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July 2017, Volume 17, Number 2

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1. Yoshida S. Cell-type specific actions of progesterone receptor modulators in the regulation of uterine leiomyoma growth. Semin Reprod Med 2010. 28(3):260-73.
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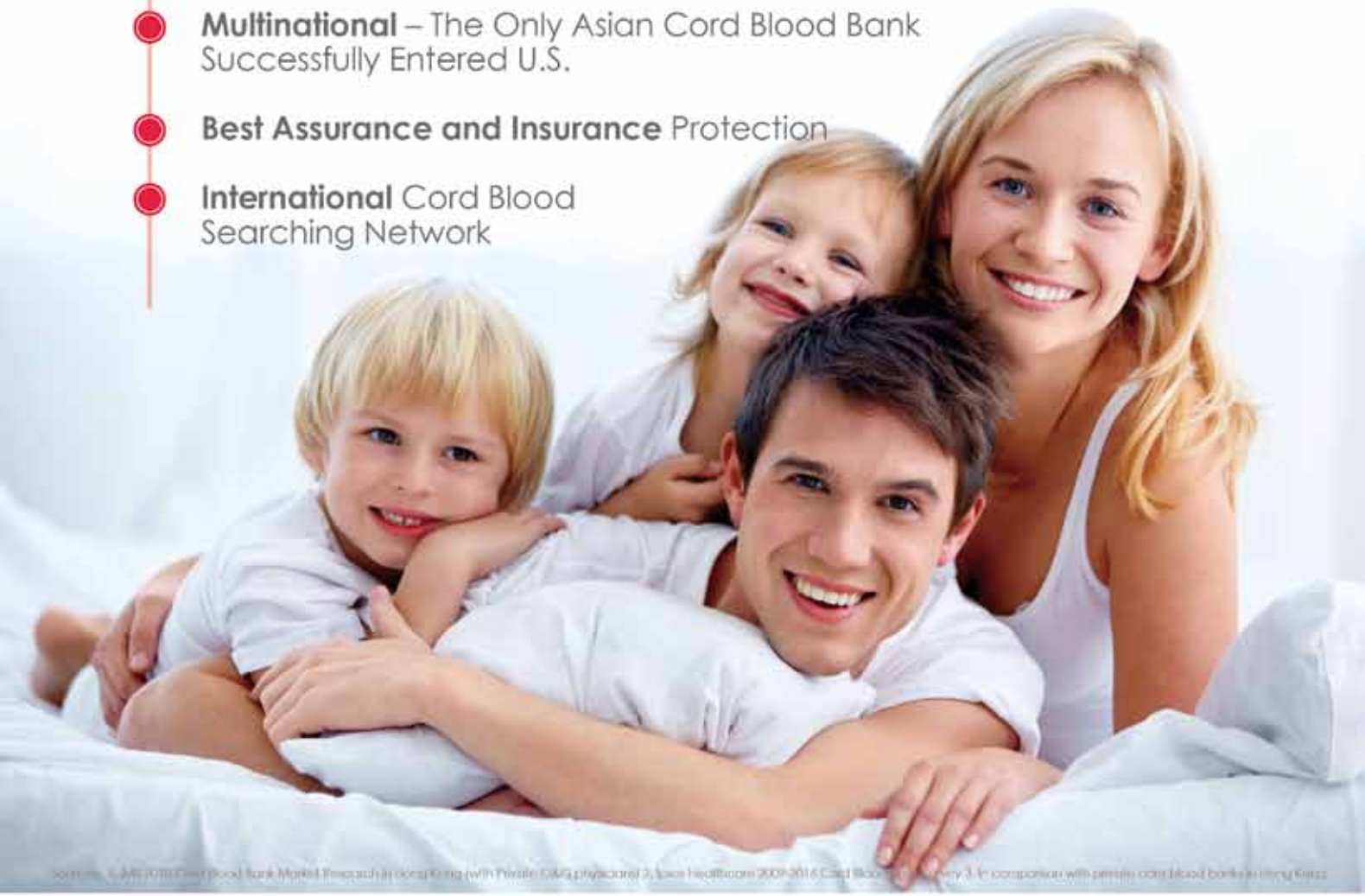

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Books edited by other authors of the article

2. Redwine DB, Perez JJ. Pelvic pain syndrome: endometriosis and mid-line dysmenorrhea. In: Arregui MW, Fitzgibbons RJ, Katkhouda N, McKerman JB, Reich H, editors. Principles of Laparoscopic Surgery – Basic and Advanced Techniques. *New York: Springer Verlag*; 1995: 545-58.

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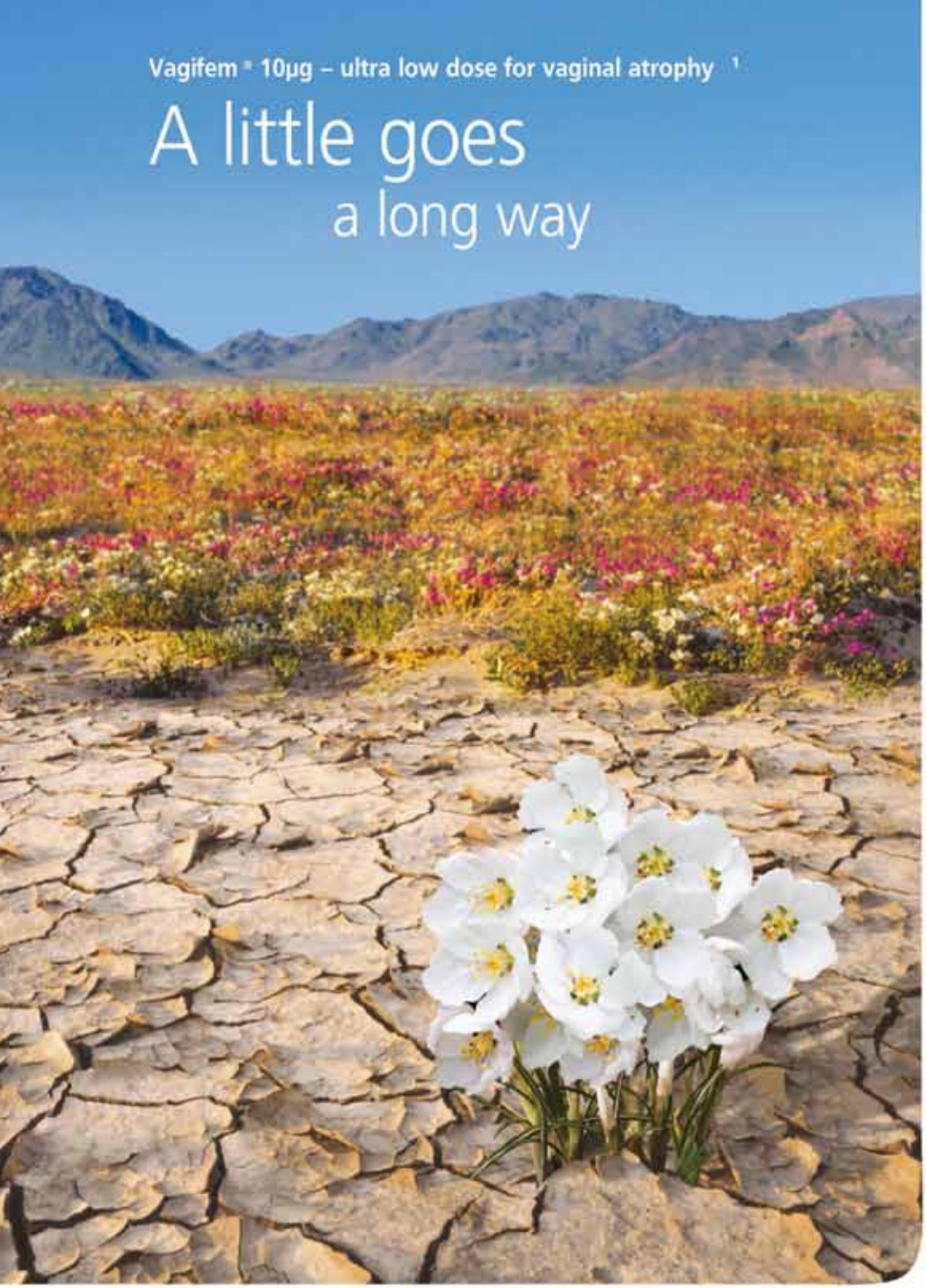

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Editorial
Medical Indemnity: Are We Safe Yet?

A medical indemnity insurance policy called Medical Professional Indemnity (MPI) was successfully launched by the Hong Kong College of Obstetricians and Gynaecologists insurance advisor Aon to compete against the Medical Protection Society (MPS) in May 2016. In a few months, more than half of practising obstetricians in Hong Kong acquired their coverage from the new provider. Colleagues needing help have received the same support as that from MPS over the past year. Trainee recruitment rebounded from our historical trough of 2015. Colleagues who continued with MPS received a Christmas present in 2016, because MPS announced the availability of long-tail cover from a third party. Obstetricians in Hong Kong who stay with MPS, however, may notice that an apparent drop in fees, related to the change of basis, was followed by an annual increase of 20% over the past 2 years, rising from nearly HK$230,000 in 2015 to HK$330,000 in 2017.

We have been led into many interesting ideas by MPS over the past 3 decades. We never asked about the sustainability of an unregulated mutual fund because it has over a century of history, although the news teaches us that history and size do not matter. We are told that the financial books of each place are independent, and we believe in transparency, but we do not know of anyone in Hong Kong who has read these books. We have been misled from our student days that discretionary cover helps doctors best, and we are now facing the same fight against ourselves. We are taught by all school teachers, and the MPS, about the core values of medicine. We are now, however, instructed by the MPS that gynaecologists should shy away from helping colleagues in obstetric disasters. All of this might answer the challenge raised by an MPS representative: "at the end of the day, it is whether you still trust the MPS or not". The problem was not just a change in the indemnity basis, it was a unilateral change in a fundamental concept even before completion of a new mode of support. In fact, a discretionary decision justifies any future overnight change.

Doctors are all concerned with the sustainability of a new product such as MPI. There is no reason to belittle ourselves on our size as a market. Hong Kong is the third largest revenue centre of the MPS, after the UK and Ireland, but Ireland is losing money. Obstetrics and Gynaecology (O&G) represents one-fifth to one-fourth of the market. Yet volatility in O&G is high. One claim could take away years of subscription fees and dishearten an insurer. It is therefore important that there is balanced exposure. The year 2017 is another critical year for the insurance indemnity product of MPI. The broker company Aon, with support from the Hong Kong Academy of Medicine and active participation by some senior doctors and the author, tried to convince private hospitals to accept the product across specialties. Private hospitals are naturally anxious about change. It is only in the best interest of doctors that we plead for competition and fairness, and O&G doctors may contribute with active persuasion by the hospital administration. It is apparent to many people that claim-based indemnity poses no material risk to the hospitals under the present legal system. In addition, after accepting claim-based insurance for the highest-risk category, obstetrics, it seems reasonable that the same product may cover other specialties.

The author wrote previously that the future is in our hands[1]. It is reasonable to be slightly relaxed about the next few years. At most, indemnity premiums could fluctuate, but indemnity is still sustainable in the short term. We have been promised transparency and we are seeing such a development from the insurers.

For historical reference, the MPS subscription rate for occurrence-based O&G cover was nearly HK$6000 in 1994, about HK$55,000 in 2003, and just over HK$360,000 in 2014. From 1994 to 2014, the number of O&G subscribers also increased by 50%! Establishment of an indemnity competitor across specialties, and one that we may influence, is therefore only the first step. It may be inadequate even for the intermediate term.

It is important to keep O&G indemnity costs down, and multiple approaches are necessary. Genuine clinical risk management has been shown to reduce claims and costs overseas. Peer review and governance measures could be targeted against asphyxia and birth trauma. Continuing medical education based on local experience improves clinical communication. Documentation about proper care is our lifeline. Such documentation includes appropriately detailed clinical notes, as well as outcome measures. The author cannot understate the importance of objective proof against asphyxia, and used it routinely to protect fellow colleagues in one busy private unit for over 10 years. Public education and appropriate information

to clients manage expectations. There is also a need to manage support mechanisms through mobilisation of experts. Doctors should not talk against one another easily, individually, as a team, or across sectors.

Competition improves performance and we obstetricians and gynaecologists advocate competition. An independent competitor has been set up in Hong Kong recently and we shall have to learn more about the product. A provider previously concentrating on general practice is also considering cover for specialists. The overall service and effectiveness will determine acceptance. An interested doctor may begin consideration by professional vetting of the policies, which are written in the language of the insurers. Other factors of concern may be overall transparency and accountability, as well as track record.

We have suffered badly from lack of information. Colleagues in other specialties who may consider alternatives to MPS have the same problem. The author is establishing an independent portal of communication, open to all to provide information at <www.facebook.com/medicalindemnity>. A doctor can visit the page and 'like' it. Future information published on the page will be 'pushed' to the Facebook wall of the doctor. The effort merely tries to level slightly the information advantage with existing provider(s).

Please pray for Hong Kong, pray for our patients to continue having a viable dual-track health care system. Pray for our trainees and students that they have a future instead of a single employer. Together, we fight a war for survival and justice, of which we have made a glorious start. The author salutes every obstetrician in Hong Kong.

Ares LEUNG FHKCOG, FHKAM (Obstetrics and Gynaecology)
Past President, Hong Kong College of Obstetricians and Gynaecologists
Email: ares@aresleung.org

Reference

1. Leung A. Changes to professional indemnity. *Hong Kong J Gynaecol Obstet Midwifery* 2015; 15:97-9.

Usefulness of Maternal Serum C-reactive Protein in Predicting Funisitis and Early-onset Neonatal Sepsis in Women with Preterm Prelabour Rupture of Membranes

Andrea Ying LEE MBBS, MRCOG
Yun-Ting LEE MBChB, MRCOG, FHKAM (Obstetrics and Gynaecology), FHKCOG
Chun-Hong SO MBChB, MRCOG, FHKAM (Obstetrics and Gynaecology), FHKCOG
Department of Obstetrics and Gynaecology, Princess Margaret Hospital, Laichikok, Hong Kong

Objectives: To evaluate the usefulness of serum C-reactive protein (CRP) in women with preterm prelabour rupture of membranes (PPROM) in the prediction of funisitis and early-onset neonatal sepsis (EONS), to determine a CRP cutoff value for their prediction, and to identify other significant risk factors associated with funisitis and EONS.
Methods: This was a retrospective study conducted in a tertiary hospital in Hong Kong. Women with a singleton pregnancy at 24 to 34 weeks of gestation and had PPROM were recruited between January 2011 and December 2015. Maternal serum CRP level, histopathological diagnosis of the placenta, and incidence of EONS were evaluated.
Results: Among the 123 women recruited, funisitis was present in 21.1% of the women and EONS in 19.5% of the newborns. Maternal serum CRP level was associated with funisitis that was in turn associated with EONS. There was, however, no significant association between maternal serum CRP and EONS. Using a CRP cutoff value of 7.65 mg/l to predict funisitis, the sensitivity, specificity, positive predictive value, and negative predictive value were 65.4%, 78.4%, 44.7%, and 89.4%, respectively. The gestational age at delivery was the most significant risk factor for funisitis and EONS. Birth weight and Apgar score were significantly lower in women with funisitis and newborns with EONS than those without. Other risk factors for EONS included a positive high vaginal swab and placental swab cultures and the presence of group B *Streptococcus* in a high vaginal swab.
Conclusions: Maternal serum CRP may be helpful in the prediction of funisitis in women with PPROM. Nonetheless, the study did not show any association between maternal serum CRP and EONS. The CRP level should be interpreted with caution in a clinical setting. The gestational age at delivery was the most significant determining factor for funisitis and EONS.
Hong Kong J Gynaecol Obstet Midwifery 2017; 17(2):79-85

Keywords: Chorioamnionitis; C-reactive protein; Fetal membranes, premature rupture; Neonatal sepsis

Introduction

Preterm premature rupture of membranes (PPROM) occurs in 1% to 3% of all pregnancies and is responsible for approximately one-third of all preterm births[1]. Gestational age at membrane rupture and delivery has a significant impact on neonatal morbidity and mortality[2]. Balancing the benefits of prolonging pregnancy for fetal maturation with the risks of infection remains a challenge to obstetricians. On the other hand, prediction and early detection of intrauterine infection and in turn early-onset neonatal sepsis (EONS) would be helpful in such conditions.

Clinical signs such as fever and fetal heart rate abnormalities often present late. In fact, several studies have attempted to identify sensitive and specific diagnostic parameters for subclinical intrauterine infection and EONS[3-5]. Some involved analysis of amniotic fluid white cell count, cytokine level, or culture results[6-8] but all are invasive and involve a long turnaround time, thus they are not practical in day-to-day clinical practice.

C-reactive protein (CRP) is an acute phase protein secreted by the liver in response to inflammation. Although not specific to infection, maternal serum CRP is widely used in clinical practice in an attempt to detect occult infection. Numerous studies have investigated such a correlation but results have been controversial[9-12]. Furthermore, some studies focused on histological chorioamnionitis / funisitis rather than neonatal outcome[13]. To the best of our knowledge, no similar studies have been conducted in our local population on determining whether maternal serum

Correspondence to: Dr Andrea Y Lee
Email: lya4482@ha.org.hk

CRP is of value in predicting funisitis and EONS in women with PPROM.

In this study, we aimed to evaluate the usefulness of maternal serum CRP in women with PPROM in the prediction of funisitis and in particular EONS, to determine a cutoff value for CRP in the prediction, and to identify other significant risk factors associated with funisitis and EONS.

Methods

This retrospective cohort study was conducted at Princess Margaret Hospital, a tertiary hospital in Hong Kong. The study was approved by the Hospital Authority Research Ethics Committee (Kowloon West Cluster), with patient consent waived.

Women admitted with a diagnosis of PPROM between January 2011 and December 2015 and delivered in the hospital were recruited. They were identified from the Obstetrics Clinical Information System, which is a well-established database containing maternal and neonatal information on all women who deliver in our hospital. The inclusion criteria of this study included: singleton pregnancy; gestational age at PPROM of >24 weeks and <34 weeks; no tocolytics, antibiotics, or steroids in the 7 days preceding admission; no clinical signs of chorioamnionitis; admission within 24 hours of PPROM; maternal serum CRP level available within 12 hours of admission and within 48 hours of delivery; and no major fetal congenital malformation. Non-Chinese women were excluded.

For each eligible woman, demographic data, pregnancy outcome, and neonatal outcome were retrieved from the medical records. Maternal data included maternal age; parity; gestational age at the time of PPROM and delivery; mode of delivery; maternal serum CRP levels; culture results; antenatal use of steroid, antibiotics, and tocolytics; and placental histology. Neonatal data included neonatal blood culture and surface swab results, birth weight, Apgar score at 1 and 5 minutes, and a diagnosis of EONS.

Rupture of membranes was diagnosed by sterile speculum examination that confirmed both pooling of amniotic fluid and a positive rapid dipstick test (Actim PROM; Medix Biochemica, Espoo, Finland). Antibiotics and steroids were administered in all women included in the study. Tocolytics were administered, if indicated, to delay delivery in order to complete the course of steroids. From admission until delivery, maternal serum CRP level was measured every 1 to 2 days depending on the clinical situation.

Concentration of CRP was measured by an immunoturbidimetric procedure using the Abbott Architect chemistry analyser (Abbott Laboratories, Abbott Park [IL], US). Clinical chorioamnionitis was defined as a body temperature of ≥37.8°C on two occasions at least 4 hours apart, and two or more of the following: uterine tenderness, foul-smelling vaginal discharge, maternal tachycardia (>100 beats/min), maternal leukoytosis (>15000/μl), or fetal tachycardia (>160 beats/min)[14].

In our unit, the standard practice is delivery at 34 weeks of gestation if there are no single features of clinical chorioamnionitis, and if the woman appears normal under close maternal and fetal surveillance. Delivery is strongly advised if there are frank signs of clinical chorioamnionitis. The option of delivery is discussed when the diagnostic criteria of clinical chorioamnionitis are partially fulfilled, or when there are early signs of maternal or fetal compromise.

The primary outcome was the incidence of funisitis and either confirmed or probable EONS. Definitions of various terms in this study are shown in Table 1[15,16].

Statistical Analysis

Statistical analysis was performed using PASW Statistics 18, Release version 18.0.0 (SPSS Inc., 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 normal distribution, independent-samples *t* test was used. 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.

A receiver operating characteristic (ROC) curve using the points on the curve closest to the (0, 1) and Youden Index was used to establish a cutoff level of serum CRP in predicting funisitis. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR+), and negative likelihood ratio (LR–) for ability of serum CRP to identify funisitis were calculated.

Statistically significant variables were adopted as potential predictors and entered into a logistic regression analysis to look for significant factors of funisitis and suspected neonatal sepsis. The multiple logistic regression

Table 1. Definition used in this study[15,16]

Term	Definition in this study
Histological funisitis	Presence of neutrophils in the wall of the umbilical vessels
Confirmed systemic neonatal sepsis	Positive culture from blood or cerebrospinal fluid
Confirmed EONS	Sepsis manifested within 72 hours of birth
Probable EONS	Presence of one or more of the clinical signs of infection from (a) to (f), together with one or more of (g) to (j): (a) Respiratory distress (i.e. requiring ventilation, continuous positive airway pressure, or supplemental oxygen for >1 hour) (b) Apnoea (c) Lethargy (d) Abnormal level of consciousness (e) Circulatory compromise (i.e. hypotension, poor perfusion, need for inotropic support, or volume expansion) (f) Temperature instability (temperature <36°C or ≥38°C) for which the baby was treated with antibiotics for ≥5 days (g) Abnormal full blood count (i.e. white cell count <5 x 10^9 cells/l or > 30 x 10^9 cells/l, platelet count <100 000 cells/ml) (h) C-reactive protein >10 mg/l (i) Growth of a known virulent pathogen from a surface swab (j) Histological diagnosis of pneumonia in an early neonatal death

Abbreviation: EONS = early-onset neonatal sepsis

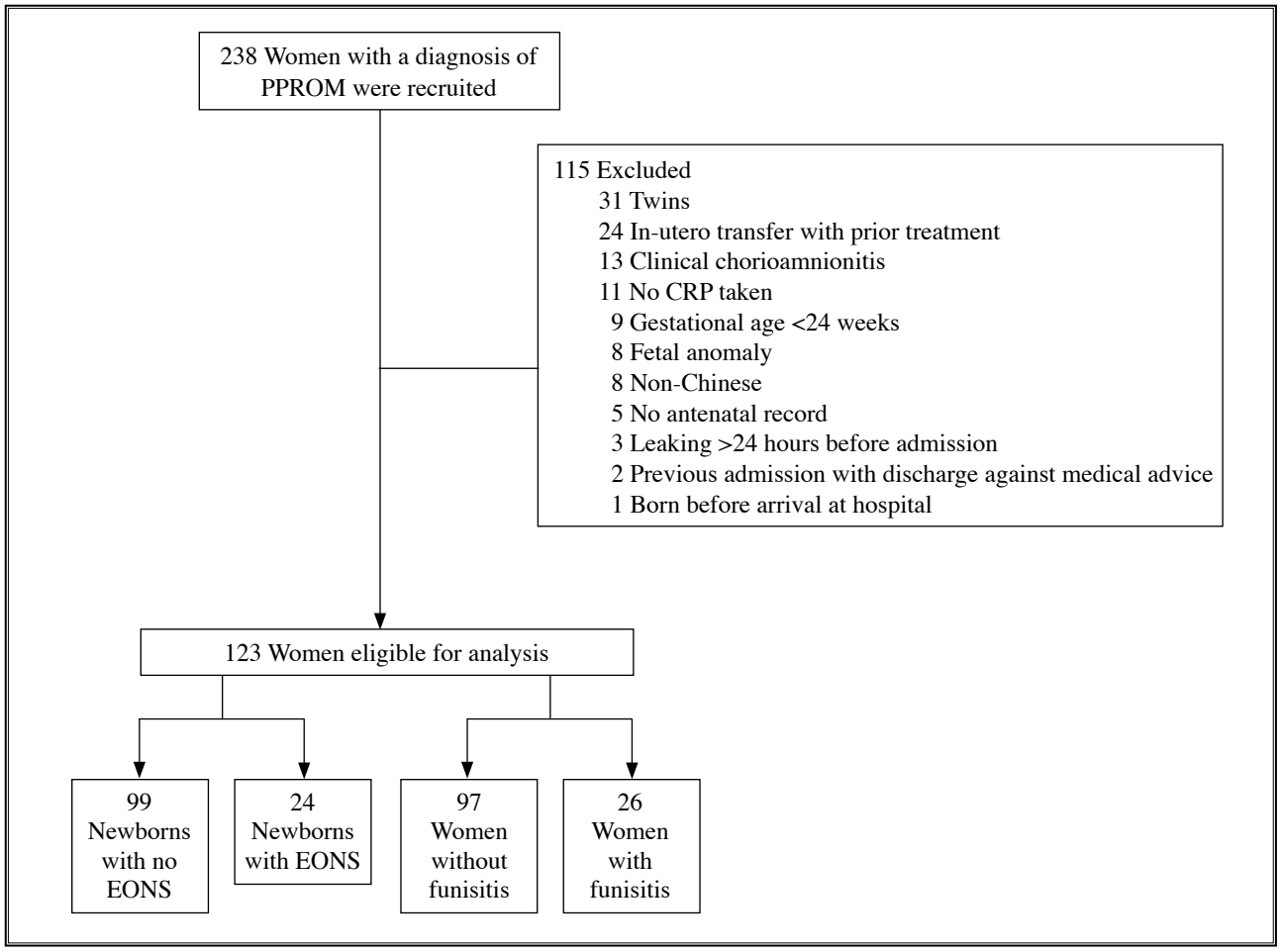

Figure 1. Flowchart showing the recruitment process and outcome (neonatal sepsis)

