)		134 (84.8)	21 (70.0)	
<7 Years / visiting visa	47 (19.3)	23 (43.4)		24 (15.2)	9 (30.0)	
Occupation			0.11			0.17
Housewife	108 (44.3)	33 (62.3)		0	0	
Clerical work	78 (32.0)	11 (20.8)		45 (28.5)	6 (20.0)	
Workman	2 (0.8)	0		26 (16.4)	10 (33.3)	
Professional	26 (10.7)	2 (3.8)		51 (32.3)	7 (23.3)	
Others	30 (12.3)	7 (13.2)		36 (22.8)	7 (23.3)	
Household income (HK$)			0.13			
<10,000	48 (19.7)	16 (30.2)		–	–	
10,001-20,000	102 (41.8)	25 (47.2)				
20,001-50,000	87 (35.7)	11 (20.8)				
>50,000	7 (2.9)	1 (1.9)				

Abbreviation: CDL = companionship during labour

* Data are shown as mean ± standard deviation or No. (%)

† Some women and their partners did not fill in this part of questions

umbilical cord by the partner as well as recording the birth process. Although videotaping is commonly not allowed in public hospitals, some public hospitals do allow cord cutting and offer facilities such as birth balls and labour massage. They may change the perception or expectation of the role of partners in accompanying labour. Whether this should be further encouraged or explored is debatable as these may distract from the care of both the parturient and the newborns. Women may also be concerned about videotaping as only 1% of them accepted taking photos and videos as a component of CDL. For the women surveyed, the focus was on safety of the labour process:

documentation of the birth process was less important to them.

According to the postulated concept of the fear-tension-pain cycle by Dick-Read[9], excessive anxiety increases endogenous release of catecholamines that reduces blood flow to and from the placenta, restricts fetal oxygen supply, reduces effectiveness of uterine contractions, and slows labour progress[10]. It has therefore been proposed that CDL can reverse this cycle. In our study, about half expected CDL to exert positive effects on the progress of labour, and about 60% to 70% expected this to increase the chance of spontaneous vaginal delivery. These findings have been similarly reported[1,11]. In a Cochrane review[1], supported women required less pain medications and were more likely to be satisfied with the experience of labour. There was no apparent impact on other intrapartum interventions, maternal or neonatal complications or breastfeeding.

There was no consensus on situations where CDL was unsuitable. In general, CDL was considered suitable for spontaneous vaginal delivery in most countries. In our study, most women and partners considered CDL suitable for spontaneous vaginal delivery although only around half considered CDL suitable during assisted vaginal delivery and only one-fourth during emergency Caesarean section. This demonstrated a concern for interference with patient care in emergency situations.

Compatible with the findings of many high-income countries, the main preferred supporter was their partner[12]: 95% of women in our study would choose their partners if they were allowed to choose only one individual for CDL.

Attendance at antenatal childbirth education classes has been shown to affect a father's ability to offer assistance[13]. Fathers who attended class were more likely to provide physical comfort to the women. Donovan[14] also showed that fathers were often unclear of their role as they lacked the information and support to meet the women's expectations. In our study, only about half of the respondents believed childbirth education classes were essential for CDL. This might be improved by scheduling antenatal classes at weekends when more working women and partners can attend together. Alternatively, provision of such classes on the internet with interactive sessions may further enhance fathers' participation and exposure.

Significantly more women who received higher education considered CDL. This might be because of the increased awareness of its existence and value. Another explanation could be that they are more cognizant of their rights, and think companions can improve communication with health care professionals in stressful situations such as labour. Although it is not unexpected that those more educated women opted for CDL, enhanced efforts should also be made to propagate the role and value of CDL to those who are less well educated.

Among the subjects recruited in this survey, most women who were not born in Hong Kong were immigrants from mainland China. Their lower preference for CDL might be due to cultural differences and a general lack of provision of CDL in mainland hospitals, so that they are not aware of the importance of CDL. The Better Births Initiative promotes labour companionship as a core element of care for improving maternal and infant health, in several low- and middle-income countries, including China[15]. It is desired that more and more women should be aware of CDL, and also agree to have CDL.

Our study had several limitations. First, the response rate of partners was relatively low. This was related to the fact that many women attended antenatal follow-up alone, and their partners were often excluded from the antenatal ward shortly after admission due to the visiting policy. Thus partners were often unavailable, or found it inconvenient to return their completed questionnaire. Another less likely explanation would be that those who did not return the questionnaire might have reservations towards CDL and not complete the questionnaires. We believe that the non-responses were more related to random non-availability of the partners: a general comparison of the epidemiological characters (age, occupation or education level) of responding and non-responding partners revealed no significant differences. Secondly, this study focused on only Chinese women: Hong Kong is an international city with multi-ethnicity and further studies should be inclusive of women and their partners from other ethnicities.

Conclusion

The CDL was highly acceptable to women and their partners. Partners should be adequately prepared so that they are able to provide effective physical and psychological support to meet the women's needs.

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The Impact of Nuchal Cord on Fetal Outcome, Mode of Delivery, and Its Management: A Questionnaire Survey of All Hong Kong Obstetricians and Gynaecologists

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Objectives: To explore the view of Hong Kong obstetrics and gynaecology specialists on the impact of nuchal cord on fetal outcome, mode of delivery, and its management.
Methods: A questionnaire was mailed to all registered Hong Kong specialists in obstetrics and gynaecology (n=381) in July 2012 with a prepaid return envelope.
Results: The overall response rate was 50.7%. About one-third and one-fifth of specialists considered that nuchal cord could cause intrauterine death and intrapartum fetal death / neonatal death, respectively. In addition, approximately half believed that it reduced the possibility of a successful normal vaginal delivery, and increased the rate of assisted vaginal delivery. Nonetheless only 4.7% would advise patients to elect for Caesarean section in the presence of nuchal cord. There were no significant differences in the opinions of the impact of nuchal cord on fetal outcome and mode of delivery between specialists working in the Hospital Authority / public institutions versus those in private practice, between Maternal-Fetal Medicine (MFM) subspecialists versus non-MFM specialists, as well as between specialists with different years of practice after obtaining Fellowship of the Hong Kong Academy of Medicine. Around one-third in private practice routinely screened for nuchal cord on ultrasound, compared with none who practised in Hospital Authority / public institutions.
Conclusion: A significant proportion of obstetrics and gynaecology specialists thought that nuchal cord would lead to adverse fetal outcome and affect the mode of delivery. A large local study of nuchal cord should be conducted in order to guide clinical management and provide evidence for patient counselling.
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Keywords: Delivery, obstetric; Fetal death; Obstetrics; Questionnaires; Umbilical cord

Introduction

The occurrence of nuchal cord is very common. In an audit of all singleton deliveries at our hospital in 2010, the incidence of nuchal cord at delivery was 26.9% of a total 5166 deliveries. The management of nuchal cord differs in different countries and among obstetricians. In mainland China, presence of nuchal cord is a strong indicator for Caesarean section. It accounted for 16% to 25% of sections at a teaching hospital and some regional hospitals in China[1,2]. Nonetheless local obstetric opinion of the impact of nuchal cord on fetal outcome, mode of delivery, and management has not been explored in Hong Kong. Therefore, we conducted this questionnaire survey.

Methods

Questionnaires about the impact of nuchal cord on fetal outcome, mode of delivery and management, in both Chinese and English versions were mailed to all registered Hong Kong specialists in obstetrics and gynaecology (O&G) in July 2012. Recipients were instructed to reply by either fax or mail in a prepaid return envelope. Each questionnaire had a serial number linked to a specialist's name in a database. This was solely used to enable a reminder to be sent after 2 months if no reply had been received. This number was blinded for subsequent analysis to maintain anonymity. The study was approved

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by the ethics committee of the Hospital Authority. The questionnaires are attached in Appendices 1 and 2.

SPSS Windows version 20.0 was used for statistical analysis. Chi-square test and Fisher's exact test were used when appropriate. All differences were defined as being statistically significant at $p<0.05$.

Results

There were a total of 381 registered O&G specialists in July 2012, of whom 160 responded within the first 2 months. After a reminder, a further 33 replied. Therefore the total response rate was 50.7% (n=193). The demographic particulars of the respondents are summarised in Table 1.

The perceived percentage of nuchal cord at term was evaluated by a visual analogue scale from 0 to 100%. Among the respondents, 51.6% considered the percentage of less than 20%. The perceived accuracy of an ultrasound scan to detect nuchal cord was similarly assessed: 55.0% viewed the accuracy to be less than 70%.

On the impact on fetal outcome, 72.4% replied that more turns of nuchal cord was associated with more adverse outcome. In all, 34% and 22.8% considered that nuchal cord could cause intrauterine death and intrapartum fetal death / neonatal death, respectively. For mode of delivery 51.6% thought that it reduced the possibility of successful normal vaginal delivery, and 53.9% thought that it increased the rate of assisted vaginal delivery. In their daily practice, 23.8% of specialists routinely screened for nuchal cord when performing prenatal ultrasound in the third trimester, and 46.9% informed their patients if the result was positive. Nonetheless only 1.1% would deliver the fetus earlier if nuchal cord was detected at term, and 4.7% would advise Caesarean section (Table 2).

There were no significant differences in the cited incidence of nuchal cord by O&G specialists working in public hospitals versus those working in private practice, nor between maternal fetal medicine (MFM) subspecialists and non-MFM specialists. A significantly higher percentage of specialists (61.8%) with more than 16 years of practice after obtaining Fellowship of the Hong Kong Academy of Medicine (FHKAM) considered the incidence of nuchal cord to be less than 20% ($p = 0.02$). For the perceived accuracy of ultrasound detection of nuchal cord, there were no differences between specialists in private / public practice or years of practice after obtaining FHKAM. Significantly fewer MFM specialists thought that the accuracy was less than 70% compared with non-MFM specialists (35.7% vs. 58.4%; $p=0.04$) [Table 3].

There were no differences in view of nuchal cord on fetal outcome and mode of delivery between public and private specialists. There were also no differences regarding MFM status and years of practice. More specialists in private practice routinely looked for nuchal cord on ultrasound scans compared with those working in the Hospital Authority / public organisations (35.7% vs. 0%, $p<0.001$). In addition, significantly more private than public specialists would inform patients when nuchal cord was detected (57.4% vs. 25.4%, $p<0.001$). More specialists with ≥16 years of practice routinely screened for nuchal cord, and more informed their patients if nuchal cord was noted. Nonetheless there were no differences between the subgroups in advice for Caesarean section (Table 4).

Discussion

Nuchal cord is common: an approximate 25% incidence revealed by our local audit is comparable with other studies[3-5]. Nonetheless in this questionnaire survey, around half of respondents underestimated the incidence. With the advance of ultrasound and use of colour flow Doppler, the sensitivity of ultrasound in detecting nuchal cord has been determined to be 79% to 96.8%[6,7]. It is thus surprising that more than half of our respondents underestimated the accuracy at less than 70%. The higher

Table 1. Demographic data of specialists in obstetrics and gynaecology (n=193)

Demographics	Data
Place of practice	
Hospital Authority or public institutions	64 (33.2%)
Private practice	129 (66.8%)
HKCOG / RCOG–accredited MFM specialist	
Yes	30 (15.5%)
No	163 (84.5%)
Years of practice after obtaining FHKAM	
0-5 Years	28 (14.5%)
6-10 Years	28 (14.5%)
11-15 Years	47 (24.4%)
≥16 Years	90 (46.6%)

Abbreviations: FHKAM = Fellow of the Hong Kong Academy of Medicine; HKCOG = Hong Kong College of Obstetricians and Gynaecologists; MFM = maternal and fetal medicine; RCOG = Royal College of Obstetricians and Gynaecologists

Table 2. Views of obstetricians and gynaecologists of nuchal cord impact on fetal outcome, mode of delivery, and their practice on nuchal cord*

Item	Yes	No
View of nuchal cord on fetal outcomes		
Nuchal cord of more turns are more dangerous	139 (72.4)	53 (27.6)
Nuchal cord can cause intrauterine death	64 (34.0)	124 (66.0)
Nuchal cord can cause intrapartum fetal death or neonatal death	42 (22.8)	142 (77.2)
View of nuchal cord on mode of delivery		
Nuchal cord will reduce the chance of successful normal vaginal delivery	99 (51.6)	93 (48.4)
Nuchal cord will increase the chance to have assisted vaginal delivery such as vacuum extraction and forceps delivery	104 (53.9)	89 (46.1)
Their practices on nuchal cord		
Will routinely look for nuchal cord when performing ultrasound at third trimester	46 (23.8)	147 (76.2)
Will inform patient if there is nuchal cord on ultrasound	90 (46.9)	102 (53.1)
Will deliver the fetus earlier on detection of nuchal cord at term	2 (1.1)	188 (98.9)
Advise patient for Caesarean section due to nuchal cord	9 (4.7)	181 (95.3)

* Data are shown as No. (%) of subjects. Percentages were calculated after exclusion of those with missing answers

Table 3. Views of obstetricians and gynaecologists on the incidence of nuchal cord and accuracy of ultrasound in detecting nuchal cord*

Demographics	Considered the incidence of nuchal cord being <20%	p Value	Considered the accuracy of ultrasound being <70%	p Value
Place of practice		0.36		0.77
Work in Hospital Authority or public institution	29/63 (46.0)		35/61 (57.4)	
Work in private practice	70/129 (54.3)		69/128 (53.9)	
Accreditation of MFM		1.00		0.04
MFM specialists	15/29 (51.7)		10/28 (35.7)	
Non-MFM specialists	84/163 (51.5)		94/161 (58.4)	
Years of practice after obtaining FHKAM		0.02		0.74
0-5 Years	13/28 (46.4)		13/28 (46.4)	
6-10 Years	15/28 (53.6)		17/28 (60.7)	
11-15 Years	16/47 (34.0)		25/46 (54.3)	
≥16 Years	55/89 (61.8)		49/87 (56.3)	

Abbreviations: FHKAM = Fellow of the Hong Kong Academy of Medicine; MFM = maternal and fetal medicine

* Data are shown as No. (%) of subjects. Percentages were calculated after exclusion of those with missing answers

accuracy estimated by MFM specialists was probably due to more liberal use of colour flow Doppler in evaluation of nuchal cord.

Whether nuchal cord is associated with poor outcome is controversial. Some studies have shown that nuchal cord is associated with an increased prevalence of variable fetal heart rate decelerations during labour and an increased incidence of umbilical artery academia, as well as a higher incidence of lower 1-minute Apgar score and meconium stained liquor[8,9]. Nuchal cord has also been proposed to result in cord compression during labour, leading to increased arterial resistance with consequent fetal bradycardia and fall in fetal cardiac output and metabolic acidosis. Nevertheless most studies have shown that nuchal cord is not associated with lower Apgar scores

Table 4. Between-group comparisons of the views of nuchal cord on fetal outcomes, mode of delivery, and the practices on nuchal cord*

Characteristic	Hospital Authority / public organisation vs. private practice		
	Public practice (n=64)	Private practice (n=129)	p Value
View of nuchal cord on fetal outcomes			
Think that nuchal cord of more turns are more dangerous	42/63 (66.7%)	97/129 (75.2%)	0.29
Think that nuchal cord can cause intrauterine death	23/63 (36.5%)	41/125 (32.8%)	0.73
Think that nuchal cord can cause intrapartum fetal death or neonatal death	13/64 (20.3%)	29/120 (24.2%)	0.68
View of nuchal cord on mode of delivery			
Think that nuchal cord will reduce the chance of successful normal vaginal delivery	28/64 (43.8%)	71/128 (55.5%)	0.17
Think that nuchal cord will increase the chance to have assisted vaginal delivery such as vacuum extraction and forceps delivery	32/64 (50.0%)	72/129 (55.8%)	0.54
Their practices on nuchal cord			
Will routinely look for nuchal cord when performing USG at third trimester	0/64	46/129 (35.7%)	<0.001
Will inform patient if there is nuchal cord on USG	16/63 (25.4%)	74/129 (57.4%)	<0.001
Will deliver the fetus earlier on detection of nuchal cord at term	1/64 (1.6%)	1/126 (0.8%)	1.00
Will advise patient for Caesarean section due to nuchal cord	1/63 (1.6%)	8/127 (6.3%)	0.28

Abbreviations: FHKAM = Fellow of the Hong Kong Academy of Medicine; MFM = maternal and fetal medicine; USG = ultrasound

* Data are shown as No. (%) of subjects. Percentages were calculated after exclusion of those with missing answers

after 5 minutes or with an increase in Caesarean sections, neonatal intensive care unit admissions, or perinatal mortality[5,10-13]. It is postulated that although cardiac output falls during acute compression of the umbilical vessels, the fetus can maintain tissue oxygenation through its reserve provided compression is not prolonged. In our study, a significant proportion of O&G specialists believed that nuchal cord could cause intrauterine death and intrapartum death / neonatal death (34% and 22.8% respectively). Half of them perceived that nuchal cord decreased the chance of successful vaginal delivery. No significant differences were found on the views of nuchal cord on fetal outcomes and mode of delivery between those working in Hospital Authority / public institutions and private practice. This may increase patient anxiety.

In our hospital, it is not routine to screen for nuchal cord on antenatal ultrasound scans and even if incidentally noted, this is not disclosed to patients, even upon active enquiry. The intention is to avoid causing unnecessary anxiety since intrapartum management and timing and mode of delivery will not be affected. This is likely to also be the case in public institutions where no specialists admitted to routine screening for nuchal cord.

It may seem to be contradictory that although one-third of private specialists routinely screen for nuchal cord and over half of them would inform their patients if there was nuchal cord on ultrasound, only 6% would advise Caesarean section for this condition. It is probable that a significant number of Caesarean sections may still be performed due to maternal request (due to induced increased anxiety).

Nuchal cord continues to be an indication for Caesarean section in mainland China[1,2]. This practice may be a source of increased anxiety for our patients, many of whom are new immigrants or have received information from friends or relatives in the mainland. There are no current local data on the impact of nuchal cord on fetal outcome and mode of delivery. There is a need to reflect the common incidence of nuchal cord and to conduct local studies on the impact of nuchal cord on fetal outcome and mode of delivery in order to provide more information and evidence to guide clinical management and patient counselling.

MFM vs. non-MFM specialists			Specialists with different years of practice after FHKAM				
MFM (n=30)	Non-MFM (n=163)	p Value	0-5 Years (n=28)	6-10 Years (n=28)	11-15 Years (n=47)	≥16 Years (n=90)	p Value
22/29 (75.9%)	117/163 (71.8%)	0.82	18/28 (64.3%)	21/28 (75.0%)	31/47 (66.0%)	69/89 (77.5%)	0.37
8/28 (28.6%)	56/160 (35.0%)	0.66	11/28 (39.3%)	7/27 (25.9%)	14/47 (29.8%)	32/86 (37.2%)	0.59
6/28 (21.4%)	36/156 (23.1%)	1.00	4/27 (14.8%)	7/28 (25.0%)	7/46 (15.2%)	24/83 (28.9%)	0.23
19/30 (63.3%)	80/162 (49.4%)	0.23	16/28 (57.1%)	13/28 (46.4%)	24/47 (51.1%)	46/89 (51.7%)	0.89
20/30 (66.7%)	84/163 (51.5%)	0.18	14/28 (50.0%)	18/28 (64.3%)	25/47 (53.2%)	47/90 (52.2%)	0.68
8/30 (26.7%)	38/163 (23.3%)	0.87	1/28 (3.6%)	4/28 (14.3%)	11/47 (23.4%)	30/90 (33.3%)	0.01
12/29 (41.4%)	78/163 (47.9%)	0.66	7/28 (25.0%)	11/28 (39.3%)	23/47 (48.9%)	49/89 (55.1%)	0.04
0/29	2/161 (1.2%)	1.00	0/28	1/28 (3.6%)	1/47 (2.1%)	0/87	0.33
2/28 (7.1%)	7/162 (4.3%)	0.62	0/28	1/28 (3.6%)	3/47 (6.4%)	5/87 (5.7%)	0.58

Conclusion

A significant proportion of O&G specialists believe that nuchal cord leads to adverse fetal outcome and affects the mode of delivery. A large local study of nuchal cord should be conducted to guide clinical management and enable accurate advice to be given to patients.

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Appendix 1. Questionnaires to obstetrics and gynaecology specialists (English version)

Part 1: View on cord round neck

1) How many fetuses will you expect to have cord round neck at term (≥37 weeks of gestation)?
(Please mark an 'X' on the line for your answer)

2) Do you think that cord round neck for more turns is more dangerous? (For example, is cord round neck for two turns more dangerous than one turn?)
☐ Yes ☐ No

3) Do you routinely look for cord round neck when ultrasound scan is performed for pregnant patients at third trimester (≥28 weeks of gestation)?
☐ Yes ☐ No

4) Do you inform patient if there is cord round neck detected on ultrasound scan?
☐ Yes ☐ No

5) What do you think is the accuracy of ultrasound in diagnosing cord round neck?
(Please mark an 'X' on the line for your answer)

6) Do you advise patient to deliver the fetus earlier if there is cord round neck detected on ultrasound at term?
☐ Yes ☐ No

7) Do you think cord round neck is a cause of intrauterine death?
☐ Yes ☐ No

8) Do you think that cord round neck reduces the chance of successful normal vaginal delivery?
☐ Yes ☐ No

9) Do you think that cord round neck increases the chance of instrumental deliveries?
☐ Yes ☐ No

10) If there is sonographically detected cord round neck, do you advise patient to have Caesarean section when there are no other medical / obstetric indications for Caesarean section? (Maternal anxiety is not considered an indication here.)
☐ Yes ☐ No

11) Do you think cord round neck is a cause of intrapartum or neonatal death?
☐ Yes ☐ No

Part 2: Demographic data

a) Where is your current place of practice?
☐ Hospital Authority
☐ Department of Health
☐ Private practice
☐ Other public organisations (e.g. Family Planning Association)

b) How many years ago did you obtain the FHKAM (O&G) ?
☐ 0-5 ☐ 6-10 ☐ 11-15 ☐ 16 Years or more

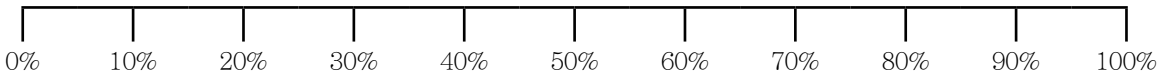
c) Are you a HKCOG / RCOG–accredited Maternal and Fetal Medicine (MFM) specialist?
☐ Yes ☐ No

- End -

Appendix 2. Questionnaires to obstetrics and gynaecology specialists (Chinese version)

第一部份：對胎兒臍帶纏頸的看法

1) 你認為有多少胎兒在足月時（懷孕37週或以上）會有臍帶纏頸的情況?
(請在線上你認為的百份比位置畫上 'X')

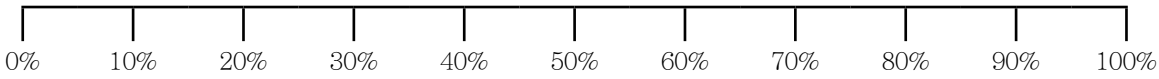


2) 你認為臍帶纏頸的圈數越多是否越危險?（例如：臍帶纏頸繞兩個圈是否比一個圈危險?）
☐是 ☐不是

3) 你為懷孕28週或以上（3rd trimester）的孕婦照超聲波時會留意胎兒有否臍帶纏頸嗎?
☐會 ☐不會

4) 若你照超聲波時發現胎兒臍帶纏頸，你會告訴病人嗎?
☐會 ☐不會

5) 你認為用超聲波去診斷胎兒臍帶纏頸有多準確?
(請在線上你認為的百份比位置畫上 'X')



6) 若胎兒在足月時超聲波發現有臍帶纏頸的情況，你會建議病人提早分娩嗎?
☐會 ☐不會

7) 你認為臍帶纏頸在懷孕期間可導致胎兒胎死腹中（intrauterine death）嗎?
☐會 ☐不會

8) 你認為臍帶纏頸會減低順產的機會嗎?
☐會 ☐不會

9) 你認為臍帶纏頸會增加需要用真空吸盤或產鉗助產的機會嗎?
☐會 ☐不會

10) 若超聲波發現胎兒有臍帶纏頸的情況，但沒有其他產科的原因必須剖腹分娩（病人擔憂maternal anxiety在此不視作產科原因），你會建議病人用剖腹分娩的方法去誕下胎兒嗎?
☐會 ☐不會

11) 你認為臍帶纏頸在分娩期間可導致胎兒死亡嗎?
☐會 ☐不會

第二部份：統計資料

a) 你在哪個機構執業?
☐醫院管理局
☐衛生署
☐私人執業
☐其他公營機構（例如：家計會）

b) 你在幾多年前獲取婦產科專科資格?
☐0-5 ☐6-10 ☐11-15 ☐16年或以上

c) 你是否香港婦產科學院或英國皇家婦產科醫學院認可的母胎醫學科（Maternal and Fetal Medicine）的專科醫生?
☐是 ☐不是

- 完 -

Physical Activity in Pregnancy: Attitudes and Practices of Hong Kong Chinese Women

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Objectives: To explore Hong Kong Chinese women's attitude towards and degree of physical activity during the first and second trimesters of pregnancy, and to identify factors that may be associated with a satisfactory level.
Methods: This prospective cohort study recruited women from a regional hospital in Hong Kong from March to July 2014. A self-administered questionnaire written in traditional Chinese was distributed in the first trimester and a follow-up questionnaire in the second trimester. Level of physical activity was assessed with the validated Pregnancy Physical Activity Questionnaire.
Results: A total of 534 questionnaires from the first trimester and 261 from the second were included for analysis. Around 94.5% of subjects agreed that exercise is necessary during pregnancy. Only 26.0% of women sought advice from medical staff. The median total physical activity level was 176.6 mean weekly energy expenditure (MET-h/week) and 179.4 MET-h/week in the first and second trimester, respectively. The level of sports activity was significantly increased in the second trimester compared with the first, with 23% to 30% of women exercising at the recommended level. Women with higher education level (p=0.002) and higher income (p=0.02) were more likely to be engaged in sports.
Conclusion: The total physical activity level was comparable in both trimesters, but sports activity significantly increased in the second trimester. Increased awareness of the recommended exercise level should be actively promoted by health care professionals.
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Keywords: Exercise; Physical fitness; Pregnancy

Introduction

Traditionally, women are advised to reduce their physical activity level during pregnancy. Nonetheless, research has provided new information about how pregnant women and their fetuses respond to moderate physical activity, and revealed no adverse maternal or neonatal outcomes[1]. There is consistent evidence that promoting physical activity in women of reproductive age may be a promising approach to prevent excessive weight gain, gestational diabetes mellitus, and subsequent complications suffered by children born from mothers with gestational diabetes[2,3]. Exercise during pregnancy not only helps reduce backache, fatigue and swelling of the extremities, it also improves women's sleep, mood, and posture[4-6].