Abbreviations: CRP = C-reactive protein; EONS = early-onset neonatal sepsis; PPROM = preterm premature rupture of membranes

Table 2. Demographic and clinical characteristics of women and newborns with and without funisitis and early-onset neonatal sepsis*

Demographics / characteristics	Funisitis			Early-onset neonatal sepsis		
	Yes (n=26)	No (n=97)	p Value	Yes (n=24)	No (n=99)	p Value
Age (years)	31.27 ± 4.85	33.15 ± 4.60	0.069	33.00 ± 5.00	32.70 ± 4.64	0.778
Gravida	2 (1-3)	2 (1-4)	0.817	2 (1-3)	2 (1-3)	0.960
Parity	1 (0-1)	0 (0-1)	0.216	1 (0-1)	0 (0-1)	0.584
Maternal length of hospital stay (days)	6 (4-10)	5 (4-8)	0.654	7 (4-8)	5 (4-9)	0.916
Gestational age at PPROM (weeks)	28 (27-31)	32 (30-33)	<0.001	30 (26-32)	32 (30-33)	0.010
Gestational age at delivery (weeks)	30 (27-31)	32 (31-33)	<0.001	31 (27-32)	32 (31-33)	0.004
Days between PPROM and delivery	2 (1-5)	2 (0-5)	0.700	3 (1-5)	2 (1-5)	0.737
Temperature on admission (°C)	36.8 (36.6-37.2)	36.7 (36.5-37.0)	0.096	36.9 (36.6-37.1)	36.8 (36.6-37.1)	0.725
Mode of delivery			0.530			0.021
Normal vaginal delivery	17 (65.4%)	58 (59.8%)		20 (83.3%)	55 (55.6%)	
Instrumental delivery	0 (0%)	3 (3.1%)		0 (0%)	3 (3.0%)	
Lower-segment Caesarean section	8 (30.8%)	35 (36.1%)		3 (12.5%)	40 (40.4%)	
Classical Caesarean section	1 (3.8%)	1 (1.0%)		1 (4.2%)	1 (1.0%)	
Birth weight (g)	1145 (1034-1704)	1790 (1548-2030)	<0.001	1435 (1057-1773)	1790 (1490-2030)	0.002
Apgar score at 1 min	7 (7-8)	8 (7-9)	0.008	7 (6-9)	8 (7-9)	0.031
Apgar score at 5 mins	9 (9-10)	10 (9-10)	0.025	9 (9-10)	10 (9-10)	0.023
Pre-existing bacterial vaginosis	1 (3.8%)	2 (2.1%)	0.513	0 (0%)	3 (3.0%)	1.000
Use of tocolytics	14 (53.8%)	58 (59.8%)	0.585	12 (50.0%)	60 (60.6%)	0.344
Serum CRP level (mg/l)						
Day 1 (n=123)	9.85 (3.38-26.75)	4.90 (2.70-8.25)	0.029	6.90 (2.83-12.75)	4.90 (2.90-9.90)	0.459
Day 2 (n=61)	6.10 (4.25-25.50) [n=13]	3.55 (2.45-8.50) [n=48]	0.013	4.50 (2.75-12.50) [n=10]	4.40 (2.60-9.10) [n=51]	0.704
Day 3 (n=61)	6.45 (3.68-15.25) [n=16]	2.40 (1.06-6.35) [n=45]	0.002	3.60 (2.00-9.25) [n=13]	3.55 (2.00-7.70) [n=48]	0.853
Day 4 (n=43)	3.50 (2.00-10.95) [n=9]	2.30 (1.18-3.05) [n=34]	0.101	2.20 (1.10-4.80) [n=7]	2.30 (1.43-3.20) [n=36]	0.881
Day 5 (n=35)	2.3 (1.33-3.78) [n=10]	2.00 (1.00-3.25) [n=25]	0.373	2.00 (1.00-3.00) [n=9]	2.30 (1.00-3.33) [n=26]	0.659
Last serum CRP level before delivery (mg/l) [n=123]	11.00 (2.58-24.25)	4.20 (2.30-7.00)	0.002	4.10 (2.30-12.50)	4.60 (2.30-8.00)	0.883
% change in serum CRP level: (last–day 1)/day 1	0 (-27.3% to 68.8%)	0 (-32.4% to 0%)	0.090	0 (-11.9% to 9.1%)	0 (-32.4% to 0%)	0.960
High vaginal swab culture positive	8 (30.8%)	22 (22.7%)	0.394	10 (41.7%)	20 (20.2%)	0.028
Midstream urine culture positive	1 (12.5%) [n=8]	2 (6.1%) [n=33]	0.488	0 (0%)	3 (9.7%) [n=31]	0.564
Placental swab culture positive	9 (34.6%)	25 (25.8%)	0.371	13 (54.2%)	21 (21.2%)	0.001
Presence of group B *Streptococcus*	6 (23.1%)	10 (10.3%)	0.104	8 (33.3%)	8 (8.1%)	0.003
Perinatal death	0 (0%)	0 (0%)	-	0 (0%)	0 (0%)	-
Histological funisitis	-	-	-	10 (41.7%)	16 (16.2%)	0.006

Abbreviations: CRP = C-reactive protein; PPROM = preterm premature rupture of membranes

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

analysis (backward / forward elimination procedure) was performed by including variables that were significant at the level of p<0.1 by univariate analysis and the importance of the demographic variable.

Results

Among the 238 deliveries with a diagnosis of PPROM, 123 met the inclusion criteria (Figure 1). Funisitis was present in 21.1% (26/123) of women and EONS in 19.5% (24/123) of newborns. None of the EONS had a positive blood or cerebrospinal fluid culture, and all were diagnosed on the basis of clinical and laboratory results using the definitions mentioned above.

Table 2 shows the demographic and clinical characteristics of patients with funisitis. Women with funisitis had a significantly lower median gestational age than those without funisitis at PPROM (28 vs. 32 weeks; p<0.001) and at delivery (30 vs. 32 weeks; p<0.001). Babies with funisitis had a lower median birth weight (1145 g vs. 1790 g; p<0.001) and Apgar score at 1 minute (7 vs. 8; p=0.008) and 5 minutes (9 vs. 10; p=0.025) after birth than those without funisitis. The median serum CRP level of women with funisitis was significantly higher on day 1, 2, and 3 of PPROM and before delivery than those without funisitis (p<0.05 for all). The first and last CRP levels did not show any significant percentage change in either group. The PPROM-to-delivery interval was comparable for the two groups.

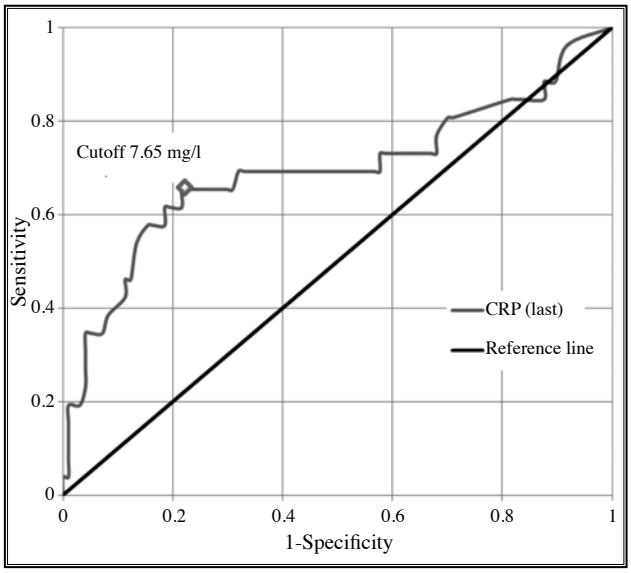

Figure 2. Receiver operating characteristic curve for the last maternal serum C-reactive protein (CRP) level for funisitis

Table 3. Logistic regression analysis of independent variables in predicting funisitis

Risk factor	OR (95% CI)	p Value
Maternal age	0.842 (0.745-0.952)	0.006
Gestational age at delivery	0.598 (0.467-0.765)	<0.001
Last serum CRP level	1.074 (1.029-1.122)	0.001

Abbreviations: CI = confidence interval; CRP = C-reactive protein; OR = odds ratio

Figure 2 shows the ROC curve of the last maternal serum CRP level before delivery in predicting funisitis. The curve is above the reference line indicating a significant relationship between CRP and funisitis (area under curve [AUC] = 0.693; 95% confidence interval [CI], 0.56-0.83; p<0.003). The best cutoff value for CRP to predict funisitis was 7.65 mg/l. Using this value, the sensitivity, specificity, PPV, and NPV were 65.4% (17/26), 78.4% (76/97), 44.7% (17/38), and 89.4% (76/85), respectively. The LR+ and LR– were 3.02 (95% CI, 1.89-4.84) and 0.44 (95% CI, 0.26-0.76), respectively. The ROC curves for CRP on day 1, 2, and 3 of PPROM were not plotted as the 95% CI of AUC crossed 0.5.

Table 3 shows the logistic regression analysis for funisitis. Maternal age, gestational age at delivery, and last maternal serum CRP level before delivery remained statistically significant after the analysis.

The demographic and clinical characteristics of patients with EONS are also shown in Table 2. Women who gave birth to babies with EONS had a significantly lower gestational age at PPROM (30 vs. 32 weeks; p=0.010) and delivery (31 vs. 32 weeks; p=0.004) than those without EONS. Babies with EONS had a lower birth weight (1435 g vs. 1790 g; p=0.002) and Apgar score at 1 minute (7 vs. 8; p=0.031) and 5 minutes (9 vs. 10; p=0.023) after birth than those without EONS. Of note, EONS was significantly associated with a positive high vaginal swab (p=0.028) and placental swab (p=0.001) cultures. The presence of group B *Streptococcus* in a high vaginal swab was significantly associated with EONS (p=0.003). The rates of histological chorioamnionitis and funisitis were higher in the EONS group than the non-EONS group. The PPROM-to-delivery interval was comparable for the two groups. Maternal serum CRP levels (including day 1-3 CRPs and last CRP before delivery) were, however, not associated with EONS.

Table 4 shows the logistic regression analysis for

Table 4. Logistic regression analysis of independent variables in predicting early-onset neonatal sepsis

Risk factor	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	p Value
Gestational age at delivery	0.721 (0.585-0.889)	0.724 (0.587-0.892)	0.002
Placental swab organism: positive (reference group: negative)	4.405 (1.63-11.906)	4.485 (1.649-12.193)	0.003

Abbreviations: CI = confidence interval; OR = odds ratio

EONS. Gestational age at delivery and positive placental swab culture remained statistically significant after the analysis.

Discussion

Funisitis was present in 21.1% of women and EONS in 19.5% of newborns in this study. Maternal serum CRP was associated with funisitis that in turn was associated with EONS. There was, however, no significant association between maternal serum CRP and EONS. The gestational age at delivery was the most significant risk factor for both funisitis and EONS. The birth weight and Apgar scores were significantly lower in women with funisitis and newborns with EONS those those without.

Maternal serum CRP has been studied for years in the prediction of chorioamnionitis and / or neonatal sepsis in patients with PPROM. Funisitis is thought to be the counterpart of a fetal inflammatory response. Nonetheless, some studies have shown a positive correlation[5,17] while others have failed to do so[11,12].

In this study, the last maternal serum CRP before delivery was associated with funisitis. Of note, an odds ratio close to 1 and a relatively small AUC (95% CI, 0.56-0.83) made the prediction of funisitis imprecise. Using the ROC curve and a cutoff value of 7.65 mg/l for serum CRP, the sensitivity, specificity, and PPV were not high and again indicated the limited use of CRP. Despite this, a relatively high NPV (89.4%) made CRP a reasonable adjunct to allow expectant management in the presence of PPROM in predicting chorioamnionitis. This cutoff value also matched that in the study by Lee et al of 8 mg/l[18].

Although there is no clear evidence to support the use of CRP as an early diagnostic test of chorioamnionitis in PPROM, a literature review for serial CRP estimations showed that a CRP level of ≥20 mg/l may be predictive[19]. This correlation, however, was not observed in this study. The serial CRP values and percentage change between first and last CRP showed no significant difference between the groups with or without funisitis or EONS. A comparable PPROM-to-delivery interval might also suggest that infection was a cause rather than a consequence of PPROM.

In this study, a significant association between funisitis and EONS was found but not between CRP and EONS. There are three postulations regarding this seemingly conflicting finding. First, the diagnostic definition of EONS varies; the definition of EONS is challenging and despite numerous reviews, there is still no consensus among paediatricians. In fact, the definition used in this study was based on clinical, biochemical, and microbiological factors. Second, the lack of an association between CRP and EONS may be due to the early intervention (i.e. delivery) for other indications before infection occurred. Third, the sample size may not have been sufficient to show a positive correlation.

Despite the insignificant correlation between CRP and EONS, we identified several other risk factors for EONS. Gestational age at delivery remained the most significant risk factor after logistic regression, but a positive maternal culture (high vaginal swab and placental swab) and the presence of group B *Streptococcus* might also alert clinicians to the need for active management.

This study has several limitations. First, randomisation and data analysis were limited by the retrospective design. Second, there might have been an inconsistent time lag between CRP measurement and delivery leading to imprecise interpretation of data. Third, there were no data regarding the long-term baby outcome, which is an important factor when considering delivery, especially at an extremely premature gestation. Larger prospective randomised trials with long-term data are needed to provide stronger evidence. Until then, CRP should be interpreted with caution.

Conclusion

Maternal serum CRP is a non-invasive, inexpensive, and readily available test useful for many clinicians in the

clinical setting of PPROM. Based on this study, however, CRP may be linked to funisitis but not directly to EONS. Other risk factors should be taken into account when managing women with PPROM such as gestational age at delivery and positive maternal cultures, especially of group B *Streptococcus*.

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Declaration

The authors have disclosed no conflicts of interest.

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Classical Caesarean Section Revisited in Modern Obstetrics

Winnie HUI MBBS, MRCOG
Vivian Kwan-Sin NG MBChB, FHKAM (Obstetrics and Gynaecology)
Wai-Lam LAU MBBS, FHKAM (Obstetrics and Gynaecology)
Wing-Cheong LEUNG MD, FHKAM (Obstetrics and Gynaecology)
Department of Obstetrics and Gynaecology, Kwong Wah Hospital, Yaumatei, Hong Kong

Objective: To review the incidence, indications, characteristics, and clinical outcomes of classical Caesarean section at a regional hospital in Hong Kong.
Methods: This was a retrospective case-series study of all women who underwent a classical Caesarean section over an 8-year period from 1 January 2008 to 31 December 2015 in our unit. Epidemiological data, indications for classical Caesarean section, and maternal and neonatal outcomes were analysed.
Results: There was an increasing trend of performing classical Caesarean section, both in our unit and other obstetrics units in Hong Kong under the Hospital Authority. Three main indications for classical Caesarean section were identified in our patients, including vascular lower segment, lower segment not well formed or inaccessible, and lower-segment uterine fibroids. The most common indication in our cohort was vascular lower segment due to placenta praevia with or without accreta. Compared with the groups of lower segment not well formed or inaccessible and lower-segment uterine fibroids, the total blood loss, need for subsequent secondary measures including compression suture and uterine artery embolisation, and admission to intensive care unit were statistically significantly highest in the vascular lower segment group.
Conclusion: Classical Caesarean section remained in its role in modern obstetrics for indications of placenta praevia, preterm delivery, as well as fibroids complicating pregnancies as demonstrated in our cohort study. As such, obstetricians should become adept at performing a classical Caesarean section because many cases will not have been predicted or will be required as an emergency procedure. With active involvement of consultants, a multidisciplinary approach and continuous training, the clinical outcome of classical Caesarean section can be reasonably good.
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Keywords: Cesarean section; Hemorrhage

Introduction

In the era of modern obstetrics, lower-segment Caesarean section has become the most common type of abdominal delivery since the last century. It is associated with less blood loss, lower risk of scar rupture, and less maternal and perinatal morbidity and mortality[1-4]. On the other hand, the classical Caesarean section remains a valid and important procedure in current practice. It was performed in 0.3% to 1% of all Caesarean sections for various indications that included transverse lie, preterm delivery[5], poor lower-segment formation, dense adhesions in the lower segment, placenta praevia[6], and invasive carcinoma of the cervix[7].

Kwong Wah Hospital is a regional hospital accounting for 5000 to 6000 deliveries per annum in Hong Kong. We can observe an increasing trend for classical Caesarean section, both in our unit and from territory-wide data in Hospital Authority. This study aimed to review the incidence and examine the current indications, characteristics, and obstetric outcome of women who underwent classical Caesarean section.

Methods

This was a retrospective case series of obstetric patients delivered by classical Caesarean section at Kwong Wah Hospital over an 8-year period from 1 January 2008 to 31 December 2015. The study was approved by the Ethics Committee of the Kowloon West Cluster, Hospital Authority, with the requirement of patient informed consent waived because of its retrospective nature.

All patients more than 24 weeks of gestation delivered by elective or emergency classical Caesarean section in our unit were included. One woman with a

Correspondence to: Dr Winnie Hui
Email: blueswinnie@gmail.com; hw029@ha.org.hk

J-shaped incision was also included as there was only one such case during the study period. Women were identified via the computerised Obstetrics Clinical Information System. All corresponding medical and operative records were reviewed in detail. Supplementary information was also retrieved from the Clinical Management System and the electronic Patient Record. Data retrieved for analysis included patient age, parity, body mass index at booking, number of previous abortions and Caesarean sections, medical history, gestation at and indications for Caesarean section, blood loss, operating time, interventions involved at and after delivery, and maternal and neonatal outcome.

Data were entered into Microsoft Office Excel 2007 and analysed using the Statistical Package for the Social Sciences (Windows version 22.0; IBM Corp, Armonk [NY], US). Categorical variables were analysed using Chi-square or Fisher's exact tests. Differences between continuous variables were analysed using analysis of variance. Level of statistical significance was set at $p<0.05$.

Results

The number of deliveries in our unit was approximately 5000 to 6000 per annum between January 2001 and December 2015 (Figure a). The total rate of Caesarean section was 23.1% in 2000 and 21.0% in 2015, with a peak incidence of 23.5% in 2008 (Figure b). The number of classical Caesarean sections performed in our unit has been increasing since 2008 (Figure c). This rise is also evident in all other Hospital Authority Obstetrics Units (Figure d). In our unit, there were only 19 cases of classical Caesarean sections from 2000 to 2007 (8 years), compared with 102 from 2008 to 2015 (8 years) [Figure c].

Among all Caesarean sections in our unit, the percentage of classical Caesarean sections varied from 0.1% to 2.7% during 2000 to 2015 (Figure b). Of the 102 classical Caesarean sections performed from 2008 to 2015, the indications were: placenta praevia type I-IV (n=56, 54.9%), fibroids (n=23, 22.5%), lower segment not well-formed (n=20, 19.6%), presence of transverse lie (n=9, 8.8%), lower-segment adhesions (n=8, 7.8%), and unstable lie (n=1, 1.0%). Among these patients, 13 had two indications and one had three.

The patients were further classified into three main groups according to their most important indication: group 1, vascular lower segment (53 cases, 52.0%); group 2, lower segment not well-formed / inaccessible (27 cases, 26.5%); and group 3, lower-segment fibroids (22 cases, 21.6%).

The mean age of all patients was 36.2 years, their mean gestation at delivery was 35.4 weeks, mean body mass index was 22.6 kg/m^2, mean operating time was 83.8 minutes, and mean blood loss was 875.5 ml. In 17 (16.7%) women, postpartum sterilisation was performed at the same surgery. Postpartum haemorrhage (PPH, defined as blood loss ≥1000 ml) occurred in 28 (27.5%) women of whom 20 (19.6% of 102) required admission to the intensive care unit (ICU). All of the patients received an oxytocin infusion after delivery as routine prophylaxis against PPH. In some instances, secondary measures were required to control PPH, including carboprost injection (n=10, 9.8%), balloon tamponade (mainly by Sengstaken Blakemore tube insertion, n=9, 8.8%), compression sutures (including Hwu's and modified B-lynch, n=22, 21.6%), and uterine artery embolisation (UAE; n=19, 18.6%). One woman required two UAEs sequentially postoperatively; 13 (12.7%) women required two or more secondary measures to control PPH.

Comparisons were made for the three groups with different main indications, including their demographics / characteristics (Table 1), maternal outcomes (Table 2), and neonatal outcomes (Table 3). The age ($p=0.01$), parity ($p=0.01$), number of previous abortions ($p=0.02$), and gestational age at delivery ($p<0.01$) were significantly different among the three groups. The mean age of the three groups exceeded 35 years signifying the impact of advanced maternal age. The mean gestational age at delivery was the lowest in group 2; and that for group 1 and group 3 was close to term. The majority of surgeons chose a midline skin incision in both group 1 and group 3.

There were significantly more patients in group 1 having a previous Caesarean section and requiring an elective classical Caesarean section under general anaesthesia compared with the other two groups (all $p<0.01$). Consultants were involved in the majority of cases, especially for group 1 with all patients having placenta praevia and group 3 with uterine fibroids, to ensure a judicious decision in the choice of classical Caesarean section as well as to offer immediate support intra-operatively. There were significantly more blood loss ($p=0.01$) and the operation was longer ($p<0.01$) in group 1 compared with the other two groups. Postoperative prophylactic antibiotics were given in more than 80% of cases in group 1 as there was a high risk of pelvic infection due to the need for multiple secondary measures to control PPH (Table 2). The placenta was retained as a conservative and fertility-preserving measure in some cases with placenta accreta, which also increased the risk of infection.

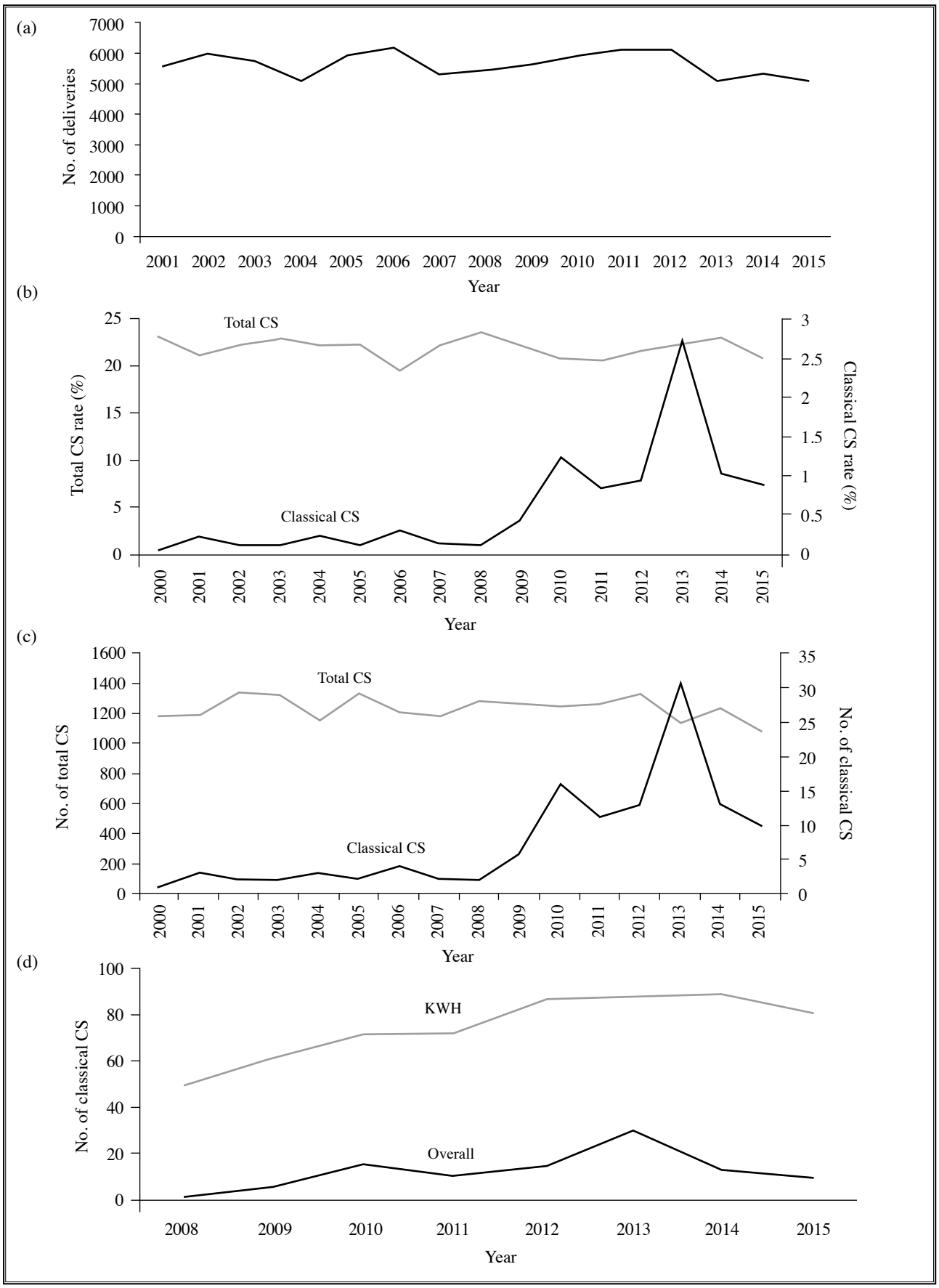

Figure. (a) Total number of births in our unit from 2001 to 2015. (b) Percentage of classical Caesarean sections over total Caesarean section in our unit during the same period. (c) Number of Caesarean sections (total and classical) in our unit from 2000 to 2015. (d) Number of classical Caesarean sections in our unit and all Hospital Authority Obstetrics Units from 2008 to 2015

Abbreviations: CS = Caesarean section; KWH = Kwong Wah Hospital

Table 1. Comparison of basic demographics and characteristics between the three groups with different main indications*

Demographics / characteristics	Group 1: vascular lower segment (n=53)	Group 2: lower segment not well formed / inaccessible (n=27)	Group 3: lower-segment fibroids (n=22)	p Value
Age (years)	35.3 ± 3.3	36.6 ± 3.1	37.9 ± 4.3	0.01
No. of parities				
0	17 (32.1)	8 (29.6)	16 (72.7)	0.01
≥1	36 (67.9)	19 (70.4)	6 (27.3)	
No. of previous abortions				
0	21 (39.6)	9 (33.3)	13 (59.1)	0.02
1	18 (34.0)	10 (37.0)	6 (27.3)	
2	4 (7.5)	5 (18.5)	0 (0)	
≥3	10 (18.9)	3 (11.)	3 (13.6)	
Gestation at delivery (weeks)	36.5 ± 2.4	32.3 ± 5.2	36.7 ± 2.4	
≤34	7 (13.2)	16 (59.3)	3 (13.6)	<0.01
>34	46 (86.8)	11 (40.7)	19 (86.4)	<0.01
BMI at booking (kg/m^2)	22.1 ± 2.9	23.7 ± 3.5	22.6 ± 3.3	0.13
Previous CS	27 (50.9)	12 (44.4)	2 (9.1)	<0.01
Elective	47 (88.7)	11 (40.7)	4 (18.2)	<0.01
General anaesthesia	47 (88.7)	12 (44.4)	4 (18.2)	<0.01
Midline skin incision	39 (73.6)	9 (33.3)	16 (72.7)	<0.01
Consultant involvement	42 (79.2)	14 (51.9)†	18 (81.8)	0.02
Postoperative prophylactic antibiotics	43 (81.1)	16 (59.3)	11 (50.0)	0.01

Abbreviations: BMI = body mass index; CS = Caesarean section

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

† Lower rate was probably because of the fact that the situation could be handled by specialist already

The mean length of hospital stay was not statistically different among the three groups.

In group 1, the reason for a vascular lower segment was solely due to placenta praevia type II to IV. There were two cases of placenta praevia type I associated with transverse lie that required classical Caesarean section due to poor lower-segment formation instead of vascularities; these were classified as group 2. One patient with a history of previous Caesarean section with placenta praevia type II was also classified in group 2 as the lower segment was inaccessible due to dense adhesions.

In group 1, seven women had placenta praevia type II, 25 had placenta praevia type III, and 21 had placenta praevia type IV. A total of 17 (32.1%) cases were diagnosed with placenta accreta intra-operatively. All were managed conservatively, with part of or the whole placenta left in situ, and none required hysterectomy. The majority (n=46, 86.8%) were delivered after 34 weeks. For those who delivered prematurely (n=7, 13.2%), all deliveries were performed as an emergency, either due to placenta praevia type III or IV with recurrent vaginal bleeding or severe pre-eclampsia. The number of patients who required blood transfusion, UAE as well as compression sutures was significantly higher in this group. The rate of ICU admission was also the highest in group 1 compared with the other two groups (p<0.01).

In group 2, the reasons for poorly formed or inaccessible lower uterine segment included mal-presentation or unstable lie (n=4, 14.8%), preterm delivery (at gestation 24-34 weeks; n=15, 55.6%), or dense adhesions (n=5, 18.5%) due to severe endometriosis, previous Caesarean section, or other pelvic surgery. There were two (7.4%) women with placenta praevia type I with malpresentation and one (3.7%) case of placenta praevia type II with dense lower-segment adhesions who were

Table 2. Maternal outcomes for the three groups with different main indications*

Maternal outcome	Group 1: vascular lower segment (n=53)	Group 2: lower segment not well formed / inaccessible (n=27)	Group 3: lower-segment fibroids (n=22)	p Value
Operating time (mins)	99.6 ± 55.6	67.4 ± 33.9	66.1 ± 26.3	<0.01
Blood loss (ml)	1096 ± 847.2	631 ± 618.2	643 ± 560.7	0.01
Length of hospital stay (postnatal) [days]	5.6 ± 2.5	5.7 ± 2.5	5.4 ± 4.4	0.94
Sterilisation	10 (18.9)	3 (11.1)	4 (18.2)	0.66
Transfusion	18 (34.0)	2 (7.4)	2 (9.1)	0.01
Secondary measures				
Carboprost	7 (13.2)	2 (7.4)	1 (4.5)	0.46
Uterine artery embolisation	19 (35.8)	0 (0)	0 (0)	<0.01
Balloon tamponade	7 (13.2)	1 (3.7)	1 (4.5)	0.27
Compression suture	20 (37.7)	1 (3.7)	1 (4.5)	<0.01
Hysterectomy	0 (0)	1 (3.7)	1 (4.5)	0.32
Postpartum fever (temperature ≥37.8°C)	6 (11.3)	5 (18.5)	3 (13.6)	0.68
Paralytic ileus	3 (5.7)	2 (7.4)	0 (0)	0.46
Wound complications	4 (7.5)	1 (3.7)	2 (9.1)	0.73
ICU admission	17 (32.1)	2 (7.4)	1 (4.5)	<0.01
Re-laparotomy	0 (0)	1 (3.7)	1 (4.5)	-
Maternal death	0 (0)	0 (0)	0 (0)	-

Abbreviation: ICU = Intensive care unit

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

Table 3. Neonatal outcomes for the three groups with different main indications*

Neonatal outcome	Group 1: vascular lower segment (n=53)	Group 2: lower segment not well formed / inaccessible (n=27)	Group 3: lower-segment fibroids (n=22)	p Value
Paediatrician standby at delivery	52 (98.1)	18 (66.7)	9 (40.9)	<0.01
Gender				
Male	34 (64.2)	14 (51.9)	10 (45.5)	0.27
Female	19 (35.8)	13 (48.1)	12 (54.5)	
Birth weight (g)	2766 ± 594	1757 ± 1065	2529 ± 577	<0.01
Apgar score at 1 min	6.7 ± 2.3	6.3 ± 2.5	7.9 ± 1.3	0.04
Apgar score at 5 mins	9.3 ± 1.3	8.0 ± 2.2	9.4 ± 0.7	<0.01
Cord blood				
pH	7.3 ± 0.1	7.3 ± 0.1	7.2 ± 0.1	0.09
BE	-5.3 ± 3.5	-7.5 ± 5.0	-7.5 ± 5.7	0.10
SCBU admission	29 (54.7)	2 (7.4)	6 (27.3)	<0.01
NICU admission	5 (9.4)	16 (59.3)	3 (13.6)	<0.01
Neonatal death†	1 (1.9)	2 (7.4)	0	

Abbreviations: BE = base excess; NICU = neonatal intensive care unit; SCBU = special care baby unit

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

† All neonatal deaths were due to preterm or complications from preterm births (2 cases at 25th week and 1 case at 29th week of gestation)

classified in this group as mentioned above.

Blood loss was significantly lower in group 2 than the other two groups (p=0.01). None of the women required UAE although two required ICU admission. One with postoperative haemoperitoneum who required repeat laparotomy and one who required a Caesarean hysterectomy were due to an intra-operative incidental finding of percreta.

In group 3, the size of the lower-segment fibroids varied from 3 to 15 cm in diameter. In four women, myomectomy was performed at the same surgery, either to facilitate uterine wound closure or to control bleeding from the fibroids. The fibroids that were removed varied from 1 to 3 cm in diameter. Blood loss volume, and number of patients who required secondary measures and ICU admission were similar in group 2 and group 3, but significantly less than those in group 1. None of the cases required UAE. In group 3, one woman underwent hysterectomy and required ICU admission.

Oxytocin infusion was administered in all women for prophylaxis of PPH. There were more secondary measures performed in group 1 including use of additional uterotonic agents, UAE, balloon tamponade, as well as compression sutures. The absolute number of patients with fever, paralytic ileus, or wound complications remained low in three groups. Most patients with fever responded well to empirical antibiotics (including cefuroxime, metronidazole, amoxicillin/clavulanate). There was only one case of severe sepsis that required use of meropenem with a prolonged stay of 23 days. The rate of re-laparotomy was low and there was no maternal mortality. The patients' subsequent pregnancy outcomes were traced but only six cases were identified from the electronic Patient Record — four required repeat Caesarean section, one had a first-trimester miscarriage, and one had a Caesarean scar pregnancy.

Table 3 shows the neonatal outcomes in the three groups. Our protocol required a paediatrician to be available at the time of delivery in women with placenta praevia. Over 60% of women in group 2 had a paediatrician standby because of preterm delivery. The mean birth weight was statistically significantly the lowest in this group for the same reason, compared with the other two groups. This also accounted for the high proportion of neonatal ICU admission (p<0.01). The Apgar scores at 1 minute and 5 minutes were statistically different between the three groups but not clinically significant.

Discussion

The overall incidence of classical Caesarean section among all Caesarean sections in our unit (0.1%-2.7%) was comparable with the literature (0.3%-1%)[3,4,8]. The general indications for classical Caesarean section in our cohort were comparable with those identified in the literature and included malpresentation, placenta praevia, inadequate lower segment, and obstruction of labour due to fibroids[3,4,8,9]. Our study results showed that there was a larger proportion of classical Caesarean section performed for placenta praevia than for other indications. The results reveal a shift of the most common indication for classical Caesarean section from preterm delivery to placenta praevia[6].

Placenta type II to IV increases the lower-segment vascularity. To avoid cutting into the blood vessels or into the placenta, surgeons elect to perform a classical Caesarean section. Placenta praevia type I does not suffice on its own as a reason for classical Caesarean section although it increases the chance of malpresentation, e.g. transverse lie, that can affect formation of the lower segment. With the increasing trend of previous Caesarean section, the incidence of placenta praevia or morbidly adherent placenta is likely to increase[10]. Classical Caesarean section is usually performed for planned conservative management of placenta accreta[11]. The expected blood loss will be higher compared with that for other indications for classical Caesarean section. Of note, PPH remains one of the major causes of morbidity. In our unit, placenta praevia with PPH accounts for most of the ICU admissions in obstetric cases[12]. Yet with the use of the secondary measures to control PPH, the rate of hysterectomy remains low[13].

The lower segment is formed when the uterine muscle fibres are stretched and occurs in the third trimester from 28 to 40 weeks. It is thinner and less vascular. Previous studies have shown that the blood loss of classical Caesarean section is higher than that following 'lower-segment Caesarean section' for preterm delivery[14]. Nonetheless, in preterm deliveries the lower segment has not yet formed. Surgeons will avoid lateral extension of the wound and consequent injury to the uterine vessels and choose classical Caesarean section. Studies have shown that the incidence of classical hysterotomy is inversely related to gestational age in both singleton and twin pregnancies[5,15]. Fetal factors such as small for gestational age and non-cephalic presentations increase the likelihood of a classical Caesarean section[5]. Systematic reviews have shown that an estimated 14.9 million babies worldwide are born preterm, accounting for 11.1% of all livebirths[16]. Multiple pregnancies and iatrogenic

preterm births caused by pre-eclampsia and fetal growth restriction remain important causes of prematurity[17]. With advancing maternal age, these factors are likely to follow an increasing trend.

On the contrary, when the lower segment is covered by dense adhesions, e.g. previous Caesarean section or previous myomectomy with bladder adhesions, surgeons will avoid injury to the visceral organs and elect to perform a classical Caesarean section. Primary Caesarean births accounted for 50% of the increasing rate of Caesarean section. According to Barber et al[18], the repeat Caesarean rate among all live births was 6.7% in 1996, 9.8% in 2003, and 14.8% in 2009, representing an increase of 120.9%. The increasing repeat Caesarean rates probably reflect the increasing number of women who present with a previous primary Caesarean as well as the reducing number of women who are willing to have trial of labour or vaginal birth after Caesarean. It is likely that classical Caesarean section will continue to play a role in this group of patients with one or more previous Caesarean sections.

There has been an increasing incidence of fibroids in the pregnant uterus varying from 0.1% to 12.5%[19]. This may be due to increased maternal age. In our cohort, the mean age of the patients with fibroids complicating pregnancy was 37.9 years (p=0.01). Previous studies suggest that Caesarean myomectomy can lead to intractable haemorrhage and may necessitate Caesarean hysterectomy with its attendant complications and loss of future fertility[20,21]. There have been some suggestions that bleeding from Caesarean myomectomy can be controlled by oxytocin and tourniquet[22]. In our cohort, four cases with myomectomy were performed to facilitate wound closure. Blood loss was essentially less than that from placenta praevia. Although there was one case of hysterectomy in group 3, myomectomy was not performed.

Conclusion

Classical Caesarean section remained its role in modern obstetrics for indications of placenta praevia, preterm delivery, as well as fibroid complicating pregnancies as demonstrated in our cohort study. Obstetricians should master the skills required to perform a classical Caesarean section since many such surgeries will have been unpredicted or performed as an emergency. As a result of an increased involvement of consultants, a multidisciplinary approach and continuous training in the techniques of classical Caesarean section, the clinical outcome of classical Caesarean section can be reasonably good.

Declaration

The authors have disclosed no conflicts of interest.

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Expectant Management Versus Induction of Labour for Intrauterine Fetal Death

Sin-Ying TSE MBChB, MRCOG
Po-Lam SO MBBS, MRCOG, FHKAM (Obstetrics and Gynaecology)
Hon-Cheung LEE MBBS, FRCOG (UK), FHKAM (Obstetrics and Gynaecology)
Department of Obstetrics and Gynaecology, Tuen Mun Hospital, Tuen Mun, Hong Kong

Objective: To compare the delivery outcome of patients managed with induction of labour versus spontaneous onset of labour following intrauterine fetal death.
Methods: Women who had an intrauterine fetal death from 1 January 2000 to 31 December 2015 in a regional hospital in Hong Kong were analysed to compare their delivery outcome following expectant management for spontaneous onset or induction of labour. The outcomes studied included the duration of labour, rate of infection, rate of coagulopathy, psychological stress, and other morbidities.
Results: A total of 193 patients fulfilled the inclusion criteria of whom 116 underwent labour induction and 51 elected spontaneous onset of labour; 26 patients were excluded from the analysis because 12 were already in active labour on admission, 13 changed their decision during the process, and one opted for Caesarean section. Patients with more advanced gestational age (p=0.004) and larger cervical dilatation (p<0.001) were more likely to opt for expectant management. The expectant group had a significantly shorter hospitalisation stay (4.8 days vs. 6.3 days; p<0.001) and shorter time from admission to delivery (4.6 days vs. 5.2 days; p=0.002) than the induction group. On the other hand, the induction group had a significantly shorter first stage of labour (4:05 hours vs. 4:52 hours; p=0.033) and less total blood loss (133.9 ml vs. 169.0 ml; p=0.013). Two cases in the induction group required emergency Caesarean section. There were no significant differences in the rate of infection, coagulopathy, or postnatal depression.
Conclusion: Both expectant management and induction of labour were safe options for intrauterine fetal death. Patients should be managed according to their preference and clinical condition.
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Keywords: Delivery, obstetric; Labor, obstetric; Perinatal death

Introduction

Intrauterine fetal death is defined as a fetus with no signs of life when the fetal weight is more than 500 g or over 24 weeks of gestation in utero as charted by the parturient[1]. In 2015 there were 2.6 million stillbirths globally, with more than 7178 deaths a day. Worldwide, the number of stillbirths has declined by 19.4% from the year 2000 to 2015, representing an annual reduction rate of 2%[2].

Intrauterine fetal death is a tragic event both for mother and her family. More than 85% of women go into labour spontaneously within 3 weeks of diagnosis[3-5]. Nonetheless there is the concern about development of complications following an intrauterine death such as disseminated intravascular coagulopathy and intrauterine infection[6,7]. The emotional burden on the mother and her family is also considerable[8]. Furthermore, postmortem and genetic assessments may be jeopardised after prolonged periods of expectant management[3]. On the other hand, inducing labour may pose risks of induction failure as well as other morbidities associated with induction[9-13].

The objective of this study was to analyse the delivery outcome of women who delivered a stillbirth following spontaneous versus induced labour.

Methods

A retrospective study was conducted of women who delivered between 1 January 2000 and 31 December 2015 at Tuen Mun Hospital, which is a regional hospital in Hong Kong. Ethics approval was obtained from the New Territories West Cluster Clinical Research Ethics Committee before commencement of the study. All women who had an intrauterine death during the study period were identified through the electronic patient records in the Clinical Management System. The case notes were retrieved and data were input into a database for thorough analysis.

Correspondence to: Dr Sin-Ying Tse
Email: tsy733@ha.org.hk

A single reviewer conducted a detailed manual review of data. Exclusion criteria included intrapartum death, multiple pregnancy, major placental abruption, placenta praevia, previous multiple Caesarean deliveries, previous classical Caesarean section, termination of pregnancy, and pre-eclampsia. Cases with either maternal or obstetric conditions that required urgent or early management and did not permit a choice of expectant management or induction were excluded. Gestational age was based on the best-estimated due date from prenatal records or ultrasound biometry at the time of intrauterine death diagnosis. The data collected included patient demographics, obstetric history, gestational age, ultrasound findings on diagnosis, cervical examination at the time of diagnosis, fetal and placental delivery time, adverse outcomes, total length of hospital stay, and the Edinburgh Postnatal Depression Scale (EPDS) score at postnatal follow-up.

Patients were stratified into the expectant management or induction group based on whether the delivery occurred after spontaneous onset of labour or induction of labour.

In Tuen Mun Hospital, all patients with suspected intrauterine death are assessed immediately by the on-duty medical officer. The diagnosis of intrauterine fetal death is confirmed by real-time ultrasonography. Patients are then counselled about the management options according to their clinical condition and delivery history. Unless the patient has an urgent need for delivery or has some exclusion criteria, they will be counselled about expectant management or induction of labour.

Patients who opt for expectant management are discharged home and followed up in the obstetric outpatient specialist clinic weekly. Blood investigations twice per week include a complete blood count, clotting profile, and serum fibrinogen. Those patients who opt for induction of labour are stratified to different induction methods according to the cervical ripening status. Prostaglandin is used for cervical ripening in patients with an unfavourable cervix. Those with a favourable cervix are given an oxytocin infusion. Amniotomy is avoided in all cases. All patients are visited by a bereavement nurse prior to discharge and all have postnatal follow-up in the postnatal clinic at Tuen Mun Hospital. At follow-up, both the medical officer and bereavement nurse assess the patient's physical and psychological health. If appropriate, referral will be made to a psychologist or psychiatrist.

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 on the scale corresponding to various clinical depression symptoms[14]. The Chinese version of the EPDS has been validated among Hong Kong Chinese women and its psychometric performance is comparable with the original scale. It has satisfactory sensitivity and specificity for detecting depression in Chinese women at 6 weeks' postpartum[15]. Mothers who score above 13 are likely to be suffering from a depressive illness of varying severity. Careful clinical assessment is carried out by an experienced specialist nurse to confirm the diagnosis.

Data were analysed using the SPSS (Windows version 21.0; IBM Corp, Armonk [NY], US). Mann-Whitney *U* test was used for continuous variables. Chi-square test and Fisher's exact test were used for discrete variables. A p value of <0.05 was considered statistically significant.

Results

During the study period, there were a total of 90,240 deliveries, including 273 cases of intrauterine death in Tuen Mun Hospital, i.e. one in 330 deliveries was an intrauterine fetal death. Of 273 cases, 80 (29.3%) were excluded based on the exclusion criteria mentioned above. Among the remaining 193 cases, 63 (23.1%) women opted for expectant management and 116 (42.5%) opted for induction of labour (Figure 1).

One 29-year-old nulliparous patient requested Caesarean section due to great maternal anxiety after the ultrasound diagnosis of intrauterine death at 37 weeks of gestation. The estimated fetal weight on ultrasound examination was 4.58 kg and the liquor volume was normal. The operation was uneventful and birth weight was 5.1 kg. Postnatal oral glucose tolerance test was normal.

One primipara patient with intrauterine death at 29 weeks of gestation originally opted for induction of labour after counselling. After 6 days of prostaglandin induction, her cervix remained unfavourable. She then switched to expectant management and refused further induction. She finally went into spontaneous labour 4 days after the last dose of prostaglandin.

Twelve patients switched from expectant management to induction for a variety of reasons. Time of change in decision ranged from 1 day to 73 days and was due to growing psychological stress. Among these, two

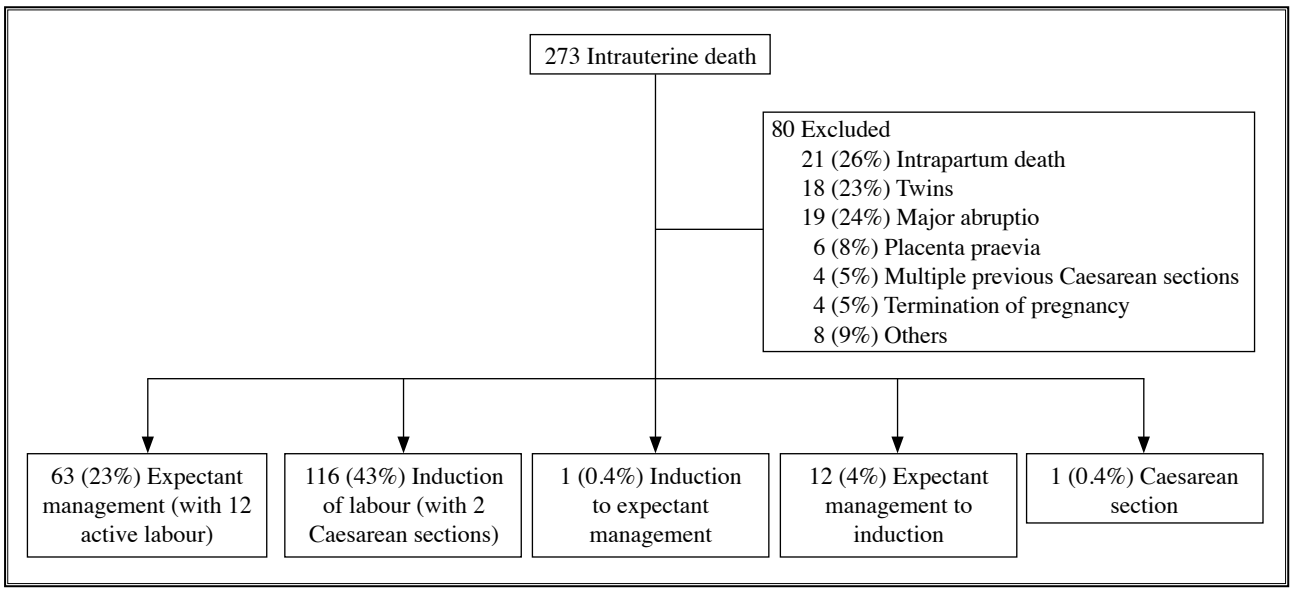

Figure 1. Flow diagram of selected patients

Table 1. Demographics and obstetric characteristics*

Demographics / characteristics	Expectant management (n=51)	Induction of labour (n=116)	p Value†
Age (years)	30.5 ± 6.0	29.0 ± 5.6	0.137
Gestational age (weeks)	34.0 ± 5.2	31.3 ± 5.6	0.004
Primiparity	23 (45.1)	59 (50.9)	0.367
Previous LSCS	7 (13.7)	7 (6.0)	0.158
Non-vertex presentation	7 (13.7)	30 (25.9)	0.055

Abbreviation: LSCS = lower-segment Caesarean section

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

† For continuous variables, p values were obtained from Mann-Whitney *U* test; for discrete variables, p values were obtained from Chi-square test

patients had no sign of labour after 46 and 73 days and finally decided to undergo induction of labour.