Based on these findings, the American College of Obstetricians and Gynecologists (ACOG) recommends that pregnant women who are free of medical or obstetric complications should follow the American College of Sports Medicine–Centers for Disease Control and Prevention general guidelines on physical activity and engage in 30 minutes of moderate exercise per day on most, if not all, days of the week[7,8].

A significant number of people in Hong Kong adopt a sedentary lifestyle. The Behavioural Risk Factor Survey conducted in April 2012[9] revealed that about half (53.9%) of female adults aged 18 to 64 years had exercised during their leisure time less than once a week in the past 30 days. Only 14.8% of female adults had exercised more than 4 to 6 times a week[9].

Pregnancy is a good time to develop healthy lifestyle habits including regular exercise. Although a recommended level of physical activity is beneficial, it may not be perceived as appropriate or feasible around the world[10-12].

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This study aimed to explore Hong Kong Chinese pregnant women's attitude towards and extent of physical activity during pregnancy, as well as any change at different stages of pregnancy. The study also aimed to identify factors associated with level of physical activity.

Methods

Participants

The subjects for this prospective cohort study were recruited from the antenatal clinic of United Christian Hospital, Hong Kong. This study was approved by the Hospital Authority Cluster Research Ethics Committee. A self-administered questionnaire written in traditional Chinese was distributed to all Chinese pregnant women who attended the clinic within their first trimester from March to July 2014. Women of other ethnic origin were excluded. Written consent was obtained by attending doctors, nurses, or paramedic staff. Once recruited, a woman was assigned a code and marked on the electronic obstetric record. A follow-up questionnaire was distributed in the second trimester at about 24 to 28 weeks of gestation to assess physical activity during that trimester.

Questionnaire

The questionnaires (Appendix) consisted of three parts: (1) questions on the attitudes and knowledge of women about physical activity in pregnancy and their sources of information; (2) the translated traditional Chinese version of Pregnancy Physical Activity Questionnaire (PPAQ) which has been validated by a Taiwan study[13]; and (3) demographic data including age, parity, education level, occupation, and household income.

The PPAQ is a self-administered, semi-quantitative questionnaire that asks respondents to report the time spent in 32 activities including household / caregiving (13 activities), occupational (5 activities), sports / exercise (8 activities), transportation (3 activities), and inactivity (3 activities)[14]. The respondents were asked to select a category for each activity that approximated the time spent by them per day or week on that activity. The time frame of recall was the current trimester of pregnancy. In the last part of the section on sports activities, an open-ended section allowed the respondent to add activities not already listed. Calculations were computed as reported previously. The compendium-based metabolic equivalent (MET) values were used to estimate the intensity of the PPAQ activities[15]. The duration of time spent on each activity was multiplied by its intensity to arrive at a measure of mean weekly energy expenditure (MET-h/week).

Statistical Analysis

Statistical analysis was performed using the Statistical Packages for the Social Sciences Windows version 22 (SPSS Inc., Chicago [IL], US). The mean weekly energy expenditure (MET-h/week) during pregnancy by PPAQ with different intensity level and

Table 1. Subjects' demographics (n=534)

Variable	Data
Age (years)	
<20	8 (1.5%)
21-30	239 (44.8%)
31-40	270 (50.6%)
>40	17 (3.2%)
Marital status (n=532)	
Single / cohabitation	64 (12.0%)
Married	465 (87.4%)
Divorced	3 (0.6%)
Occupation (n=527)	
Housewife	194 (36.8%)
Clerical work	158 (30.0%)
Manual work	14 (2.7%)
Professional	70 (13.3%)
Self-employed	15 (2.8%)
Others	76 (14.4%)
Income (HK$) [n=510]	
<10,000	82 (16.1%)
10,000-20,000	222 (43.5%)
20,001-50,000	157 (30.8%)
>50,000	49 (9.6%)
Education level	
Primary	17 (3.2%)
Secondary	311 (58.2%)
Tertiary	206 (38.6%)
Parity	
0	258 (48.3%)
≥1	276 (51.7%)
History of miscarriage	
0	386 (72.3%)
1	88 (16.5%)
≥2	60 (11.2%)
Conception (n=531)	
Natural	515 (97.0%)
Assisted reproduction (other than in-vitro fertilisation)	11 (2.1%)
In-vitro fertilisation	5 (0.9%)

types of activity were calculated. Women who satisfied the ACOG guidelines (≥7.5 MET-h/week) in the study period were regarded as physically active. Factors observed to be associated with changes in physical activity from the first to second trimester were calculated with non-parametric tests including Mann-Whitney *U* test, Kruskal-Wallis test, Wilcoxon signed rank test, and considered as statistically significant if p value was <0.05.

Results

A total of 600 questionnaires were distributed to eligible pregnant women in their first trimester. A total of 542 questionnaires were returned, giving a response rate of 90.3%. There were 534 (89%) questionnaires that were adequately completed and included for analysis. Adequately filled was defined as more than 70% of questions answered. A total of 270 women were successfully contacted in their second trimester and questionnaires were distributed for follow-up, of which 261 (96.7%) were returned and included for analysis.

For demographics (Table 1), the mean age of

Table 2. Attitudes and knowledge of the women on exercise and pregnancy (n=534)

Question	Data
Do you have regular exercise before pregnancy? (n=532)	
Yes	120 (22.6%)
No	412 (77.4%)
Does pregnancy affect your exercise habit? (n=528)	
No	272 (51.5%)
Yes, slightly limited	194 (36.8%)
Yes, considerably limited	62 (11.7%)
Reason(s) for decreased physical activity during pregnancy	
Fatigue during pregnancy	435 (81.5%)
Worry about fetal growth being affected	186 (34.8%)
Physical discomfort during exercise	102 (19.1%)
Advice from family / friends	55 (10.3%)
Advice from medical staff	9 (1.7%)
Others	20 (3.8%)
Appropriate level of exercise is necessary during pregnancy (n=542)	
Agree	512 (94.5%)
Not agree	30 (5.5%)
Benefit(s) of exercise during pregnancy	
Shortened delivery process	457 (85.6%)
Improve general health of mother / fetus	325 (60.9%)
Minimise excessive weight gain	244 (45.7%)
Decrease low back pain / muscle pain	217 (40.6%)
Improve blood glucose control	113 (21.2%)
Others	4 (0.8%)
Source(s) of information about pregnancy and exercise	
Internet / website	258 (48.3%)
Friends / family	255 (47.8%)
Books	221 (41.4%)
Medical staff	139 (26.0%)
Newspaper / magazines	128 (24.0%)
Television / radio	101 (18.7%)
Others	5 (0.9%)

subjects was 30.5 years. About 95% were between 20 and 40 years of age and about 3% were over 40 years. Most women (87.4%) were married, almost half (48.3%) were nulliparous, and approximately 2% conceived by assisted reproduction. Approximately a quarter (28%) of participants had had one or more miscarriage before this pregnancy.

Table 2 shows the attitudes towards and knowledge of the subjects about exercise and pregnancy. In all, 120 (22.6%) claimed to have exercised regularly before pregnancy. Most (94.5%) agreed that exercise was necessary during pregnancy. About half (51.5%) considered that pregnancy did not affect their exercise routine but 11.7% believed it had been considerably limited. The main reason for this limitation was reported to be fatigue (81.5%) followed by worry about fetal growth (34.8%). In terms of the benefits of exercise during pregnancy, most thought that labour may be shortened (85.6%) and general health of the mother or fetus would be improved (60.9%). Most women obtained their information from the internet / website (48.3%), family / friends (47.8%), and books (41.4%). Only a quarter (26.0%) obtained information from medical staff.

For physical activity level calculated by the PPAQ (Table 3), the median total activity was 176.6 MET-h/week in the first trimester and 179.4 MET-h/week in the second. An evaluation of activity level according to the classes of intensity showed that light activity constituted 40% of the total activity of the women, followed by moderate activity 34%, and sedentary activity 24%.

Through analysis of activity according to the domains of activity, household activity constituted the largest component of physical activity, being about 40% in both trimesters, followed by occupation activity (23%). For sports / leisure activity, it constituted only 2.2% (2.4 MET-h/week) in the first trimester and 3.2% (3.5 MET-h/week) in the second. There was a significant increase in sport-related activity in the second trimester compared with the first ($p < 0.001$): significantly more women in the second trimester (79/261, 30.3%) than the first (126/534, 23.6%) fulfilled the advice of the ACOG to have moderate physical activity of more than 7.5 MET-h/week (p=0.05, Fisher's exact test).

For the 261 women who completed questionnaires in both trimesters, there was no statistically significant change in total activity level and by classes of intensity between the two trimesters. Nonetheless, similar to the cross-sectional analysis, there was significant increase in sports activity in the second trimester (3.5 MET-h/week) compared with the first (2.4 MET-h/week; p=0.001, Wilcoxon signed rank test).

The total physical activity level was significantly higher in the multiparous group (212.8 MET-h/week) than the nulliparous group (144.1 MET-h/week) [$p < 0.001$]. Women with higher income were also more physically active (p=0.01). For level of sports activity, women with higher education level (p=0.002) and higher income (p=0.02) were more likely to engage in sports. For conception method, the median level of sport activity for the natural conception group was 2.4 MET-h/week and artificial reproduction

Table 3. Physical activity of women according to Pregnancy Physical Activity Questionnaire in the first and second trimesters

	Mean ± SD (Met-h/week)		Median (IQR) [Met-h/week]		Proportion of total activity		p Value*
	First trimester	Second trimester	First trimester	Second trimester	First trimester	Second trimester	
Total (intensity)	205.2 ± 139.3	206.9 ± 127.7	176.6 (115.0-261.6)	179.4 (114.5-268.7)	100.0	100.0	0.68
Sedentary	49.3 ± 26.8	47.8 ± 26.4	48.7 (25.9-68.9)	47.8 (24.5-64.6)	24.0	23.1	0.39
Light	86.5 ± 79.4	87.6 ± 61.0	72.5 (40.1-111.7)	76.1 (40.6-115.3)	42.2	42.4	0.40
Moderate	68.9 ± 83.8	70.7 ± 69.1	48.6 (11.8-99.8)	54.8 (16.2-105.4)	33.6	34.2	0.19
Vigorous	0.4 ± 1.8	0.7 ± 3.3	0.0 (0.0-0.0)	0.0 (0.0-0.2)	0.2	0.3	0.32
Household	81.2 ± 92.8	82.1 ± 73.2	53.8 (0.0-107.7)	63.4 (30.1-110.6)	39.6	39.7	0.21
Occupation	47.8 ± 56.5	47.1 ± 55.6	33.6 (0.0-70.3)	33.6 (0.0-74.2)	23.3	22.8	0.94
Sports	4.4 ± 6.2	6.5 ± 10.0	2.4 (0.0-6.5)	3.5 (0.8-8.4)	2.2	3.2	<0.001

Abbreviations: IQR = interquartile range; MET-h/week = mean weekly energy expenditure; SD = standard deviation

* Comparison of the means between first and second trimesters by Mann-Whitney *U* test

group was 0.8 MET-h/week, but the difference was not statistically significant (p=0.24) [Table 4].

Discussion

In this prospective study among Chinese women in Hong Kong, the validated traditional Chinese version of the PPAQ from Taiwan was used[13]. For the PPAQ results, the total physical activity level was lower in Hong Kong when compared with Taiwan (Table 5[13,16]). Household and sport-related activity were comparable but occupation activity was significantly lower (Hong Kong 47 MET-h/week vs. Taiwan 120 MET-h/week) in both trimesters. About 40% of our participants were housewives and 30% were employed in clerical work; this accounted for the low occupational activity. The level of sports activity was comparable with other Asian countries[16].

According to the World Health Organization recommendations, adults aged 18 to 64 years should have at least 150 minutes of moderate-intensity, or 75 minutes of

Table 4. Distribution of total and sports activities across different categories (n=534)

	No. (%)	Median physical activity level (Met-h/week)	
		Total activity	Sports activity
Age (years)			
<20	8 (1.5%)	115.2	1.4
21-30	239 (44.8%)	160.1	2.0
31-40	270 (50.6%)	186.1	2.4
>40	17 (3.1%)	182.7	2.0
p Value*		0.22	0.48
Parity			
0	258 (48.3%)	144.1	2.0
≥1	276 (51.7%)	212.8	2.4
p Value†		<0.001	0.22
Conception (n=531)			
Natural	515 (97.0%)	175.6	2.4
Assisted reproduction	16 (3.0%)	180.6	0.8
p Value†		0.54	0.24
History of miscarriage			
0	386 (72.3%)	177.6	2.4
1	88 (16.5%)	175.9	0.8
≥2	60 (11.2%)	175.2	2.4
p Value*		0.83	0.07
Education level			
Primary	17 (3.2%)	183.1	0.8
Secondary	311 (58.2%)	169.8	2.0
Tertiary	206 (38.6%)	192.5	2.4
p Value*		0.09	0.002
Income (HK$) [n=510]			
<10,000	82 (16.1%)	151.3	0.8
10,000-20,000	222 (43.5%)	167.4	2.0
20,001-50,000	157 (30.8%)	182.5	2.4
>50,000	49 (9.6%)	222.0	2.4
p Value*		0.01	0.02

* Mann-Whitney *U* test

† Kruskal-Wallis test

Table 5. Comparison of physical activity level using Pregnancy Physical Activity Questionnaire among different Asian countries[13,16]

	Present study (Hong Kong)		Lee (2011), Taiwan[13]	Matsuzaki (2014), Japan[16]
	Mean	Median	Mean	Median
First trimester				
Total activity	222.5	176.6	251.17	137.9
Household	81.2	53.8	89.9	79.1
Occupation	47.8	33.6	120.0	0.0
Sports	4.4	2.4	3.4	4.2
Second trimester				
Total activity	206.9	179.4	253.2	151.9
Household	82.1	63.4	84.7	79.0
Occupation	47.1	33.6	120.1	0.0
Sports	6.5	3.5	4.6	2.8

vigorous-intensity aerobic physical activity throughout the week, or an equivalent combination of both[17]. The ACOG adopted this recommendation for pregnant women and advised engagement in 30 minutes of moderate exercise per day on most days of the week, equivalent to 7.5 MET-h/week[7,8]. In our study, 23.6% and 30.3% of women fulfilled the criteria in the first and second trimester, respectively. Studies from other countries have also shown poor compliance with exercise during pregnancy with less than half of the population complying. Only 10.2% of women fulfilled the recommendations in Brazil[18], 17.4% in United States[19], 20.3% in Spain[20], 47% in France[21], and 48% in United Kingdom[22]. The French[21] and British[22] studies showed that this level of activity was similar throughout the entire pregnancy, even in the third trimester.

It is not surprising that the level of sports activity was significantly increased in the second trimester compared with the first. It is well known that in the first trimester, women experience more physical discomfort, i.e. nausea, vomiting, and fatigue. In addition, they may be less worried about the possibility of miscarriage after the end of the first trimester. Finally, antenatal exercise classes in our hospital are not usually scheduled until after the first trimester and may account for the increase in sports activity then.

Our study showed that multiparous women were more physically active than nulliparous ones, in agreement with prior studies[18,23,24]. Women are better adapted to physical changes during pregnancy after one or more deliveries and are more likely to remain active. Women with a higher education level and income engaged in more sports. This may be because they are better informed about exercise in pregnancy as shown in the first part of the questionnaire. The sports activity was much lower in women who conceived following artificial reproduction techniques (0.8 MET-h/week) than in those who conceived naturally (2.4 MET-h/week), although it was not statistically significant as the sample size of assisted reproductive technology group was very small, accounting for only 3% of the participants.

Our study showed that although women had some knowledge about exercise in pregnancy and their attitude towards exercise was favourable, few exercised in reality. The main reason for reduced physical activity was fatigue and concern about fetal growth. Only a quarter of women sought relevant information from medical staff. Counselling should be offered starting at the first antenatal visit about the recommended level of exercise during pregnancy, preferably accompanied by informative pamphlets and internet resources. A physiotherapist can also be involved to organise a structured exercise programme (including birth ball, yoga, etc.) to increase motivation.

The response rate to our questionnaire in the first trimester of above 90% was satisfactorily high although disappointingly low in the second trimester, around half. Nonetheless a comparison was made of level of physical activity in the first trimester between those who had completed a follow-up questionnaire in the second trimester and those who had not. There was no significant difference between them (p=0.83). There was also no significant difference between the two groups in parity, conception

method, history of miscarriage, education level, or income, only age. Thus, we can assume that their behaviour in the second trimester may also be similar.

We suggest that future study may examine changes that occur in the third trimester and postpartum. An interventional study that offers written information at the first visit and a repeat questionnaire in a subsequent trimester to identify any improvement in level of sports activity would also be beneficial.

Conclusion

This study showed that in local Chinese women, the level of sports activity was significantly increased in the second trimester compared with the first. In addition, those with higher education level and higher income had increased physical activity. About 23% to 30% of women fulfilled the ACOG recommendations for exercise during pregnancy, comparable with prior studies in foreign countries. It would be optimal if medical staff can take a more active role in promoting physical exercise during pregnancy.

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Appendix. Questionnaire for the study

研究題目: 本地婦女在懷孕期間的身體活動量之研究

孕期：早期 / 中期 / 後期

請你花十五分鐘完成問卷，在適當空間填上剔號 (✓)

第一部份：孕婦對懷孕期間身體活動的看法

1. **你在懷孕前有沒有慣常的運動習慣？** ☐1. 有 ☐2. 沒有

2. **懷孕有沒有影響你的運動習慣？** ☐1. 沒有 ☐2. 少量影響 ☐3. 非常影響

3. **在懷孕期間使你減少身體活動的原因：(可選多於一項)**
   - ☐1. 怕影響胎兒成長
   - ☐2. 身體疲倦
   - ☐3. 活動造成身體不適
   - ☐4. 家人或朋友建議
   - ☐5. 醫護人員建議
   - ☐6. 其他 _____

4. **你認同懷孕期間應該有適量的運動？** ☐1. 是 ☐2. 否

5. **你認為運動對懷孕的好處包括：(可選多於一項)**
   - ☐1. 減少腰背痛等身體不適
   - ☐2. 令生產過程更順利
   - ☐3. 有利媽媽與孩子的健康
   - ☐4. 減少體重過量增加
   - ☐5. 幫助身體的血糖控制
   - ☐6. 其他 _____

6. **你從以下哪些途徑獲得懷孕與運動的資訊：(可選多於一項)**
   - ☐1. 電視、電台
   - ☐2. 報章、雜誌
   - ☐3. 書本
   - ☐4. 互聯網
   - ☐5. 朋友、家人
   - ☐6. 醫護人員
   - ☐7. 其他 _____

Appendix. (cont'd)

第二部份：孕期身體活動問卷

親愛的孕婦們：這份問卷的問題是由不同方面來看您在此懷孕期間的身體活動狀態，請您回答以下問題，在適當空間填上剔號 (✓)，選出最符合您狀況的答案。

	無	一天少於半小時	一天約半小時-1小時	一天約1-2小時	一天約2-3小時	一天3小時以上
在此懷孕期，當妳下班後或沒工作時，您通常花多少時間：						
1. 準備餐點（煮飯、擦桌子、洗盤子）						
2. 坐著幫孩子穿衣、洗澡、餵食						
3. 站著幫孩子穿衣、洗澡、餵食						
4. 站著或坐著和小孩玩						
5. 走路或跑步和小孩玩						
6. 帶小孩						
7. 照顧長輩						
8. 使用電腦或寫字						
9. 看電視或影片						
10. 坐著讀書、說話、講電話						
11. 和寵物玩						
12. 輕鬆簡單的打掃（整理床舖、送洗衣物、熨衣服、整理東西）						
13. 逛街購物（為了買食物、衣服或其他）						
14. 做粗重的打掃（吸塵器、打掃、洗窗戶）						
15. 準備午晚餐（從烹煮、整理餐桌到飯菜上桌）						
16. 洗瓦斯爐或抽油煙機						
去某地方……在此懷孕期間，妳通常花多少時間做下列事情：						
17. 用慢走的方式去某個地方（例如搭公車、工作、拜訪），但不是為了玩樂或運動						
18. 用快走的方式去某個地方（例如搭公車、工作、學校），但不是為了玩樂或運動						
19. 開車或搭公車						
為了玩樂或運動……在此懷孕期妳通常花多少時間做下列事情：						
20. 用慢走的方式去玩樂或運動						
21. 用快走的方式去玩樂或運動						
22. 為了玩樂或運動，以快走方式登山						
23. 慢跑						
24. 參加產前運動課程						
25. 游泳						
26. 跳舞						

Appendix. (cont'd)

第二部份：孕期身體活動問卷（續）						
親愛的孕婦們：這份問卷的問題是由不同方面來看您在此懷孕期間的身體活動狀態，請您回答以下問題，在適當空間填上剔號 (✓)，選出最符合您狀況的答案。						
	無	一天少於半小時	一天約半小時-1小時	一天約1-2小時	一天約2-3小時	一天3小時以上
請告訴我們，除了上述外，妳還有參加那些活動是為了玩樂或運動？						
27. （活動名稱）						
28. （活動名稱）						
若妳是學生或是有工作收入者請寫填下欄。若妳是家庭主婦、無法工作者、沒有工作者則不需填寫下欄。在工作時……在此懷孕期間，妳通常花多少時間做下列事情：						
29. 坐著工作或上課						
30. 工作時，需拿著東西，站著或慢步走（重量超過3瓶家庭號鮮奶）						
31. 工作時，不需拿任何東西站著或慢步走						
32. 工作時，需拿著東西快走（重量超過3瓶家庭號鮮奶）						
33. 工作時，不需拿著任何東西快步走						

第三部份：孕婦資料統計（圈出最符合您狀況的答案）	
年齡	20歲以下 / 21-30歲 / 31-40歲 / 40歲以上
教育水平	小學程度或以下 / 中學程度 / 副學士或文憑 / 大專或以上
婚姻狀況	未婚 / 已婚 / 分居 / 離居 / 同居
是次懷孕	自然懷孕 / 人工輔助懷孕 / 試管嬰兒
生產次數	沒有 / 一次或以上
小產次數	沒有 / 一次 / 多於一次
職業	家庭主婦 / 文職 / 工人 / 專業人士 / 自僱人士 / 其他 _____
家庭收入	少於$10,000 / $10,000-20,000 / $20,001-50,000 / 多於$50,000

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Outcome of Twin Reversed Arterial Perfusion Sequence: 15-Year Experience in a Tertiary Hospital in Hong Kong

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Objective: To evaluate our local experience of twin reversed arterial perfusion sequence.
Methods: This was a retrospective cohort study of all twin pregnancies complicated by twin reversed arterial perfusion sequence that were managed at a university teaching hospital in Hong Kong from 1 January 1998 to 31 December 2012.
Results: Of 16 cases identified, two were excluded and 14 were analysed. The median (range) gestation at diagnosis was 16.0 (10.8-24.3) weeks. Seven cases were treated conservatively and seven were treated with surgical intervention. Comparison of surgical and conservative treatment showed that the former was associated with a trend for better survival (71% vs. 43%), and less miscarriage (14% vs. 43%), preterm delivery (20% vs. 33%), and small for gestational age (0 vs. 33%), although these were not statistically significant. There was no significant difference in median gestation at delivery (37.0 vs. 37.4 weeks). Two cases (28.6%) with treatment failure and one other case (14.3%) had procedure-related complications. In the small-size acardiac twin subgroup (acardiac-to-pump twin size ratio <50%), both surgical and conservative treatments had excellent survival (100%). Of the six cases diagnosed in the first trimester, three (50%) ended in miscarriage before 16 weeks of gestation, and all were associated with a large-size (i.e. acardiac-to-pump twin size ratio ≥50%) acardiac twin.
Conclusions: Surgical intervention for twin reversed arterial perfusion sequence tended to improve survival with few adverse events. Our surgical intervention results were comparable with other studies. Conservative management appears to be safe for twin reversed arterial perfusion with a small acardiac twin. Diagnosis of twin reversed arterial perfusion sequence in the first trimester was associated with a high miscarriage rate at or before 16 weeks, especially with a large-size acardiac twin.
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Keywords: Diseases in twins; Heart defects, congenital; Hong Kong

Introduction

Twin reversed arterial perfusion (TRAP) sequence is a rare condition unique to monochorionic (MC) twin pregnancy, occurring in approximately 1 in 35,000 pregnancies, 1 in 100 MC twin pregnancies, and 1 in 30 MC triplet pregnancies[1,2]. Twin reversed arterial perfusion sequence is a condition in which one twin (termed the acardiac twin) has a non-functioning or absent heart and receives all of its perfusion from its structurally normal co-twin (termed the pump twin). The acardiac twin has no placental share and perfusion occurs through a superficial arterial-arterial placental anastomosis between the structurally normal pump twin and the acardiac twin. Blood flows in a retrograde fashion from the pump twin towards, rather than away from, the acardiac twin through the umbilical artery and then back towards (but not into) the placenta through the umbilical vein. The returning blood bypasses the placenta and returns to the pump twin through vein-vein anastomosis[3]. The overall perinatal mortality rate

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of the pump twin without any intervention ranges from 35% to 55%[4,5]. Contributors to perinatal death of the pump twin are congestive heart failure, preterm delivery due to polyhydramnios, and mass effect of the acardiac twin. Intrauterine growth restriction and development of fetal hydrops may further complicate the wellbeing of the pump twin. In case of monoamniotic (MA) twins, the umbilical cord of the pump twin may become entangled with that of the acardiac twin[6].