In the analysis of delivery outcomes, patients were stratified into expectant management or induction groups depending on whether delivery occurred following spontaneous onset of labour or after induction of labour. Women who changed their decision were not included in the study to ensure fair comparison of outcomes between the two groups. Twelve (4.40%) patients from the expectant group were excluded as they were already in active labour on admission. The definition of active labour used in this study was the documentation of regular uterine contractions with cervical dilatation greater than 4 cm at the time of first assessment at diagnosis of intrauterine death.

Maternal demographics and obstetric characteristics of the expectant and induction groups are summarised in Table 1. There were no significant differences between the two groups with respect to mean age, parity, and in the history of previous Caesarean section. The mean gestational age in the expectant group was significantly greater than that in the induction group (mean ± standard deviation: 34.0 ± 5.2 vs. 31.3 ± 5.6 weeks; p=0.004) [Table 1].

Labour characteristics and outcomes of the expectant and induction groups are summarised in Table 2. The mean cervical dilatation in the expectant group was significantly larger than that in the induction group (1.5 cm vs. 0.8 cm; p<0.001) and their mean birth weight of babies was also significantly greater (2081 g vs. 1641 g; p=0.015). The time from onset of labour to full cervical dilatation was significantly shorter in the induction group than the

Table 2. Labour characteristics and outcomes*

Characteristic / outcome	Expectant management (n=51)	Induction of labour (n=116)	p Value†
Cervical dilatation (cm)‡	1.5 ± 1.1	0.8 ± 0.8	<0.001
Birth weight (g)	2081 ± 1077	1641 ± 1088	0.015
Duration of first stage (hours)	4:52 ± 4:11	4:05 ± 4:45	0.033
Duration of second stage (hours)	0:12 ± 0:14	0:12 ± 0:22	0.056
Duration of third stage (hours)	0:07 ± 0:07	0:14 ± 0:29	0.510
Time from admission into hospital to delivery (days)	4.6 ± 6.3	5.2 ± 7.0	0.002
Length of hospital stay (days)	4.8 ± 3.0	6.3 ± 3.9	<0.001
Mode of delivery, No.			-
Normal vaginal delivery	45	90	
Instrumental	0	1	
Assisted breech	6	23	
Caesarean section	0	2	

* Data are shown as mean ± standard deviation, unless otherwise stated
† For continuous variables, p values were obtained from Mann-Whitney *U* test
‡ Cervical dilatation was documented at the time of diagnosis of intrauterine death in terms of width of dilatation irrespective of the thickness of cervix

Table 3. Maternal complications*

Complication	Expectant management (n=51)	Induction of labour (n=116)	p Value†
Blood loss (ml)	169.0 ± 104.7	133.9 ± 101.4	0.013
Blood transfusion	0	0	-
Retained placenta	1 (2.0)	10 (8.6)	0.109
Major perineal injury (3rd- or 4th-degree tear)	0	1 (0.9)	0.319
Shoulder dystocia	0	2 (1.7)	0.158
Surgical evacuation	0	2 (1.7)	0.158
Endometritis‡	3 (5.9)	10 (8.6)	0.509
Disseminated intravascular coagulopathy	0	0	-
Uterine rupture	0	0	-
Readmission after delivery	1 (2.0)	2 (1.7)	0.924
Side-effects			
Vomiting	-	1 (0.9)	-
Diarrhoea	-	2 (1.7)	-
Hyperstimulation	-	0	-

* Data are shown as mean ± standard deviation or No. (%) of subjects
† For continuous variables, p values were obtained from Mann-Whitney *U* test; for discrete variables, p values were obtained from Chi-square test or Fisher's exact test
‡ Based on clinical diagnosis and the need of antibiotics treatment

expectant group (4:05 hours vs. 4:52 hours; p=0.033), although their time from hospital admission to delivery was significantly longer (5.2 days vs. 4.6 days; p=0.002). The total length of hospital stay, meaning the total number of days spent in hospital since diagnosis, was also longer in the induction group than the expectant group (6.3 days

Table 4. Maternal psychological impact*

	With postnatal follow-up		p Value†
	Expectant management (n=42)	Induction of labour (n=100)	
EPDS questionnaire			0.707
Completed questionnaire	34 (81.0)	50 (50.0)	
Score ≥13	12 (35.3)	12 (24.0)	
Referral to psychologist or psychiatrist	21 (50.0)	32 (32.0)	0.542

Abbreviation: EPDS = Edinburgh Postnatal Depression Scale

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

† For discrete variables, p values were obtained from Chi-square test

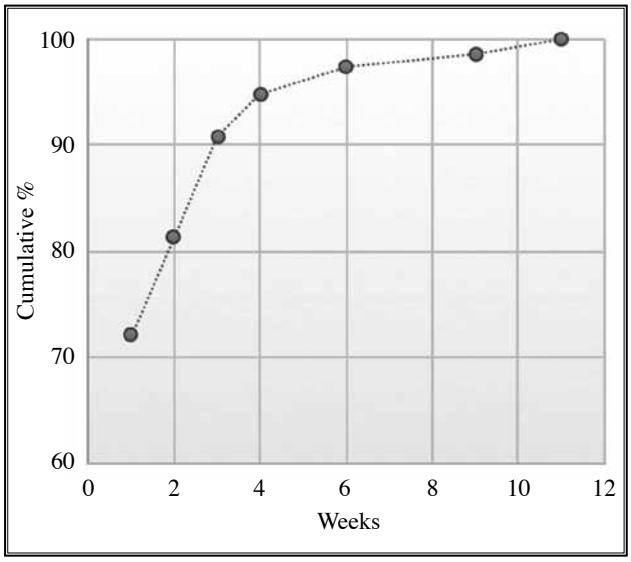

Figure 2. Cumulative percentage of spontaneous delivery versus number of weeks after diagnosis

vs. 4.8 days; p<0.001). There was no significant difference in the duration of second or third stage between the two groups. Two patients in the induction group required an emergency Caesarean section. Of these, one woman who failed induction was para 1 with a favourable cervix (Bishop score of 8) at diagnosis. The cervix, however, remained unchanged despite 3 days of good regular uterine contractions with oxytocin induction during the daytime. Another patient was para 1 with intrauterine fetal death and breech presentation. The fetus moved to a transverse lie in the active phase of labour and emergency lower-segment Caesarean section was required (Table 2).

Data on maternal complications of the expectant and induction groups are listed in Table 3. There was significantly more blood loss in the expectant group than in the induction group (169.0 ml vs. 133.9 ml; p=0.013), but no differences were found in the need for blood transfusion, the incidence of retained placenta, major perineal injury, shoulder dystocia, or uterine rupture. The occurrence of endometritis was not statistically different and there was no documented case of disseminated intravascular coagulopathy in either group during the study period. There were also no differences in the need for surgical evacuation after delivery or readmission rate in both groups. Side-effects due to the induction agent were few (Table 3).

With regard to the psychological impact on patients, choice of management did not appear to have a statistically significant effect on the incidence of postnatal depression or need for referral to a psychologist or psychiatrist (Table 4).

The cumulative percentage of patients who had a spontaneous delivery after diagnosis is plotted in Figure 2. Over 90% of patients had a spontaneous delivery within 3 weeks of diagnosis. The longest time awaiting spontaneous onset of labour was 73 days. This patient switched to induction of labour and delivered after 26 hours.

Discussion

In our study, approximately one (0.3%) in 330 deliveries in our hospital had an intrauterine fetal death. This number is comparable with other developed countries with an estimated incidence of approximately 0.5%[16]. There is no strong evidence to dictate the choice of either management option in an otherwise uncomplicated patient. As consideration of the fetus is no longer essential, the safety of the mother is the most important issue.

The Royal College of Obstetricians and Gynaecologists recommends that labour and delivery take account of the mother's preference as well as her medical condition and previous intrapartum history. Women should

be strongly advised to take immediate steps towards delivery if there is sepsis, pre-eclampsia, placental abruption or membrane rupture, while a more flexible approach can be discussed in the absence of these factors. Physically well women with intact membranes and no laboratory evidence of disseminated intravascular coagulopathy should be advised that they are unlikely to come to physical harm if labour is delayed for a short period, but that they may develop severe medical complications and had greater anxiety if the interval is prolonged[3]. Guidelines from the National Institute for Health and Care Excellence suggest that if the woman appears to be physically well, her membranes are intact and there is no evidence of infection or bleeding, she should be offered a choice of immediate induction of labour or expectant management[17]. In our study, the management plans of our medical officers concurred with the above recommendations.

In our study, patients in both groups had comparable demographics and obstetric characteristics except for gestational age. Women with more advanced gestation tended to opt for expectant management. This might be because these mothers were more psychologically attached to the dead fetus at a more advanced gestation and might need more time to accept the fact of intrauterine death. They might not be psychologically prepared to be separated immediately from the dead baby.

For labour characteristics, patients in the expectant group had greater mean cervical dilatation than the induction group at the time of diagnosis. They were generally at a more advanced gestation and thus their cervical status was better at the time of diagnosis. This also explained the larger mean birth weight of babies in the expectant group. As expected, the first stage of labour was short in the induction group but the time from admission to delivery was shorter in the expectant group. It is because those patients who were not in active labour were discharged home and managed in the outpatient setting. They were admitted to hospital only when signs or symptoms of labour were present or they were in active labour. Thus, their mean length of hospital stay was shorter. These results are comparable with those obtained in other studies[18].

In the induction group, two women required Caesarean section, with one of them due to a failed induction. This is one of the most feared risks that leads to emergency Caesarean section. Caesarean section is known to bear anaesthetic and surgical risks and may affect future pregnancies. The chance of placenta praevia, accreta, or even percreta is higher in patients with previous Caesarean section[19,20]. Moreover, the chance of postpartum haemorrhage with consequent need for hysterectomy is higher during Caesarean section[21]. Such important information should be included in counselling the couple. Another patient had lower-segment Caesarean section due to malpresentation, which is quite uncommon. One may consider the role of internal podalic version in managing transverse lie in labour but this requires an experienced obstetrician and poses a risk of uterine rupture. Apart from failed induction of labour, there is also the concern of possible side-effects from the induction agent including vomiting and diarrhoea[9-12]. In our study, the side-effects noted from labour induction were minimal.

The total blood loss in the induction group was less than that in the expectant group. The mean gestation in the expectant group was greater in this study and may explain the greater blood loss. The shorter mean duration of labour in the induction group may also explain the smaller blood loss.

In our hospital, all patients who opt for expectant management are closely monitored twice weekly. There was no case of disseminated intravascular coagulopathy noted throughout the study period (the longest duration of expectant management was >10 weeks). And the incidence of endometritis and postnatal depression was not statistically significant when compared with the induction group.

In our study, over 90% of patients achieved a spontaneous delivery within 3 weeks of diagnosis, comparable with other studies in which more than 85% of patients delivered in 3 weeks[3-5]. This is helpful in the counselling of patients as most couples who opt for expectant management are frustrated and obviously eager to know the approximate time of spontaneous delivery. However, it may also cause more anxiety for the already-stressed mother and her family. Although no statistical significance was evident in our study with regard to psychological impact, induction of labour may be a better option for the really desperate couples[8].

Strengths and Limitations

To the best of our knowledge, this is the first study in Hong Kong to compare the delivery outcome following expectant and induction management of intrauterine fetal death. Its strength lies in the relatively long study period and large sample size.

This study is limited by its retrospective design, dependent on retrospective review of medical records.

However, it may be unethical to perform a prospective randomised study for this type of cases. In addition, 18% of patients in the expectant group and 14% in the induction group defaulted from postnatal follow-up so the assessment was incomplete. Long-term follow-up of patients with regard to the psychological and psychiatric impact was also lacking in this study.

Further study is required to evaluate not only the delivery outcomes between induction and expectant management, but also the different induction regimens, including their effectiveness and safety.

Conclusion

In our study, both management options appeared safe. Practitioners should counsel patients with clear and adequate information about the pros and cons of each option. Full support should also be provided for patients and their partner, irrespective of their choice.

Declaration

The authors have disclosed no conflicts of interest.

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The Impact of Education on Patients' Understanding of the Implications of Nuchal Cord for Fetal Outcomes, Mode of Delivery, and Management

Choi-Wah KONG MBChB, MRCOG, FHKAM (Obstetrics & Gynaecology)
Diana Ho-Yin LEE MBBS, MRCOG
Lin-Wai CHAN MBChB, FRCOG
William Wing-Kee TO MD, FRCOG
Department of Obstetrics and Gynaecology, United Christian Hospital, Kwun Tong, Hong Kong

Objective: To explore whether education can change a pregnant woman's understanding of the impact of nuchal cord on fetal outcomes, mode of delivery, and management.
Methods: A questionnaire survey was conducted between August and October 2012 among all pregnant women when they attended the antenatal clinic of two regional hospitals in Hong Kong for the first time. After completion of the questionnaire, the women were given an information pamphlet about the impact of nuchal cord. A second questionnaire asking the same questions about the impact of nuchal cord was mailed to these women at 36 weeks of gestation. Answers to the first and second questionnaires were compared.
Results: There were no statistically significant differences in the proportion of women who were worried about nuchal cord between the first and second questionnaires, i.e. before or after receipt of the information pamphlet. Results of the second questionnaire revealed that there were significantly fewer women continued to wrongly believe that nuchal cord would likely cause adverse fetal outcomes, or affect the mode of delivery and management.
Conclusion: Education can correct women's misconceptions about the impact of nuchal cord. More patient education about the impact of nuchal cord is suggested to reduce anxiety and misconceptions. This may involve organisation of specific antenatal health talks and promulgation of correct concepts through the media.
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Keywords: Health education; Nuchal cord; Pamphlets; Surveys and questionnaires

Introduction

The incidence of nuchal cord at delivery has been reported to be 14.7% to 33.7%[1-6]. Most studies show that nuchal cord is not associated with lower Apgar score at 5 minutes or with an increase in Caesarean section rates, neonatal intensive care unit admissions, or perinatal mortality[1,2,4,6-8]. Nonetheless in our daily practice, women often request an antenatal ultrasound scan to look out for nuchal cord, or ask the sonographer to specifically look for the presence of nuchal cord during ultrasound scans performed for other obstetric indications. In addition, many women request elective Caesarean sections when nuchal cord is suspected during an ultrasound scan near term. This study was conducted to explore whether simple patient education using an information pamphlet to explain evidence-based facts about 'cord around the neck' can alter their misconceptions.

Methods

In 2015, a study reported the results of a questionnaire to evaluate women's understanding of the impact of nuchal cord on fetal outcome, mode of delivery, and management[9]. The questionnaire was distributed to all pregnant women at their first antenatal visit to the United Christian Hospital and Tseung Kwan O Hospital in Hong Kong from August to October 2012[9]. The questionnaire was available in traditional Chinese, simplified Chinese, and English (Appendix 1). All respondents were asked to choose the questionnaire in their preferred language. Those who were unable to understand Chinese or English were excluded from the study. The questionnaires were collected by nursing staff after completion. An information pamphlet (also available in three versions: traditional Chinese, simplified Chinese, and English; Appendix 2) about the true impact of nuchal cord was then distributed to respondents

Correspondence to: Dr Choi-Wah Kong
E-mail address: melizakong@gmail.com

by the staff. The pamphlet included information that nuchal cord is not associated with adverse perinatal outcomes or an increase in the rate of Caesarean section or instrumental deliveries.

The respondents were then asked to complete a second questionnaire at 36 weeks of gestation. The questionnaire was mailed to the respondents' home address with a request to return it by fax or mail on completion. In addition to the questions included in the first questionnaire, the second questionnaire asked whether the respondent had undergone an ultrasound scan in the third trimester and whether nuchal cord was specifically looked for. The second questionnaire was also available in three languages as in the first questionnaire (Appendix 3). The two questionnaires were then compared to determine whether the women's understanding on the impact of nuchal cord had altered. Ethics approval was obtained from the Clinical Research Ethics Committee of the Hospital Authority. SPSS (Windows version 20.0; IBM Corp, Armonk [NY], US) was used for statistical analysis. Chi-square test and Fisher's exact test were used when appropriate. McNemar's test was used to compare any change in respondents' views between the first antenatal visit and at 36 weeks of gestation. A p value of <0.05 was considered statistically significant.

Results

A total of 869 questionnaires were collected at the first antenatal visit[9] and 510 (58.7%) respondents returned the second questionnaire at 36 weeks of gestation. The demographic data of the respondents who returned the second questionnaire (respondents) and those who did not (non-respondents) are shown in Table 1. The respondents had a significantly lower educational level than the non-respondents (P=0.001). There were, however, no significant difference in the understanding about the impact of nuchal cord on fetal outcome, mode of delivery, or management for the first questionnaire between the two groups (Table 2).

Table 1. Demographic data of respondents and non-respondents*

Demographics	No. (%) of patients†		p Value
	Respondents (n=510)	Non-respondents (n=359)	
Maternal age (years)			0.109
<35	394 (78.2)	260 (73.4)	
≥35	110 (21.8)	94 (26.6)	
Not indicated	6	5	
Parity			0.210
0	263 (53.6)	205 (57.9)	
≥1	228 (46.4)	149 (42.1)	
Not indicated	19	5	
Ethnicity			0.373
Chinese	485 (96.4)	337 (95.2)	
Non-Chinese	18 (3.6)	17 (4.8)	
Not indicated	7	5	
Marital status			0.426
Single	47 (9.4)	39 (11.1)	
Married	451 (90.6)	312 (88.9)	
Not indicated	12	8	
Educational level			0.001
Non-tertiary	345 (68.6)	205 (57.9)	
Tertiary or above	158 (31.4)	149 (42.1)	
Not indicated	7	5	

* Respondents were those who returned the completed second questionnaire at 36 weeks of gestation, and non-respondents were those who did not return the second questionnaire

† %s were calculated after exclusion of those with an incomplete questionnaire

Table 2. Comparison of understanding about nuchal cord between respondents and non-respondents at first visit, and between respondents at first visit and at 36 weeks of gestation*

	Non-respondents' view at first visit (n=359)†	Respondents' view at first visit (n=510)†	p Value‡ (non-respondents vs. respondents at first visit)	Respondents' view at 36 weeks of gestation (n=510)	p Value‡ (respondents' view at first visit vs. at 36 weeks of gestation)
	Answer yes	Answer yes		Answer yes	
Worrying about nuchal cord	260 (72.6)	360 (71.1)	0.634	363 (72.5)	0.611
Impact of nuchal cord on fetal outcomes					
Nuchal cord can cause intrauterine death	287 (80.2)	388 (77.0)	0.264	316 (62.8)	<0.001
Nuchal cord can cause fetal death during labour	312 (87.9)	432 (87.6)	0.909	343 (70.3)	<0.001
Effect of nuchal cord on mode of delivery					
Nuchal cord will reduce the chance of a successful normal vaginal delivery	306 (87.2)	441 (87.1)	0.830	363 (72.5)	<0.001
Nuchal cord will increase the chance of an assisted vaginal delivery such as vacuum extraction or forceps delivery	196 (56.0)	279 (56.7)	0.838	215 (44.1)	<0.001
Management of nuchal cord					
It is necessary to have an ultrasound to detect nuchal cord at term	337 (94.4)	471 (93.8)	0.726	395 (79.0)	<0.001
It is necessary to deliver the fetus earlier if there is nuchal cord	258 (72.5)	335 (66.2)	0.051	266 (52.7)	<0.001
Caesarean section must be performed for nuchal cord alone, without other medical indications	250 (71.6)	366 (73.6)	0.518	263 (53.5)	<0.001

* Respondents were those who returned the completed second questionnaire at 36 weeks of gestation, and non-respondents were those who did not return the second questionnaire

† Data are shown as No. (%) of subjects calculated after exclusion of those with an incomplete questionnaire

‡ Chi-square test

For the respondents, there were no statistically significant differences in their proportion who were worried about nuchal cord at the first antenatal visit and after education at 36 weeks of gestation (p=0.611). Nonetheless, significantly fewer women who, after reading the pamphlet, were concerned about possible adverse fetal outcomes related to nuchal cord including intrauterine death and intrapartum death (all p<0.001). There was also a significantly lower proportion of women who believed nuchal cord should affect mode of delivery, including decreasing the chance of normal vaginal delivery or increasing the instrumental delivery rate (all p<0.001) after reading the pamphlet. In addition, after education, fewer women thought that nuchal cord would affect antenatal management including the need to detect nuchal cord by ultrasound scan, the need to deliver the fetus earlier, and the need for Caesarean section (all p<0.001) [Table 2].

A total of 160 (31.4%) respondents had an ultrasound scan performed in the private sector during the third trimester. Of them, 81 (50.6%) respondents specifically searched for the presence of nuchal cord, and 26 (32.1%) were told they had nuchal cord. Two were offered Caesarean section.

Discussion

This study showed that education of women about nuchal cord can significantly alter their belief about the possible consequences. Although there were fewer misconceptions after receiving the information pamphlet, many women remained ill-informed. After reading the pamphlet, approximately 60% to 70% still believe that nuchal cord could lead to intrauterine death and intrapartum death, 73% thought that nuchal cord would decrease the chance of a successful normal vaginal delivery, 79%

thought that an ultrasound scan was required to detect nuchal cord at term, and 54% thought that Caesarean section should be arranged in the presence of nuchal cord. An information pamphlet might have helped in patient education but was insufficient to change the long-standing misconceptions held by some women. Further education should be provided such as organising specific antenatal talks about nuchal cord so that evidence-based facts can be elaborated in more detail and patient's concerns and questions about nuchal cord can be addressed directly.

This study showed that although significantly fewer women had misconceptions, their anxiety was not reduced after education. Approximately 73% of respondents still worried about nuchal cord. This anxiety in such a high proportion of women should be addressed by obstetricians. Apart from providing more patient education about the true impact of nuchal cord, the absence of adverse fetal outcomes as a result of nuchal cord should be publicised widely by media to the general population in order to alleviate women's anxiety due to the long-standing misconceptions.

Of the women who had an ultrasound scan performed by their private doctor during the third trimester, around half of them specifically searched for the presence of nuchal cord. This re-enforces the misconception that such practice is necessary. An earlier questionnaire survey of all Hong Kong obstetricians showed that none who practised in the public sector would search for nuchal cord while 35.7% of private obstetricians would[10]. Nonetheless only 1.6% of obstetricians from the public sector and 6.3% of private obstetricians would offer Caesarean section to women with nuchal cord[10]. The findings from our study were compatible. Of the 26 respondents who were found to have nuchal cord by their private doctor following an ultrasound scan, only two (7.7%) were offered Caesarean section. Searching specifically for the presence of nuchal cord during ultrasound scans performed near-term should be abandoned as this will not alter antenatal management. Various studies have revealed an incidence of nuchal cord as high as 33% so such practice will only heighten maternal anxiety[1-6].

Limitations of the Study

This study had limitations. First, the response rate of the second questionnaire was only 58.7%, which can introduce bias into survey results. However, there was no statistically significant difference in the opinions about nuchal cord on the first antenatal visit between women who responded to the second questionnaire and those who did not. As such, we believe that our respondents at 36 weeks of gestation were not from a biased population and that the result from the second questionnaire should truly reflect the view of our patient population after education. Second, the respondents of the second questionnaire apparently had a lower educational level than the non-respondents. Whether a lower education background implies that such respondents were more amendable to health education, or whether non-respondents with a higher education background would show an even greater improvement in eradicating misconceptions after education requires further study.

Conclusion

Health education can reduce women's misconceptions about nuchal cord. More patient education in the form of antenatal talks about the true impact of nuchal cord is suggested. The absence of evidence of a direct adverse fetal outcome due to nuchal cord should be publicised widely by the media to the general population to reduce anxiety and misconceptions. Routine searching for the nuchal cord during ultrasound scan by obstetricians should be abandoned.

Conflict of Interest

No author has declared any conflicts of interest in this study.

Appendix

Additional material related to this article can be found on the HKJGOM website. Please go to <http://www.hkjgom.org/>, search for the appropriate article, and click on Full Text (PDF) following the title.

Declaration

The authors have disclosed no conflicts of interest.

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Incidence, Risk Factors, and Natural History of Ovarian Cysts in Postmenopausal Chinese Women: a Retrospective Cohort Study

Ho-Yan WAN MBBS, MRCOG, MHKCOG
Daniel WONG MBBS, MRCOG, FHKCOG, FHKAM (Obstetrics and Gynaecology)
Kwok-Keung TANG MBChB, FRCOG, FHKCOG, FHKAM (Obstetrics and Gynaecology)
Department of Obstetrics and Gynaecology, Pamela Youde Nethersole Eastern Hospital, Chai Wan, Hong Kong
Ho-Chi WAN BSc(ActuarSc), MEcon
Former Research Manager, Census and Statistics Department, Hong Kong

Objective: To evaluate the incidence of and risk factors for ovarian cysts in postmenopausal Chinese women, and the resolution rate of various morphological cysts and their association with ovarian cancer with use of serum CA-125 level and risk of malignancy index (RMI).
Methods: This was a retrospective cohort study conducted at a regional hospital in Hong Kong. All women who were first assessed in our clinic from May 2014 to January 2016 were included. We reviewed the ultrasound reports of their 6- to 9-monthly interval rescan, as well as the demographics, clinical history, and ultrasound findings of women who presented with postmenopausal bleeding. For women with any ovarian cysts on rescans or in surgery, ultrasonographic findings on interval scans and pathological reports from surgery up to 1 year were reviewed.
Results: A total of 1158 Chinese women were included. The overall incidence of ovarian cysts on a single ultrasound scan was 6.6%. The age-related incidence increased after 50 years of age and peaked at 60 to 64 years, then dropped until a second peak occurred at 75 to 79 years of age. No other potential risk factors for an increased incidence of ovarian cysts were identified. Chance of resolution of simple cysts was 26% in a single rescan. The resolution rate for a non-simple cyst was low (6%). All ovarian cysts with RMI score of <200 were benign. A RMI score of ≥200 was associated with a higher risk of ovarian cancer.
Conclusion: The resolution rate of ovarian cysts was comparable with that of overseas studies. Current management guidelines from overseas are appropriate for the Chinese population. The age-related incidence of postmenopausal cysts among Chinese women may support focusing on a target age-group in the population if a screening programme were to be implemented. Further prospective studies are warranted.
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Keywords: Incidence; Natural history; Ovarian cysts; Postmenopause; Risk factors

Introduction

Ovarian cysts are common in postmenopausal women. Although the majority of these cysts are benign, it is important to identify those that are potentially malignant because ovarian cancer is associated with high mortality[1]. Ovarian cancer is now the most common cause of death in Hong Kong due to cancer of the female genital tract although it has a lower overall prevalence[2]. Early disease is often asymptomatic and many women present late with advanced disease.

Although early diagnosis is associated with improved prognosis, there remains a lack of established screening programmes worldwide for ovarian cancer, due to the limited specificity of non-invasive screening tests[3-5] and the increase in unnecessary morbidities from invasive procedures. A recent breakthrough from a national randomised controlled trial in the UK[6] showed that annual screening for ovarian cysts with ultrasonography (USG) and serum CA-125 in low-risk postmenopausal women was associated with a significant reduction in mortality after 7 to 14 years of screening. Therefore, the efficacy and cost-effectiveness of an ovarian cancer screening programme is now being further evaluated in national studies in the UK.

With increasing evidence that screening for postmenopausal ovarian cysts may reduce mortality from ovarian cancer, data on the incidence of and risk factors for postmenopausal ovarian cysts will be helpful in clinical counselling, recommendations, and policy planning. Previous overseas studies have estimated the incidence of postmenopausal ovarian cysts to be 5% to 17%[7-10], but no

Correspondence to: Dr Eric Ho-Yan Wan
Emails: why667@ha.org.hk, ericwan124816@yahoo.com.hk

data have been published for the Chinese population. The primary aim of this study was to evaluate the incidence of and risk factors for ovarian cysts detected on a single USG scan in postmenopausal Chinese women. We also explored the natural history of postmenopausal cysts in a low-risk population and the risk of ovarian cancer associated with a morphological complex ovarian cyst, elevated CA-125 level, and high risk of malignancy index (RMI). This study therefore also attempted to determine the value of applying international guidelines for the management of postmenopausal cysts to our predominantly Chinese population.

Methods

This was a retrospective cohort study conducted at the postmenopausal bleeding assessment (PMBA) clinic of a regional hospital in Hong Kong. All women who were first assessed in the PMBA clinic from May 2014 to January 2016 were included, and the ultrasound reports of their 6- to 9-monthly interval rescan were reviewed. Ethics approval was obtained from the local institutional research ethics committee with patient consent waived due to its retrospective nature (Ref: HKEC-2016-098).

All patients who presented to the PMBA clinic during the study period were managed according to the latest departmental operational guidelines, in which their clinical history, physical examination, and pelvic USG findings were documented on a standardised electronic template.

Clinical history of postmenopausal bleeding and presence of associated symptoms including lower abdominal pain and abdominal distension were documented. Further details including the patient's obstetric history, medical history, medication history (e.g. hormone contraception or hormone replacement therapy), social history (e.g. ethnicity and smoking history), and family history of gynaecological, breast, or colorectal cancers were also recorded.

Pelvic USG was performed in every patient by medical officers who had completed and passed the accredited examination of the Obstetrics and Gynaecology Ultrasound Training Programme of the Hospital Authority of Hong Kong. Transvaginal scans were routinely performed except in patients who had never been sexually active, in which case a transabdominal or transrectal approach was adopted. Endometrial thickness was routinely screened as well as bilateral ovaries and adnexa. A 5-7.5 MHz transvaginal probe was used to measure each ovary and describe any observed abnormalities. The examiner spent at least 5 minutes searching for both ovaries, but the scan was halted if the iliac vessels were visualised and the ovaries were not visible.

Presence of ovarian or adnexal cysts were documented with the following details: (1) size measured along the major and minor axes of both transverse and longitudinal planes; (2) laterality; (3) non-simple features including presence of loculations, any mixed (solid / cystic) component, any solid area or papillary projection that extended into the cyst cavity; and (4) presence of ascites.

Serum CA-125 was measured in any woman with ovarian cyst(s) and the RMI calculated (RMI I score was used[11]). For patients with simple ovarian cysts and Ca-125 level of <35 U/ml — defined in this study by cyst size of <5 cm; unilateral; and absence of non-simple features as mentioned above or ascites — a repeat pelvic USG assessment was arranged in 6 to 9 months' time. If the cysts persisted on two consecutive scans or had altered features, bilateral oophorectomy was offered.

Women with non-simple ovarian cysts or elevated CA-125 level and RMI I score were counselled about surgical intervention. In patients who opted for surgery, an USG assessment was arranged as part of their preoperative assessment. In those who declined surgery, pelvic USG assessment was repeated after a further 6 months.

In this study, clinical data of women who attended the PMBA clinic were extracted from medical records of the electronic patient record database of the Hospital Authority, Hong Kong. The overall incidence of ovarian cysts and possible risk factors for developing ovarian cysts were studied. The natural history of either simple or complex cysts of these patients was also reviewed to determine the chance of resolution on follow-up scans. For patients who underwent surgery, operative findings and clinical pathological reports of the ovaries were reviewed.

Statistical analysis was performed using Stata Windows version 14.0. To measure the relative risk of potential risk factors, comparison between the outcome groups was made by Fisher's exact test for binary and categorical variables. A p value of <0.05 was considered statistically significant.

Inclusion and Exclusion Criteria

All women who were assessed in the PMBA clinic from May 2014 to January 2016 were included. Since the target group in this study was the low-risk Chinese

population, patients were excluded if they fulfilled any of the following criteria: non-Chinese; not postmenopausal according to clinical history (in our study, postmenopausal was defined as a women who had no menstruation for 12 consecutive months in the absence of any identified secondary causes); history of gynaecological malignancy; history of salpingo-oophorectomy or oophorectomy; history of hysterectomy as it reduces sensitivity in detecting an adnexal cyst; or known carrier of *BRCA1*, *BRCA2*, or Lynch syndrome.

Results

A total of 1243 patients attended the PMBA clinic during the study period, of which 85 were excluded based on our exclusion criteria. In patients who were referred with confirmed *BRCA1*, *BRCA2* gene mutation or Lynch syndrome, follow-up with regular ultrasound surveillance was arranged in the gynaecology clinic, not the PMBA clinic. As a result, data of 1158 (93%) women were reviewed (Figure 1). Table 1 summarises their demographics and characteristics.

Incidence of Ovarian Cysts

Among the 1158 women enrolled in this study, 76 (6.6%) had ovarian or adnexal cysts identified during a single episodic pelvic USG, of whom 29 had either non-simple ovarian cysts and / or elevated CA-125 level. In our study, the incidence of ovarian cysts increased with age after 50 years and peaked in the 60-64 years. The incidence then dropped until a second smaller peak at 75-79 years (Table 2).

When samples were allocated to various 2x2 contingency tables according to the bisecting ages, the odds ratio (OR) of having an ovarian cyst was significantly higher at the age of ≥65 years (OR=1.725, p=0.027) compared with the age of <65 years (Table 3).

Risk Factors for Ovarian Cyst

Multivariate analysis was performed to assess the association of traditional risk factors or protective factors for ovarian cancer with development of postmenopausal ovarian cyst. There was no significant increase in risk for having a first-degree family history of colorectal, breast or ovarian cancer; or a history of metabolic disease (diabetes, hypertension, obesity, hyperlipidaemia). There was also no associated risk for parity or history of hormone replacement therapy (Table 4).

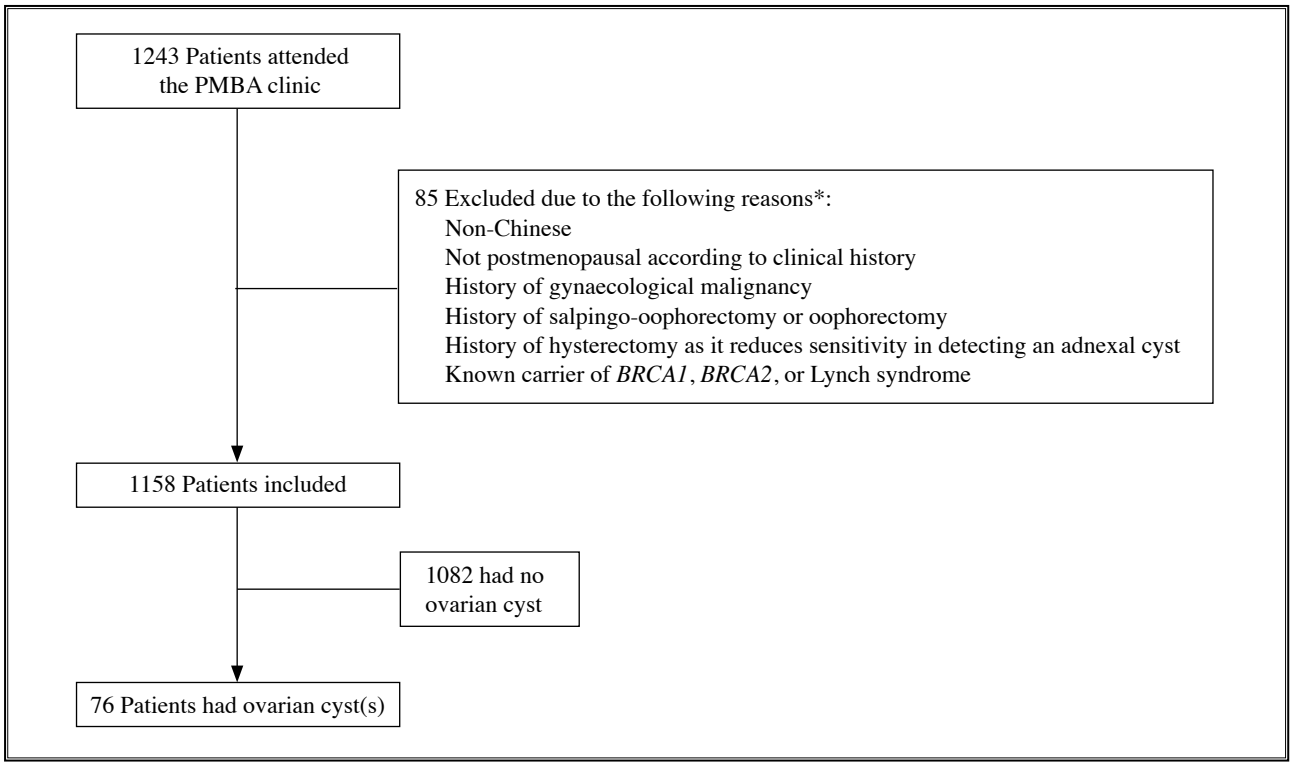

Figure 1. Study flow diagram of ovarian cyst study cohort

Abbreviation: PMBA = post-menopausal bleeding assessment

* Some patients might meet more than one exclusion criterion

Table 1. Demographics and characteristics of the ovarian cyst study cohort (population of effective data = 1158)

Demographics / characteristic	No. (%) of patients
Age-group (years)	
40-44	6 (0.52)
45-49	35 (3.02)
50-54	207 (17.88)
55-59	322 (27.81)
60-64	174 (15.03)
65-69	156 (13.47)
70-74	62 (5.35)
75-79	69 (5.96)
80-84	59 (5.09)
85-90	46 (3.97)
90-94	15 (1.30)
95-99	7 (0.60)
Parity	
Nulliparous	156 (13.47)
Primiparous / multiparous	1002 (86.53)
Sexual history	
Never sexually active	70 (6.04)
Ever sexually active	1084 (93.61)
Missing data	4 (0.35)
First-degree family history of colorectal, breast or ovarian cancer	
Yes	199 (17.18)
No	954 (82.38)
Missing data	5 (0.43)
History of hormone replacement therapy	
Yes	33 (2.85)
No	1121 (96.8)
Missing data	4 (0.35)
History of metabolic diseases (diabetes / hypertension / obesity / hyperlipidaemia)	
Yes	507 (43.78)
No	648 (55.96)
Missing data	3 (0.26)

Natural History of Ovarian Cyst

The serial re-imaging of ovarian cysts at standard intervals in this study provided information about the natural history of various ovarian cysts. Of 76 patients who had ovarian or adnexal cysts identified during a single episodic pelvic USG, 47 (62%) had simple ovarian cysts with normal CA-125 level and RMI I score of <200. Among these, 38 were re-imaged and 10 were cyst-free on one USG performed after 6 to 9 months, yielding a resolution rate of 26%. In women with persistent ovarian cysts, there was no change to cyst morphology (Figure 2).

Table 2. Age-related incidence of postmenopausal ovarian cyst

Age-group (years)	Absence of cyst	Presence of cyst	Incidence (%)
50-54	196	11	5.31
55-59	298	24	7.45
60-64	159	15	8.62
65-69	149	7	4.49
70-74	60	2	3.23
75-79	65	4	5.80
80-84	56	3	5.08
≥85	65	3	4.41

Table 3. Risk of postmenopausal ovarian cyst in various bisecting ages

Age-group (years)	Odds ratio	p Value (1-sided Fisher's exact test)
<55 vs. ≥55	1.150	0.354
<60 vs. ≥60	1.230	0.166
<65 vs. ≥65	1.725	0.027
<70 vs. ≥70	1.569	0.100

Of the remaining 29 patients who were diagnosed with non-simple cyst, 17 (94%) of 18 women with an RMI-I score of <200 who underwent interval USG re-imaging had persistent ovarian cysts. Seven opted for surgery and cysts were benign in all cases. Among four women with RMI I score of ≥200, one was not medically fit for surgery and died before workup, and another defaulted follow-up. Of the two patients who were further evaluated, one had a benign ovarian tumour and underwent subsequent laparotomy; the other was diagnosed with metastatic ovarian cancer. This last patient aged 63 years and attended for postmenopausal bleeding; she was otherwise asymptomatic except for a non-specific bloating sensation. USG revealed a 10-cm complex adnexal cyst and CA-125 level was 30096 U/ml. Computed tomographic scan of thorax, abdomen, and pelvis showed a left adnexal mass with ascites suspicious of omental cakes, enlarged lymph nodes in the para-aortic and common iliac regions, as well as unilateral pleural effusion with soft tissue nodules over the left chest wall.

Table 4. Risk factors for ovarian cyst

Risk factor	Prevalence of ovarian cyst		Adjusted association	
	No. of women	Rate of ovarian cyst (%)	Odds ratio	p Value (1-sided Fisher's exact test)
Parity	1158			
Nulliparous	156	5.77		
Primiparous / multiparous	1002	6.67	1.170	0.413
Sexual history	1154			
Never sexually active	70	7.14		
Ever sexually active	1084	6.55	0.911	0.496
Family history of colorectal, breast, or ovarian cancer (first-degree relative)	1153			
No	954	6.50		
Yes	199	7.04	1.089	0.441
History of hormonal replacement therapy	1154			
No	1121	6.51		
Yes	33	9.10	1.436	0.372
History of metabolic diseases	1155			
No	648	5.86		
Yes	507	7.50	1.301	0.161

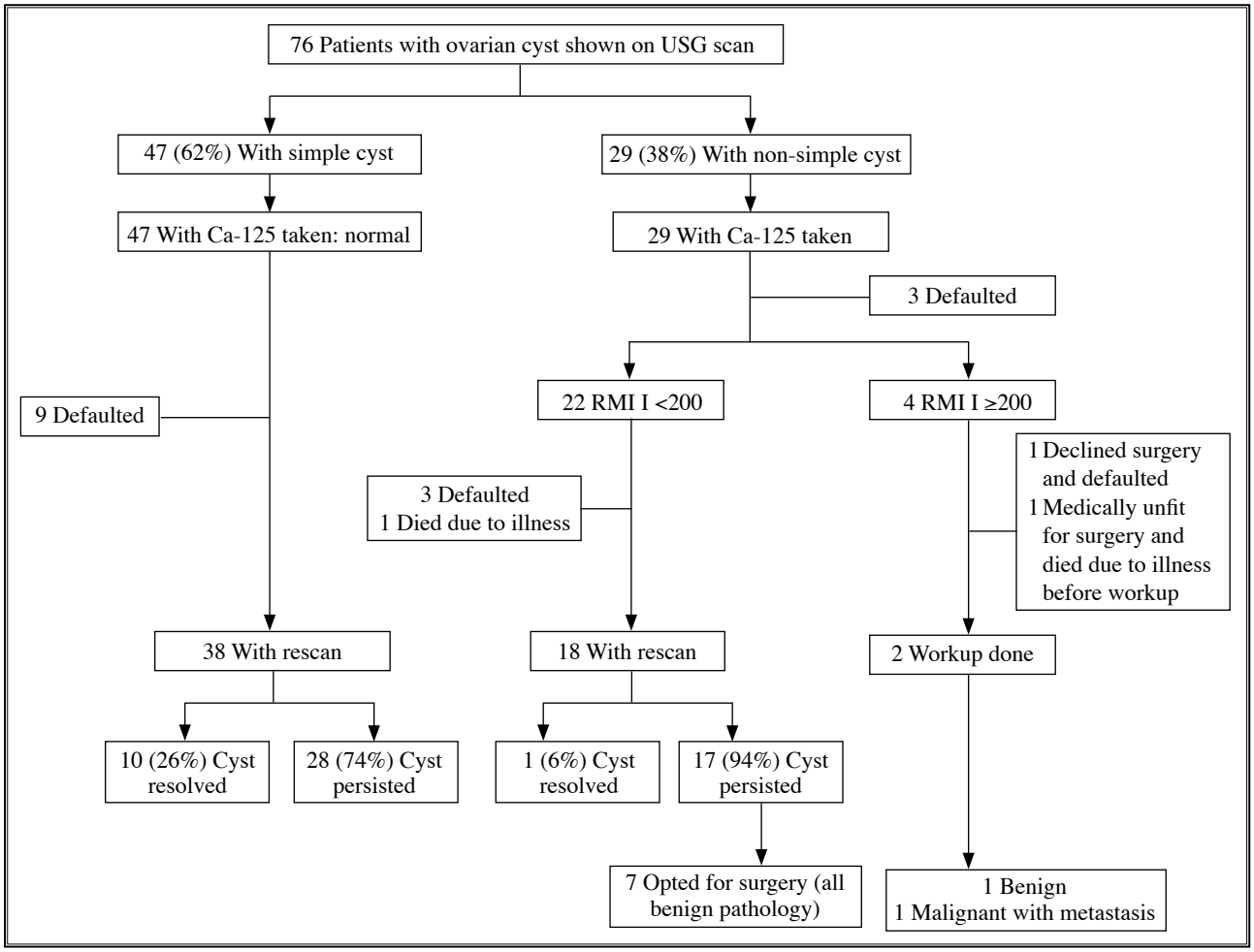

Figure 2. Study flow diagram of patients with ovarian cysts shown on ultrasonographic scan

Abbreviations: RMI = risk of malignancy index; USG = ultrasonography

Biopsy was taken and histopathology confirmed high-grade serous adenocarcinoma. USG-guided aspirated pleural fluid cytology and chest wall nodule biopsy confirmed metastasis from the female genital tract. The patient was referred to a clinical oncologist and underwent chemotherapy.

In summary, cysts were benign in all patients with simple cysts, and those with non-simple cysts and RMI I score of <200. Patients with RMI I score of ≥200 had a 50% risk of having ovarian cancer (Figure 2).

Discussion

Ovarian cysts are common findings on ultrasonography in postmenopausal women. The incidence of postmenopausal ovarian cysts on a single USG in our study was 6.6%, which is comparable with previous overseas cancer screening trials[1].

The incidence of postmenopausal ovarian cyst correlated with age in our study. A double peak pattern was observed, with the incidence increasing by the age after 50 years, peaking at the 60-64 years' age-group, then dropping until a second smaller peak at the age of 75-79 years. When the bisecting age reached 65 years, the OR of having ovarian cysts was maximised and there was a statistically significantly higher risk of having ovarian cysts between menopause and the age of 65 years. Whether this group of patients is at a higher risk of ovarian cancer requires further larger-scale prospective study.

Multivariate analysis revealed that traditional ovarian cancer risk factors (metabolic disease, family history of breast or colorectal or ovarian cancer, nulliparity) were not associated with a significant increase in ovarian cysts, probably due to the small sample size. The occurrence of postmenopausal cysts does not directly reflect risk of ovarian cancer. Nonetheless, we still advise health care providers and patients to be conscious about these health risks.

The overall findings in our follow-up studies of the natural history of both simple and non-simple ovarian cysts support the current management guidelines of the Royal College of Obstetricians and Gynaecologists[1] (RCOG) and the American College of Obstetricians and Gynecologists (ACOG)[12].

Simple cysts resolved or persisted without progression in all patients who were followed up with no apparent increased risk of malignancy. The resolution rate in one rescan was 26% in our study after 6 to 9 months, similar to that of other overseas studies with an annual resolution rate of 23% to 32%[8,13]. In our study, the follow-up period was relatively short and it was not possible to determine the long-term resolution rate. The University of Kentucky trial further followed up patients and suggested that up to 83% of simple cysts would resolve spontaneously over a mean of 4.6 years of follow-up[13].

On the contrary, the chance of resolution of a non-simple cyst with RMI I score of <200 was less than 6% in our study, which is lower than the 16.1% quoted in a previous study[14]. The figures, however, may not be directly comparable since we took the RMI I score into account and the rescan interval was also different. In view of the low resolution rate, surgical intervention should be included as one of the management options during counselling after the first scan, even when CA-125 level is normal and RMI I score is <200.

Apart from the resolution rate, management of patients with non-simple cyst should take account of the RMI I score. Our data suggest that using the new cut-off RMI I score of 200 to stratify risk of invasive ovarian cancer appears to be reliable[1]. However, patients should be informed during discussion about management of its limited sensitivity[15,16]. A prospective study with a larger sample size should be considered to evaluate this cutoff.

This is the first study to evaluate the prevalence and natural history of ovarian cysts in a Chinese population. A strength of this study is the well-structured clinical protocol for management of women with postmenopausal bleeding, and the standardised follow-up for those with ovarian cysts. All clinical data including history, physical findings, and USG reports were well-documented on a standardised electronic template so data collection was complete and accurate with less than 1% of missing data despite its retrospective nature. All USG scans were performed by an accredited medical doctor and the findings were documented in a standard format.