The goal of treating TRAP sequence is to maximise the likelihood of term delivery and survival of the pump twin in a safe and effective manner. The definitive treatment of this condition is obliteration of the arterial-arterial and vein-vein anastomoses via fetal intervention. However, fetal intervention has significant risks of preterm delivery (PTD), preterm prelabour rupture of membranes (PPROM), miscarriage, intrauterine death (IUD), and treatment failure. As a result, conservative management, with a survival rate of 90%, has been advocated[7]. There are many issues regarding the management of TRAP sequence, such as whether to intervene and, if so, when to intervene, and which method of intervention, such as cord occlusion or intrafetal ablation, to use.

This study aimed to review the local experience of twin pregnancies complicated by TRAP sequence managed by conservative treatment or surgical intervention.

Methods

This retrospective cohort study was conducted at the Fetal Medicine Unit, Tsan Yuk Hospital, and Queen Mary Hospital, The University of Hong Kong. The unit provides tertiary hospital care and manages high-risk pregnancies that are referred from other local hospitals in Hong Kong. There are around 4000 deliveries annually. More than 90% of the patients are ethnic Chinese. Ethical approval for this study was obtained from the local institutional human research ethics committee. All consecutive cases of TRAP sequence that were managed between 1 January 1998 and 31 December 2012 were identified by reviewing the departmental database. Details of all identified cases were obtained from the case notes and hospital electronic systems (Clinical Management System and Obstetrics Clinical Information System). The data were collected from prenatal records, ultrasound (USG) reports, operation records, delivery charts, and neonatal records.

All cases underwent detailed USG examination by maternal fetal medicine subspecialists to confirm the diagnosis of TRAP sequence. Women were counselled regarding the prognosis of the pump twin. The various options were offered, namely, termination of pregnancy (TOP), conservative management, or surgical intervention. For women who opted for conservative management, the pregnancies were followed up weekly until there was no growth and no blood flow in the acardiac twin. Thereafter, the pregnancies were evaluated every 2 to 3 weeks to monitor the growth of the pump twin. Surgical intervention was not recommended until after at least 16 weeks of gestation (up to 2007) and 12 weeks of gestation (after 2007) or when there was a significant risk of death for the pump twin, such as increase in size of the acardiac twin, acardiac-to-pump twin size ratio of ≥50%, abnormal Doppler or cardiac decompensation of the pump twin, or polyhydramnios[8]. Surgical intervention was also recommended for monochorionic monoamniotic (MCMA) cases to prevent the death of the pump twin from cord entanglement[9]. The acardiac-to-pump twin size ratio was calculated by comparing abdominal circumferences or estimated fetal weights, or by comparing the upper pole-rump length of the acardiac and the crown-rump length of the pump twin[10]. Estimated fetal weight of the acardiac twin was calculated by measuring in three dimensions (anteroposterior, transverse, and longitudinal) and using the equation for a prolate ellipsoid to estimate volume (in mL); fetal weight was then obtained by assuming that 1 mL is equal to 1 gm[11]. All women gave written informed consent prior to treatment.

Intrafetal monopolar thermocoagulation was performed under local anaesthesia. An 18-gauge needle was introduced transabdominally under USG guidance targeted near to the major intra-abdominal vessel of the acardiac twin. The stylet was then removed. A 1-mm wire electrode, which was insulated along most of its length with 3 mm of wire left bare at the tip, was passed through the lumen of the needle until the 3-mm length of bare wire had passed the end of the needle. The wire electrode was connected to a standard monopolar diathermy machine. Thermocoagulation was applied several times at 30 to 40 W for 5 to 15 seconds until cessation of blood flow in the acardiac twin was demonstrated by colour Doppler USG[12].

Fetoscopic laser cord coagulation was performed under general anaesthesia. A 1-mm mini-fetoscope (Karl Storz, Tuttlingen, Germany) was used. The trocar was inserted into the amniotic cavity under USG guidance. The fetoscope was passed through the trocar and the umbilical cord insertion of the acardiac twin was identified. Neodymium-doped yttrium aluminium garnet laser fibre was then passed through the operative channel of the

fetoscope. Laser coagulation pulses of 30 W for 3 seconds each were delivered until arrest of flow was detected by colour Doppler USG.

Bipolar cord coagulation was performed under general anaesthesia. A 3.5-mm laparoscopic trocar and 3-mm bipolar forceps (Karl Storz, Tuttlingen, Germany) were used. After the trocar was inserted into the amniotic cavity under USG guidance, the bipolar forceps was passed through the trocar and the umbilical cord insertion to the acardiac twin was identified and grasped under USG guidance. Bipolar coagulation of 20 to 55 W for 15 seconds each was applied until arrest of flow was detected via colour Doppler USG.

Treatment failure was defined as incomplete cessation of blood flow, a second procedure needed to achieve complete occlusion, procedure abandoned, or death of the pump twin within 24 hours of the procedure. Procedure-related miscarriage, PTD, and PPROM were defined as occurring within 4 weeks of the procedure.

After fetal intervention, patients were discharged either on the same day or the next day. Ultrasound was performed before discharge to ensure that there was no blood flow in the acardiac twin and that the pump twin was normal. The pregnancies were followed up weekly until stable and then every 2 to 3 weeks to monitor the growth of the pump twin. Patients were referred back to their local hospitals to continue antenatal care and for delivery if their condition was stable.

Statistical analysis was performed using the Statistical Package for the Social Sciences Windows version 16.0 (SPSS Inc., Chicago [IL], US). Variables were expressed as median and range for non-normally distributed variables. Comparison between the outcome groups was by Mann-Whitney *U* test for continuous variables and Fisher's exact test for categorical variables. A p value of ≤0.05 was considered statistically significant.

Results

There were 16 cases of TRAP sequence diagnosed in the study period. Two cases were excluded due to missing case notes for one and TOP at the patient's request for the other. Therefore, 14 cases were included in the analysis. Of these, 12 (85.7%) cases were Chinese. Thirteen (92.8%) cases involved spontaneous conception. There were 13

Table 1. Clinical characteristics of twin reversed arterial perfusion sequence with conservative management

Case No.	Year	Type of twinning	Median gestational age at diagnosis (weeks)	Size ratio (%)	Sign of pump twin compromise	Progress	Outcome	Median gestational age at delivery (weeks)	Mode of delivery	Birth weight (g)
1	1998	MCDA	22+1	166	Hydrops, oligohydramnios	-	IUD at 24+4 weeks	25+3	-	-
2	2002	MCDA	10+6	63	-	-	Miscarriage at 13 weeks	-	-	-
3	2004	MCDA	24+2	28	-	Pump twin SGA, oligohydramnios	Live birth	32+0	LSCS	1260
4	2005	MCDA	14+0	14	-	Acardiac twin without blood flow at 14+6 weeks	Live birth	38+0	NSD	2610
5	2005	MCDA	13+3	73	Sinus bradycardia, UA REDF	-	Miscarriage at 13+5 weeks	-	-	-
6	2009	MCDA	11+2	64	-	-	Miscarriage at 12+5 weeks	-	-	-
7	2012	MCDA	12+4	34	-	Acardiac twin without blood flow at 15+4 weeks	Live birth	37+3	LSCS	2550

Abbreviations: IUD = intrauterine death; LSCS = lower segment Caesarean section; MCDA = monochorionic diamniotic; NSD = normal spontaneous delivery; SGA = small for gestational age; UA REDF = umbilical artery Doppler reversed end-diastolic flow

Table 2. Clinical characteristics of twin reversed arterial perfusion sequence with surgical management

Case No.	Year	Type of twinning	Median gestational age at diagnosis (weeks)	Size ratio (%)	Sign of pump twin compromise	Progress
8	1999	MCDA	16+0	20	-	Increased size of acardiac twin
9	2001	MCDA	20+2	94	Polyhydramnios	-
10	2001	MCDA	16+0	22	-	Increased size of acardiac twin, polyhydramnios
11	2003	MCDA	20+1	21	-	Increased size of acardiac twin
12	2004	MCDA	17+1	93	Cardiomegaly, polyhydramnios	-
13	2007	MCMA	16+0	151	-	-
14	2007	MCDA	12+2	52	-	Increased size of acardiac twin

Abbreviations: IUD = intrauterine death; LSCS = lower segment Caesarean section; MCDA = monochorionic diamniotic; MCMA = monochorionic monoamniotic; NSD = normal spontaneous delivery; PPROM = preterm prelabour rupture of membranes; VE = vacuum extraction

(92.8%) pairs of MC diamniotic twins and one (7.2%) pair of MCMA twins. There were no high-order pregnancies. The median (range) maternal age was 31.5 (23-42) years. Six (42.9%) patients were nulliparous. The overall median (range) gestational age at diagnosis was 16.0 (10.9-24.3) weeks. In eight cases the pump twin survived, for an overall survival rate of 57.1%. The overall median (range) gestation at delivery was 37.0 (25.4-39.7) weeks. Fetal karyotypes were available in eight (57.1%) cases and all were normal. In eight (51.7%) cases, USG revealed that the acardiac twin had acardius acephalus, which was the most common morphology. The remaining six cases had acardius anceps (n=5) or acardius amorphous (n=1). Seven cases were managed conservatively and seven underwent fetal intervention.

In the conservative management group (Table 1), the median (range) gestational age at diagnosis and delivery were 13.4 (10.9-24.3) weeks and 37.4 (32.0-38.0) weeks, respectively. Three of the seven cases had live birth of the pump twin, achieving a survival rate of 42.9%. The median birth weight was 2550 (range, 1260-2610) g. Among the pump twins that survived, one had both PTD before 34 weeks and small for gestational age (SGA), and two had spontaneous cessation of blood flow of the acardiac twin during follow-up, with both having small acardiac-to-pump twin size ratios of <50%. Three (42.9%) cases had miscarriage, all of which had large acardiac-to-pump twin size ratios of ≥50%. Two cases, which occurred before 2007, presented in the first trimester with acardiac-to-pump twin size ratio of ≥50%; at the time, departmental policy was to delay intervention until ≥16 weeks in such cases, and the miscarriages happened at <16 weeks. One case, which was diagnosed at 11.3 weeks, presented after 2007 when the departmental policy had changed to allow earlier surgical intervention at ≥12 weeks, although miscarriage occurred at 12.7 weeks. One case had IUD at 24.5 weeks, and that the TRAP sequence was first diagnosed at 22.1 weeks with a large acardiac-to-pump twin size ratio of >100% and signs of compromise of the pump twin. However, the patient declined fetal intervention or TOP.

In the surgical intervention group (Table 2), the median (range) gestational age at diagnosis, time of procedure, and time of delivery of live births were 16.0 (12.3-20.3) weeks, 18.0 (14.1-25.0) weeks, and 37.0 (33.0-40.3) weeks, respectively. Five of the seven cases had live birth of the pump twin, achieving a survival rate of 71.4%. The median (range) birth weight was 2815 (2045-3075) g. The median treatment-to-delivery interval for live birth cases was 16.0 (range, 11.0-26.2) weeks. Among the surviving pump twins, one (20.0%) case underwent PTD before 34 weeks but none were SGA. There was one

Median gestational age at treatment (weeks)	Method	Complication	Outcome	Median gestational age at delivery (weeks)	Mode of delivery	Birth weight (g)
17+1 (First attempt); 17+3 (second attempt)	Intrafetal monopolar thermocoagulation	Partially successful after second attempt	Live birth	39+5	VE	3075
21+0	Intrafetal monopolar thermocoagulation	Successful	Live birth	37+0	LSCS	2950
17+0	Intrafetal monopolar thermocoagulation	Successful	Live birth	33+0	NSD	2045
25+0	Intrafetal monopolar thermocoagulation	Successful	Live birth	36+0	LSCS	2700
19+4 (First attempt); 20+0 (second attempt)	Intrafetal monopolar thermocoagulation	Successful after second attempt	PPROM, miscarriage at 23+2 weeks	-	-	-
18+2	Bipolar cord coagulation	Successful	IUD at 24 weeks	-	-	-
14+1	Laser cord coagulation	Successful	Live birth	40+2	VE	2815

(14.3%) miscarriage and one (14.3%) IUD, at 3 and 6 weeks after the procedure, respectively. Four cases had acardiac-to-pump twin size ratios of ≥50% at the time of diagnosis. Of these, two had polyhydramnios and one of them had cardiomegaly of the pump twin. The remaining three cases had small initial acardiac-to-pump twin size ratios (<50%), but serial monitoring showed that the acardiac twin size was increasing. Thus, treatment was indicated in these cases. For the treatment modality, five (71.4%) cases underwent intrafetal monopolar thermocoagulation, one (14.3%) underwent bipolar cord coagulation (BCC), and one (14.3%) underwent fetoscopic laser cord coagulation. In five cases successful cessation of blood flow was achieved after a single procedure. The case of BCC involved MCMA twins with acardiac-to-pump twin size ratio of 150%; the procedure was smooth and dislodged of cord of the acardiac twin, but it was complicated by IUD 6 weeks after the procedure. Two of the cases undergoing intrafetal monopolar thermocoagulation needed a second procedure to achieve cessation of blood flow; the treatment failure rate was therefore 28.6%. One of the two cases still had low blood flow after the second attempt, but with spontaneous cessation 5 weeks after the second procedure resulting in the live birth of the pump twin. Although the other case had successful complete occlusion after the second procedure, the case was complicated by PPROM and miscarriage 3 weeks after the procedure (14.3%).

When comparing surgical to conservative management, there was a trend for the surgical group to have a better survival rate of the pump twin, and less chance of PTD, SGA, miscarriage, and IUD, although these did not reach statistical significance. When comparing only the small acardiac-to-pump twin size ratio (<50%) subgroups, both surgical and conservative management had excellent survival rates of the pump twin (100%) [Table 3].

In subgroup analysis, six cases of TRAP sequence were confirmed in the first trimester. Four of the six cases had acardiac-to-pump twin size ratios of ≥50%. Three (50%) ended in miscarriage with fetal death before 16 weeks of gestation. One case underwent surgical treatment at 14.1 weeks and survived. The other two cases had acardiac-to-pump twin size ratios of <50%, and both had spontaneous cessation of blood flow during follow-up and underwent term live birth deliveries (Table 4).

Discussion

Since Van Allen et al[3] reported the pathophysiology of TRAP sequence in 1983, numerous types of intervention have been described to interrupt the vascular supply of the acardiac twin in order to improve the outcome of the pump twin. These techniques target the umbilical cord vessels, the intrafetal vessel or the vascular anastomoses on the placental surface, and include cord occlusion by

Table 3. Outcomes of conservatively and surgically managed cases*

Characteristic	Conservative (n=7)	Surgical (n=7)	p Value
Gestation at diagnosis (weeks)	13.4 (10.9-24.3)	16.0 (12.3-20.3)	0.38
Pump twin survival rate	3 (43%)	5 (71%)	0.59
Gestation at delivery for live birth (weeks)†	37.4 (32.0-38.0)	37.0 (33.0-40.3)	0.79
Adverse outcome	6 (86%)	3 (43%)	0.27
Preterm delivery ≤34 weeks†	1/3 (33%)	1/5 (20%)	1
SGA (<10th centile)†	1/3 (33%)	0	0.38
Miscarriage	3 (43%)	1 (14%)	0.56
IUD	1 (14%)	1 (14%)	1
Survival in cases with small acardiac twin‡	3/3 (100%)	3/3 (100%)	1

Abbreviations: IUD = intrauterine death; SGA = small for gestational age

* Data are shown as median (range) or No. (%)

† For live births only (3 conservative cases and 5 surgical cases)

‡ Defined as an acardiac-to-pump twin size ratio of <50% (3 conservative cases and 3 surgical cases)

Table 4. Clinical characteristics of twin reversed arterial perfusion sequence diagnosed in the first trimester

Case No.	Year	Type of twinning	Median gestational age at diagnosis (weeks)	Size ratio (%)	Sign of pump twin compromise	Progress	Treatment	Outcome	Median gestational age at delivery (weeks)	Mode of delivery	Birth weight (g)
Large-size acardiac twin*											
2	2002	MCDA	10+6	63	-	-	-	Miscarriage at 13 weeks	-	-	-
5	2005	MCDA	13+3	73	Sinus bradycardia, UA REDF	-	-	Miscarriage at 13+5 weeks	-	-	-
14	2007	MCDA	12+2	52	-	Increased size of acardiac twin	Laser cord coagulation	Live birth	40+2	VE	2815
6	2009	MCDA	11+2	64	-	-		Miscarriage at 12+5 weeks	-	-	-
Small-size acardiac twin†											
4	2005	MCDA	14+0	14	-	Acardiac twin without blood flow at 14+6 weeks	-	Live birth	38+0	NSD	2610
7	2012	MCDA	12+4	34	-	Acardiac twin without blood flow at 15+4 weeks		Live birth	37+3	LSCS	2550

Abbreviations: LSCS = lower segment Caesarean section; MCDA = monochorionic diamniotic; NSD = normal spontaneous delivery; UA REDF = umbilical artery Doppler reversed end-diastolic flow; VE = vacuum extraction

* Defined as acardiac-to-pump twin size ratio of ≥50%

† Defined as acardiac-to-pump twin size ratio of <50%

coil[13], ligation[14], cord coagulation with bipolar diathermy[15], or laser[16], or intrafetal ablation by alcohol[17], monopolar[12], laser[18], radiofrequency ablation (RFA)[19] or, most recently, high-intensity focused USG[20]. Laser coagulation of the vascular anastomoses on the placental surface has also been proven to be a safe and effective alternative[21]. However, no single technique has been shown to be unequivocally optimal[9,22].

Our study shows that surgical intervention has a trend for better survival of the pump twin, and less chance of PTD, SGA, and miscarriage, although these advantages did not reach statistical significance. The pump twin survival rate with surgical intervention in our cohort was 71%, which is comparable with large systematic reviews and meta-analyses of individual types of interventions (65-85%)[16,18,19,21-24]. Our results also have similar treatment failure rate (28.6% vs. 0-35%), procedure-related complication rate (14.3% vs. 19-30%), and PTD rate (20% vs. 11%-71.4%)[16,18,19,21-24].

In our study, five cases underwent intrafetal ablation and two underwent cord occlusion. Because of the small number of cases, we cannot draw any conclusion about which intervention had the better outcome. A systematic review by Tan and Sepulveda[22] suggests that the intrafetal technique was preferred because of significantly later gestational age at delivery (37 weeks vs. 32 weeks, p=0.04), lower technical failure rate (13% vs. 35%, p=0.03), lower rate of PTD or PPROM before 32 weeks (23% vs. 58%, p=0.003), and higher clinical success rate (77% vs. 50%, p=0.02). On the basis of recent publications, it appears that the most commonly used techniques are RFA, intrafetal laser, and BCC[25]. These techniques all have survival rates for the pump twin ratio of >80% in large systematic reviews and meta-analyses with TRAP sequence diagnosed and treated at or after 16 weeks of gestation[14,15,17,18,19,23,25,26]. Two studies comparing RFA and BCC for a variety of complications in MC twins reported similar rates of survival for the two techniques[26,27]. Our department had stopped using intrafetal monopolar thermocoagulation for the most recent cases, after 2007, as it is less effective than the other treatments.

There are ongoing discussions regarding the decision to intervene and the timing of such intervention. Some authors propose conservative treatment, waiting for evidence of compromise in the pump twin before undertaking any intervention. The advantage of such an approach is possible avoidance of an adverse outcome from the intervention (e.g. miscarriage, PPROM). Other authors favour prophylactic intervention at 16 to 18 weeks, after obliteration of the coelomic cavity, to reduce the risk of miscarriage and to preclude the difficulty of achieving cessation of blood flow in a large, and often hydropic, acardiac twin in advanced gestation[10,16]. The results of this latter approach were promising, with 80% to 90% survival rates in most of the large series[11,16,28]. This approach is still popular in many fetal therapy centres.

In recent years, however, with increasing introduction of universal first trimester Down syndrome screening worldwide as well as in Hong Kong, TRAP is increasingly being diagnosed in the first trimester. This was also observed in our study. Despite the trend for earlier diagnosis, surgical intervention is still often delayed until after 16 weeks. Reluctance to perform surgical intervention before 16 weeks primarily stems from the concern that the persistence of the coelomic cavity before this gestation time may lead to higher risks of membrane rupture and miscarriage. However, studies have shown high miscarriage rates reported in the pump twin between 12 and 16 weeks[10,18,29]. Lewi et al[10] demonstrated that eight of 24 (33%) TRAP sequences diagnosed in the first trimester resulted in spontaneous death of the pump twin before 16 weeks. Other authors reported fetal mortality following diagnosis in the first trimester of 83% to 100%, with all losses occurring at or before 16 weeks[18,29]. Our study was consistent with these findings — when TRAP sequence was diagnosed in the first trimester, fetal mortality was high (50%), and all fetal deaths occurred at or before 16 weeks. The actual incidence of fetal death following diagnosis in the first trimester might have been higher because of referral bias, with a subset of cases possibly having miscarried at local hospitals without referral. Also, some authors found that there are no USG features that could help to distinguish between pregnancies resulting in death of the pump twin from those that will survive until prophylactic intervention after 16 weeks[10,25]. Moreover, there have been reports of successful results of minimally invasive intervention for TRAP sequence before 16 weeks utilising intrafetal laser[18], RFA[19], mini-fetoscopic laser coagulation[16], as in our study or, most recently, non-invasive high-intensity focused USG[20]. Furthermore, a recent meta-analysis by Chaveeva et al[25] demonstrated that in 104 TRAP sequence cases treated with intrafetal laser, the pump twin survival rate was unrelated to the gestational age at surgical intervention, so there is no benefit to delaying intervention. The same study[25] also showed that there was an inverse association between gestational age at treatment and gestational age at birth, so early intervention may have the additional benefit of reducing the risk of preterm delivery. These observations have led to a tendency to recommend earlier prophylactic intervention from 12 weeks[10,18,25,30].

Our study showed that all the fetal deaths occurring at or before 16 weeks had a large acardiac-to-pump twin size ratio (≥50%). The only case with large acardiac twin size and in which the pump twin survived had undergone surgical intervention. So large acardiac twin size could

possibly be a poor predictor for pump twin death when TRAP sequence is diagnosed in the first trimester, and this could constitute a group with a particular need for early prophylactic treatment from 12 weeks.

The technique of choice for early intervention is likely to be intrafetal laser or RFA rather than BCC because both intrafetal laser and RFA employ smaller instruments. Intrafetal laser was more commonly used as more clinical evidence was available to support its favourable outcome. In a recent meta-analysis of 51 cases of intrafetal laser therapy, including cases from 10 studies and a large cohort from the authors, the overall neonatal survival rate was 80% with the preterm birth rate before 32 weeks being 11%. For the subgroup with treatment before 16 weeks, the outcome was significantly better, with survival of 16 of 18 (88.9%) cases, with two IUDs and two preterm births before 32 weeks[18]. However, there is a scarcity of data on the use of RFA before 16 weeks. A large multicentre study reported that the rate of IUD of the pump twin was significantly higher in cases undergoing RFA at 15 to 19 weeks than that in those treated after 19 weeks (33.3% vs. 10.7%)[23].

Our study found that for a small-size acardiac twin (<50%), both conservative and surgical management had excellent survival rates for the pump twin, reaching 100%. All small-size acardiac twins diagnosed in the first trimester (≤14 weeks) had spontaneous cessation of blood flow during follow-up and delivery of a healthy pump twin at term. This concurred with previous studies that suggested conservative management with close monitoring to be safe in pregnancies in which the acardiac twin was <50% the weight of the pump twin. Jelin et al[31] showed that in a retrospective cohort of 18 cases of small acardiac twin, 11 underwent conservative management and seven underwent surgical management by RFA; pump twin survival was 91% for the overall conservative management group, 88% for the conservative management group that had blood flow, and 100% for RFA. In their cohort there were no statistically significant differences in gestational ages at delivery, birth weights, and survival rates between these groups, even after stratification by blood flow[31].

The retrospective design of the current study only allowed categorisation of cases by the final treatment modalities (observation vs. in-utero intervention). Together with the sample size, bias was potentially introduced. It is difficult to make definitive conclusions based on our finding. Despite these limitations, our study adds some evidence that surgical intervention had a trend for better survival rates for the pump twin, and less chance of PTD, SGA, and miscarriage. Our local data showed that the outcomes of surgical intervention were comparable with other studies. In cases with small acardiac-to-pump twin size ratio (<50%), conservative management with close monitoring appeared to be a safe option. However, when TRAP sequence was diagnosed in the first trimester, it was associated with high fetal mortality (50%) at or before 16 weeks, especially for those with large acardiac-to-pump twin size ratios, which could be a possible predictor for pump twin death when TRAP sequence is diagnosed in the first trimester. Early prophylactic intervention from 12 weeks may benefit this group. A larger study will be necessary to examine whether prophylactic intervention at 12 weeks can prevent the deaths of those who would have died before 16 weeks as well as to explore the optimal early surgical intervention technique in such gestations.

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Clinical Analysis of CA125, CA72-4, and Risk of Malignancy Index in Distinguishing Benign and Malignant Ovarian Masses

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Objective: To analyse CA125, CA72-4, and risk of malignancy index in distinguishing benign and malignant ovarian masses.
Methods: This was a retrospective study of patients with ovarian mass. Patients were divided into four groups according to the pathology results: group A included follicular cyst, corpus luteum cyst, and ovarian cyst; group B comprised chocolate ovarian cyst; group C included benign ovarian tumour; and group D involved malignant ovarian tumour. Serum CA125 and CA72-4 were measured. Risk of malignancy index was calculated by CA125 value, menopause status, and ultrasound status.
Results: A total of 249 patients were included. The median values of CA125 (178.7 U/mL), CA72-4 (6.05 U/mL), and risk of malignancy index (873.2) in group D patients were significantly higher than the normal cut-off value as well as in the other three groups. In group B, the median CA125 was higher than the cut-off value (51.15 U/mL), but CA72-4 and risk of malignancy index were normal. The sensitivities of CA125, CA72-4, and risk of malignancy index were 80.95%, 52.38%, and 73.81%, respectively; respective values for specificity were 70.97%, 79.29%, and 95.41%; for positive predictive value were 35.78%, 31.88%, and 75.61%; and for negative predictive value were 95.06%, 90%, and 94.97%.
Conclusions: Serum CA125 had the highest sensitivity and risk of malignancy index had the highest specificity. Combination of the three factors, CA125, CA72-4, and risk of malignancy index could be used to differentiate benign ovarian mass from ovarian cancer and increased the specificity to 98%. The positivity rates of the three factors increased in line with the clinical status of ovarian cancer, and could be used to better evaluate the risk of ovarian cancer, especially epithelial ovarian cancer.
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Keywords: Antigens, tumor-associated, carbohydrate; CA-125 antigen; Ovarian neoplasms; Risk factors

Introduction

Ovarian mass comprises several types of cysts and tumours, including benign tumour, malignant tumour, chocolate cyst, and ovarian cyst, of which ovarian tumour (benign and malignant) is the most common. Ovarian cancer is a malignant tumour of women, with a wide range of pathological (histological) types, and is the primary cause of death from the female reproductive tract[1]. According to global statistics, most ovarian cancers are diagnosed at an advanced stage, and less than 20% of women with advanced ovarian cancer (stages III and IV) are cured[2]. Less than 25% of ovarian cancers are identified at stage I[3], although the 5-year survival for early-stage ovarian cancer is more than 90%[4,5], and most patients can be cured by cytoreductive surgery with no need for chemotherapy or radiotherapy. Hence, early detection of ovarian cancer is very important, as are effective methods for diagnosis and evaluating preoperative risk. CA125 is a widely used tumour marker, but it has low sensitivity for early-stage ovarian cancer and its presence in some benign ovarian masses makes its specificity low. The specificity of CA72-4 is higher than that of CA125, but its sensitivity is lower, thus a combination of both tumour markers provides a better tool for diagnosis of ovarian cancer. Differentiation of ovarian masses is challenging preoperatively. According to Jacobs et al[6], increasing risk of malignancy index (RMI) score, CA125 level, menopausal status, and ultrasound status could be used to evaluate the risks for patients with ovarian tumours and to differentiate between benign and malignant ovarian masses. This study systematically

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analysed CA125, CA72-4, and RMI with the aim of differentiating ovarian cancer from benign ovarian mass. The study also analysed the relationship of these three factors with ovarian cancer status and pathological type for early detection of ovarian cancer.

Methods

Study Design and Population

This was a retrospective study of hospitalised patients presenting with ovarian mass in Jiamusi University First Affiliated Hospital, China from 1 December 2011 to 31 May 2013. All patients had newly diagnosed ovarian mass. Patients with polycystic ovary syndrome, previous oophorectomy, previous related treatment, such as surgery, radiotherapy, chemotherapy, or hormonal therapy, previous diagnosis of ovarian mass, and other related diseases or cancers were excluded. Patients were divided into four groups according to the postoperative pathology report: group A included follicular cyst, corpus luteum cyst, and ovarian cyst, group B comprised chocolate ovarian cyst; group C included benign ovarian tumour; and group D involved malignant ovarian tumour.

Methods and Determination of CA125, CA72-4, and Risk of Malignancy Index

Patients' venous blood samples (2 mL) were collected after 12 hours of fasting. The samples were collected without undergoing any anticoagulation procedures and were left for at least 30 minutes before centrifugation, and were then centrifuged for 20 minutes at 3000 rpm. After centrifugation, the serum was collected and stored in cryovials. In keeping with procedure, if there was any sediment present then re-centrifugation was done. Haemolysis and cell granules were not present. The serum was stored in a freezer at a temperature of 4°C to 5°C and assayed within 24 hours at the Nuclear Medicine Laboratory of the First Affiliated Hospital of Jiamusi University using ECLIA (electrochemiluminescence immunoassay) to check the serum levels of CA125 and CA72-4. The RMI was calculated according to patient's menopausal status, preoperative ultrasound status, and CA125 value as below:

RMI = M x U x serum CA125

M stands for menopausal status: 1 point for premenopausal patients or those having menstruation within 1 year of the blood collection; 3 points for postmenopausal patients, those who had had no menstruation for >1 year, those aged >50 years had had a hysterectomy, or those aged >55 years whose last menstruation was not known. U stands for ultrasound status: 1 point was given for the each of the following criteria: multilocular cysts, solid areas, metastases, ascites, and bilateral lesions. Then we added up the scores and got the U value according to the following criteria: U = 0 if the score was 0; U = 1 if the score was 1; and U = 3 if the score was 2 to 5. Serum CA125 was measured in IU/mL[7]. The respective cut-off values for CA125, CA72-4, and RMI were 35 U/mL, 6 U/mL, and 200.

Statistical Analyses

The Statistical Package for the Social Sciences version 19.0 (IBM Corp., Armonk [NY], US) was used to analyse relevant data. Medians and interquartile ranges were used for determination of the four groups, and non-parametric tests were used to compare the three factors among the four groups. Analysis of the relationship of pathology type and clinical stage to the three factors was done for group D. Specificity, sensitivity, positive predictive value, negative predictive value, and area under curve of the three factors and the combination of the three factors were determined for group D. Kruskal-Wallis test was used to analyse the differences among the four groups. Mann-Whitney test and Wilcoxon W test were used for pairwise comparisons. A p value of <0.05 was considered statistically significant.

Results

A total of 249 patients were included in this study, including 27 in group A, 64 in group B, 116 in group C, and 42 in group D; their respective mean ± standard deviation age was 41.93 ± 13.23, 37.70 ± 6.99, 41.27 ± 12.20, and 53.62 ± 8.45 years. Group D patients' age ranged from 35 to 74 years, with 28 postmenopausal and 14 premenopausal patients. Among these four groups, group D patients were significantly older ($p<0.05$) and group B patients were significantly younger ($p<0.05$).

As shown in Table 1, the medians and interquartile ranges of all three markers in group A and group C patients were within the normal ranges. The median CA125 in group B patients (51.15 U/ml) was higher than the normal cut-off value, but those of CA72-4 (3.17 U/mL) and RMI (56.51) were within the normal ranges. In group D patients, their median CA125 (178.7 U/mL), CA72-4 (6.05 U/mL), and RMI (873.2) were all significantly higher than the normal range. Comparison of CA125, CA72-4, and RMI in the four groups showed statistical significance ($p<0.05$) [Table 2].

Values of CA125 and RMI of group D were significantly higher than the other three groups. CA125

Table 1. Values of CA125, CA72-4, and risk of malignancy index among four groups of ovarian mass*

Group†	CA125 (U/mL)	CA72-4 (U/mL)	Risk of malignancy index
Group A	19.46 (11.53-25.51)	2.48 (1.01-5.08)	22.63 (13.07-30.51)
Group B	51.15 (31.91-84.20)	3.17 (1.73-6.12)	56.51 (39.64-101.86)
Group C	14.2 (9.90-23.83)	3.12 (1.43-5.89)	18.45 (11.70-35.55)
Group D	178.7 (53.02-838.33)	6.05 (2.24-22.46)	873.2 (187.32-4095.80)

* Values are shown as median (interquartile range)

† Group A = follicular cyst, corpus luteum cyst, and ovarian cyst; group B = chocolate ovarian cyst; group C = benign ovarian tumour; group D = malignant ovarian tumour

Table 2. Comparison of CA125, CA72-4, and risk of malignancy index among four groups of ovarian mass (using Kruskal-Wallis test)

Factor	Chi-square	Degrees of freedom	p Value
CA125	109.666	3	<0.001
CA72-4	12.135	3	0.01
Risk of malignancy index	109.177	3	<0.001

Table 3. Pairwise comparisons of CA125, CA72-4, and risk of malignancy index among four groups of ovarian mass*

Pairwise comparison*	CA125				CA72-4				Risk of malignancy index			
	Mann-Whitney *U*	Wilcoxon W	Z	p Value†	Mann-Whitney *U*	Wilcoxon W	Z	p Value†	Mann-Whitney *U*	Wilcoxon W	Z	p Value†
Groups A vs. D	109.50	487.50	-5.625	0.000	336.00	714.00	-2.840	0.005	65.00	443.00	-6.172	0.000
Groups B vs. D	696.00	2776.00	-4.186	0.000	950.50	3030.50	-2.542	0.011	389.00	2469.00	-6.169	0.000
Groups C vs. D	430.00	6646.00	-7.772	0.000	1621.50	7837.50	-2.901	0.004	301.00	6517.00	-8.299	0.000
Groups A vs. B	223.00	601.00	-5.569	0.000	675.00	1053.00	-1.642	0.101	273.00	651.00	-5.135	0.000
Groups B vs. C	971.00	7187.00	-7.996	0.000	3386.50	9602.50	-0.513	0.608	1379.00	7595.00	-6.732	0.000
Groups A vs. C	1288.00	7504.00	-1.130	0.26	1307.00	1685.00	-1.028	0.304	1439.50	7655.50	-0.317	0.752

* Group A = follicular cyst, corpus luteum cyst, and ovarian cyst; group B = chocolate ovarian cyst; group C = benign ovarian tumour; group D = malignant ovarian tumour

† $\alpha = 0.0083$; p values of <0.0083 (i.e. p of 0.05 / 6 pairs) had statistical significance

in group B was significantly higher than groups A and C, whereas values of CA72-4 in group D were significantly higher than groups A and C, but no significant differences were shown when compared with group B (i.e. p>0.0083). Comparisons of CA125, CA72-4, and RMI between groups A and C showed no statistical significance (Table 3).

The sensitivity (80.95%) and negative predictive value (95.06%) of CA125, as well as the specificity (95.41%), positive predictive value (75.61%) and diagnosis rate of RMI (95.98%) were highest in group D patients. The sensitivity of CA72-4 was lower for this group, but the specificity was higher than that of CA125. The combination of the three factors decreased the sensitivity to 42.86%, but increased the specificity to 98.07%. The positive predictive value was higher with the three factors combined than for any single factor alone (81.82%; Table 4).

The area under the receiver operating characteristic curve (ROC AUC) value used to evaluate the relationship of sensitivity and specificity of CA125, CA72-4, and RMI in group D were 0.854, 0.657, and 0.911, respectively, in which the AUC of RMI was the greatest (Table 5 and Fig).

According to International Federation of Gynaecology and Obstetrics (FIGO), Spearman test of the

Table 4. Comparison of sensitivity, specificity, positive predictive value, and negative predictive value in ovarian cancer

	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Accuracy (%)
CA125 (35 U/mL)	80.95 (34/42)	70.97 (154/215)	35.78 (34/95)	95.06 (154/162)	75.50 (188/249)
CA72-4 (6 U/mL)	52.38 (22/42)	79.29 (180/227)	31.88 (22/69)	90.00 (180/200)	81.12 (202/249)
Risk of malignancy index (200)	73.81 (31/42)	95.41 (154/218)	75.61 (31/41)	94.97 (154/219)	95.98 (239/249)
Combination of all markers	42.86 (18/42)	98.07 (203/207)	81.82 (18/22)	89.43 (203/227)	88.76 (211/249)

Table 5. ROC AUC comparisons of the three factors in ovarian cancer

Factor	ROC AUC	(95% Confidence interval)
CA125	0.854	0.787-0.921
CA72-4	0.657	0.556-0.759
Risk of malignancy index	0.911	0.854-0.968

Abbreviation: ROC AUC = area under the receiver operating characteristic curve

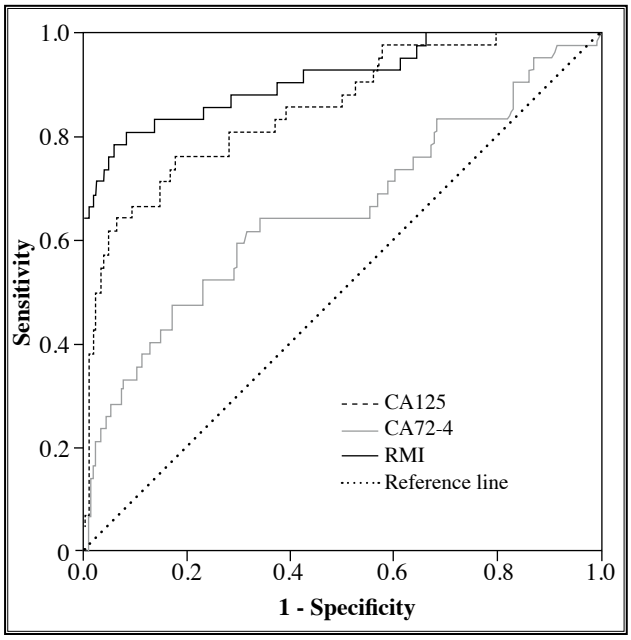

*Figure. Receiver operating characteristic (ROC) curve analysis of CA125, CA72-4, and risk of malignancy index (RMI) for diagnosis of ovarian cancer**

* Diagonal segments are produced by ties

median of the three factors in different stages of ovarian cancer showed a p value of <0.01, with CA125, CA72-4, and RMI having positive relationships with FIGO clinical stage. According to FIGO clinical stage, the median, interquartile ranges, and positivity rates of CA125, CA72-4, and RMI all increased according to the development of the clinical stage (Tables 6 and 7).

According to the pathological type of ovarian cancer, the median CA125 in epithelial ovarian cancer was 210.00 U/mL, and that the value was highest in serous cystadenocarcinoma (422.05 U/mL). The median CA72-4 in epithelial ovarian cancer was 6.63 U/mL, and that the value was highest in clear cell carcinoma (20.99 U/mL). The median RMI of epithelial ovarian cancer was 786.87, and that the value was highest in serous cystadenocarcinoma (2051.40) and for clear cell carcinoma it was 305.10. The median values of CA125, CA72-4, and RMI in some types of non-epithelial ovarian cancer were higher than the normal range (Table 8).

Discussion

Ovarian cancer is the seventh most common cause of cancer death for woman worldwide[8]; according to the Global Burden of Disease Study in 2010, about 160,000 women died from ovarian cancer, up from 113,000 in 1990[9]. In the US, about 1.7% to 2.5% (1 in every 40 to 60) women have the possibility of developing ovarian cancer. The risk is greater among elderly women[10]. In 2010, a survey found that 21,880 women were diagnosed ovarian cancer, with 13,850 deaths[11]. The risk increases with age, and decreases as the number of pregnancies has increased[12]. The lifetime risk is approximately 1.6%, but the risk increases to 5% for women with a first-grade relative who has had ovarian cancer. Survival dramatically increases for women who are diagnosed at an early stage; however, about 70% of cases are diagnosed at stages III or IV, with greatly decreased 5-year survival rates[13].

Table 6. Values and positivity of CA125, CA72-4, and RMI in ovarian cancer by FIGO stage

FIGO stage	CA125		CA72-4		RMI	
	Median (interquartile range)	Positivity	Median (interquartile range)	Positivity	Median (interquartile range)	Positivity
I (n=10)	24.26 (18.35-231.03)	4 (40%)	2.02 (1.09-5.02)	2 (20%)	59.40 (19.81-693.75)	5 (50%)
II (n=10)	77.85 (59.20-428.83)	9 (90%)	6.05 (2.48-19.41)	6 (60%)	577.26 (187.32-1434.52)	7 (70%)
III and IV (n=20)*	609.50 (155.50-2186.00)	20 (100%)	13.41 (4.84-42.19)	13 (65%)	3313.50 (720.78-8896.50)	19 (95%)
Unstaged (n=2)†	-	1/2	-	0/2	-	1/2
Total (n=42)	**178.7 (53.02-838.33)**	**34 (80.95%)**	**6.05 (2.24-22.46)**	**21 (50.00%)**	**873.2 (187.32-4095.80)**	**32 (76.19%)**

Abbreviations: FIGO = International Federation of Gynaecology and Obstetrics; RMI = risk of malignancy index

* Since there are only two cases of stage IV ovarian cancer, we combined stages III and IV, which is considered to be 'late stage'

† Two cases of ovarian cancer were unstaged, and were not put into test analysis in this comparison

Table 7. Relativity of CA125, CA72-4, and RMI and ovarian cancer by FIGO stage

	Spearman Rs*	p Value
CA125 (n=40)	0.629	<0.001
CA72-4 (n=40)	0.472	0.001
RMI (n=40)	0.629	<0.001

* When the confidence level (one-sided) was 0.01, the relativity was significant

FIGO = International Federation of Gynaecology and Obstetrics; RMI = risk of malignancy index

Effective methods for diagnosis and evaluating preoperative risk, such as tumour markers, imaging, and consideration of risk factors are important. CA125 is a widely used tumour marker, but it has low sensitivity in the early stages of ovarian cancer and its presence in some women with benign ovarian masses reduces its specificity.

It is recommend that women older than 30 years should have a physical examination every year and, if ultrasound shows a mass, they should have their serum tumour markers checked and undergo further investigation to evaluate the risk of developing ovarian cancer. CA125 and CA72-4 are widely used in clinical practice. Jacobs et al[6] proposed an evaluation tool for ovarian cancer in the form of the RMI, which uses menopausal status, ultrasound status, and CA125 level to calculate the risk of cancer in a patient with an ovarian mass.

This research systematically analysed CA125, CA72-4, RMI, and a combination of the three factors in order to distinguish ovarian cancer from benign ovarian mass, as well as to analyse the relationship of the three factors with ovarian cancer status and pathological type for early detection of ovarian cancer. The serum level of CA125 in chocolate ovarian cyst patients (group B) was higher than the normal range, while CA72-4 and RMI levels were within the normal range. The CA125 range could be used to differentiate ovarian chocolate cyst (31.91-84.20 U/mL) from ovarian cancer (53.02-838.33 U/mL), with their respective medians being 51.15 U/mL and 178.7 U/mL ($p<0.01$). From this study, for patients with an ovarian mass presenting with high CA125, a combination of CA72-4 and RMI could be used; if they were both within the normal range, it was highly likely that the ovarian mass was a chocolate ovarian cyst, and ovarian cancer could be excluded and evaluated as low risk ($p<0.01$).

We can evaluate the risk of cancer for patients with ovarian mass using this method. According to the RMI, preoperative evaluation can assign women into high-risk and low-risk groups, with RMI of >200 being high risk for ovarian cancer when CA125 and CA72-4 were higher than the normal range. For ovarian cancer patients, RMI specificity was 95.41%, the positive predictive value was the highest at 75.61%, and the diagnostic rate being the highest at 95.98%. CA125 sensitivity was the highest at 80.95%, with negative predictive value also being the highest at 95.06%. Regarding CA72-4, its sensitivity was lower than that of CA125, yet its specificity being higher. The combination of the three factors could increase the

Table 8. Values and positivity of CA125, CA72-4, and risk of malignancy index according to ovarian cancer pathology

Histological classification	CA125	
	Median (interquartile range)	Positivity
Epithelial ovarian cancer		
Serous cystadenocarcinoma (n=24)	422.05 (77.85-1901.50)	21 (87.5%)
Mucinous cystadenocarcinoma (n=3)*	56.74	2 (66.7%)
Endometrioid adenocarcinoma (n=1)*	64.34	1 (100%)
Clear cell carcinoma (n=7)	120.20 (26.81-295.50)	5 (71.4%)
Overall (n=35)	**210.00 (57.56-1000.33)**	**29 (82.9%)**
Sex cord (stromal)		
Granular cell tumour (n=1)*	10.98	-
Thecoma (n=2)*	483.75	2/2
Fibroma (n=1)*	1066.00	1/1
Overall (n=4)	**167.50**	**3/4**
Germ cell		
Malignant teratoma (n=1)*	17.55	-
Metastatic ovarian cancer (n=2)*	138.67	2/2

* Interquartile ranges were not stated in view of too few cases for analysis

specificity to 98.07% and the positive predictive value to 81.82%, while the sensitivity was decreased.