An ideal study design for this cohort would be to recruit asymptomatic women from the general population into a large screening USG programme. Nonetheless there is a lack of established screening programmes in Hong Kong. In most of the regional hospitals in Hong Kong, under the current clinical practice, ovarian cysts in postmenopausal women are identified either following emergency admission or by referral from an outpatient setting. In this study, we reviewed those women presented with postmenopausal

bleeding as it is an uncommon presenting symptom for ovarian cysts or ovarian cancer, except in rare cases such as a hormone-secreting tumour. The selected patient group in this study therefore represented a generally low-risk Chinese population in current clinical practice in Hong Kong.

This study has some limitations. The final histological pathology was not available for every woman with an ovarian cyst. In addition, with the small sample size and relatively short follow-up period, an accurate malignancy risk as well as long-term resolution rate could not be ascertained.

Conclusion

The incidence of postmenopausal ovarian or adnexal cysts in Chinese women was 6.6% in a single episodic pelvic USG. The incidence of postmenopausal cysts follows the double-peak pattern of the age-related incidence of ovarian cancer in Hong Kong, which increases with age and reaches its highest peak at 60-64 years, and a second peak at 75-80 years. No other risk factors or protective factors for occurrence of postmenopausal cysts were identified. The chance of resolution of ovarian cysts in the Chinese population is comparable with overseas studies. Our finding supports the current management guidelines of the RCOG and ACOG on postmenopausal ovarian cysts and their appropriateness to our local Chinese population.

Declaration

The authors have disclosed no conflicts of interest.

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Maternal and Neonatal Outcomes under the Comprehensive Child Development Service at Princess Margaret Hospital: a One-year Experience

Lai-Fong HO RN, RM, MSc
Mei-Fung CHAN RN, RM, BSc
Hoi-Ying LAU RN, RM, MSc
Lai-Fun TSE RN, RM, BSc
Yan-Yan AU RN, RM, BSc
Judy WY NG RN, RM, MSSc, MHSc(Edu)
Department of Obstetrics and Gynaecology, Princess Margaret Hospital, Laichikok, Hong Kong

Objective: To review the demographic characteristics of the women under the care of the Comprehensive Child Development Service (CCDS) and their neonatal outcomes.
Methods: Patient records under the care of the CCDS team in 2014 in a regional hospital in Hong Kong were retrieved for data analysis.
Results: Of the 275 women included in the final cohort, 21 (7.6%) were teenagers, 86 (31.3%) were a substance abuser, and 168 (61.1%) had mental health problems. With regard to the neonatal outcome, 14.2% were delivered preterm and 44.0% were admitted to the neonatal unit. Of the babies admitted to neonatal unit, 33.9% were due to neonatal drug withdrawal syndrome. Ketamine (50.0%) and amphetamine (44.2%) were the illicit drugs most commonly used by the mother, followed by cocaine (26.7%), heroin (17.4%), and ecstasy (17.4%); 34.9% of these women did not avoid the substance during pregnancy. When compared with the overall statistics in the hospital in 2014, the women in this study had more preterm birth (14.2% vs. 7.2%), more operative deliveries (26.8% vs. 21.1%), and more babies who required special care (44.0% vs. 31.1%).
Conclusion: Women with active substance abuse disorders are at risk for unplanned pregnancy. Effective contraceptive methods should be emphasised to this group of women after delivery. It is also crucial to appreciate the impact of the adverse consequences of substance abuse during pregnancy.
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Keywords: Drug users; Infant, newborn; Mental disorders; Pregnancy complications; Substance-related disorders

Introduction

Many studies have shown that mental health problems, substance abuse, and teenage pregnancies are associated with poor outcomes for fetal and child development[1,2]. The Hong Kong Hospital Authority introduced the Comprehensive Child Development Service (CCDS) in 2005 to improve the health outcomes of these pregnant women and their babies. CCDS is a government-funded community-based programme that aims to ensure early identification of the various needs of children (0-5 years old) and their family. Through collaboration and communication of different health care disciplines, timely support can be provided to families with special needs.

The scope of the CCDS consists of the following four main components: (1) identification and holistic management of at-risk pregnant women; (2) identification and management of mothers with postnatal depression; (3) identification and management of families with psychosocial needs; and (4) identification and management of toddlers with physical, developmental, and behavioural problems. At the hospital level, the clinic serves as a platform for antenatal and postnatal screening[3]. The at-risk groups that include teenage pregnant women, women with mental health problems, and women with substance abuse can be identified and monitored by the CCDS team.

Pre-existing mental illness, history of significant life events, experience of postnatal depression, or issues relating to grief and loss may all place women at risk of antenatal depression and / or postnatal depression[4]. Maternal mental health has become an area of increasing concern for researchers, clinicians, and public policymakers since

Correspondence to: Dr Lai-fong Ho
Email: hlf208@ha.org.hk

evidence has been accumulating that the consequences of perinatal mental illness are not limited to the suffering of the affected women, but extend to the mother-infant relationship and eventually the developing child[5]. The process of childbirth involves many psychological and emotional changes that may cause pre-existing mental health problems to relapse or recur, including psychotic symptoms[6].

Another high-risk group under the CCDS team is women with substance abuse. Drug misuse and dependence during pregnancy is associated with a wide variety of adverse maternal and child outcomes[7,8]. Neonatal complications include microcephaly, intrauterine growth retardation, opioid withdrawal syndrome, postnatal growth deficiency, neurobehavioural problems, and sudden infant death[9,10]. The adverse obstetric outcomes are mainly attributable to poor nutrition as money is spent on purchase of the illicit drug / substance, loss of appetite due to the side-effects of the illicit drug / substance or smoking, and a poor social relationship with family members with consequent lack of social support. Significant risk may occur with drug-induced psychosis, paranoid schizophrenia, auditory or sensory hallucination, and suicidal ideation. It creates not only a substantial impact on perinatal outcomes, but also a long-term ill effect on the health of women and their children[11].

In relation to teenage pregnancy, many studies have shown an increased risk of adverse birth outcomes, such as preterm delivery[12], increased risk of congenital anomalies[13], and neonatal death. In the long term, babies are more likely to be admitted to hospital as a result of accident or gastroenteritis[14,15]. The additional measures undertaken during antenatal visits by pregnant teenagers should include discussion of future childcare plans, improving knowledge about parenting, introducing contraception methods as early as possible in antenatal care, and a review of legal issues if the mother is aged under 16 years.

Local experience of the services provided to these women under the care of the CCDS team has not been reported. As we started referring pregnant women who were habitual / occasional / potential psychotic substance abusers to the CCDS team in 2013 after getting their verbal consent, we reviewed the demographic characteristics of these women under the care of the CCDS team in 2014 and their neonatal outcomes.

Methods

This was a retrospective hospital-based study of women who were Hong Kong residents, delivered at our hospital, and under the care of the CCDS team in 2014. Data were collected from the initial assessment form completed at the first interview and the postnatal assessment form completed after delivery. Analyses were performed using the SPSS (Windows version 16.0; SPSS Inc, Chicago [IL], US). Baseline descriptive statistics were used to present data. Chi-square test and one-way analysis of variance were adopted to assess the relationship between variables.

Results

In the database of 375 women, 100 were excluded (68 did not require follow-up, 3 had termination of pregnancy, and 29 delivered in other hospitals).

Patients were classified into three groups (teenage problem, substance abuse problem, and mental health problem) based on their major problem that needed to be addressed first. For instance, if a teenage woman presented with a history of substance abuse within a year before the expected date of confinement, then she would be classified in the substance abuse group.

Of the 275 women included in the final cohort, 21 (7.6%) were a teenager, 86 (31.3%) engaged in substance abuse, and 168 (61.1%) had mental health problems. The demographic data for each group are shown in Table 1.

Neonatal outcomes are shown in Table 2. 14.2% (39/275) were delivered preterm and 44.0% (121/275) were admitted to the special care baby unit (SCBU) or neonatal intensive care unit (NICU). Of the admissions to SCBU, 33.9% (41/121) were due to neonatal drug withdrawal syndrome. Compared with figures in the Annual Report of 2014[16], our study has more preterm births (14.2% vs. 7.2%), more operative deliveries (26.9% vs. 21.1%), and more babies who required special care (44.0% vs. 31.1%).

Of 86 women (1.8% of the 4701 women delivered in our hospital in year 2014) with substance abuse, 53 were active substance abusers and 33 had more than 1-year history of substance abuse prior to the expected date of confinement. With regard to marital status, 45 (52.3%) were single and nine (10.5%) were separated / divorced; whereas 59 (68.6%), 10 (11.6%), and 13 (15.1%) claimed to have a stable, fair, or poor relationship with their husband / partner, respectively. Of the patients, 72 (83.7%) and 34 (39.5%) had a smoking and drinking habit, respectively. In 67 (77.9%) cases, pregnancy was unplanned and 61 (70.9%) reported no previous use of contraception. For the neonatal outcome, 15 (17.4%) women delivered their baby

Table 1. Demographic data of the three groups

Demographics	No. (%) of subjects		
	Teenage (n=21)	Substance abuse (n=86)	Mental health problem (n=168)
Age-group (years)			
≤18	21 (100)	4 (4.7)	1 (0.6)
19-34	0	71 (82.6)	124 (73.8)
≥35	0	11 (12.8)	43 (25.6)
Primiparous	19 (90.5)	46 (53.5)	74 (44.0)
Marital status: single	21 (100)	45 (52.3)	24 (14.3)
Stable relationship with husband / partner	17 (81.0)	59 (68.6)	137 (81.5)
Financial problem	5 (23.8)	21 (24.4)	43 (25.6)
Smoking habit	10 (47.6)	72 (83.7)	41 (24.4)
Drinking habit	8 (38.1)	34 (39.5)	27 (16.1)
Unplanned pregnancy	17 (81.0)	67 (77.9)	98 (58.3)

Table 2. Neonatal outcome

Outcome	No. (%) of subjects or mean ± SD			p Value
	Teenage (n=21)	Substance abuse (n=86)	Mental health problem (n=168)	
Caesarean section	4 (19.0)	18 (20.9)	52 (31.0)	0.123
Admission to SCBU / NICU	6 (28.6)	58 (67.4)	57 (33.9)	<0.001
Preterm (<37 weeks)	2 (9.5)	15 (17.4)	22 (13.1)	0.504
Birth weight (g)				
<1500	2 (9.5)	2 (2.3)	10 (6.0)	0.583
1500-2499	1 (4.8)	8 (9.3)	13 (7.7)	
≥2500	18 (85.7)	76 (88.4)	145 (86.3)	
Apgar score				
At 1 min	8.73 ± 1.10	8.52 ± 1.40	8.83 ± 0.89	0.414
At 5 mins	9.73 ± 0.77	9.67 ± 0.94	9.93 ± 0.45	0.228

Abbreviations: NICU = neonatal intensive care unit; SCBU = special care baby unit; SD = standard deviation

preterm, and 18 (20.9%) had an operative delivery.

Ketamine (50.0%, 43/86) and amphetamine (44.2%, 38/86) were the most commonly used illicit drugs in this group, followed by cocaine (26.7%, 23/86), heroin (17.4%, 15/86), and ecstasy (17.4%, 15/86). Some had taken methadone, marijuana and cannabis, and 34.9% (30/86) did not stop the abuse during pregnancy. A total of 58 (67.4%) babies were transferred to the SCBU or NICU. For birth weight, 76 (88.4%) weighed more than 2500 g. Babies were being cared for by their mother in 87.8% of cases, and by relatives in 5.4%. In 6.8% of cases the baby was handed over for foster care.

Discussion

Under CCDS, midwives play a significant role as case managers to provide in-depth assessment, health counselling, and appropriate and timely referral of the teenage mother to a psychiatric nurse or psychiatrist, medical social worker or social worker, community psychiatric nurse, detoxification institution, or non-governmental organisation. These vulnerable women also require additional antenatal care and hence a multidisciplinary approach, which consists of appropriate obstetric and

neonatal care, can reduce the rate of complications in these pregnancies and improve maternal and child outcomes[15].

Women with active substance abuse disorders are at risk of unplanned pregnancy. Upon diagnosis of pregnancy, the parental role should be discussed and counselling should be offered about pregnancy options. The importance of effective contraceptive methods should be reiterated after delivery. Most women did not abstain from illicit drugs during pregnancy, and babies needed to be admitted to the SCBU as a consequence of this substance abuse or because of neonatal withdrawal syndrome. Therefore, effective counselling, referral, and intervention for this high-risk group is an important component of the CCDS programme.

Results of this study revealed that there were an increased number of babies admitted to SCBU or NICU, this added an extra workload to the neonatal unit. Therefore, it is crucial to appreciate the impact of the adverse consequences of substance abuse in pregnancy.

This study included the data in 1 year only, which does not reflect the full extent of the problem or its impact on service requirements. Nevertheless, no evaluation has been carried out since the CCDS programme was introduced to our hospital in 2006. Continuous evaluation and quality management of the CCDS team are essential to optimise the service. Examination of maternal and neonatal outcomes over a minimum of 5-year period will provide a valid means to evaluate the quality and effectiveness of service provided, and form the basis of future improvements and direction of our CCDS and management teams.

Declaration

The authors have disclosed no conflicts of interest.

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Use of Next-generation Sequencing for Prenatal Diagnosis of Hypophosphatasia

Choi-Wah KONG MBChB, MRCOG, FHKAM (Obstetrics and Gynaecology)
William Wing-Kee TO MBBS, MPH, M Phil, MD, Dip Med, FRCOG, FHKAM, Cert HKCOG(MFM)
Department of Obstetrics and Gynaecology, United Christian Hospital, Kwun Tong, Hong Kong

We report on a patient who had recurrent skeletal dysplasia in three of four of her pregnancies which all resulted in termination of pregnancies. The ultrasound and / or histological findings of her first and fourth pregnancy were suggestive of osteogenesis imperfecta while those in her second pregnancy were more suggestive of achondrogenesis. The exact diagnosis could not be made clinically at that time. With the emergence of next-generation sequencing (NGS), the stored placental tissue from her second pregnancy was retrieved for testing 4 years after the pregnancy was terminated. NGS detected two heterozygous pathogenic variants in the *ALPL* gene which were associated with autosomal recessive hypophosphatasia. This case demonstrated the usefulness of NGS in making an exact diagnosis on the type of skeletal dysplasia which was important in counselling the patients on the risk of recurrence, and offering prenatal diagnosis in their future pregnancies.
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Keywords: Hypophosphatasia; Prenatal diagnosis; Sequence analysis, DNA

Case Report

A patient, who enjoyed good past health, presented with hypophosphatasia. She and her husband were of average height and there was no family history of skeletal dysplasia. During her first pregnancy in 2010, when she aged 28 years, ultrasonography (USG) at 22 weeks of gestation revealed a fetus with severely shortened long bones with multiple fractures. The patient opted for termination of pregnancy. Babygram (Figure 1) and histological examination of the fetus showed that the upper and lower limbs were shortened with inward bowing and multiple fractures, including the ribs. A normal karyotype was found. The patient was counselled by the Clinical Genetics Service about a suspected diagnosis of osteogenesis imperfecta (OI) type 2. Although most cases are de novo, there is a risk of germline mosaicism with a consequent estimated risk of recurrence of 6%.

In her second pregnancy in 2011, USG at 17 weeks of gestation showed grossly shortened limb bones with poor bone mineralisation but no fractures (Figure 2). The patient underwent termination of pregnancy. Babygram and histological examination of the fetus showed markedly shortened limb bones but no fractures (Figure 3). Sections of the diaphysis and cortex showed lack of ossification. The clinical picture was more suggestive of achondrogenesis than OI. The patient was again referred to the Clinical Genetics Service and advised that her case was likely to be an autosomal recessive type of skeletal dysplasia, although the exact diagnosis was uncertain.

The patient had her third pregnancy in 2012. Serial USG scans showed normal growth of the fetus with normal long bone length. Subsequently she delivered a normal healthy baby.

She had her fourth pregnancy in 2013 and received no antenatal care until 32 weeks of gestation. USG at that time indicated that the bi-parietal diameter and abdominal circumference corresponded to the gestation, but again the long bones were severely shortened and corresponded to only around 17 weeks of gestation. There were multiple fractures and the thoracic chest wall was narrow and compressed. There was polyhydramnios with amniotic fluid index of 30 cm. The patient subsequently underwent termination of pregnancy in China.

Next-generation sequencing (NGS) was performed by the Clinical Genetics Service in 2015 on the placental tissue stored from the 2011 pregnancy. Two heterozygous pathogenic variants in exon 7 of *ALPL* gene were detected (c.650delinsCTAA and c.736A>T). These were reported to be associated with autosomal recessive hypophosphatasia.

The patient is currently pregnant in 2017. The

Correspondence to: Dr Choi-Wah Kong
E-mail address: melizakong@gmail.com

Figure 1. Babygram of the first pregnancy in 2010 shows grossly shortened long bones of the appendicular with multiple fractures

couple have been advised that they are both likely to be carriers of the hypophosphatasia gene with an associated 25% risk of fetal hypophosphatasia in this pregnancy. They have been offered blood tests to confirm their carrier status. If status is confirmed, prenatal diagnosis by genetic testing of the *ALPL* gene can be offered. As of March 2017, serial USG scans at 14, 17, and 20 weeks of gestation revealed a fetus with normal long bones, indicating a likely unaffected pregnancy.

Discussion

Hypophosphatasia is caused by missense mutations in the *TNSALP* gene on chromosome 1p36.1-p34, and it impairs bone mineralisation[1]. It is subdivided into six clinical types according to the age of onset: perinatal, prenatal benign, infantile, childhood, adult, and odontohypophosphatasia. The perinatal type is fatal and is inherited in an autosomal recessive manner, affecting 1 in 100,000 pregnancies[2].

Traditional diagnosis of hypophosphatasia was made by USG, features of which include severe micromelia, decreased thoracic circumference, and bone demineralisation[2]. The demineralisation of the long bones may be patchy or generalised with bowing of the bones, and fractures are occasionally seen. The skull size is typically normal but the demineralised calvarium causes the brain to be more easily visualised on USG scan and the cranial vault may be compressible under gentle transducer pressure. Skin-covered osteochondral spurs (Bowdler spurs) protruding from the midshaft or around the elbow or knee joints are specific features diagnostic of hypophosphatasia[2,3].

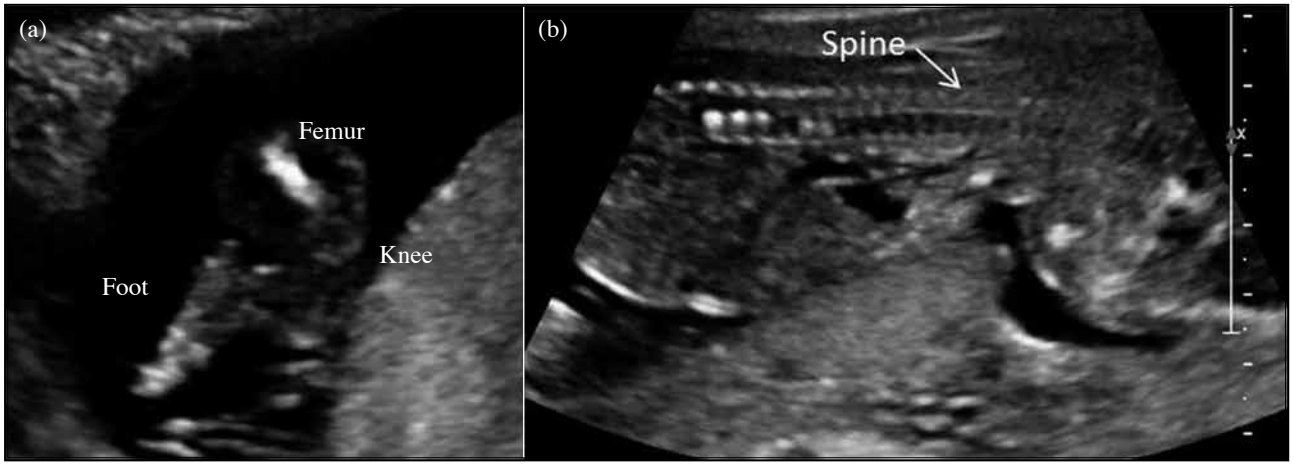

Figure 2. Ultrasonogram at 17 weeks of gestation in the second pregnancy in 2011. (a) The femur is grossly shortened with underdevelopment of the tibia and fibula. (b) Poor mineralisation of the vertebral column is shown

Figure 3. (a) Abortus of second pregnancy in 2011; bone spur in the right knee is shown (arrow). (b) Babygram showing poor mineralisation of the calvarial bones, most part of the vertebral column, rib cage, and lack of ossification of the sacrum and ischial bones

These spurs are often unossified and difficult to detect on USG imaging, but they may be evident on histological examination. On close scrutiny of our patient, such spurs were present in the abortus of the second pregnancy (Figure 3; spur on right knee of the abortus). A low serum alkaline phosphatase (ALP) level and a high pyridoxal-5-phosphate level are helpful in the detection of heterozygous hypophosphatasia carriers[4]. Retrospective review of liver function tests of our patient revealed that serum ALP at 18 weeks of gestation in her second pregnancy was below normal at 21 IU/L (reference range, 35-104 IU/L), and in her current pregnancy it was at the lower normal range (35 IU/L) at 24 weeks of gestation. This is compatible with a maternal carrier of hypophosphatasia with a lower-than-normal serum ALP. As gestation advances, however, there will be a physiological increase in maternal ALP level due to placental ALP and this may mask the previous abnormal findings[4]. Therefore, in the prenatal diagnosis of suspected fetal hypophosphatasia detected by USG scan at or after mid-second trimester, analysis of these biochemical markers in maternal blood may not be useful. Confirmation can probably only be made after the pregnancy. Paternal blood should be analysed in parallel to determine carrier status of the father.

Hypophosphatasia has considerably overlapping clinical features with other types of skeletal dysplasia such as OI type 2 and achondrogenesis[2,3,5,6]. As these types of skeletal dysplasia all show severe micromelia and decreased thoracic circumference, a specific diagnosis based on radiological / pathological findings alone is achievable in only 55% of patients[2]. Furthermore, long bone fractures are sometimes present in hypophosphatasia that mimicks OI type 2 as in the first pregnancy of our patient. Both hypophosphatasia and achondrogenesis show bone demineralisation on radiological and histological examination that makes diagnosis of a specific skeletal dysplasia difficult. OI type 2 is inherited in an autosomal dominant pattern. Almost all cases are due to de-novo mutations. The risk of recurrence in a future pregnancy should be very low. Allowing for the possibility of a germ-line mutation, risk is usually estimated to be approximately 6%[6]. On the contrary, hypophosphatasia is inherited in an autosomal recessive fashion with a recurrence risk of 25%

in future pregnancy. Since the recurrence risk of these two conditions is so different, an accurate diagnosis is essential so that genetic counselling can provide precise information about risk of recurrence in future pregnancy.

Traditionally, genetic diagnosis of hypophosphatasia is performed by sequencing the *TNSALP* gene for mutations, of which over 300 have been reported[7]. Previous studies have reported a 95% detection rate of these mutations for hypophosphatasia by sequencing the 12 exons and intron/exons borders in the *ALPL* gene by Sanger method[8]. The remaining undetected mutations probably affect intronic or regulatory sequences, or correspond to large deletions partly detected by quantitative polymerase chain reaction (PCR) or semi-quantitative methodologies like quantitative multiplex PCR of short fluorescent fragments[9]. However, the Sanger method supplemented by PCR methods is expensive and time-consuming[7]. In addition, since OI, campomelic dysplasia, and various other skeletal dysplastic conditions are often the main differential diagnoses, in the presence of a negative result for *ALPL* mutations, these specific conditions would have to be analysed and excluded sequentially, lengthening the time before diagnosis. Advances in NGS technology now enable one-time sequencing of several genes (targeted NGS) or all the coding sequences of genes (exome sequencing) or the full genome. An NGS 'bone panel' can now be used to establish the diagnosis in these cases. Typically, the panel can include the *ALPL* gene, genes of differential diagnosis *COL1A1* and *COL1A2* that represent 90% of OI cases, *SOX9* responsible for campomelic dysplasia, as well as an additional 8 to 10 potential modifier genes of hypophosphatasia[7]. Molecular genetic analysis using such a comprehensive panel will allow us to diagnose a specific type of skeletal dysplasia as in our patient in a single sequencing run. The carrier status of the couple can then be checked by NGS and prenatal diagnosis can be offered. Such NGS techniques are therefore particularly useful in prenatal diagnosis when time is of the essence. Recent studies have also supported the use of NGS in diagnosing specific types of skeletal dysplasia to help in counselling couples about the recurrence risk and to provide prenatal diagnosis for future pregnancies[7-10]. With technological advances, pre-implantation genetic diagnosis by NGS for carrier couples will likely be feasible in the near future.

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Declaration

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Hysterectomy for Benign Disease

Ting-Chung PUN MBBS, FRCOG, FHKAM (Obstetrics & Gynaecology)
Department of Obstetrics and Gynaecology, Queen Mary Hospital, Hong Kong

The number of hysterectomies performed is decreasing because of the availability of less-invasive alternatives and a general trend towards more conservative management. Historically, hysterectomy was performed through the vagina, which is the preferred approach. Nonetheless, a laparoscopic approach can be used to avoid open surgery when the vaginal route is not feasible. Total hysterectomy should be performed and intrafascial hysterectomy may have some advantage over extrafascial hysterectomy. The age of the patient, risk of ovarian carcinoma, and risk of reoperation should be considered prior to performing prophylactic salpingo-oophorectomy. Salpingectomy should be discussed with the patient who wishes to conserve her ovaries. There is now a trend towards shorter hospital stay and same-day discharge following hysterectomy. Criteria for audit on the operations are suggested.
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Keywords: Hysterectomy, vaginal; Laparoscopy; Salpingectomy

Introduction

Hysterectomy is one of the most common major gynaecological operations. In Hong Kong, 4000 to 6000 hysterectomies are performed each year (Table 1[1-3]). It appears that this number is now reducing, which is a trend that has also been observed elsewhere. Predisposing factors are multiple and include the availability of less-invasive alternatives and a general trend towards more conservative non-surgical management[4]. Despite this, hysterectomy remains one of the most common major operations and this review focuses on its application in benign disease.

History

The first authenticated case of partial vaginal hysterectomy was reported by Berengarius da Carpi in 1507. Schenck of Grabenberg reported 26 cases during the early 17th century. Baudelocque from France introduced the technique of artificially prolapsing and then cutting away the uterus and appendages. He performed 23 such procedures during the 16 years following 1800. The first attempt at abdominal hysterectomy was reported in 1843[5]. In the early 20th century, subtotal abdominal hysterectomy was the universal approach[6]. The first total abdominal hysterectomy was performed in 1929 by Edward Richardson and his technique remains the standard of care today[7]. Harry Reich performed the first laparoscopy-assisted hysterectomy in 1988. In search of a simpler approach, laparoscopic subtotal hysterectomy[8]—the classic intrafascial serrated edged macro morcellator hysterectomy (CISH)—was reported[9]. Of note, robot-assisted laparoscopic hysterectomy is another way to simplify a minimally invasive approach[10], and vaginal hysterectomy is increasingly performed in some countries[11,12].

Indications

Uterine leiomyoma and adenomyosis have been the two most common indications associated with abdominal and laparoscopic hysterectomy in Hong Kong. On the other hand, genital prolapse is probably the most common condition associated with vaginal hysterectomy[1].

Choice of Routes

The American College of Obstetricians and Gynecologists (ACOG) and the Society of Obstetricians and Gynaecologists of Canada have recommended vaginal hysterectomy as the optimum route for hysterectomy[13,14]. The ACOG recommendation is based on the Cochrane Review published in 2009 that showed vaginal hysterectomy to be associated with better outcomes and few complications[15]. The review was last assessed as up-to-date in August 2014 and the authors remained firm in their recommendation that vaginal hysterectomy was superior to laparoscopic and abdominal hysterectomy with a more rapid return to normal activity. If vaginal hysterectomy is not possible, laparoscopic hysterectomy should be performed. A comparison of different approaches to hysterectomy is shown in Table 2[16]. In a debate about the choice between laparoscopic versus vaginal hysterectomy, Bongers[17] suggested that most advantages of vaginal hysterectomy are related to skill and will change if surgeons have more exposure to total laparoscopic hysterectomy. Whilst this may be true in future, vaginal hysterectomy should remain

Correspondence to: Dr Ting-Chung Pun
Email: puntc@ha.org.hk

Table 1. Number of abdominal hysterectomies performed in Hong Kong according to the Hong Kong College of Obstetricians and Gynaecologists Territory-wide Audits[1-3]

Year	Total abdominal hysterectomy for benign conditions	Laparoscopic hysterectomy	Vaginal hysterectomy	Total
1999[1]	4146	255	450	4851
2004[2]	5058	798	507	6363
2009[3]	4136	1091	460	5687

Table 2. Comparison of different approaches to hysterectomy[16]

Comparison	Details
Vaginal hysterectomy vs. abdominal hysterectomy	Faster return to normal activities More rapid recovery Fewer postoperative febrile episodes
Vaginal hysterectomy vs. laparoscopic hysterectomy	Shorter operating time Less urinary tract injuries than total laparoscopic hysterectomy
Laparoscopic hysterectomy vs. abdominal hysterectomy	Faster return to normal activities Fewer febrile episodes Fewer wound or abdominal wall infections Longer operating time

Table 3. Contraindications to vaginal hysterectomy[20]

- Uterus >12 weeks' size
- Uterine volume >300 cm^3
- Restricted uterine mobility
- Adnexal pathology
- Diminished vaginal space
- Cervix flush with vagina
- Inaccessible cervix
- Vesicovaginal fistula repair
- Invasive cancer of the cervix

the route of choice until we have evidence to the contrary. In fact, the same conclusion is reiterated by other more recent reports and meta-analysis[18,19].

There is no universally accepted list of contraindications to vaginal hysterectomy but Sheth[20] has proposed a list as guidance (Table 3). The author remarked that many of these contraindications are relative and vary with the skill of the surgeon. He has the experience of operating on several patients with a cervix flush with the vagina as a result of a previous large loop excision of transformation zone or cone biopsy. Nonetheless this list is helpful at the initial learning phase.

Of note, robotic and single-port hysterectomy should not be considered a standard alternative until more evidence is available[16].

The Technique

Vaginal Hysterectomy

Vaginal hysterectomy is performed under general anaesthesia with prophylactic antibiotics given at induction. After making a circumferential incision at the vaginal forni, the bladder is dissected from the uterus and the anterior vesico-uterine space and the pouch of Douglas are entered. Uterosacral ligaments and transverse cervical ligaments are clamped, cut, and transfixed together with the uterine vessels. The uterus is bisected or morcellated as appropriate whenever difficulty is encountered due to uterine size. The upper uterine pedicles including the round ligaments, uterine tubes, and ovarian ligaments are then clamped, cut, and transfixed. After inspection of the adnexal organs (ovaries and fallopian tubes) and confirmation of haemostasis, the vaginal vault is closed[21].

For a large uterus, it is reasonable to pre-treat the patient with a 3-monthly dose of gonadotropin-releasing hormone agonist. Reducing the size of the uterus may make vaginal hysterectomy more feasible[22]. It may also reduce the operating time and consequent blood loss[23]. Bisection or morcellation are important techniques as the uterus is removed intact in only 16% of the patients. Coring is particularly useful for patients with endometrial hyperplasia as it avoids opening the uterine cavity in case

the patient had carcinoma of corpus. It is important to look for bleeders at 4 and 8 o'clock regions before closure of the vault. This can probably reduce the chance of vaginal haematoma. Currently, the author advises suturing of the uterosacral ligaments to the vault to reduce the chance of vault prolapse[24].

Perhaps the main obstacle to the adoption of vaginal hysterectomy is the acquisition of the necessary skill. In the author's experience, laparoscopy-assisted vaginal hysterectomy can serve as a stepping stone to the adoption of vaginal hysterectomy[23].

Laparoscopic Hysterectomy

There are many variations in the degree of laparoscopic involvement when performing laparoscopic hysterectomy, ranging from laparoscopy-directed preparation for vaginal hysterectomy to a complete laparoscopic procedure[25]. Equally variable is the exact technique in performing the procedure. A good discussion of the technique can be found in the review by King and Giles[26].

All those interested in performing laparoscopic hysterectomy must be aware of the eVALuate study by Garry et al[27]. The study concluded that laparoscopic hysterectomy was associated with a significantly higher rate of major complications than abdominal hysterectomy. The major complications included major haemorrhage, haematoma, bowel injury, ureteric injury, bladder injury, pulmonary embolus, major anaesthesia problem, unintended laparotomy, and wound dehiscence. Whether the same conclusion can be drawn today is questionable. The original author, Garry[28], suggests that changes in methods of haemostasis mean that the conclusions are no longer valid. This is a reasonable statement but has yet to be supported by more evidence.

Vaginal cuff dehiscence and evisceration are rare complications of hysterectomy although a higher rate was reported following laparoscopic hysterectomy (Table 4[29]). Specific factors related to laparoscopic hysterectomy explaining the increase may include the use of electrosurgery, shallow suture placement, and compromised knots.

Table 4. Estimated rates of vault dehiscence[29]

	Incidence (%)
Vaginal hysterectomy	0.15
Laparoscopy-assisted vaginal hysterectomy	0.20
Total laparoscopic hysterectomy	0.87
Total abdominal hysterectomy	0.28

Abdominal Hysterectomy

Most surgeons perform total abdominal hysterectomy following the technique of Richardson[30]. In his original description, he named the common problems associated with the existing methods of hysterectomy including haemorrhage, ureteric injuries, and postoperative *Streptococcus* infection. He then summarised the five features of his method (Table 5[31]). In a detailed description of his technique, he stated that the cervix is covered with a thin layer of fascia after the bladder has been pushed down. This fascia is to be cut a little below the level of the internal os so that the vascular plexus in the fascia layer will be freed from the cervix. Another transverse incision is made through the posterior peritoneal reflection 1 cm above the level of attachment of the two uterosacral ligaments and the dissection is continued for at least 2 cm. The uterosacral ligaments are clamped, divided, and ligated close to their cervical attachment before division of the basal segment of the broad ligament on both sides of the cervix[31]. It is therefore clear that the original technique described by Richardson is intrafascial hysterectomy.

The advantages of intrafascial hysterectomy may include minimisation of urinary tract and bowel injury, reduction of postoperative infection, and preservation of the anatomic relationship between the endopelvic fascia and the vagina[32]. It may also be helpful when dealing with difficult anatomy from adhesive disease such as endometriosis and large myomas that increase the risk of injury to the surrounding structures[33]. Unfortunately, the theoretical advantages of intrafascial hysterectomy have not been proven by direct comparison with extrafascial hysterectomy. Conceptually speaking, this can be considered the third way in the dichotomy between subtotal and total abdominal hysterectomy[34]. In the United Kingdom, the extrafascial technique of hysterectomy is more commonly used. The clamps are placed directly onto the uterine vessels and the cardinal and uterine ligaments without entering the vesico-uterine or recto-uterine space[35]. The author suspects that this is also the case in Hong Kong. This change can be observed in standard textbooks. For example, in the 8th edition of *Te Linde's operative gynecology*[36], the existence of the pubovesicocervical fascia was mentioned categorically whilst from the 9th edition on, this fascia is no longer named[37]. It was also remarked that dissection of the posterior peritoneum off the cul-de-sac was considered unnecessary[37]. In addition, if one learns hysterectomy from an oncologist, it is likely to be extrafascial. Intrafascial hysterectomy should only be performed for benign disease. Oncologists are more likely to use the extrafascial technique for both benign and malignant diseases.

Table 5. The five features of Richardson's method of hysterectomy[31]

Feature	Principle	Effect
1. Complete separation of the cervix posteriorly, as well as anteriorly by means of blunt dissection confined to its relatively avascular mid-section	Segregation of the loosely attached, fan-shaped plexus of veins on each side to a narrow zone adjacent to the basal portion of the broad ligament so that these veins can be included in a single clamp (in addition to separation of the bladder and rectum)	Avoid bleeding encountered in the lower lateral cervical region
2. Detachment of the divided and ligated uterine vessels from the lateral margins of the cervix down to the basal portions of the broad ligaments	Drop the ureters considerably further away	Ureters are safe from injury
3. Preliminary surgical toilet of the vagina and cervix; cervix not squeezed by the application of forceps, not drawn into pelvic cavity; finger or hook not introduced into vagina; only knife enters the vagina and this is discarded after vaginal detachment	-	Reduction of postoperative *Streptococcus* peritonitis
4. Reattachment of basal segments of the broad ligaments, uterosacral ligaments, and round ligament to the lateral angle of the vaginal vault	-	Guarantee adequate vault support
5. Complete absence of haemorrhage	-	Simplifies the technique and permits perfect exposure

More information on intrafascial hysterectomy can be found in the article written by Aldridge and Meredith[38]. In summary, the peritoneum and fascial cuff are opened at the level of the ligated uterine vessels just above the attachment of the uterosacral ligaments. The fascial cuff is detached from the posterior surface of the cervix. This can reduce the risk of bowel injury in case of adhesion at the pouch of Douglas. A similar incision is made at the pubovesicocervical ligament anteriorly at the same level and similarly, the ligament is detached from the cervix. The transverse cervical ligaments are clamped in stages inside the fascial cuff until the cervix can be cut from the vaginal vault. The vault and fascial cuff are then closed. One advantage of this technique is that the uterosacral ligaments are kept intact rather than cut and then reattached to the vault. This can avoid any dissection in the pouch of Douglas. Very clear diagrams can be found in the article illustrating the technique[38].

Subtotal Hysterectomy

From the 1960s onwards, removal of the uterine cervix has been performed to prevent carcinoma of cervix[39]. In a review, the incidence of carcinoma of the cervical stump was reported as 0.32% to 1.9%[40]. Although some authors suggested that the risk may be similar to the rate of vaginal cancer after total abdominal hysterectomy, the validity of this claim has not been proven[7]. It is difficult to understand why the incidence is much lower after removal of the uterine corpus alone. The efficacy of additional procedures, e.g. CISH[9] or electrocoagulation of endocervical mucosa to remove the transformation zone[41], to reduce the risk remains to be confirmed.

Apart from prevention of carcinoma, there are other disadvantages to keep the cervix. These include cyclical or acyclical vaginal bleeding, pelvic pain, vaginal discharge, deep dyspareunia and reduced libido, post-coital bleeding, and abnormal cytology[42].

Is there any advantage to conserving the cervix? A Cochrane review on the subject found no evidence to support the claims of improved outcomes for sexual, urinary, or bowel function following subtotal hysterectomy[43]. The rekindled interest is probably more a response to the search for a simpler approach to laparoscopic hysterectomy[7], thus retracing the development of the open procedure. The claims to improve outcomes are excuses that try to justify this backward step.

Concomitant Procedures

Prophylactic Bilateral Salpingo-oophorectomy

Removal or conservation of the adnexa at the same time with the uterus was already a common question during ward rounds when the author started his training. A significant change in practice has been observed. Mikhail et al[44] reported that from 1998 to 2001, there was a 2.2% increase in the rate of bilateral salpingo-oophorectomy per year. From 2001 onwards, however, there was a 3.6% annual decline from 49.7% to 33.4% in 2011.

One of the main indications for bilateral salpingo-oophorectomy is to reduce the risk of carcinoma of ovary. The lifetime risk of developing ovarian cancer in the general population is one in 70 or 1.4%[45]. It is also well known that hysterectomy can reduce the risk of carcinoma of the ovary by 26% to 30%[39]. Various mechanisms including screening effect, protection from carcinogens, decreased blood supply to the ovary, and triggering of an immune response to the surface glycoprotein MUC1 have been proposed to explain this observation. The exact degree of protection can therefore only be estimated from comparative studies. According to a recent systematic review, the prevalence of ovarian cancer in women who underwent hysterectomy with ovarian conservation was 0.14% to 0.7% compared with 0.02% to 0.04% in those who underwent hysterectomy with bilateral salpingo-oophorectomy[46]. The benefit would be much higher in patients at a higher risk of carcinoma of ovary, e.g. those with hereditary cancer syndrome.

Another advantage of bilateral salpingo-oophorectomy is avoidance of the need for reoperation because of adnexal pathology, the 'residual ovary syndrome'. The risk has been estimated to be 2% to 3%[47] although the ACOG quoted a risk of 7.6% when one ovary was conserved and 3.6% when both were conserved[45]. The risk is higher in patients with endometriosis, pelvic inflammatory disease, and chronic pelvic pain[45]. For example, the risk of reoperation was found to be 47% in a small series of patients with endometriosis[48]. One has to distinguish this from the 'ovarian remnant syndrome' that develops following previous bilateral salpingo-oophorectomy.

Hysterectomy alone can affect ovarian function. Siddle et al[49] reported that the mean age of ovarian failure reduced from 49.5 years to 45.4 years after hysterectomy. The finding was confirmed in a more recent prospective study, in that the risk of ovarian failure after 4 years of follow-up was doubled after hysterectomy[50]. Underlying reasons include the effect of hysterectomy on blood supply to the ovaries and also on secretion of follicle-stimulating hormone, and the condition that led to the hysterectomy. Whatever the mechanism, this should be kept in mind when advising patients whether or not to have their ovaries removed.

Another factor to consider is the effect of adnexae removal on overall mortality. The review mentioned above identified three observational studies that examined all-cause mortality[46]. Two studies favoured hysterectomy alone in women younger than 45 or 50 years in terms of all-cause mortality. No difference was found in the third study but this may be due to shorter follow-up, long interval between the oophorectomy and recruitment into the study, and exclusion of outcomes present at the time of recruitment[51,52]. Similar results have been reported in a recent study[53]. Currently, the author usually advises removal of adnexae in postmenopausal women although there is evidence to suggest that postmenopausal ovaries are still metabolically active[54,55].

Vaginal bilateral salpingo-oophorectomy can be performed at the same time as vaginal hysterectomy. In the author's experience, 15% of patients had planned vaginal removal of adnexae and in all cases the concomitant procedure was performed successfully. There was no conversion because of this additional procedure[23]. These findings echo the ACOG conclusion that the choice of whether to perform prophylactic oophorectomy at the time of hysterectomy is based on the patient's age, risk factors and informed wishes, but not on the route of hysterectomy[13].

Prophylactic Bilateral Salpingectomy

Prophylactic bilateral salpingectomy is a more recently introduced concomitant procedure. There has been a rapidly increasing body of evidence that the fallopian tube is the site of origin of non-uterine pelvic high-grade serous carcinomas[56]. The annual increase in concomitant salpingectomy was approximately 8% from 1998 to 2008, to 24% from 2009 to 2011[44].

Clinical evidence of the efficacy of bilateral salpingectomy in reducing ovarian cancer risk is accumulating. In a population-based cohort study, Falconer et al[57] reported that the risk of ovarian cancer among women with previous salpingectomy was lower (hazard ratio=0.65). Bilateral salpingectomy was associated with a 50% decrease in the risk of ovarian cancer compared with the unilateral procedure. A meta-analysis also showed that the odds ratio of developing ovarian cancer was 0.51 after bilateral salpingectomy[58]. Although the evidence cannot be considered conclusive, prophylactic bilateral salpingectomy

Table 6. Mean duration of hospital stay after hysterectomy in Hong Kong[1-3,60] *

Year	Duration of hospital stay (days)		
	Abdominal hysterectomy	Laparoscopic hysterectomy	Vaginal hysterectomy without pelvic floor repair
1994[60]	8.1 ± 4.6	-	7.8 ± 5.5
1999[1]	7.4 ± 4.0	6.5 ± 3.8	6.3 ± 3.9
2004[2]	6.3 ± 3.7	4.0 ± 2.5	4.4 ± 2.2
2009[3]	5.7 ± 3.3	3.5 ± 2.5	4.4 ± 2.9

* Data are shown as mean ± standard deviation

should be considered when planning hysterectomy.

The author has also performed bilateral salpingectomy during vaginal hysterectomy. In the author's experience, the procedure is more technically challenging than bilateral salpingo-oophorectomy because of the risk of tearing the mesosalpinx. In a large retrospective cohort study of 425 patients who underwent vaginal hysterectomy[59], the overall success rate of salpingectomy was 88% and pelvic adhesion significantly predicted failure. The postoperative complication rate attributed to salpingectomy was 3.8%, including pelvic bleeding, pelvic abscess/infection, fever, drainage of pelvic haematoma, reoperation, and ileus.

Enhanced Recovery

The duration of hospital stay after hysterectomy is decreasing in Hong Kong (Table 6[1-3,60]). In many overseas centres, same-day discharge is practised. In a systematic review, same-day discharge appeared feasible for patients who underwent a minimally invasive hysterectomy, although only articles studying robot-assisted surgery and laparoscopic surgery were included[61]. Same-day discharge has been reported as feasible in 31.8% of patients in retrospective studies[61]. Among some prospective studies, 78.4% of patients were discharged on the same day[61]. Preoperative inclusion criteria included support from a social network, American Society of Anesthesiologists score of 1 or 2, age younger than 60 years, and adequate motivation and understanding to consent and participate. Similar results have been reported for vaginal hysterectomy[62,63]. Apart from selection of suitable patients, a perioperative multimodal evidence-based recovery protocol to optimise same-day discharge is an indispensable element for early discharge or same-day discharge. These protocols have been named differently as enhanced recovery pathway, enhanced recovery after surgery, and fast-track surgery. More information on the principles and practices of such protocols can be found in the review article by Kalogera and Dowdy[64].

Audit on Hysterectomy

An audit on hysterectomy can be performed on the indication, route, procedure and complications, concomitant procedures, and hospital stay. Alternative less-invasive treatments should be tried or at least discussed with the patient before hysterectomy[65]. Reasonable audit criteria can be derived from local publications[21,66]. These criteria include: 10% as a reasonable target for using the vaginal approach in patients without genital prolapse; a minimal access approach should be used for a uterus smaller than 12 weeks' gestation; total hysterectomy should be the target for most hysterectomies; healthy ovaries should not be routinely removed at the time of hysterectomy; the option of prophylactic salpingectomy should be discussed; prophylactic antibiotics should be given before incision; and the incidence of peri-operative complications should be around 10%.

Conclusion

Hysterectomy is one of the most common major gynaecological operations. Development has gone full circle, from a vaginal to an abdominal approach and now a rekindling of interest in vaginal hysterectomy. The indication tends to be more stringent with the adoption and development of less-invasive alternatives. Prophylactic bilateral salpingo-oophorectomy has also undergone a similar pattern of change. Total versus subtotal hysterectomy has a different pattern and currently, the application of subtotal hysterectomy should be very limited. Nonetheless prophylactic bilateral salpingectomy should be considered in all patients who wish to conserve their ovaries. In general, the duration of hospital stay after hysterectomy is also reducing.

Declaration

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Lichen Sclerosus: a Review of the Condition and Its Management

Elizabeth YY LI MBChB
Mona WC LAM MBChB, MPH, FRCOG, FHKAM (Obstetrics and Gynaecology)
Department of Obstetrics and Gynaecology, United Christian Hospital, Kwun Tong, Hong Kong

Lichen sclerosus is a chronic vulvar condition that is the most prevalent in pre-pubertal girls and post-menopausal women. It manifests as vulvar pruritus or distortion of the normal vulval architecture in later stages of the disease. It is mainly a clinical diagnosis, sometimes requiring histological confirmation by vulval biopsies. Superpotent topical steroid is the mainstay of treatment, aiming to relieve symptoms and prevent anatomical destruction and progression to premalignant or malignant conditions. Other treatment modalities include immunomodulating drugs for steroid-resistant disease, and surgical management in cases of intractable symptoms, failed medical treatment, or when restoration of anatomy and function is required.
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Introduction

Lichen sclerosus is a chronic dermatological disorder with features of marked inflammation and epithelial thinning[1]. The original term 'lichen sclerosus et atrophicus' described a hard, thickened, and atrophic rash. It is a benign but progressive condition characterised by symptoms of pruritus and pain. This review article aimed to discuss the clinical background, manifestations, diagnosis, and management of this disorder.

Epidemiology

Lichen sclerosus is often underdiagnosed and undertreated with the exact incidence and prevalence unknown. It is 10 times more common in women than in men[2]. The prevalence is estimated to range from one in 30 menopausal women[3] and one in four patients who attend specialist vulval clinics[4]. Bimodal peaks have been identified for the onset of the disease that mostly occurs in pre-pubertal girls and peri- or post-menopausal women.

Aetiology

The aetiology of lichen sclerosus is still unknown although associations have been identified with immunological, hormonal, genetic, and local factors.

Immunological factor

Up to 20% of women with vulvar lichen sclerosus have co-existing autoimmune diseases, especially thyroid disease, type 1 diabetes mellitus, vitiligo, and alopecia areata. Immunoglobulin auto-antibodies have been identified in 44% to 74% of affected women[3,5,6].

Hormonal factor

The role of hormones has been postulated in the pathogenesis of the disease as lichen sclerosus is mostly found in those with low oestrogen status before menarche and after menopause[3,4].

Genetic factor

In an observational study in the United Kingdom, up to 12% of patients had a positive family history. A possible genetic link was suggested although the responsible gene has yet to be identified[6].