Using the normal range to ascertain the ROC AUC of CA125, CA72-4, and RMI in ovarian cancer, the ROCs were 0.854, 0.657, and 0.911, respectively. The ROC AUC of the RMI was the greatest, with the highest diagnosis rate meaning that RMI is the most effective value for evaluating the risk of ovarian cancer. This information will help to decide such factors as the tests needed, whether to move the patient to a specialised hospital, the best treatment plan, and the best time for treatment, thus obtaining the best treatment outcome and prognosis.

This study used Spearman's correlation to analyse the relationship between FIGO clinical stage and the three factors, and the results were statistically significant. The correlation was positive for CA125, CA72-4, and RMI and increased with the development of each clinical stage. Therefore, using the three factors, we can evaluate the risk of ovarian cancer, the prognosis, and the 5-year survival rate. This method enables risk evaluation and appropriate treatment of patients with ovarian mass.

In conclusion, in a comparison of CA125, CA72-4, and RMI, RMI was the better tool to distinguish benign and malignant ovarian mass, and can help in evaluating the risk of cancer for patients with ovarian mass. The combination of CA125, CA72-4, and RMI can be used to better evaluate the risk of ovarian cancer, especially epithelial ovarian cancer, for early detection and prognosis.

Declaration

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CA72-4		Risk of malignancy index	
Median (interquartile range)	**Positivity**	**Median (interquartile range)**	**Positivity**
7.74 (4.71-24.91)	15 (62.5%)	2051.40 (423.90-7508.25)	20 (83.3%)
2.49	-	170.22	1 (33.3%)
0.20	-	193.02	-
20.99 (1.87-44.76)	4 (57.1%)	305.10 (120.20-2034.90)	5 (71.4%)
6.63 (2.45-25.39)	**19 (54.3%)**	**786.87 (205.09-4698.60)**	**26 (74.3%)**
2.64	-	32.94	-
16.71	-	4353.75	1/2
5.01	-	3198.00	1/1
2.64	**-**	**1507.50**	**2/4**
1.95	-	17.55	-
6.02	1/2	1248.03	2/2

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MENARINI

Intraoperative Frozen Section Versus Intraoperative Gross Examination in the Assessment of Myometrial Invasion in Clinical Stage I Endometrial Cancer

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Objective: To evaluate the accuracy of frozen section and gross examination in assessing myometrial invasion in endometrial cancer with respect to definitive histological examination.
Methods: A retrospective study of women who underwent surgical treatment for clinical stage I endometrial cancer at the Pamela Youde Nethersole Eastern Hospital between 1 July 2003 and 30 June 2013 was conducted. The women underwent intraoperative gross examination or frozen section for assessment of myometrial invasion. Deep myometrial invasion was defined as involvement of ≥50% of the thickness of the myometrium. The final histopathology was considered the reference standard. The accuracy, sensitivity, specificity, positive predictive value, and negative predictive value for both modalities were analysed.
Results: Of 115 women included in the study, 49 had gross examination and 66 had frozen section. Gross examination correctly identified (accuracy) the depth of myometrial invasion in 67.3% of cases with sensitivity, specificity, and positive and negative predictive values of 33.4%, 78.4%, 33.3%, and 78.4%, respectively. Frozen section correctly identified (accuracy) 95.5% of cases with sensitivity, specificity, and positive and negative predictive values of 92.3%, 96.2%, 85.7%, and 98.1%, respectively.
Conclusion: Frozen section appeared to be more effective than gross examination in assessing myometrial invasion and hence should be preferred as a basis for selective lymphadenectomy for clinical stage I endometrial cancer.
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Keywords: Endometrial neoplasms; Frozen sections; Intraoperative period; Neoplasm invasiveness

Introduction

Endometrial cancer is the sixth most common cancer in women worldwide, and the twelfth most common cancer overall[1]. In 2012, endometrial cancer occurred in 320,000 women and caused 76,000 deaths. In 2011, carcinoma of the corpus was the fourth leading cancer for women in Hong Kong, with an incidence of 685 cases and a relative frequency of 5.3%[2]. Fortunately, most patients with carcinoma of the uterus present early with abnormal bleeding and therefore approximately 70% to 75% of patients are diagnosed with stage I disease, with high 5-year survival rates of 88% and 75% for stage IA and 1B, respectively[3].

In 1988, the International Federation of Gynaecology and Obstetrics (FIGO) Cancer Committee changed the staging of endometrial carcinoma from a clinical to a surgicopathological system[4]. While there is general agreement about the necessity of complete surgical staging for high-risk endometrial carcinoma as the risk of nodal metastasis is high, the management of low-risk endometrial cancer is controversial. There has been an emerging dichotomy between European and North American treatment protocols for the management of low-risk endometrial cancer. Some authors advocate only hysterectomy and bilateral salpingo-oophorectomy without lymphadenectomy, while others suggest comprehensive surgical staging for all patients with low-risk disease[5,6].

Data have shown that the risk of lymph node metastasis is directly related to the depth of myometrial invasion[7]. Patients with more than 50% gross myometrial invasion had a 6.4-fold higher prevalence of pelvic

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lymph node metastases, a 6.9-fold higher prevalence of para-aortic lymph node metastases, and a 6.7-fold higher prevalence of advanced surgical stage than those with less than 50% myometrial invasion[7]. In what can be considered as early-stage carcinomas, i.e. when there is superficial myometrial invasion of less than 50% of the thickness of the myometrium, no invasion of the cervical stroma, tumour measurement <2 cm, and a less aggressive histological type (grades 1 and 2), it has been demonstrated that patients do not benefit from lymphadenectomy in terms of recurrence and survival[5]. Assessment of the degree of myometrial invasion is therefore essential to avoid under- or over-treatment.

Gross visual examination of the tumour cut surface during the operation is a common method to evaluate the depth of myometrial invasion. Several studies have proposed that intraoperative gross examination is comparable to the final histological evaluation[7-9]. Intraoperative frozen section (FS) was shown to be more accurate in assessing depth of myometrial invasion and enabling the tumour grade and cell type to be assessed; however, marked variability in reported accuracy has been found among institutions that used this method[10]. Frozen section has the disadvantage of prolonging operative time and requires a skilled histologist, thereby increasing the overall cost of the procedure. Since the introduction of selective pelvic lymphadenectomy for low-risk endometrial carcinoma in our unit, FS is preferred to gross examination for assessment of the depth of myometrial invasion. This study aimed to compare the validity of intraoperative FS compared with gross examination in predicting the depth of myometrial invasion.

Methods

This was a retrospective consecutive case note review of all patients who were diagnosed with endometrial cancer on curettage or office endometrial biopsy and were surgically treated at Pamela Youde Nethersole Eastern Hospital (PYNEH) from 1 July 2003 to 30 June 2013.

Only patients with clinical stage I disease with preoperative histological diagnosis of grade 1 or 2 endometrial cancer of low-risk cell types were included in this cohort. Clinical stage I disease was defined as tumour confined to the uterus on preoperative clinical examination, imaging, and intraoperative gross examination prior to hysterectomy. Women with clinical stage 2 or above or with synchronous ovarian cancer were excluded from this study as the extent of surgery would depend on factors other than grading or myometrial invasion. All patients with preoperative diagnosis of grade 3 endometrial cancer or demonstrated clear cell, serous papillary differentiation, or carcinosarcoma were classified as high-risk cell types and were excluded from the study. Any patients without a definite preoperative tumour grade were also excluded from the study. Detailed patient demographics, operation details, and histology results were retrieved from the clinical records. The primary treatment for all recruited patients was hysterectomy and bilateral salpingo-oophorectomy done via open surgery, laparoscopy, or robot-assisted laparoscopy.

In the gross examination group, almost all patients were operated in or before 2009 and had routine pelvic lymphadenectomy regardless of the myometrial invasion. All the gross examinations were performed by one of the consultant gynaecologists who had a special interest in oncology. After removal of the uterus, its anterior wall was incised and opened along the uterine fundus to the cervix using a scalpel. At gross inspection of the uterine cavity and wall, the depth of myometrial invasion was noted as less or greater than 50% after a full-thickness incision was made through the tumour. The estimated depth of myometrial invasion was noted in the patient's operative record. These operative findings were compared with the final histological report.

In the FS group, the uterus, fallopian tubes, and ovaries were removed and submitted fresh for FS evaluation intraoperatively. The level of expertise for FS evaluation varied from fellow to senior consultant pathologists. The pathologist reporting the FS had the presenting pathology grade available for reference. The uterus was sliced at 3 to 5 mm intervals to look for possible myometrial invasion foci; the deepest focus was sampled. One to three blocks were taken for FS depending on the distribution and macroscopic appearance of the tumour. With myometrial invasion ≥50% on the FS, the decision of whether to perform lymph node dissection was taken by the surgeon.

Accurate FS pathology was defined as complete concordance between FS reporting and definitive reporting of paraffin sections with regard to the depth of myometrial invasion (<50% or ≥50%). Any degree of discordance between the FS and final histopathology was defined as inaccurate FS pathology. The same comparison was made between gross examination and paraffin sections on depth of myometrial invasion for degree of concordance.

The study was approved by the Cluster Research Ethics Committee of Hong Kong East Cluster under the

Hospital Authority. Statistical analysis was carried out by Predictive Analytics Software 18 (formerly the Statistical Package for the Social Sciences; SPSS, Inc., Chicago [IL], US) and Statistical Analysis System version 9.1 (SAS Institute, Inc., Cary [NC], US). For the association of categorical data, Chi-squared test and Fisher's exact test were used according to the data pattern. For continuous data with a highly skewed distribution, a non-parametric test (i.e. Mann-Whitney *U* test) was used. A p value of <0.05 was considered statistically significant.

Results

A total of 203 women were diagnosed with uterine cancer and underwent hysterectomy at PYNEH during the study period, of whom 196 were diagnosed with endometrial cancer. Only 115 patients fulfilled the criteria of clinical stage I disease with low-grade tumour on preoperative histology; 49 had gross examination and 66 had frozen section. The general baseline epidemiological data were similar in both groups (Table 1).

Gross examination only correctly identified (accuracy) the depth of myometrial invasion in 67.3% of the 49 patients. A positive test was defined as deep myometrial invasion with involvement of ≥50% of the thickness of the myometrium.

The false-negative and false-positive rates were 66.7% (8/12) and 21.6% (8/37), respectively (Table 2). The sensitivity, specificity, positive predictive value, and negative predictive value were 33.3%, 78.4%, 33.3%, and 78.4%, respectively.

Table 1. Demographics and surgicopathological factors*

	Gross examination (n=49)	Frozen section (n=66)	Total (n=115)	p Value
Age at operation (years)	58 (52.5-73.5)	56 (52-65.25)	58 (52-68)	0.19
Body weight (kg)†	60.75 (51.63-65.93)	58.75 (51-66.63)	60.3 (51.25-66.35)	0.82
Menopausal status				
Premenopausal	16 (32.7)	22 (33.3)	38 (33.0)	0.94
Postmenopausal	33 (67.3)	44 (66.7)	77 (67.0)	
Postmenopausal age (years)	50 (47-54)	51 (50-53)	50 (50-54)	0.21
Hypertension	27 (55.1)	28 (42.4)	55 (47.8)	0.18
Diabetes mellitus	6 (12.2)	11 (16.7)	17 (14.8)	0.51
Tamoxifen	3 (6.1)	2 (3.0)	5 (4.3)	0.65
Polycystic ovarian syndrome	0	2 (3.0)	2 (1.7)	0.51
Hereditary non-polyposis colorectal cancer gene carrier	1 (2.0)	3 (4.5)	4 (3.5)	0.64
Unopposed hormone replacement therapy	1 (2.0)	0	1 (0.9)	0.43
Preoperative tumour grade				0.71
1	40 (81.6)	52 (78.8)	92 (80.0)	
2	9 (18.4)	14 (21.2)	23 (20.0)	

* Data are shown as median (interquartile range) or No. (%)
† Missing data of 1 patient in the gross examination group

Table 2. Depth of myometrial invasion in gross examination and frozen section compared with final histopathology

Final histopathology	Gross examination (n=49)		Frozen section diagnosis (n=66)	
	<50%	≥50%	<50%	≥50%
<50%	29/37 (78%)	8/37 (22%)	51/53 (96%)	2/53 (4%)
≥50%	8/12 (67%)	4/12 (33%)	1/13 (8%)	12/13 (92%)

The FS correctly identified (accuracy) the depth of myometrial invasion in 95.5% of the 66 patients. The false-negative rate was 7.7% (1/13) and false-positive rate was 3.8% (2/53) [Table 2]. The sensitivity, specificity, positive predictive value, and negative predictive value were 92.3%, 96.2%, 85.7%, and 98.1%, respectively.

Discussion

Because of the prognostic importance of intraoperative findings, FIGO adopted a surgicopathological system for the staging of endometrial carcinoma in 1988[11]. The incidence of lymph node metastasis increases with grade of tumour, depth of myometrial invasion, cervical or adnexal involvement, lymphovascular invasion, and poor histological type[4].

The role of lymphadenectomy in the management of early endometrial cancer has been discussed extensively since the introduction of surgicopathological staging. A significant number of women with clinical early-stage disease have extrauterine disease within the pelvic or para-aortic lymph nodes[4]. However, routine lymphadenectomy increases morbidity, such as bleeding, lymphocyst formation, and lymphoedema[12-14]. Also, addition of lymphadenectomy to the staging surgery of early-stage endometrial cancer has been shown not to improve the survival[5] despite earlier data that demonstrated survival benefits[15]. In order to avoid morbidity due to overtreatment, identification of the risk factors that can accurately predict pelvic lymph node involvement and therefore guide the need for selective lymphadenectomy in high-risk patients is indicated.

The key finding from our study was that FS analysed by general anatomic pathologists appeared to be much more accurate than gross examination by experienced surgeons in the assessment of myometrial invasion in endometrial cancer, with accuracies of 95.5% and 67.3%, respectively.

Unlike previous studies of FS and gross examination, which included all cases of endometrial cancer, this study is clinically relevant as it concentrated on the subgroup of patients for whom the decision to perform full surgical staging is made during surgery.

Gross examination of the depth of myometrial invasion is an inexpensive, fast and, in some studies, accurate method for identifying patients at increased risk for extrauterine metastases. The accuracy of intraoperative gross examination of myometrial invasion has been evaluated in several studies with controversial results. Several studies[7,8,16] found the procedure to be highly accurate (>86%). However, Larson et al[7] and Franchi et al[8] both did prospective studies of larger sample sizes that included endometrial cancer of all cell types, grades, and stages. The uteri were incised along the lateral walls along the course of the uterine vessels for examination instead of being cut on the anterior wall along the uterine fundus to the cervix as in our study. Doering et al[16] conducted a study limited to patients with clinical stage I endometrial cancer, but all cell types and grades of tumour were included. Noumoff et al[17] found that the depth of myometrial invasion by gross evaluation was in accordance with the final specimen in only 67.7% of cases, which corresponds to our findings of 67.3% accuracy.

In this study, we found that FS assessment of the depth of myometrial invasion in patients with endometrial cancer was considerably higher than gross examination, with accuracy of 95.5%. Other studies evaluating the accuracy of FS support our findings. A retrospective analysis of 209 patients in which presenting histology of grade 3 or high-risk cell types were excluded also demonstrated accuracy of 94.7%[18]. An older study of 204 patients also demonstrated accuracy of 95%[19]. However, other prospective studies have reported accuracy as low as 67%[20]. Since the sample for FS is taken from the point of deepest macroscopically visible invasion, sampling error is possible. It has been commented that it would be particularly difficult to determine the best spot for sampling if the tumour macroscopically appeared to be confined to the endometrium and showed no signs of discrimination such as change of colour or consistency[21].

The discrepancies between the different studies described above could lie with the expertise of the surgeons who performed gross examination or of the pathologists who performed FS. In the present study, all the gross examinations were performed by the few consultant gynaecologists who had a special interest in oncology, whereas FSs were performed by pathologists who had obtained their fellowship, albeit with varying levels of experience. Interobserver and intraobserver errors could be present, and further prospective studies to evaluate the impact of such errors and to correlate with the experience of individual observers would be worthwhile.

With FS, the duration of operation is prolonged resulting in longer exposure to general anaesthesia and higher risk of infection for the patient. In addition, since the extent of the operation will be dictated by the result of the FS, the exact time allocated for each operation will be difficult

to estimate beforehand, thus creating problems in resource management. In order to avoid these shortcomings, other imaging techniques such as ultrasonography, computed tomography, and magnetic resonance imaging (MRI) have also been employed to evaluate the depth of myometrial invasion with different degrees of reliability[7]. Among these methods, MRI is currently seen as the best technique for myometrial assessment. However, Furukawa et al[10] reported the diagnostic accuracy with MRI to be as low as 54.8% whereas Manfredi et al[22] reported diagnostic accuracy of 89%. Further studies have yet to be performed to compare the diagnostic accuracy of FS or gross examination with MRI in predicting the degree of myometrial invasion. Apart from accuracy, there could also be concerns about the cost-effectiveness and availability of such expensive imaging technology, especially in developing countries.

Our study have several limitations. First, this retrospective study could be subjected to data bias, as only records with complete data were included for analysis. Second, despite the fact that the study period spanned more than 10 years, the number of cases that satisfied the preset inclusion criteria of clinical low-risk stage I endometrial cancer and could therefore be analysed was limited. Third, there could be interobserver and intraobserver errors as surgeons and pathologists with varying experience were performing the gross examinations and FSs.

Nevertheless, we believe this local study still provides valuable information for other centres in Hong Kong, which may still be relying purely on gross examination to decide which subgroup of patients require lymphadenectomy in clinical stage I endometrial cancer.

Although MRI may provide better preoperative planning of the indicated surgical procedure and time allocated for each operation, as well as allowing more precise preoperative counselling to the patient, its accuracy for myometrial invasion assessment is still controversial and requires further evaluation. To date, there is still no consensus on a gold standard for preoperative or intraoperative assessment of myometrial invasion in clinical stage I endometrial cancer. According to our data, FS is highly accurate and so, in terms of decision-making, it should be valuable and effective. Moreover, FS has benefit over MRI and gross examination in providing assessment of tumour grade. This is particularly important as some studies have suggested that correlation between presenting tumour grade and final histopathology is often poor[23,24].

In conclusion, this study suggests that FS is more accurate than gross examination in the assessment of myometrial invasion in early-stage endometrial cancer, so the decision on the need for selective lymphadenectomy should be based on FS findings.

Declaration

The authors declared no conflicts of interest in connection with this article.

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A Cross-sectional Study of the Relationship of Serum Folic Acid, Vitamin B_{12}, Zinc, Magnesium with Semen Parameters in Infertile Couples in Hong Kong

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Objectives: The primary objective was to evaluate the association of serum folate, vitamin B_{12}, zinc, magnesium with semen parameters in infertile couples in Hong Kong. The secondary objective was to explore whether the study participants were deficient in any of these micronutrients. The impact of smoking on semen parameters was also analysed.
Methods: This cross-sectional study recruited 196 Chinese men from the Subfertility Clinic of the Department of Obstetrics and Gynaecology, Kwong Wah Hospital between August 2012 and November 2013. Semen and blood samples were collected on the same day for analysis.
Results: Higher levels of serum magnesium were significantly associated with higher percentages of normal sperm morphology (p=0.02). The median levels of micronutrients studied were within the normal range, indicating that deficiency of these nutrients was rare in our locality, although such deficiency is common in western countries. Both median semen volume and sperm concentration were within the normal range but the median percentages of normal sperm morphology and motility were below the normal range. We postulate that sperm morphology might be improved by an increased intake of magnesium. Smoking was significantly associated with low semen volume (p=0.01).
Conclusion: This is the first study to evaluate the relationship between serum micronutrients and semen parameters in infertile Chinese couples in our locality. Male subfertility is a multifactorial disorder. Although both nutritional and lifestyle factors are important and modifiable, further research on these subjects would provide a platform for potential fertility treatments.
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Keywords: Folic acid; Magnesium; Semen; Vitamin B 12; Zinc

Introduction

Approximately 16% of couples in Hong Kong are involuntarily childless[1]. This has a great influence on the quality of life[2]. Male infertility contributes to 30% to 50% of all infertility cases[3]. Several animal studies have demonstrated the effects of micronutrients such as folate, vitamin B_{12}, zinc, and magnesium on spermatogenesis[4-7].

Folate is essential for processes that are important for spermatogenesis including DNA synthesis[8], regulation of DNA transcription via methylation[3], as well as transfer RNA and proteins. Vitamin B_{12} is an essential component of DNA synthesis and is also a cofactor in the folate-dependent conversion of homocysteine to methionine. The impact of folate and vitamin B_{12} on semen parameters is controversial. Serum folate and vitamin B_{12} levels have been reported to be lower in infertile subjects[9], although other studies have shown no such association[10,11].

Zinc serves as a cofactor for more than 80 metalloenzymes involved in DNA transcription, expression of steroid receptors and protein synthesis[12-15]. A lowered serum zinc level has been shown to be more common in infertile patients[16]. Zinc is important in testicular development, spermatogenesis, and sperm motility[17]. It

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improves spermatogenesis in animals[15], and increases sperm concentration[18,19], motility[20], and morphology in subfertile males[21].

Magnesium is an essential ion for enzyme activations in the body that are related to male sexual functions[22], including various biochemical processes of spermatogenesis, and functions in sperm motility. Biochemical processes include synthesis of ATP, cAMP, proteins and DNA, ATP hydrolysis, and the functioning of enzymes and non-enzymatic factors involved in proper protective antioxidant mechanisms[23-25]. It is proposed that ATPase releases energy required for sperm motility from ATP[26]. According to Morisawa and Okuno[27], sperm motility requires both cAMP and magnesium ATP, and the formation of them is magnesium-intensive. In-vivo magnesium has been shown to increase sperm motility and sperm production by up to 80%[28], although studies of the impact of serum magnesium on semen variables are scarce.

Most studies have been conducted among a western population. We hypothesised that deficiency in these serum micronutrients would also aggravate semen quality in our Chinese population. The primary objective of our study was to thus evaluate the association of serum folate, vitamin B_{12}, zinc, and magnesium, with semen parameters in infertile couples in Hong Kong. The secondary objective was to explore whether a deficiency of the studied micronutrients was present among the study participants. We also analysed the impact of smoking on semen variables. Although causes of male subfertility are multifactorial, nutrition and lifestyle factors are modifiable. We hoped to gain an invaluable insight into the potential nutrients that improve semen quality, and thus explore the options for fertility treatment.

Methods

This was a cross-sectional study. Chinese couples were recruited when they attended the Subfertility Clinic of the Department of Obstetrics and Gynaecology, Kwong Wah Hospital between August 2012 and November 2013. Infertility was defined as failure to conceive over 1 year of regular intercourse without contraception. Subjects who were non-Chinese and mentally incompetent were excluded. Participants were given written information regarding the objectives and details of the study and informed consent was obtained prior to study recruitment. The sample size was calculated based on the formula:

$$n = \frac{z^2_{1-\frac{\alpha}{2}}\, p(1-p)}{d^2}$$

where α is the significance level ($\alpha = 0.05$), $z_{1-\frac{\alpha}{2}}$ means the corresponding z value from standard normal distribution (mean = 0, standard deviation = 1), p being the response rate, and d being the margin of error. Assuming p (response rate) to be 80% and d (margin of error) to be 0.06, the required sample size (n) was 171.

Study subjects who attended the Subfertility Clinic were asked to save a semen sample for analysis and blood was taken. One semen sample and blood sample were collected from each subject on the same day. Demographic and clinical data were obtained from the subfertility assessment forms in the electronic patient record through the Clinical Management System of the Hospital Authority, Hong Kong, and included age, occupation, smoking status, history of medical illness or operations, history of genital infection or injury and any coital problem. The study was approved by the Ethics Committee of Kowloon West Cluster, Hospital Authority, Hong Kong.

Semen Analysis

The participant produced a semen sample by masturbation. Self-reported duration of ejaculation abstinence and time of ejaculation were obtained. The whole ejaculate of semen was required to be collected without a condom at home by masturbation into the container provided, then tightly capped. Time of semen collection was recorded; 2 to 3 days of sexual abstinence was advised prior to semen collection. The samples were delivered to the Andrology Laboratory within 1 hour of collection. Once received, the semen was allowed to liquefy for 30 to 60 minutes at room temperature before semen analysis was performed. Semen analysis was performed according to the fifth edition of the World Health Organization (WHO) laboratory manual for the examination and processing of human semen[29]. Motility of sperm was classified as progressive (PR) or non-progressive (NP). Semen analysis was performed in the Andrology Laboratory of Dr Stephen Chow Chun-kay Assisted Reproduction Centre of Kwong Wah Hospital by trained medical technicians. Semen variables were categorised as normal if they were equal or above the reference values, and abnormal if below the reference values according to the WHO 2010's reference values[29].

Blood Measurements

Venous blood samples were drawn into vacutainer tubes and analysed in the Laboratory of Department of Pathology, Kwong Wah Hospital. For serum folate and serum vitamin B_{12}, 4 mL clotted blood was analysed using

chemiluminescent microparticle immunoassay on Abbott Architect i2000SR System (Abbott, US). For serum zinc, 4 mL clotted blood was analysed using ICP-AES (inductively coupled plasma atomic emission spectroscopy) on Varian Vista-MPX CCD Simultaneous ICP-AES System (Varian, Australia). For serum magnesium, 4 mL clotted blood was analysed using calmagite spectrophotometry on Beckman Coulter UniCel DxC800 Synchron Clinical System (Beckman Coulter Inc., US). The normal reference ranges of the laboratory of the Department of Pathology of Kwong Wah Hospital for each micronutrient level were as follows: serum folate (3.10-20.50 ng/mL), serum vitamin B_{12} (187-883 pg/mL), serum zinc (10-19 μmol/l), and serum magnesium (0.70-1.05 mmol/l). The serum level of these micronutrients in each blood sample was categorised as deficient if it was below normal range, sufficient if it was within the normal range, and high for those above the normal range.

Statistical Analyses

Analyses were performed using SPSS version 20 for Mac (SPSS Inc., Chicago [IL], US). The association between semen parameters and micronutrient levels was examined as categorical data using exact Chi-square test and Fisher's exact test. A p value of <0.05 was considered statistically significant. Continuous variables were presented as median (interquartile range). The multiple logistic regression analysis (stepwise) was performed to include variables found to be significant at $p<0.2$ by univariate analysis, if considered to be an important demographic variable.

Results

Demographic and Clinical Data

A total of 235 couples were approached during the study period from August 2012 to November 2013. Of the 200 couples recruited, four non-Chinese men were excluded, thus semen and blood samples from 196 Chinese men were analysed. The response rate was 85.1% (200/235).

Table 1[29,30] summarises the demographic and clinical data of the participants as well as their semen variables. The median age of participants (n=196) was 37 years. Demographic details were as follows: 91 (46.4%) worked at administrative levels and as professionals while 26 (13.3%) engaged in labouring work; 122 (62.2%) were non-smokers, 57 (29.1%) were smokers and 17 (8.7%) were ex-smokers. Nine had hypertension, four had diabetes mellitus, three had hyperlipidaemia, two were obese, two had gout, two had hypothyroidism and were prescribed T4 supplementation, 12 had a history of mumps, two had varicocele diagnosed in the male subfertility clinic following referral for azoospermia, and one had previous surgery for varicocele. For history of genital infection or injury, two had a history of prostatitis. Semen samples were collected throughout the year, 45 (23.0%) in spring (March to May), 48 (24.5%) in summer (June to August), 67 (34.2%) in autumn (September to November), and 36 (18.4%) in winter (December to February).

The median duration of abstinence was 3 days and the median time of liquefaction was 44 minutes. There were four subjects with azoospermia and therefore the association between serum micronutrient level and sperm motility and normal morphology could not be studied in these samples. Among these four cases of azoospermia, all had the diagnosis confirmed by repeat semen analysis and were referred to the Male Subfertility Clinic in Queen Mary Hospital for assessment and further investigations. Three individuals attended the clinic for assessment and one did not; two had non-obstructive azoospermia with the presence of varicocele and microdissection testicular sperm extraction with or without intracytoplasmic sperm insemination was discussed. One was diagnosed to be likely obstructive azoospermia and was scheduled for scrotal exploration. The median (range) semen volume was 2.5 (2.0-3.8) mL, the median sperm concentration was 30 (14-48) M/mL, the median PR motility was 27.5% (18%-34%), the median total motility (PR+NP) was 37% (30%-45%), and the median normal form was 2% (1%-4%). Both median semen volume and sperm concentration of the participants were within the normal range, but median motility and normal form were below the normal range.

Serum Folate and Vitamin B_{12}

Two samples were cancelled due to gross haemolysis. The median serum folate and vitamin B_{12} level was 7.60 (5.68-9.73) ng/mL and 448.50 (365-562.75) pg/mL, respectively, both within the normal range recommended by our laboratory. The majority of Chinese participants (97.4%) had a normal serum level of folate. There was no statistically significant association between serum folate (Table 2) and vitamin B_{12} (Table 3) levels respectively with each semen parameter.

Serum Zinc

One haemolysed sample was excluded from analysis. The median (range) serum zinc level was 12 (11-13) μmol/l. There was no statistically significant association between serum zinc level and each semen parameter (Table 4).

Table 1. Demographics of participants (n=196)

Demographics	Data*
Age (years)	37 (34-42)
21-30	18 (9.2%)
31-40	117 (59.7%)
41-50	51 (26%)
51-60	9 (4.6%)
61-70	1 (0.5%)
Occupation†	
Managers and administrators	12 (6.1%)
Professionals	16 (8.2%)
Associate professionals	63 (32.1%)
Clerks	30 (15.3%)
Service workers and shop sales workers	38 (19.4%)
Plant and machine operators and assemblers	18 (9.2%)
Elementary occupations	8 (4.1%)
Self-employed	4 (2.0%)
Unemployed	3 (1.5%)
Retired	1 (0.5%)
Missing data	3 (1.5%)
Smoking status	
Non-smoker	122 (62.2%)
Smoker	57 (29.1%)
Ex-smoker	17 (8.7%)
Disease	
Hypertension	9 (4.6%)
Diabetes	4 (2.0%)
Hyperlipidaemia	3 (1.5%)
Obesity	2 (1.0%)
Gout	2 (1.0%)
Hypothyroidism on T4 supplement	2 (1.0%)
History of mumps	12 (6.1%)
Varicocele	2 (1.0%)
Varicocele with operation done	1 (0.5%)
History of prostatitis	2 (1.0%)

* Data are shown as median (interquartile) or No. (%) of subjects

† Classified according to the International Labour Organization[30]

‡ Classified according to the Hong Kong Observatory

§ Determination according to the World Health Organization (2010) laboratory manual for the examination and processing of human semen, 5th edition[29] were employed as reference values. Normal reference values were semen volume of 1.5 mL, sperm concentration of 15 M/mL, motility PR of 32%, total motility (PR+NP) of 40%, and normal morphology of 4%

¶ Four semen samples were azoospermia and were excluded from analysis

Table 1. (cont'd)

Demographics	Data*
Season of semen collection‡	
Spring	45 (23.0%)
Summer	48 (24.5%)
Autumn	67 (34.2%)
Winter	36 (18.4%)
Days of abstinence	3 (3-5)
0-1	1 (0.5%)
2-3	100 (51.0%)
4-7	92 (46.9%)
>7	3 (1.5%)
Time of liquefaction (mins)	44 (33.5-55.0)
Within 1 hour	177 (90.3%)
1-2 Hours	19 (9.7%)
Semen parameters§	
Volume (mL)	2.5 (2.0-3.8)
Concentration (M/mL)	30 (14-48)
Motility PR¶ (%)	27.5 (18-34)
Total motility (PR+NP)¶ [%]	37 (30-45)
Normal form¶ (%)	2 (1-4)

Serum Magnesium

Low serum magnesium level was not found in any sample. The median (range) serum magnesium level was 0.92 (0.88-0.97) mmol/l. There was no statistically significant association between serum magnesium and semen volume, sperm concentration or motility (Table 5). Nonetheless there was a significant association between serum magnesium and normal morphology of sperm (p=0.02). Those who had a high serum magnesium level were less likely to have an abnormal form of sperms (odds ratio [OR]=0.13, 95% confidence interval [CI], 0.03-0.61, p=0.01) but were more likely to be older (OR=1.12, 95% CI, 1.02-1.24, p=0.02) [Table 5 and 6].

Smoking Status

Current smoker status was significantly associated with low semen volume compared with non-smoker and ex-smoker (Table 7).

Discussion

Our study demonstrates a significant association between serum magnesium and normal sperm morphology (p=0.02): a higher serum magnesium level was less likely to be associated with abnormal sperm morphology. The

Table 2. Serum folate level and semen parameters in Chinese infertile men (n=194)*

	Serum folate level (ng/mL)			p Value
	Deficient (<3.10)	Sufficient (3.10-20.50)	High (>20.50)	
Current smoking status				0.28
No	1 (0.5%)	134 (69.1%)	2 (1.0%)	
Yes	2 (1.0%)	55 (28.4%)	0	
Hypertension				1
No	3 (1.5%)	180 (92.8%)	2 (1.0%)	
Yes	0	9 (4.6%)	0	
Diabetes				1
No	3 (1.5%)	186 (95.9%)	2 (1.0%)	
Yes	0	3 (1.5%)	0	
Hyperlipidaemia				1
No	3 (1.5%)	186 (95.9%)	2 (1.0%)	
Yes	0	3 (1.5%)	0	
Obesity				1
No	3 (1.5%)	187 (96.4%)	2 (1.0%)	
Yes	0	2 (1.0%)	0	
Gout				1
No	3 (1.5%)	187 (96.4%)	2 (1.0%)	
Yes	0	2 (1.0%)	0	
Hypothyroidism on T4 supplement				1
No	3 (1.5%)	187 (96.4%)	2 (1.0%)	
Yes	0	2 (1.0%)	0	
History of mumps				1
No	3 (1.5%)	177 (91.2%)	2 (1.0%)	
Yes	0	12 (6.2%)	0	
Varicocele				1
No	3 (1.5%)	187 (96.4%)	2 (1.0%)	
Yes	0	2 (1.0%)	0	
Varicocele with operation				1
No	3 (1.5%)	188 (96.9%)	2 (1.0%)	
Yes	0	1 (0.5%)	0	
History of prostatitis				1
No	3 (1.5%)	187 (96.4%)	2 (1.0%)	
Yes	0	2 (1.0%)	0	
Season of collection				0.61
Spring	2 (1.0%)	43 (22.2%)	0	
Summer	0	46 (23.7%)	1 (0.5%)	
Autumn	1 (0.5%)	65 (33.5%)	1 (0.5%)	
Winter	0	35 (18.0%)	0	
Duration of abstinence (days)				0.66
0-1	0	1 (0.5%)	0	
2-3	2 (1.0%)	95 (49.0%)	2 (1.0%)	
4-7	1 (0.5%)	90 (46.4%)	0	
>7	0	3 (1.5%)	0	

Abbreviations: NP = non-progressive motility; PR = progressive motility

* Two blood samples were grossly haemolysed and were excluded from analysis

† Four semen samples were azoospermia and were excluded from analysis

Table 2. (cont'd)

	Serum folate level (ng/mL)			p Value
	Deficient (<3.10)	Sufficient (3.10-20.50)	High (>20.50)	
Time of liquefaction				1
Within 1 hour	3 (1.5%)	170 (87.6%)	2 (1.0%)	
1-2 Hours	0	19 (9.8%)	0	
Semen parameters				
Volume (mL)				
Normal	3 (1.5%)	172 (88.7%)	2 (1.0%)	1
Abnormal	0	17 (8.8%)	0	
Concentration (M/mL)				
Normal	3 (1.5%)	141 (72.7%)	1 (0.5%)	0.37
Abnormal	0	48 (24.7%)	1 (0.5%)	
Motility PR (%)†				
Normal	0	67 (35.3%)	0	0.48
Abnormal	3 (1.6%)	118 (62.1%)	2 (1.1%)	
Total motility (PR+NP) [%]†				
Normal	0	85 (44.7%)	0	0.17
Abnormal	3 (1.6%)	100 (52.6%)	2 (1.1%)	
Normal form (%)†				
Normal	0	56 (29.5%)	0	0.59
Abnormal	3 (1.6%)	129 (67.9%)	2 (1.1%)	

median level of each micronutrient studied was within the normal range, indicating that deficiency of these nutrients is rare in our locality. Of note, serum folate deficiency is common in western countries. We also demonstrated that smoking was significantly associated with low semen volume.

In our study, we demonstrated that a higher level of serum magnesium was significantly associated with a higher percentage of normal sperm morphology. Daily magnesium intake in the human diet is often below the daily requirement that may be even higher for many patients who engage in high levels of physical activity and / or who experience high levels of stress[31,32]. Thus, a relative hypomagnesaemia may occur despite the fact that the serum magnesium level is within the clinically physiological reference range.

A prospective pilot study was conducted by Kiss et al[33] and Viski et al[34] to evaluate the effectiveness of oral magnesium therapy on human semen parameters. They reported that 1 mg oral magnesium-citrate, administered daily for 3 continuous months, increased sperm volume, sperm count, motile sperm ratio, and normal morphology ratio. However, Závaczki et al[35] have conducted a randomised, placebo-controlled clinical pilot study among 20 men who suffered from idiopathic infertility to examine the effect of magnesium orotate on male idiopathic infertility, and shown that treatment at a dose of 3000 mg/day for 90 consecutive days led to neither a significant improvement in sperm variables nor an increased pregnancy rate in female partners of treated males compared with the controls.

Nonetheless, it does suggest that magnesium supplementation is advisable for patients if their daily dietary magnesium intake is less than the required amount, or if magnesium loss is increased due to chronic illness, high physical activity, or stress[35]. Among our participants, occupation could be a source of stress in the case of administrators and professionals, or a high degree of physical activity required by jobs such as labouring work; nonetheless the problem of infertility was also an important stressor. Magnesium is abundant in nature, found in green vegetables, chlorophyll, cocoa derivatives, nuts, wheat, seafood, and meat. Although further research on magnesium supplementation is needed, an increased dietary intake is a considerable alternative.

Table 3. Serum vitamin B_{12} level and semen parameters in Chinese infertile men (n=194)*

	Vitamin B_{12} level (pg/mL)			p Value
	Deficient (<187)	Sufficient (187-883)	High (>883)	
Current smoking status				0.77
No	1 (0.5%)	130 (67.0%)	6 (3.1%)	
Yes	0	56 (28.9%)	1 (0.5%)	
Hypertension				0.08
No	0	178 (91.8%)	7 (3.6%)	
Yes	1 (0.5%)	8 (4.1%)	0	
Diabetes				1
No	1 (0.5%)	183 (94.3%)	7 (3.6%)	
Yes	0	3 (1.5%)	0	
Hyperlipidaemia				1
No	1 (0.5%)	183 (94.3%)	7 (3.6%)	
Yes	0	3 (1.5%)	0	
Obesity				1
No	1 (0.5%)	184 (94.8%)	7 (3.6%)	
Yes	0	2 (1.0%)	0	
Gout				1
No	1 (0.5%)	184 (94.8%)	7 (3.6%)	
Yes	0	2 (1.0%)	0	
Hypothyroidism on T4 supplement				1
No	1 (0.5%)	184 (94.8%)	7 (3.6%)	
Yes	0	2 (1.0%)	0	
History of mumps				0.41
No	1 (0.5%)	175 (90.2%)	6 (3.1%)	
Yes	0	11 (5.7%)	1 (0.5%)	
Varicocele				1
No	1 (0.5%)	184 (94.8%)	7 (3.6%)	
Yes	0	2 (1.0%)	0	
Varicocele with operation				1
No	1 (0.5%)	185 (95.4%)	7 (3.6%)	
Yes	0	1 (0.5%)	0	
History of prostatitis				0.08
No	1 (0.5%)	185 (95.4%)	6 (3.1%)	
Yes	0	1 (0.5%)	1 (0.5%)	
Season of collection				0.21
Spring	0	41 (21.1%)	4 (2.1%)	
Summer	0	45 (23.2%)	2 (1.0%)	
Autumn	1 (0.5%)	65 (33.5%)	1 (0.5%)	
Winter	0	35 (18.0%)	0	
Duration of abstinence (days)				0.15
0-1	0	1 (0.5%)	0	
2-3	0	96 (49.5%)	3 (1.5%)	
4-7	1 (0.5%)	87 (44.8%)	3 (1.5%)	
>7	0	2 (1.0%)	1 (0.5%)	

Abbreviations: NP = non-progressive motility; PR = progressive motility

* Two blood samples were grossly haemolysed and were excluded from analysis

† Four semen samples were azoospermia and were excluded from analysis

Table 3. (cont'd)

	Vitamin B_{12} level (pg/mL)			p Value
	Deficient (<187)	Sufficient (187-883)	High (>883)	
Time of liquefaction				1
Within 1 hour	1 (0.5%)	167 (86.1%)	7 (3.6%)	
1-2 Hours	0	19 (9.8%)	0	
Semen parameters				
Volume (mL)				
Normal	1 (0.5%)	169 (87.1%)	7 (3.6%)	1
Abnormal	0	17 (8.8%)	0	
Concentration (M/mL)				
Normal	1 (0.5%)	140 (72.2%)	4 (2.1%)	0.53
Abnormal	0	46 (23.7%)	3 (1.5%)	
Motility PR (%)†				
Normal	0	65 (34.2%)	2 (1.1%)	1
Abnormal	1 (0.5%)	117 (61.6%)	5 (2.6%)	
Total motility (PR+NP) [%]†				
Normal	1 (0.5%)	82 (43.2%)	2 (1.1%)	0.34
Abnormal	0	100 (52.6%)	5 (2.6%)	
Normal form (%)†				
Normal	0	56 (29.5%)	0	0.13
Abnormal	1 (0.5%)	126 (66.3%)	7 (3.7%)	

Table 4. Serum zinc level and semen parameters in Chinese infertile men (n=195)*

	Serum zinc level (μmol/L)			p Value
	Deficient (<10)	Sufficient (10-19)	High (>19)	
Current smoking status				0.33
No	8 (4.1%)	130 (66.7%)	0	
Yes	2 (1.0%)	54 (27.7%)	1 (0.5%)	
Hypertension				0.11
No	8 (4.1%)	177 (90.8%)	1 (0.5%)	
Yes	2 (1.0%)	7 (3.6%)	0	
Diabetes				0.21
No	9 (4.6%)	181 (92.8%)	1 (0.5%)	
Yes	1 (0.5%)	3 (1.5%)	0	
Hyperlipidaemia				1
No	10 (5.1%)	181 (92.8%)	1 (0.5%)	
Yes	0	3 (1.5%)	0	
Obesity				1
No	10 (5.1%)	182 (93.3%)	1 (0.5%)	
Yes	0	2 (1.0%)	0	

Abbreviations: NP = non-progressive motility; PR = progressive motility

* One blood sample was haemolysed and were excluded from analysis

† Four semen samples were azoospermia and were excluded from analysis

Table 4. (cont'd)

	Serum zinc level (µmol/L)			p Value
	Deficient (<10)	Sufficient (10-19)	High (>19)	
Gout				1
No	10 (5.1%)	182 (93.3%)	1 (0.5%)	
Yes	0	2 (1.0%)	0	
Hypothyroidism on T4 supplement				1
No	10 (5.1%)	182 (93.3%)	1 (0.5%)	
Yes	0	2 (1.0%)	0	
History of mumps				1
No	10 (5.1%)	172 (88.2%)	1 (0.5%)	
Yes	0	12 (6.2%)	0	
Varicocele				1
No	10 (5.1%)	182 (93.3%)	1 (0.5%)	
Yes	0	2 (1.0%)	0	
Varicocele with operation				1
No	10 (5.1%)	183 (93.8%)	1 (0.5%)	
Yes	0	1 (0.5%)	0	
History of prostatitis				1
No	10 (5.1%)	182 (93.3%)	1 (0.5%)	
Yes	0	2 (1.0%)	0	
Season of collection				0.41
Spring	4 (2.1%)	41 (21.1%)	0	
Summer	1 (0.5%)	46 (23.6%)	0	
Autumn	3 (1.5%)	64 (32.8%)	0	
Winter	2 (1.0%)	33 (16.9%)	1 (0.5%)	
Duration of abstinence (days)				0.63
0-1	0	1 (0.5%)	0	
2-3	4 (2.1%)	94 (48.2%)	1 (0.5%)	
4-7	6 (3.1%)	86 (44.1%)	0	
>7	0	3 (1.5%)	0	
Time of liquefaction				
Within 1 hour	9 (4.6%)	166 (85.1%)	1 (0.5%)	
1-2 Hours	1 (0.5%)	18 (9.2%)	0	
Semen parameters				
Volume (mL)				
Normal	10 (5.1%)	167 (85.6%)	1 (0.5%)	0.64
Abnormal	0	17 (8.7%)	0	
Concentration (M/mL)				
Normal	7 (3.6%)	138 (70.8%)	1 (0.5%)	0.79
Abnormal	3 (1.5%)	46 (23.6%)	0	
Motility PR (%)†				
Normal	1 (0.5%)	65 (34.0%)	1 (0.5%)	0.08
Abnormal	9 (4.7%)	115 (60.2%)	0	
Total motility (PR+NP) [%]†				
Normal	2 (1.0%)	82 (42.9%)	1 (0.5%)	0.11
Abnormal	8 (4.2%)	98 (51.3%)	0	
Normal form (%)†				
Normal	3 (1.6%)	54 (28.3%)	0	1
Abnormal	7 (3.7%)	126 (66.0%)	1 (0.5%)	

Table 5. Serum magnesium level and semen parameters in Chinese infertile men (n=196)

	Serum magnesium level (mmol/L)		p Value
	Sufficient (0.70-1.05)	High (>1.05)	
Median (interquartile range) age (years)	36 (33-42)	41 (38-45.5)	0.05
Current smoking status			0.72
No	133 (67.9%)	6 (3.1%)	
Yes	54 (27.6%)	3 (1.5%)	
Hypertension			0.35
No	179 (91.3%)	8 (4.1%)	
Yes	8 (4.1%)	1 (0.5%)	
Diabetes			1
No	183 (93.4%)	9 (4.6%)	
Yes	4 (2.0%)	0	
Hyperlipidaemia			1
No	184 (93.9%)	9 (4.6%)	
Yes	3 (1.5%)	0	
Obesity			1
No	185 (94.4%)	9 (4.6%)	
Yes	2 (1.0%)	0	
Gout			1
No	185 (94.4%)	9 (4.6%)	
Yes	2 (1.0%)	0	
Hypothyroidism on T4 supplement			1
No	185 (94.4%)	9 (4.6%)	
Yes	2 (1.0%)	0	
History of mumps			0.10
No	177 (90.3%)	7 (3.6%)	
Yes	10 (5.1%)	2 (1.0%)	
Varicocele			1
No	185 (94.4%)	9 (4.6%)	
Yes	2 (1.0%)	0	
Varicocele with operation			1
No	186 (94.9%)	9 (4.6%)	
Yes	1 (0.5%)	0	
History of prostatitis			1
No	185 (94.4%)	9 (4.6%)	
Yes	2 (1.0%)	0	
Season of collection			0.18
Spring	43 (21.9%)	2 (1.0%)	
Summer	47 (24.0%)	1 (0.5%)	
Autumn	61 (31.1%)	6 (3.1%)	
Winter	36 (18.4%)	0	0.18
Duration of abstinence (days)			0.25
0-1	1 (0.5%)	0	
2-3	98 (50.0%)	2 (1.0%)	
4-7	85 (43.4%)	7 (3.6%)	
>7	3 (1.5%)	0	

Abbreviations: NP = non-progressive motility; PR = progressive motility

* Four semen samples were azoospermia and were excluded from analysis

Table 5. (cont'd)

	Serum magnesium level (mmol/L)		p Value
	Sufficient (0.70-1.05)	High (>1.05)	
Time of liquefaction			0.21
Within 1 hour	170 (86.7%)	7 (3.6%)	
1-2 Hours	17 (8.7%)	2 (1.0%)	
Semen parameters			
Volume (mL)			
Normal	170 (86.7%)	9 (4.6%)	1
Abnormal	17 (8.7%)	0	
Concentration (M/mL)			
Normal	139 (70.9%)	8 (4.1%)	0.46
Abnormal	48 (24.5%)	1 (0.5%)	
Motility PR (%)*			
Normal	65 (33.9%)	2 (1.0%)	0.50
Abnormal	118 (61.5%)	7 (3.6%)	
Total motility (PR+NP) [%]*			
Normal	81 (42.2%)	5 (2.6%)	0.52
Abnormal	102 (53.1%)	4 (2.1%)	
Normal form (%)*			
Normal	52 (27.1%)	6 (3.1%)	0.02
Abnormal	131 (68.2%)	3 (1.6%)	

Table 6. Correlation between having sufficient / high serum magnesium level with morphology of sperm and age

Variable	Odds ratio (95% confidence interval)	p Value
Morphology of sperm [Reference group: normal form (%)]	0.13 (0.03-0.61)	0.01
Age	1.12 (1.02-1.24)	0.02

Of note, our study shows that the majority of Chinese participants (97.4%) had a normal serum level of folate, contrary to western studies, and folate deficiency was rare; hence echoing the studies by Tso and Wong[36] and Lee et al[37,38]. These data revealed that there is a very low incidence of folate deficiency in Hong Kong Chinese: the Chinese style of food consumption in Hong Kong is characterised by a high daily intake of leafy green vegetables, in addition to soybean, green tea, and to a lesser extent animal liver, all of which represent rich sources of folate[39-42].

Among the participants, the median normal morphology of sperm was below the normal range. It is to be determined whether an increased dietary intake or supplementation of magnesium can improve these semen variables and this will be the subject of our future research.

In our study, smoking was significantly associated with low semen volume (p=0.01). The mechanism whereby cigarette smoking affects sperm function is not well understood. Some studies have shown that smoking has a detrimental effect on sperm quality, most significantly sperm concentration, motility, and morphology[43-47]. Since cigarette smoke contains many substances including nicotine, carbon monoxide, heavy metals, benzopyrene, dimethylbenzanthracene dimethylnitrosamine, naphthalene and metanaphtalene[48], smoking can increase inflammatory agents and effect sperm genome and gonads and failure in sperm-ovum fecundation and thus decrease fertility[49]. Contrary to this though, some studies have shown no

Table 7. Current smoking status and semen parameters in Chinese infertile men (n=196)

Semen parameters	Current smoking status		p Value
	Non-smokers and ex-smokers	Smokers	
Volume (mL)			0.01
Normal	132 (67.3%)	47 (24.0%)	
Abnormal	7 (3.6%)	10 (5.1%)	
Concentration (M/mL)			0.32
Normal	107 (54.6%)	40 (20.4%)	
Abnormal	32 (16.3%)	17 (8.7%)	
Motility PR (%)*			0.63
Normal	46 (24.0%)	21 (10.9%)	
Abnormal	90 (46.9%)	35 (18.2%)	
Total motility (PR+NP) (%)*			0.54
Normal	59 (30.7%)	27 (14.1%)	
Abnormal	77 (40.1%)	29 (15.1%)	
Normal form (%)*			0.18
Normal	45 (23.4%)	13 (6.8%)	
Abnormal	91 (47.4%)	43 (22.4%)	

Abbreviations: NP = non-progressive motility; PR = progressive motility

* Four semen samples exhibited azoospermia and were excluded from analysis

association between smoking and sperm quality[50,51], or sperm function[52].

The impact of cigarette smoking on male fertility thus remains a highly controversial issue. Since male smokers are very susceptible to oxidative damage induced by free radicals, infertile men who smoke cigarettes should be advised to quit given the potential adverse effects of seminal oxidative stress[48].

Strengths and Limitations

Our study is the first research study in a Chinese population in our locality to examine the relationship of serum folic acid, vitamin B_{12}, zinc, and magnesium, to semen parameters in infertile couples. We have demonstrated a significant association between serum magnesium and sperm normal morphology. Since a higher serum magnesium level is associated with a higher percentage of normal sperm morphology, this will aid in further exploration of potential treatments for male subfertility.

There were some limitations of our study. Semen parameters vary between samples from the same individual, and in our study only one semen sample was collected and studied from each participant. Hence it might not truly reflect the quality of semen of the study subject. In addition the serum micronutrient level will vary over time due to dietary intake and physical consumption. We therefore collected the semen and blood samples on the same day assuming that the serum micronutrients studied were involved in the spermatogenesis of semen samples being analysed.

A multi-centre WHO study on the influence of varicocele on fertility parameters demonstrated that varicocele is associated with impaired testicular function and infertility[53]. Whether surgery can help improve semen quality remains controversial. One of the participants in our study had a history of varicocele surgery and the remaining two were identified to have varicocele upon examination in the male subfertility clinic; since there was no routine physical examination of men in our subfertility clinic, the prevalence of varicocele might have been underestimated.

Conclusion

Our study is the first research study in a Chinese population in our locality to examine the relationship of serum folic acid, vitamin B_{12}, zinc, and magnesium to semen parameters in infertile couples. We demonstrated

a significant association between serum magnesium and normal morphology of sperm as well as the detrimental effect of smoking on semen volume, contributing to male infertility. Male factor subfertility is a multifactorial disorder. Nutritional factors, unlike genetic factors, can be adjusted by altering dietary intake. Whether an improvement in normal sperm morphology following magnesium supplementation or increased dietary intake will result in an increase in pregnancy rates remains to be established. This should further stimulate research on nutrition and environmental factors in the pathogenesis and prevention of fertility disorders.

Declaration

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Effects of Paternity Leave on Maternal Postpartum Depression in Hong Kong Chinese

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Objectives: To examine the effects of paternity leave on maternal postpartum depression, paternal involvement in neonatal care, and maternal perception of social support in Hong Kong Chinese.
Methods: A prospective study was conducted from July to September 2013 in Tuen Mun Hospital, Hong Kong, among postpartum women with liveborn babies. The subjects were assessed by a self-administered survey between 1 and 5 days postpartum, and again at 6 to 8 weeks postpartum. Postpartum depression and social support were assessed using the Edinburgh Postnatal Depression Scale and the Multidimensional Scale of Perceived Social Support, respectively. Paternal involvement in baby care was rated on a Likert scale.
Results: A total of 424 (65.1%) of the 651 subjects responded to the second survey between 6 and 8 weeks postpartum. The prevalence of postpartum depression was 31.4% (133/423). Postpartum depression was associated with shorter duration of stay in Hong Kong, lower family income, lower perceived social support, and lower paternal involvement. The prevalence of paternity leave was 61.6% (261/424) with a mean duration of 8.9 days. Paternity leave was associated with paternal involvement, partner companionship during labour, and some demographic variables (marital status, maternal work status, education level, duration of stay in Hong Kong, family income, household size, number of existing children, helper availability, and pregnancy plan). Paternity leave had no statistically significant effect on maternal perception of social support or postpartum depression.
Conclusion: Although paternity leave was associated with increased paternal involvement in baby care, which was in turn associated with a reduced risk of postpartum depression, it had no direct effect on postpartum depression.
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Keywords: Depression, postpartum; Parental leave; Paternal behavior; Pregnancy complications; Social support

Introduction

Paternity leave is a form of parental leave offered to the father of a newborn so that he can give support to the mother, bond with the newborn, and participate in baby care. Laws about paternity leave vary around the world, with some places offering very generous terms up to months, and others fewer measures in place to promote and protect parental leave. Paternity leave can be taken both before and after a birth, for varying lengths of time. In some places, people are entitled to full or partial pay during their paternity leave. In places where paternity leave is not required by law, it is still provided by some proactive employers. In other instances, the employee has to negotiate with the employer to obtain leave to care for a newborn, and may be forced to take limited time off without pay. Other employers may grant annual leave to facilitate the new father who wants to spend some time at home. In this study, paternity leave refers to leave taken around the time of delivery that can be paid or unpaid paternity leave, annual leave, or other kinds of leave, and is equally applicable to births within both marital and non-marital partnerships.

The Hong Kong community attaches increasing importance to the father's responsibilities in the family.

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There is an increasing trend for provision of paternity leave by private enterprises for their employees. According to statistics from the Labour Department of the Hong Kong SAR Government, the percentage of respondent private organisations who offer paternity leave on their own volition has increased from 16% in 2006 to 32.5% in 2010[1]. Starting from April 2012, eligible government employees can enjoy 5 working days of full-pay paternity leave on each occasion of childbirth. There are views that the Government should legislate for the provision of paternity leave by all employers.

Postpartum depression is a common disorder, with a prevalence estimated at about 12.7% to 24.2% of deliveries in Hong Kong Chinese women[2]. Maternal depression has deleterious effects on the new mother, her baby, and her family[3]. Risk factors for postpartum depression include stressful life events during pregnancy, difficult birth, marital difficulties, lack of social support, personal history of mood disorders, and depressed mood and / or anxiety during pregnancy[4]. The lack of social support as a risk factor for postpartum depression has been particularly studied. Women who perceive to receive more social support have less psychological distress in the postpartum period[5]. Depressed women tend to have less social support than others[6] and report less support from their partner[7]. The partner's supportive role seems to be a protective factor against the development of postpartum depression[8,9]. The lack of paternal involvement in baby care may predict the intensity of maternal depressive symptoms[10,11]. The provision of paternity leave may encourage paternal support for the mother and paternal involvement in baby care, and thus prevent postpartum depression.

To our knowledge, there has been no local research about the relationship between paternity leave and postpartum health. In this study we examined the effects of paternity leave on maternal postpartum depression, paternal involvement in neonatal care, and maternal perception of social support in the Chinese population of Hong Kong.

Methods

Study Design

A prospective observational study was conducted from July 2013 to September 2013 at Tuen Mun Hospital, Hong Kong. Ethics approval was obtained from the New Territories West Cluster Clinical and Research Ethics Committee before commencement of the study. Postpartum women with liveborn babies were invited to participate in the study by the authors while they were in the postnatal ward. Women who: (1) had active psychiatric disease; (2) were not ethnic Chinese; (3) were not permanent residents in Hong Kong; (4) did not have a partner (husband or boyfriend); or (5) whose partner was not in full-time employment were excluded.

Informed consent was obtained from women who agreed to participate. Each woman was assigned a unique research number and asked to complete a demographic questionnaire, the Edinburgh Postnatal Depression Scale (EPDS) and the Multidimensional Scale of Perceived Social Support (MSPSS) between the first and fifth day postpartum (time 1). The subjects were given another self-administered survey, along with a stamped envelope, to be completed and returned 6 weeks postpartum (time 2). The subjects would be asked several questions about paternity leave, paternal involvement, EPDS, and MSPSS. If the subjects did not return the survey, they would be reminded by phone to complete and return the second survey before 8 weeks postpartum. This study was conducted in Chinese. All printed materials for the subjects, including information leaflets, consent forms and questionnaires, were in traditional Chinese.

Study Instruments

Postpartum depression was assessed using the Chinese version of the EPDS. The original EPDS is a 10-item self-report scale widely used to screen for postpartum depression, with items of the scale corresponding to various clinical depressive symptoms[12]. The Chinese version of the EPDS has been validated among Hong Kong Chinese women. Its psychometric performance is comparable with the original scale. It has been shown to have satisfactory sensitivity and specificity using a cut-off point of 9/10 for detecting depression in Chinese women at 6 weeks postpartum[13].

The MSPSS was used to assess social support perceived by the mother. This scale consists of 12 questions divided equally between three sources of perceived social support: family members including the husband; friends; and a significant other[14]. The Chinese version of the MSPSS has been validated among Hong Kong Chinese and its psychometric performance is comparable with the original scale[15].

Paternal involvement in baby care was assessed over four areas (overall care, changing clothes and napkins, play, and taking care of the baby alone). Subjects were asked to rate the father's level of participation in each area through a Likert item ranging from 0 ('never') to 4 ('all the time'), and the responses were summed to give a maximum

score of 16. Cronbach's alpha for the scale used in a study[10] was 0.85.

We used a demographic questionnaire to collect socio-demographic information from subjects based on known risk factors for postpartum depression. The information included age, education, marital status, number of existing children, whether the pregnancy was unplanned, employment, family income, housing, financial assistance, social support including presence of domestic helper or peiyue maid, and father's disappointment with the baby's gender[16].

Obstetric and neonatal data were also collected. These included age and parity, gestation at delivery, mode of delivery, partner companionship during labour, history of medical or psychiatric illness, obstetric complications, and neonatal complications.

Sample Size Calculation

Assuming a prevalence of postpartum depression of 15%, prevalence of paternity leave of 50% and precision of 3.8%, a total of 190 subjects would be required to achieve a 5% level of significance[17]. With an estimated response rate of 50%, 380 cases were required for the study.

Statistical Analysis

Data were analysed using the Statistical Package for the Social Sciences Windows version 20.0 (SPSS Inc., Chicago [IL], US). For continuous variables, p values were obtained from the Mann-Whitney *U* test. For discrete variables, p values were obtained from the Fisher's exact test. Logistic regression models were used to control for the effect of several significant variables on postpartum depression. For all analyses, a $p<0.05$ was considered statistically significant.

Results

A total of 872 mothers were approached during the study period. In all, 99 mothers were excluded based on the exclusion criteria; 122 mothers opted out of the study. A total of 651 mothers agreed to participate in the study. Written informed consent was obtained and the first survey completed while they were on our postnatal ward.

Among the subjects, 424 (65.1%) responded ('respondents') to the second survey between 6 and 8 weeks postpartum and their data were valid for analysis (Table 1). Those who completed the first survey but failed to respond to the second survey between 6 and 8 weeks postpartum are classified as 'non-respondents'. In all, 37.7% of them required a phone reminder to return the second survey. The sample sizes for individual items in the surveys varied slightly because inadmissible or incomplete responses were rejected for analysis. For example, because a small number of respondents neglected to specify the duration or type of paternity leave, the denominators used in the corresponding analyses ranged from 421 to 424 (Table 2).

The mean EPDS score at time 1 for respondents (7.5) and non-respondents (7.9) were not significantly different (p=0.39) [Table 1]. Respondents and non-respondents also shared similar demographic characteristics, except that respondents were more likely to be older ($p<0.001$) and more likely to have obstetric complications (p=0.01).

The prevalence of postpartum depression at 6 to 8 weeks postpartum (i.e. EPDS score at time 2 ≥10) was 31.4% (133/423) [Table 2]. The mean ± standard deviation EPDS score at time 2 for all respondents was 7.6 ± 5.0.

The prevalence of paternity leave was 61.6% (261/424) [Table 2] with an overall mean duration (among those with paternity leave) of 8.9 days. In all, 23% (98/423) had paid paternity leave ranging from 1 to 31 days (mean, 4.7 days). A further 12.6% (53/421) had non-paid paternity leave ranging from 1 to 35 days (mean, 6.4 days). In addition 27.7% (117/422) took annual leave ranging from 2 to 50 days (mean, 7.6 days), and 8.8% (37/421) took other kinds of leave, such as event leave and leave from own business, ranging from 1 to 120 days (mean, 16.1 days).

Postpartum depression was associated with duration of stay in Hong Kong, family income, MSPSS at time 1, MSPSS at time 2, and paternal involvement individually. The prevalence of postpartum depression increased with shorter duration of stay in Hong Kong (p=0.01-0.04) [Table 3], lower family income (p=0.03) [Table 4], lower MSPSS scores ($p<0.001$) [Table 5], and lower scores of paternal involvement (p=0.001) [Table 6].

Paternity leave was associated with increased paternal involvement (p=0.001) [Table 6], but had no statistically significant effect on MSPSS score at time 2 (p=0.48) [Table 5]. Paternity leave increased the scores for each of the assessed areas of paternal involvement in baby care (overall care, p=0.001; changing clothes and napkins, p=0.002; playing with the baby, p=0.01; and taking care of the baby alone, p=0.01).

Table 1. Characteristics of respondents and non-respondents*

Characteristics	Respondents† (n=424)	Non-respondents† (n=227)	Overall (n=651)	p Value‡
Maternal age (years)				<0.001
Mean	31.2 ± 4.8	29.0 ± 5.2	30.5 ± 5.1	
<18	1 (0.2)	1 (0.4)	2 (0.3)	
18-24	36 (8.5)	47 (20.7)	83 (12.7)	
25-34	278 (65.6)	143 (63.0)	421 (64.7)	
≥35	109 (25.7)	36 (15.9)	145 (22.3)	
Parity	0.6 ± 0.8	0.5 ± 0.7	0.6 ± 0.7	0.14
Marital status				0.06
Cohabitation	20 (4.7)	21 (9.3)	41 (6.3)	
Married	396 (93.4)	200 (88.1)	596 (91.6)	
Divorced / single	8 (1.9)	6 (2.6)	14 (2.2)	
Duration of stay in Hong Kong				0.31
0-1 Year	14 (3.3)	5 (2.2)	19 (2.9)	
2-5 Years	48 (11.4)	29 (12.9)	77 (11.9)	
6-9 Years	19 (4.5)	17 (7.6)	36 (5.6)	
>10 Years	340 (80.8)	173 (77.2)	513 (79.5)	
Work status				0.12
Full-time work	219 (51.7)	110 (48.5)	329 (50.5)	
Part-time work	14 (3.3)	12 (5.3)	26 (4.0)	
Housewife	189 (44.6)	100 (44.1)	289 (44.4)	
Others	2 (0.5)	5 (2.2)	7 (1.1)	
Education level				0.32
Primary school	4 (0.9)	3 (1.3)	7 (1.1)	
Secondary school	294 (69.3)	167 (73.6)	461 (70.8)	
Forms 6-7	30 (7.1)	19 (8.4)	49 (7.5)	
Tertiary or above	96 (22.6)	38 (16.7)	134 (20.6)	
Family income (HK$)				0.49
<10,000	46 (10.9)	25 (11.1)	71 (11.0)	
10,000-29,999	249 (59.1)	146 (64.6)	395 (61.1)	
30,000-49,999	100 (23.8)	45 (19.9)	145 (22.4)	
≥50,000	26 (6.2)	10 (4.4)	36 (5.6)	
Living environment				0.53
Owned private housing	135 (32.2)	64 (29.0)	199 (31.1)	
Rented private housing	66 (15.8)	44 (19.9)	110 (17.2)	
A part of rented private housing	9 (2.1)	4 (1.8)	13 (2.0)	
Owned public housing	53 (12.6)	19 (8.6)	72 (11.3)	
Rented public housing	132 (31.5)	78 (35.3)	210 (32.8)	
Temporary housing	6 (1.4)	4 (1.8)	10 (1.6)	
Others	18 (4.3)	8 (3.6)	26 (4.1)	
Economic support				0.09
No	414 (98.6)	217 (96.4)	631 (97.8)	
Yes	6 (1.4)	8 (3.6)	14 (2.2)	

Abbreviations: EPDS = Edinburgh Postnatal Depression Scale; MSPSS = Multidimensional Scale of Perceived Social Support; time 1 = first survey

* Data are shown as No. (%) of respondents or mean ± standard deviation. A minority of subjects did not answer all questions in the survey, hence the total number of subjects for each item may vary

† Respondents refer to those who responded to the second survey between 6 and 8 weeks postpartum. Non-respondents refer to those who completed the first survey but failed to respond to the second survey between 6 and 8 weeks postpartum

‡ For continuous variables, p values were obtained from Mann-Whitney *U* test. For discrete variables, p values were obtained from Fisher's exact test

Table 1. (cont'd)

Characteristics	Respondents† (n=424)	Non-respondents† (n=227)	Overall (n=651)	p Value‡
Household size	3.0 ± 1.7	3.0 ± 1.6	3.0 ± 1.7	0.74
No. of existing children	0.7 ± 0.8	0.7 ± 0.9	0.7 ± 0.9	0.16
Living with parents				0.14
No	371 (88.3)	188 (83.9)	559 (86.8)	
Yes	49 (11.7)	36 (16.1)	85 (13.2)	
Living with parents-in-law				0.17
No	312 (74.3)	155 (68.9)	467 (72.4)	
Yes	108 (25.7)	70 (31.1)	178 (27.6)	
Helper availability				0.92
No	322 (76.8)	171 (76.3)	493 (76.7)	
Yes	97 (23.2)	53 (23.7)	150 (23.3)	
Planned pregnancy				0.13
No	126 (30.0)	81 (36.0)	207 (32.1)	
Yes	294 (70.0)	144 (64.0)	438 (67.9)	
Partner disappointment about the baby's gender				1.00
No	402 (95.7)	215 (95.6)	617 (95.7)	
Yes	18 (4.3)	10 (4.4)	28 (4.3)	
Gestation at delivery				0.99
<28 Weeks	1 (0.2)	1 (0.4)	2 (0.3)	
28-31+ Weeks	2 (0.5)	1 (0.4)	3 (0.5)	
32-33+ Weeks	4 (0.9)	2 (0.9)	6 (0.9)	
34-36+ Weeks	32 (7.5)	18 (7.9)	50 (7.7)	
37-41+ Weeks	385 (90.8)	205 (90.3)	590 (90.6)	
Mode of delivery				0.52
Normal spontaneous delivery	265 (62.5)	149 (65.6)	414 (63.6)	
Assisted vaginal delivery	41 (9.7)	25 (11.0)	66 (10.1)	
Elective Caesarean section	37 (8.7)	20 (8.8)	57 (8.8)	
Emergency Caesarean section	81 (19.1)	33 (14.5)	114 (17.5)	
Partner companionship during labour				0.80
No	195 (49.4)	108 (50.7)	303 (49.8)	
Yes	200 (50.6)	105 (49.3)	305 (50.2)	
History of medical illness				0.14
No	365 (86.1)	185 (81.5)	550 (84.5)	
Yes	59 (13.9)	42 (18.5)	101 (15.5)	
History of psychiatric illness				0.87
No	396 (93.4)	211 (93.0)	607 (93.2)	
Yes	28 (6.6)	16 (7.0)	44 (6.8)	
Obstetric complications				0.01
No	213 (50.2)	138 (60.8)	351 (53.9)	
Yes	211 (49.8)	89 (39.2)	300 (46.1)	
Neonatal complications				0.77
No	324 (76.4)	171 (75.3)	495 (76.0)	
Yes	100 (23.6)	56 (24.7)	156 (24.0)	
EPDS score at time 1	7.5 ± 4.2	7.9 ± 4.6	7.7 ± 4.4	0.39
EPDS score at time 1 ≥10				0.66
No	282 (67.5)	148 (65.8)	430 (66.9)	
Yes	136 (32.5)	77 (34.2)	213 (33.1)	
MSPSS score at time 1	69.5 ± 13.9	68.3 ± 14.9	69.1 ± 14.3	0.50

Table 2. Characteristics of paternity leave taken by partners of respondents with and without postpartum depression*

Variable	EPDS score <10	EPDS score ≥10	Total	p Value†
Presence of PL				0.75
No	110 (37.9)	53 (39.8)	163 (38.5)	
Yes	180 (62.1)	80 (60.2)	260 (61.5)	
Total duration of leave (for respondents with / without paternity leave)	5.7 ± 8.9	4.9 ± 11.3	5.4 ± 9.7	0.43
Paid PL	1.0 ± 2.6	1.2 ± 3.4	1.1 ± 2.9	0.70
Non-paid PL	0.9 ± 3.5	0.6 ± 2.0	0.8 ± 3.1	0.57
Annual leave	2.2 ± 5.5	1.8 ± 3.7	2.1 ± 5.0	0.72
Other kinds of leave	1.5 ± 6.7	1.3 ± 10.5	1.4 ± 8.1	0.74
Comparison of paid PL with other categories				0.91
Paid PL	66 (23.1)	32 (24.1)	98 (23.4)	
No PL	110 (38.5)	53 (39.8)	163 (38.9)	
Non-paid / annual / others	110 (38.5)	48 (36.1)	158 (37.7)	
Comparison of non-paid PL with other categories				0.86
Non-paid PL	38 (13.3)	15 (11.3)	53 (12.6)	
No PL	110 (38.5)	53 (39.8)	163 (38.9)	
Paid / annual / others	138 (48.3)	65 (48.9)	203 (48.4)	

Abbreviations: EPDS = Edinburgh Postnatal Depression Scale; PL = paternity leave

* Data are shown as No. (%) of respondents or mean ± standard deviation. A minority of subjects did not answer all questions in the survey, hence the total number of subjects for each item may vary

† For continuous variables, p values were obtained from Mann-Whitney *U* test. For discrete variables, p values were obtained from Fisher's exact test

It was also associated with partner companionship during labour (p=0.01) [Table 7], and some demographic variables (marital status, maternal work status, education level, duration of stay in Hong Kong, family income, household size, number of existing children, helper availability, and pregnancy plan) [Table 3].

Paternity leave had no statistically significant effect on maternal postpartum depression (p=0.75) [Table 2], even after controlling for significant variables (duration of stay in Hong Kong, family income, MSPSS score at time 2, and paternal involvement) using logistic regression (p=0.85). Sub-categories of paternity leave also had no statistically significant effect on postpartum depression (p values, 0.57-0.74). Subgroup analyses of paid and non-paid paternity leave likewise showed no statistically significant effect on postpartum depression (Table 2).

Discussion

The prevalence of postpartum depression in Asian countries ranges from 3.5% to 63.3%, and the prevalence in Hong Kong Chinese women ranges from 12.7 to 24.2%[2]. In our study, the prevalence of postpartum depression at 6 to 8 weeks postpartum was 31.4%, relatively high compared with previous studies of Hong Kong Chinese[2]. The women in our locality might be more prone to develop postpartum depression because of their socio-economic characteristics. The obstetric population in the New Territories West Cluster tended to be younger, less educated, and of lower income compared with those in other parts of Hong Kong[18]. Our estimation of the prevalence was limited by self-selection bias, as our subjects might differ significantly in their susceptibility to depression from women who opted out of the study. Despite a reasonably high response rate, the risk of non-response bias, where depressed subjects would be more likely or less likely to respond to the second survey, could not be eliminated. The characteristics of respondents and non-respondents were largely comparable, except that the respondents tended to be older and suffer from obstetric complications (which were not shown to be associated with postpartum depression in this study). Finally, direct comparison with previous studies might be inappropriate because of differences in timing and methods for detection of postpartum depression, cut-off scores for diagnosis, and inclusion criteria.

Table 3. Maternal age, parity, marital status, duration of stay in Hong Kong, work status, and education level of respondents with and without postpartum depression and paternity leave*

Variable	EPDS score <10	EPDS score ≥10	Total	p Value†
Maternal age (years)	31.2 ± 4.8	31.2 ± 4.9	31.2 ± 4.8	0.73
Maternal age-group (years)				0.99
<18	1 (0.3)	0	1 (0.2)	
18-24	25 (8.6)	11 (8.3)	36 (8.5)	
25-34	190 (65.5)	87 (65.4)	277 (65.5)	
≥35	74 (25.5)	35 (26.3)	109 (25.8)	
Parity	0.6 ± 0.8	0.6 ± 0.8	0.6 ± 0.8	0.64
Marital status				0.44
Cohabitation	13 (4.5)	7 (5.3)	20 (4.7)	
Married	273 (94.1)	122 (91.7)	395 (93.4)	
Divorced / single	4 (1.4)	4 (3.0)	8 (1.9)	
Duration of stay in Hong Kong category 1 (years)				0.03
0-1 Year	11 (3.8)	3 (2.3)	14 (3.3)	
2-5 Years	24 (8.3)	24 (18.2)	48 (11.4)	
6-9 Years	12 (4.2)	7 (5.3)	19 (4.5)	
≥10 Years	241 (83.7)	98 (74.2)	339 (80.7)	
Duration of stay in Hong Kong category 2 (years)				0.04
0-5 Years	35 (12.2)	27 (20.5)	62 (14.8)	
≥6 Years	253 (87.8)	105 (79.5)	358 (85.2)	
Duration of stay in Hong Kong category 3 (years)				0.03
0-9 Years	47 (16.3)	34 (25.8)	81 (19.3)	
≥10 Years	241 (83.7)	98 (74.2)	339 (80.7)	
Duration of stay in Hong Kong category 4 (years)				0.01
2-5 Years	24 (8.3)	24 (18.2)	48 (11.4)	
Others	264 (91.7)	108 (81.8)	372 (88.6)	
Work status				0.19
Full-time work	155 (53.4)	63 (47.4)	218 (51.5)	
Part-time work	12 (4.1)	2 (1.5)	14 (3.3)	
Housewife	121 (41.7)	68 (51.1)	189 (44.7)	
Others	2 (0.7)	0	2 (0.5)	
Education level				0.24
Primary school	1 (0.3)	3 (2.3)	4 (0.9)	
Secondary school	204 (70.3)	89 (66.9)	293 (69.3)	
Forms 6-7	22 (7.6)	8 (6.0)	30 (7.1)	
Tertiary or above	63 (21.7)	33 (24.8)	96 (22.7)	

Abbreviation: EPDS = Edinburgh Postnatal Depression Scale

* Data are shown as No. (%) of subjects or mean ± standard deviation. A minority of subjects did not answer all questions in the survey, hence the total number of subjects for each item may vary

† For continuous variables, p values were obtained from Mann-Whitney *U* test. For discrete variables, p values were obtained from Fisher's exact test

Table 3. (cont'd)

Variable	With paternity leave	Without paternity leave	Total	p Value†
Maternal age (years)	31.4 ± 4.6	31.0 ± 5.1	31.2 ± 4.8	0.51
Maternal age-group (years)				
<18	0	1 (0.6)	1 (0.2)	
18-24	21 (8.0)	15 (9.2)	36 (8.5)	
25-34	171 (65.5)	107 (65.6)	278 (65.6)	
≥35	69 (26.4)	40 (24.5)	109 (25.7)	
Parity	0.6 ± 0.8	0.7 ± 0.8	0.6 ± 0.8	0.07
Marital status category 1				0.02
Cohabitation	13 (5.0)	7 (4.3)	20 (4.7)	
Married	247 (94.6)	149 (91.4)	396 (93.4)	
Divorced / single	1 (0.4)	7 (4.3)	8 (1.9)	
Marital status category 2				0.01
Cohabitation / married	260 (99.6)	156 (95.7)	416 (98.1)	
Divorced / single	1 (0.4)	7 (4.3)	8 (1.9)	
Duration of stay in Hong Kong category 1 (years)				<0.001
0-1 Year	6 (2.3)	8 (5.0)	14 (3.3)	
2-5 Years	18 (6.9)	30 (18.6)	48 (11.4)	
6-9 Years	8 (3.1)	11 (6.8)	19 (4.5)	
≥10 Years	228 (87.7)	112 (69.6)	340 (80.8)	
Duration of stay in Hong Kong category 2 (years)				<0.001
0-5 Years	24 (9.2)	38 (23.6)	62 (14.7)	
≥6 Years	236 (90.8)	123 (76.4)	359 (85.3)	
Duration of stay in Hong Kong category 3 (years)				<0.001
0-9 Years	32 (12.3)	49 (30.4)	81 (19.2)	
≥10 Years	228 (87.7)	112 (69.6)	340 (80.8)	
Duration of stay in Hong Kong category 4 (years)				<0.001
2-5 Years	18 (6.9)	30 (18.6)	48 (11.4)	
Others	242 (93.1)	131 (81.4)	373 (88.6)	
Work status				<0.001
Full-time work	156 (59.8)	63 (38.7)	219 (51.7)	
Part-time work	10 (3.8)	4 (2.5)	14 (3.3)	
Housewife	94 (36.0)	95 (58.3)	189 (44.6)	
Others	1 (0.4)	1 (0.6)	2 (0.5)	
Education level				<0.001
Primary school	1 (0.4)	3 (1.8)	4 (0.9)	
Secondary school	160 (61.3)	134 (82.2)	294 (69.3)	
Forms 6-7	23 (8.8)	7 (4.3)	30 (7.1)	
Tertiary or above	77 (29.5)	19 (11.7)	96 (22.6)	

Table 4. Demographics of household of respondents with and without postpartum depression and paternity leave*

Variable	EPDS score <10	EPDS score ≥10	Total	p Value†
Family income category 1‡ (HK$)				0.03
<10,000	25 (8.7)	21 (15.8)	46 (11.0)	
10,000-29,999	168 (58.5)	81 (60.9)	249 (59.3)	
30,000-49,999	78 (27.2)	22 (16.5)	100 (23.8)	
≥50,000	16 (5.6)	9 (6.8)	25 (6.0)	
Family income category 2‡ (HK$)				0.04
<10,000	25 (8.7)	21 (15.8)	46 (11.0)	
≥10,000	262 (91.3)	112 (84.2)	374 (89.0)	
Living environment				0.31
Owned private housing	97 (33.9)	37 (28.0)	134 (32.1)	
Rented private housing	44 (15.4)	22 (16.7)	66 (15.8)	
A part of rented private housing	3 (1.0)	6 (4.5)	9 (2.2)	
Owned public housing	39 (13.6)	14 (10.6)	53 (12.7)	
Rented public housing	87 (30.4)	45 (34.1)	132 (31.6)	
Temporary housing	4 (1.4)	2 (1.5)	6 (1.4)	
Others	12 (4.2)	6 (4.5)	18 (4.3)	
Economic support				0.08
No	284 (99.3)	129 (97.0)	413 (98.6)	
Yes	2 (0.7)	4 (3.0)	6 (1.4)	
Household size	3.0 ± 1.6	2.9 ± 1.8	3.0 ± 1.7	0.15
No. of existing children	0.8 ± 0.8	0.7 ± 0.9	0.7 ± 0.8	0.68
Living with parents				0.74
No	251 (87.8)	119 (89.5)	370 (88.3)	
Yes	35 (12.2)	14 (10.5)	49 (11.7)	
Living with parents-in-law				1.00
No	212 (74.1)	99 (74.4)	311 (74.2)	
Yes	74 (25.9)	34 (25.6)	108 (25.8)	
Helper availability				0.17
No	213 (74.7)	108 (81.2)	321 (76.8)	
Yes	72 (25.3)	25 (18.8)	97 (23.2)	
Planned pregnancy				0.26
No	81 (28.3)	45 (33.8)	126 (30.1)	
Yes	205 (71.7)	88 (66.2)	293 (69.9)	
Partner disappointment with the baby's gender				0.30
No	276 (96.5)	125 (94.0)	401 (95.7)	
Yes	10 (3.5)	8 (6.0)	18 (4.3)	

Abbreviation: EPDS = Edinburgh Postnatal Depression Scale

* Data are shown as No. (%) of subjects or mean ± standard deviation. A minority of subjects did not answer all questions in the survey, hence the total number of subjects for each item may vary

† For continuous variables, p values were obtained from Mann-Whitney *U* test. For discrete variables, p values were obtained from Fisher's exact test

‡ Family income was grouped into two categories, including 4 subgroups as category 1 and 2 subgroups as category 2

Table 4. (cont'd)

Variable	With paternity leave	Without paternity leave	Total	p Value†
Family income category 1‡ (HK$)				<0.001
<10,000	14 (5.4)	32 (20.0)	46 (10.9)	
10,000-29,999	146 (55.9)	103 (64.4)	249 (59.1)	
30,000-49,999	78 (29.9)	22 (13.8)	100 (23.8)	
≥50,000	23 (8.8)	3 (1.9)	26 (6.2)	
Family income category 2‡ (HK$)				<0.001
<10,000	14 (5.4)	32 (20.0)	46 (10.9)	
≥10,000	247 (94.6)	128 (80.0)	375 (89.1)	
Living environment				<0.001
Owned private housing	99 (38.4)	36 (22.4)	135 (32.2)	
Rented private housing	41 (15.9)	25 (15.5)	66 (15.8)	
A part of rented private housing	3 (1.2)	6 (3.7)	9 (2.1)	
Owned public housing	36 (14.0)	17 (10.6)	53 (12.6)	
Rented public housing	67 (26.0)	65 (40.4)	132 (31.5)	
Temporary housing	1 (0.4)	5 (3.1)	6 (1.4)	
Others	11 (4.3)	7 (4.3)	18 (4.3)	
Economic support				0.21
No	256 (99.2)	158 (97.5)	414 (98.6)	
Yes	2 (0.8)	4 (2.5)	6 (1.4)	
Household size	2.8 ± 1.6	3.2 ± 1.8	3.0 ± 1.7	0.04
No. of existing children	0.7 ± 0.8	0.9 ± 0.9	0.7 ± 0.8	0.01
Living with parents				0.21
No	232 (89.9)	139 (85.8)	371 (88.3)	
Yes	26 (10.1)	23 (14.2)	49 (11.7)	
Living with parents-in-law				0.49
No	195 (75.6)	117 (72.2)	312 (74.3)	
Yes	63 (24.4)	45 (27.8)	108 (25.7)	
Helper availability				0.02
No	188 (72.9)	134 (83.2)	322 (76.8)	
Yes	70 (27.1)	27 (16.8)	97 (23.2)	
Planned pregnancy				0.002
No	63 (24.4)	63 (38.9)	126 (30.0)	
Yes	195 (75.6)	99 (61.1)	294 (70.0)	
Partner disappointment with the baby's gender				0.81
No	246 (95.3)	156 (96.3)	402 (95.7)	
Yes	12 (4.7)	6 (3.7)	18 (4.3)	

Table 5. MSPSS score with and without postpartum depression and paternity leave*

Variable	EPDS score <10	EPDS score ≥10	Overall	p Value†
MSPSS score at time 1	71.5 ± 12.9	65.3 ± 15.1	69.5 ± 13.9	<0.001
MSPSS score at time 2	69.6 ± 13.0	60.0 ± 16.9	66.6 ± 15.0	<0.001
Variable	**With paternity leave**	**Without paternity leave**	**Overall**	**p Value†**
MSPSS score at time 1	69.7 ± 13.4	69.2 ± 14.7	69.5 ± 13.9	0.94
MSPSS score at time 2	67.2 ± 14.6	65.8 ± 15.7	66.6 ± 15.0	0.48
Correlation	**Overall**		**EPDS score at time 1 ≥10**	
	Change in EPDS score	**p Value**	**Change in EPDS score**	**p Value†**
MSPSS score at time 2	-0.146	0.003	-0.197	0.02

Abbreviations: EPDS = Edinburgh Postnatal Depression Scale; MSPSS = Multidimensional Scale of Perceived Social Support; time 1 = first survey; time 2 = second survey

* Data are shown as mean ± standard deviation

† For continuous variables, p values were obtained from Mann-Whitney *U* test. For discrete variables, p values were obtained from Fisher's exact test

Table 6. Rating of paternal involvement with and without postpartum depression and paternity leave*

Variable	EPDS score <10	EPDS score ≥10	Overall	p Value†
Paternal involvement in baby care	12.1 ± 3.9	10.8 ± 4.0	11.7 ± 3.9	0.001
Taking care of the baby	3.2 ± 1.0	3.0 ± 1.0	3.1 ± 1.0	0.04
Changing clothes and napkins	2.9 ± 1.2	2.6 ± 1.3	2.8 ± 1.3	0.002
Playing with the baby	3.4 ± 0.9	3.1 ± 1.0	3.3 ± 0.9	0.002
Taking care of the baby alone	2.6 ± 1.3	2.2 ± 1.3	2.5 ± 1.3	0.003
Variable	**With paternity leave**	**Without paternity leave**	**Overall**	**p Value†**
Paternal involvement in baby care	12.3 ± 3.5	10.8 ± 4.4	11.7 ± 3.9	0.001
Taking care of the baby	3.3 ± 0.9	2.9 ± 1.1	3.1 ± 1.0	0.001
Changing clothes and napkins	3.0 ± 1.1	2.5 ± 1.4	2.8 ± 1.3	0.002
Playing with the baby	3.4 ± 0.8	3.1 ± 1.0	3.3 ± 0.9	0.01
Taking care of the baby alone	2.6 ± 1.2	2.2 ± 1.4	2.5 ± 1.3	0.01
Correlation	**Overall**		**EPDS score at time 1 ≥10**	
	Change in EPDS score	**p Value**	**Change in EPDS score**	**p Value†**
Paternal involvement in baby care	-0.177	<0.001	-0.344	<0.001
Taking care of the baby	-0.160	0.001	-0.306	<0.001
Changing clothes and napkins	-0.155	0.002	-0.314	<0.001
Playing with the baby	-0.185	<0.001	-0.429	<0.001
Taking care of the baby alone	-0.130	0.01	-0.189	0.03

Abbreviation: EPDS = Edinburgh Postnatal Depression Scale

* Data are shown as mean ± standard deviation, unless otherwise specified

† For continuous variables, p values were obtained from Mann-Whitney *U* test. For discrete variables, p values were obtained from Fisher's exact test

Table 7. Obstetric characteristics and co-morbidities of respondents*

Variable	EPDS score <10	EPDS score ≥10	Total	p Value†
Gestation at delivery				0.23
<28 Weeks	1 (0.3)	0	1 (0.2)	
28-31+ Weeks	1 (0.3)	1 (0.8)	2 (0.5)	
32-33+ Weeks	3 (1.0)	1 (0.8)	4 (0.9)	
34-36+ Weeks	17 (5.9)	15 (11.3)	32 (7.6)	
37-41+ Weeks	268 (92.4)	116 (87.2)	384 (90.8)	
Mode of delivery				0.84
Normal spontaneous delivery	182 (62.8)	82 (61.7)	264 (62.4)	
Assisted vaginal delivery	26 (9.0)	15 (11.3)	41 (9.7)	
Elective Caesarean section	27 (9.3)	10 (7.5)	37 (8.7)	
Emergency Caesarean section	55 (19.0)	26 (19.5)	81 (19.1)	
Partner companionship during labour				0.11
No	125 (46.6)	70 (55.6)	195 (49.5)	
Yes	143 (53.4)	56 (44.4)	199 (50.5)	
History of medical illness				0.45
No	252 (86.9)	112 (84.2)	364 (86.1)	
Yes	38 (13.1)	21 (15.8)	59 (13.9)	
History of psychiatric illness				1.00
No	271 (93.4)	124 (93.2)	395 (93.4)	
Yes	19 (6.6)	9 (6.8)	28 (6.6)	
Obstetric complications				0.47
No	149 (51.4)	63 (47.4)	212 (50.1)	
Yes	141 (48.6)	70 (52.6)	211 (49.9)	
Neonatal complications				0.11
No	228 (78.6)	95 (71.4)	323 (76.4)	
Yes	62 (21.4)	38 (28.6)	100 (23.6)	
Variable	**With paternity leave**	**Without paternity leave**	**Total**	**p Value†**
Gestation at delivery				0.22
<28 Weeks	1 (0.4)	0	1 (0.2)	
28-31+ Weeks	1 (0.4)	1 (0.6)	2 (0.5)	
32-33+ Weeks	4 (1.5)	0	4 (0.9)	
34-36+ Weeks	16 (6.1)	16 (9.8)	32 (7.5)	
37-41+ Weeks	239 (91.6)	146 (89.6)	385 (90.8)	
Mode of delivery				0.10
Normal spontaneous delivery	155 (59.4)	110 (67.5)	265 (62.5)	
Assisted vaginal delivery	24 (9.2)	17 (10.4)	41 (9.7)	
Elective Caesarean section	29 (11.1)	8 (4.9)	37 (8.7)	
Emergency Caesarean section	53 (20.3)	28 (17.2)	81 (19.1)	
Partner companionship during labour				0.01
No	108 (44.1)	87 (58.0)	195 (49.4)	
Yes	137 (55.9)	63 (42.0)	200 (50.6)	
History of medical illness				0.39
No	228 (87.4)	137 (84.0)	365 (86.1)	
Yes	33 (12.6)	26 (16.0)	59 (13.9)	
History of psychiatric illness				0.55
No	242 (92.7)	154 (94.5)	396 (93.4)	
Yes	19 (7.3)	9 (5.5)	28 (6.6)	
Obstetric complications				0.23
No	125 (47.9)	88 (54.0)	213 (50.2)	
Yes	136 (52.1)	75 (46.0)	211 (49.8)	
Neonatal complications				0.91
No	200 (76.6)	124 (76.1)	324 (76.4)	
Yes	61 (23.4)	39 (23.9)	100 (23.6)	

Abbreviation: EPDS = Edinburgh Postnatal Depression Scale

* Data are shown as No. (%) of subjects. A minority of subjects did not answer all questions in the survey, hence the total number of subjects for each item may vary

† For continuous variables, p values were obtained from Mann-Whitney *U* test. For discrete variables, p values were obtained from Fisher's exact test

Obstetric complications, neonatal complications, and a history of psychiatric illness were not shown to be statistically significant risk factors for postpartum depression in this study (Table 7). Nonetheless all obstetric and neonatal complications and a history of psychiatric illnesses (after exclusion of active psychiatric illness) were included, and their nature and severity were not further categorised or studied. Therefore, the effects of severe complications and a history of major psychiatric illness might be lessened by the inclusion of minor conditions in the analysis.

Consistent with previous studies[2,10,11], paternal involvement in baby care and high MSPSS scores at time 1 and time 2 were shown to be protective against postpartum depression (Tables 5 and 6). This highlights the importance of encouraging paternal involvement and social support in the postpartum period. Our result was limited by the use of a non-validated questionnaire for the mother to rate paternal involvement in baby care. Women with postpartum depression might perceive their partners to be less supportive than others[7]. This could affect the correlation between maternal perception of paternal involvement and actual paternal involvement. The reduced paternal involvement demonstrated in women with postpartum depression could be attributable to bias in maternal perception.

Consistent with the studies by Séjourné et al[10,11] in France, our study did not demonstrate any significant effect of paternity leave on postpartum depression in Hong Kong Chinese (Table 2). This could not be attributed to the limited duration of paternity leave, as there was no difference in the mean duration of paternity leave between those with or without postpartum depression. Hence, we did not stratify the duration of paternity leave for further analysis. It is possible that some paternity leave was taken in response to the development of maternal depressive symptoms in the postpartum period. This might offset the possible reduction in postpartum depression caused by longer paternity leave taken in the absence of depressive symptoms.

Although it was shown that those with paternity leave experienced higher paternal involvement, and that higher paternal involvement was associated with a lower risk of developing postpartum depression (Table 6), the magnitude of the association might be small. This might explain why this study failed to demonstrate any direct statistically significant effect of paternity leave on postpartum depression.

There were likely other factors associated with postpartum depression and paternity leave that were not addressed in this study. Such confounding factors might include marital conflict, relationship problems with in-laws, active psychiatric illness such as antepartum depression, and severe obstetric or neonatal complications. The sample size of this study may also not have been sufficiently large to demonstrate the 'small' effect in the presence of confounding factors.

Actual paternal involvement in maternal and neonatal care might be more important in the prevention of maternal postpartum depression than paternity leave per se. The provision of paternity leave did not necessarily lead to increased paternal involvement. Differences in the fathers' motivation for taking paternity leave, which was not explored in our study, might lead to differences in paternal support for the mother and newborn.

Given the positive effects of paternity leave on paternal involvement, we consider paternity leave to be a desirable component of postpartum care. In addition, our study showed that paternity leave was positively associated with partner companionship during labour (Table 7). Previous studies[19] have shown that partner companionship is associated with better maternal satisfaction and obstetric outcomes.

Strengths and Limitations

To our knowledge, this is the first study to examine the effects of paternity leave on postpartum depression in Hong Kong women. Its strengths included the large sample size, reasonably high response rate, prospective design, and use of validated instruments.

It might not be appropriate to extrapolate the results of our study to all Chinese women in Hong Kong. Socio-demographic characteristics of the obstetric population vary across Hong Kong[18] and this study was conducted in one regional hospital only. One-third of the subjects did not respond to the second survey, and there were some demographic differences between respondents and non-respondents. Other limitations of this study included a lack of data on the fathers' motivation for taking paternity leave, and the lack of an objective instrument to measure actual paternal involvement in baby care.

Conclusion

Although paternity leave was associated with increased paternal involvement in baby care, which

was in turn associated with a reduced risk of developing postpartum depression, paternity leave had no statistically significant direct effect on the prevalence of maternal postpartum depression. Our study highlights the importance of paternal involvement and social support in the prevention of postpartum depression.

Future research may explore the timing and duration of and motivation for paternity leave to clarify its relationship with postpartum depression. Data on known risk factors for postpartum depression such as antepartum depression and marital conflict[2] may be collected to study the effects of paternity leave on high-risk women who are especially in need of family support. Future research may also study other possible beneficial effects of paternity leave, for example, its influence on breastfeeding rate.

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