Local factor

Koebner phenomenon, the development of isomorphic pathological lesions in traumatised uninvolved skin of a patient with a cutaneous disease, is observed in lichen sclerosus. Trauma, burn injury, irradiation, and sexual abuse have been suggested as triggering factors for development of the disease[7].

Clinical Manifestations

Vulvar pruritus is the hallmark of lichen sclerosus. It is usually the chief complaint and the most distressing symptom to affect a patient's daily life. If the disease involves the perianal area, it may manifest as anal discomfort, pain on defaecation, anal fissures, or even per-

Correspondence to: Dr Elizabeth YY Li
Email: lyy699@ha.org.hk

rectal bleeding. If there is fusion of the labia minora with consequent obstruction of the urethral opening, it can result in dysuria. Dyspareunia and sexual dysfunction are late symptoms of the disease when anatomical destruction has already set in leading to stenosis of the introitus and fusion of the labia[5,6].

The classical manifestation of lichen sclerosus is the presence of porcelain white plaques and atrophic depigmented areas over the vulvae known as leukoplakia. Some individuals may have ecchymosis changes such as purpura. In later stages of the disease, fissuring or even erosion may be seen. Hyperkeratosis characterised by waxy skin can result from the chronic insult to the affected skin. Chronic scratching due to the intense pruritus can lead to excoriation and lichenification which is thickening of the epidermis with exaggeration of normal skin lines[6,8].

The most commonly affected areas of the vulva include the medial labia majora, interlabial creases, labia minora, clitoral hood, and clitoris. Lesions may extend to the perianal region causing a 'figure-of-eight' pattern. Mucosal regions like the vagina, however, are seldom involved. In cases of extragenital involvement, the thighs, breasts, wrists, shoulders, neck, and back can be affected.

As the disease progresses, the normal vulvar architecture is lost. It begins with a loss of distinction between the labia majora and minora, followed by shrinkage of the introitus, possibly burying the clitoris. In the final stage, only a posterior pinhole orifice remains as a result of midline fusion of the vulvae[9] (Figure).

Figure. Leukoplakia with fusion of vulvae

Diagnosis

The diagnosis of lichen sclerosus can be made clinically in cases with typical manifestations and dermatological changes. Histological confirmation by vulval biopsy is indicated if a diagnosis cannot be made clinically or when there is a need to exclude a premalignant or malignant condition[10]. When initial treatment of lichen sclerosus fails, vulval biopsy should be performed to re-evaluate the diagnosis. As vulval leukoplakia has a wide range of differential diagnoses including underlying malignancy, some advocate biopsy in all cases of adult-onset vulvar lichen sclerosus. It is suggested that biopsy be performed before starting treatment as the characteristic histological features may be less evident after application of topical steroids[6].

Histopathology

A 4-mm punch or incisional biopsy, which provides sufficient tissue for evaluation, can be performed under local anaesthesia and should be taken from the most abnormal-looking area. Under the microscope, thinned epidermis and sub-epidermal hyalinisation with deeper inflammatory lymphocytic infiltrates can be identified[11].

Investigations

If there is a clinical suspicion of secondary infection over the areas with lichen sclerosus, wound swabs should be taken for culture to exclude any co-existant bacterial or fungal infections[6]. As lichen sclerosus is associated with autoimmune diseases, symptoms and signs of thyroid disease, type 1 diabetes mellitus, and pernicious anaemia should be sought and investigations performed when indicated[6,12].

Premalignant and Malignant Conditions

Patients with lichen sclerosus are at a higher risk of developing future malignancy or a premalignant condition of the vulva[13-15].

Vulvar Intraepithelial Neoplasia

Vulvar intraepithelial neoplasia (VIN) is a premalignant condition that may progress to invasive squamous cell carcinoma (SCC). Lichen sclerosus is associated with the differentiated type of VIN, while the usual-type VIN is more often related to human papillomavirus.

Vulvar Squamous Cell Carcinoma

In patients with lichen sclerosus, the lifetime risk of developing vulvar SCC has been quoted to be less than 5%, based on some retrospective case series[16]. The relationship between lichen sclerosus and melanoma, basal cell carcinoma, and verrucous carcinoma has not been identified[12]. It is suggested that early detection, use of potent topical steroids, more liberal biopsy, and excision of abnormally thickened skin resistant to treatment may reduce the risk of developing SCC[12,17].

Management

Treatment of lichen sclerosus aims to relieve symptoms to reduce the dysfunction and disfigurement caused by the disease. It should be initiated soon after diagnosis and within 2 years to prevent long-standing disease and progression causing irreversible distortion to normal vulvar architecture. Multidisciplinary input from the gynaecologist, dermatologist, urologist, or paediatrician may be necessary to provide optimal care[12].

Counselling and Patient Education

In chronic diseases, counselling and patient education play an important role in management. Information about the nature of the disease and the mainstay of treatment should be given, including the regimen and instructions about application of topical medication. Patients are advised against scratching the vulvar skin and to avoid any skin irritants, with emphasis placed on the importance of maintaining good perineal hygiene. Education should include the technique of regular self-examination using a mirror to detect any abnormal thickening or non-resolving ulcers that may indicate neoplastic changes[6].

Symptomatic Relief

Emollients and lubricants can be applied to the affected areas to reduce symptoms and dysfunction, but they cannot alter the course of the disease[17].

First-line Treatment: Topical Corticosteroids

Topical corticosteroids are the mainstay of treatment. Steroids of super-high potency are effective treatments for lichen sclerosus of which clobetasol propionate is the most commonly prescribed. Its use is well supported by multiple randomised controlled trials[18-20]. Mometasone furoate is less potent than clobetasol but is said to have a greater anti-inflammatory activity and a longer duration of action, although more evidence is needed to support its use as an effective alternative to clobetasol[21,22]. The optimal treatment regimen is unknown. A fingertip unit per application of clobetasol propionate 0.05% ointment is approximately 0.5 g. A thin film is applied over the affected area.

Treatment is divided into three phases. During the initial phase, topical steroid is applied daily or at night for 6 to 12 weeks, then treatment response is evaluated in terms of resolution of pruritus, pain, and skin changes including hyperkeratosis, fissuring, and ecchymoses. It is followed by tapering therapy with application of topical steroid at night for 4 weeks, reducing to alternate-day application for another 4 weeks, followed by twice weekly application for 4 weeks. If there is recurrence of symptoms during the tapering phase, frequency of treatment should be adjusted in order to achieve good control. Maintenance therapy aims to prevent recurrence of symptoms and to maintain normal anatomy. There is a suggestion that continuation of maintenance therapy is associated with a reduced incidence of differentiated VIN and vulvar SCC[23]. Common side-effects of topical steroids include cutaneous atrophy, telangiectasia, and striae. These can occur as early as 2 to 3 weeks following daily application and may be irreversible in some cases[24].

Second-line Treatment: Calcineurin Inhibitors

Topical calcineurin inhibitors, namely tacrolimus and pimecrolimus, have been shown by two small-scale randomised controlled trials to be effective in treating lichen sclerosus[18,25]. They are immunosuppressants that act by suppressing the T-lymphocyte response and reducing inflammation. It has been suggested that daily use of tacrolimus was less effective than daily use of clobetasol propionate, whereas twice daily use had similar clinical efficacy but lesser histological efficacy than super-high potency topical steroids[3]. Discrete case reports have demonstrated improvement when calcineurin inhibitors were used in patients with steroid-refractory vulvar lichen sclerosus[26-29], but more evidence of their efficacy is required. Calcineurin inhibitors do not cause cutaneous atrophy and are generally better tolerated than topical steroid, although some patients may experience a burning sensation during application. Concerns have been raised about their long-term safety, especially the risk of potential malignant transformation, so use for longer than 2 years is not advised[18,30].

Controversial Treatments

Other treatments have been suggested but their use is controversial. As well as oral acitretin and retinoids, topical progesterone and topical testosterone, non-pharmacological treatments such as ultraviolet A1 phototherapy and photodynamic therapy have also been used[31-34]. However, data for their efficacy are limited or conflicting. Moreover, some of these treatments are not easily accessible and some have poorly tolerated side-effects.

Surgical Management

In the majority of cases, surgery will not be considered unless there are complications as a result of anatomical distortion or intractable vulval symptoms that fail medical treatment. Vulvoperineoplasty can be considered if there is loss of normal vulvar architecture leading to malfunctioning and disfigurement including severe introital fissuring, stenosis, and clitoral adhesion. During the procedure, scarring and adhesions are freed, and repair is performed using tissue taken from the posterior vaginal wall. Postoperatively, manual dilation will help restore anatomy and function[35,36]. Simple vulvectomy is the last resort. If the disease is extensive and primary re-approximation of the vulva is not feasible, a skin flap or graft from the buttock or lateral thigh may be required. Great care should be taken to monitor for any infection or haematoma formation after surgery[37].

Follow-up and Recommendations

Follow-up is important to evaluate treatment response. When treatment fails to control symptoms or achieve disease regression, efforts should be made to ensure proper use of medication at the correct area, with the appropriate amount and frequency. Superimposed infection should be excluded and treated with antibiotics or antifungal agents if confirmed. Use of intralesional steroid can be considered for thick hyperkeratotic plaques[38]. Other causes or exacerbating factors such as menopausal changes and neuropathic vulvodynia should be identified and treated accordingly. A biopsy should be taken or repeated if malignancy is suspected.

It is suggested that women with lichen sclerosus are reviewed 3 months following treatment for active disease and annually by a general practitioner in cases of stable disease. Referral for specialist care should be made if treatment response is inadequate or disease has progressed[39]. Some have suggested specialist care because patients with lichen sclerosus are regarded as a high-risk group with a 2% to 4% lifetime risk of invasive vulval cancer[40].

Conclusion

Lichen sclerosus of the vulva is a chronic disease that presents with vulval leukoplakia and pruritus. The majority of cases can be diagnosed clinically by characteristic features. In severe cases, there is malfunctioning, anatomical destruction, and a potential risk of developing malignancy. Ultra-high potency topical steroid remains the gold standard and the first-line management. Second-line or surgical treatment can be considered if topical steroid fails.

Declaration

The authors have disclosed no conflicts of interest.

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Role of Intrapartum Ultrasound in Modern Obstetrics

Viola YT CHAN MBBS, MRCOG, FHKAM (Obstetrics and Gynaecology)
Winnie HUI MBBS, MRCOG
Wai-Lam LAU MBBS, FRCOG, FHKAM (Obstetrics and Gynaecology)
Department of Obstetrics and Gynaecology, Kwong Wah Hospital, Yaumatei, Hong Kong

Intrapartum ultrasound has become more popular over the last decade. It provides a more objective assessment of fetal head position and station than traditional digital vaginal examination, which is now known to be inaccurate. Correct identification of fetal head position is particularly useful before instrumental delivery, although it should not be used in the first stage of labour to predict successful vaginal delivery. Fetal head station can be assessed by determining the relationship between maternal and fetal structures transperineally, such as head-perineum distance and angle of progression. Intrapartum ultrasound has potential use before and during labour. Current evidence, however, shows it is most useful during the second stage of labour, especially when choice of optimal mode of delivery is not apparent. We believe that intrapartum ultrasound is a promising diagnostic tool that will ultimately improve the wellbeing of mothers and babies.
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Introduction

Use of ultrasound in obstetrics and gynaecology first started in 1958 following the legendary publication by Ian Donald and his team in *Lancet* in which the physics, techniques, safety, and potential of ultrasound were described[1]. Since then, the development of ultrasound has accelerated and it has become indispensible in modern obstetrics.

Intrapartum ultrasound is a relatively new concept that has developed in the last 10 years, and is becoming more popular in developed countries as part of the assessment of labour progress. It is well established that clinical examination of fetal head position, station, and descent is often inaccurate, especially in the second stage of labour when the fetus may already have had significant caput succedaneum and moulding. With the help of transabdominal and transperineal ultrasound, the fetal spine, head position, station, and descent can be assessed objectively, thereby assisting clinical decision-making, such as choosing the optimal mode of delivery in a prolonged second stage.

In this article, we discuss the various ultrasound parameters proposed for labour assessment, and their current and future clinical applications.

Fetal Head and Spine Position

Traditionally, fetal head position is assessed by identifying the location of the posterior fontanelle by digital vaginal examination. Such clinical assessment is often inaccurate, with only 30% in complete agreement and 69% in agreement within 45 degrees when compared with actual fetal head position obtained by transabdominal ultrasound[2]. Fetal head position can be ascertained by transabdominal ultrasound according to the 'clock-face' method proposed by Akmal et al[3], as shown in Figure 1. Fetal occiput, cerebral midline, or the orbits in the transverse plane or fetal spine in the longitudinal plane can be used as markers to identify different fetal head positions (Figure 2). Accurate assessment of the fetal head position during labour is particularly useful when the fetus is in an occiput-posterior (OP) position, since certain manoeuvres can be performed to reduce maternal discomfort[4]. A local study[5] as well as a recent multicentre randomised controlled trial by Ramphul et al[6] have shown that compared with digital vaginal examination, determination of fetal head position with ultrasound prior to instrumental delivery reduces misplacement of the vacuum cup. Prediction of persistent OP position at delivery is also possible with a sensitivity of approximately 70% to 80%[7,8], although it is important to remember that fetal head position during the first stage of labour should not be used to predict successful vaginal

Correspondence to: Dr Wai-Lam Lau
Email: lauwl@hotmail.com

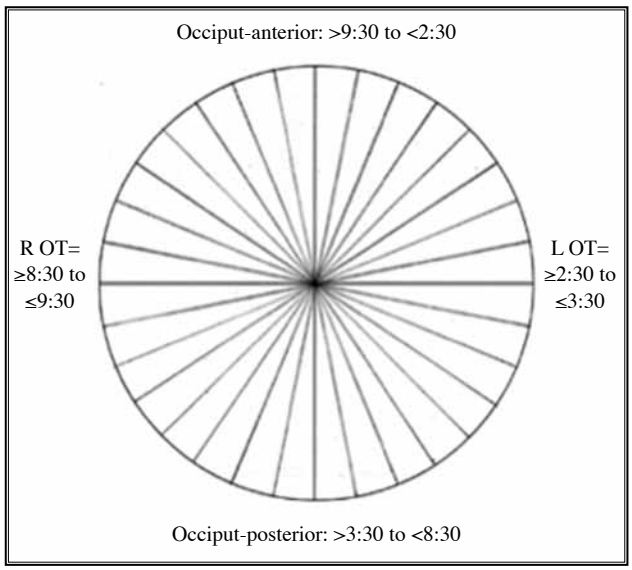

Figure 1. 'Clock-face' concept of fetal head position proposed by Akmal et al[3]

Abbreviations: L = left; OT = occiput-transverse; R = right

delivery. In a prospective cohort study by our group in which 100 assessments were obtained from 94 labouring women in the first and second stage of labour, the incidence of OP position was approximately 20%, 15%, and 4% during the first stage, second stage, and at birth, respectively[9].

Apart from fetal head position, fetal spine position can be ascertained using transabdominal ultrasound. Knowledge of both improves prediction of persistent OP position at birth from 70-80% to 100%[4].

Fetal Head Station: Head-perineum Distance and Angle of Progression

Fetal head station by digital vaginal examination of the relationship between fetal head and maternal ischial spine[10] has been proven to be subjective, inaccurate and poorly reproducible, with numerical errors occurring in 36% to 88% of cases, of which 20% were undiagnosed high

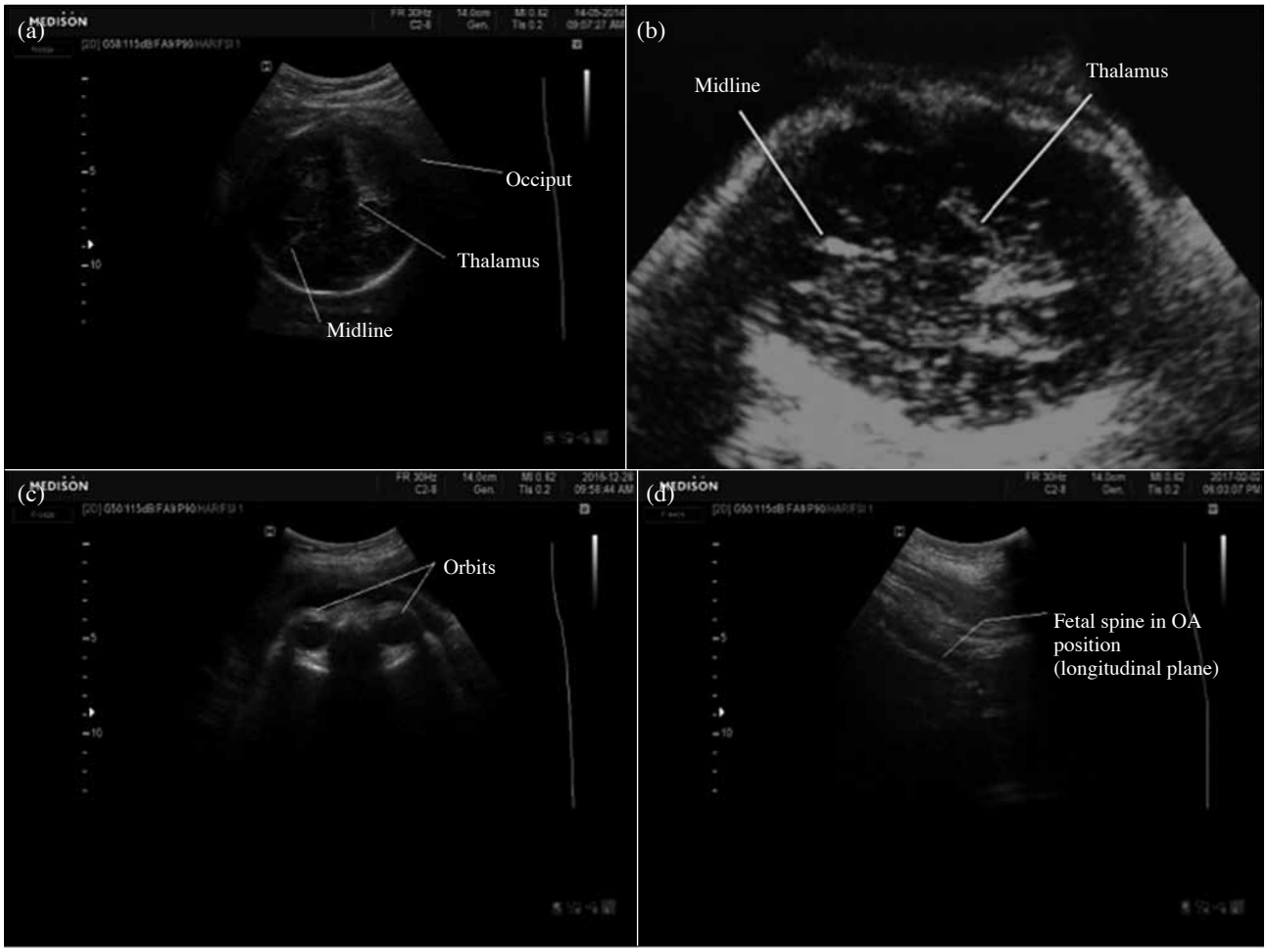

Figure 2. Images of fetal head position obtained by transabdominal ultrasound (transverse plane), with (a) occiput visualised anteriorly in OA position; (b) transversely positioned midline in OT position; (c) anterior pointing orbits in OP position; (d) spine (longitudinal plane) in OA position

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

stations[11,12]. Nonetheless, accurate assessment of fetal head station and descent is paramount to the assessment of labour progress as it enables the correct decision to be made about mode of delivery when labour is prolonged. Transperineal ultrasound allows visualisation and measurement of the relationship between the fetal head and maternal tissue, therefore overcoming the shortcomings of digital vaginal examination that is rather arbitrary. Different transperineal ultrasound parameters have been proposed and evaluated for their reproducibility, including head-perineum distance (HPD), angle of progression (AoP), head progression distance, head-symphysis distance, and midline angle[13]. They have been shown to be objective, highly correlated, and reliable in the assessment of fetal head station. These measurements are obtained by placing the ultrasound probe transversely or sagittally onto the maternal perineum as shown in Figures 3 and 4. HPD and AoP are discussed in detail below as they are easy to learn and extensively used. In brief, the shorter the HPD or the larger the AoP, the lower is the fetal head station.

Steps of Transperineal Ultrasound Examination

The following shows the steps of transperineal ultrasound examination:

1. The woman should lie in the lithotomy position, and her bladder should be empty.
2. Ultrasound gel should be applied to the transducer before covering it with a glove.
3. The ultrasound probe should be pressed firmly and transversely onto the perineum to obtain the HPD.
4. The ultrasound probe should then be rotated 90 degrees to a sagittal plane, to determine the AoP and head direction.
5. These measurements should be repeated during uterine relaxation and contraction with pushing.

Head-perineum Distance

HPD is the shortest distance from the outer bony limit of the fetal skull to the skin surface of the perineum[14]. It is obtained by simply pressing the ultrasound probe firmly onto the soft tissue between the labia majora until the probe can advance no further. After freezing the image, the HPD is measured on screen (Figure 3). The measurement should be taken during both uterine relaxation and contraction with pushing. A shorter distance indicates that the fetal head is closer to the perineum. In our previous study, HPD was correlated linearly with clinical head station (f= –0.497, p<0.001)[15]. A recent multicentre prospective cohort study of prolonged second stage by Kahrs et al[16] showed that the duration of vacuum extraction was shorter in women with HPD of 25 mm (log rank test <0.01). In women with HPD

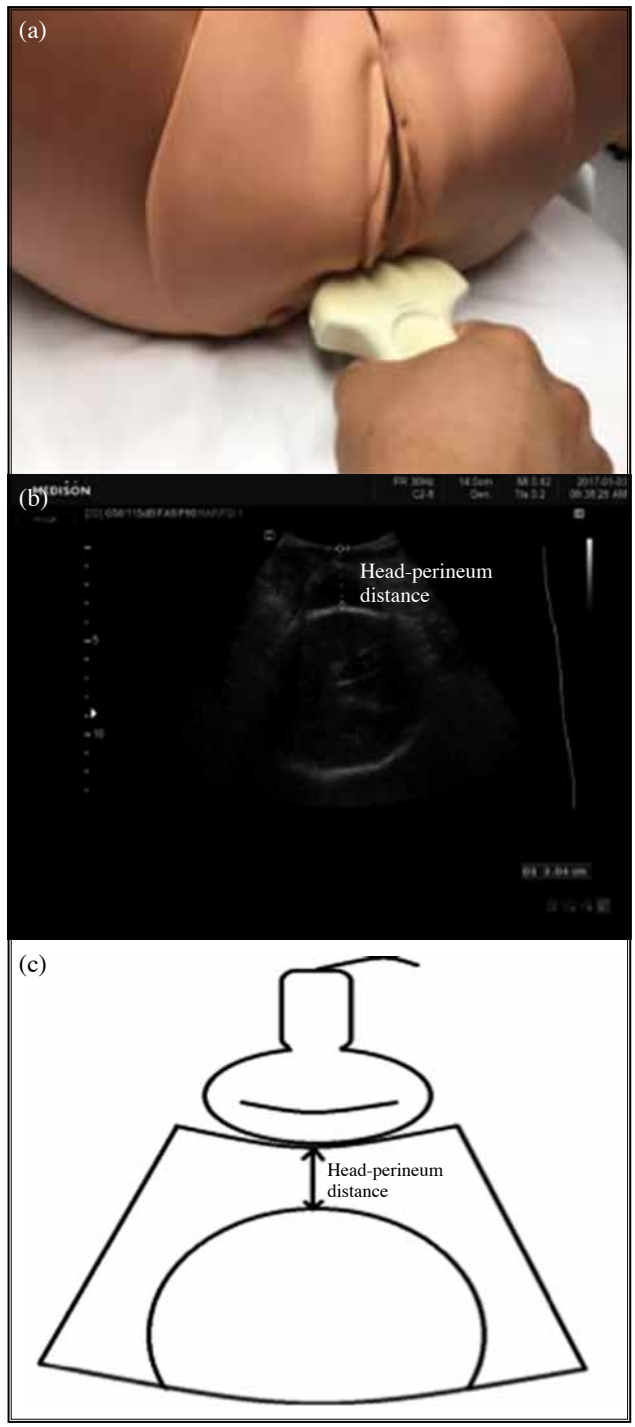

Figure 3. Placing the ultrasound probe transversely on the maternal perineum to obtain the head-perineum distance: illustrated by (a) manikin, (b) ultrasound image, and (c) schematic diagram

of ≤35 mm, 7/181 (3.9%) were delivered by Caesarean section compared with 9/41 (22.0%) in women with HPD of >35 mm (p<0.01). In addition, umbilical cord arterial pH was <7.10 in 2/144 (1.4%) women with HPD of ≤35 mm compared with 8/40 (20.0%) with HPD of >35 mm (p<0.01).

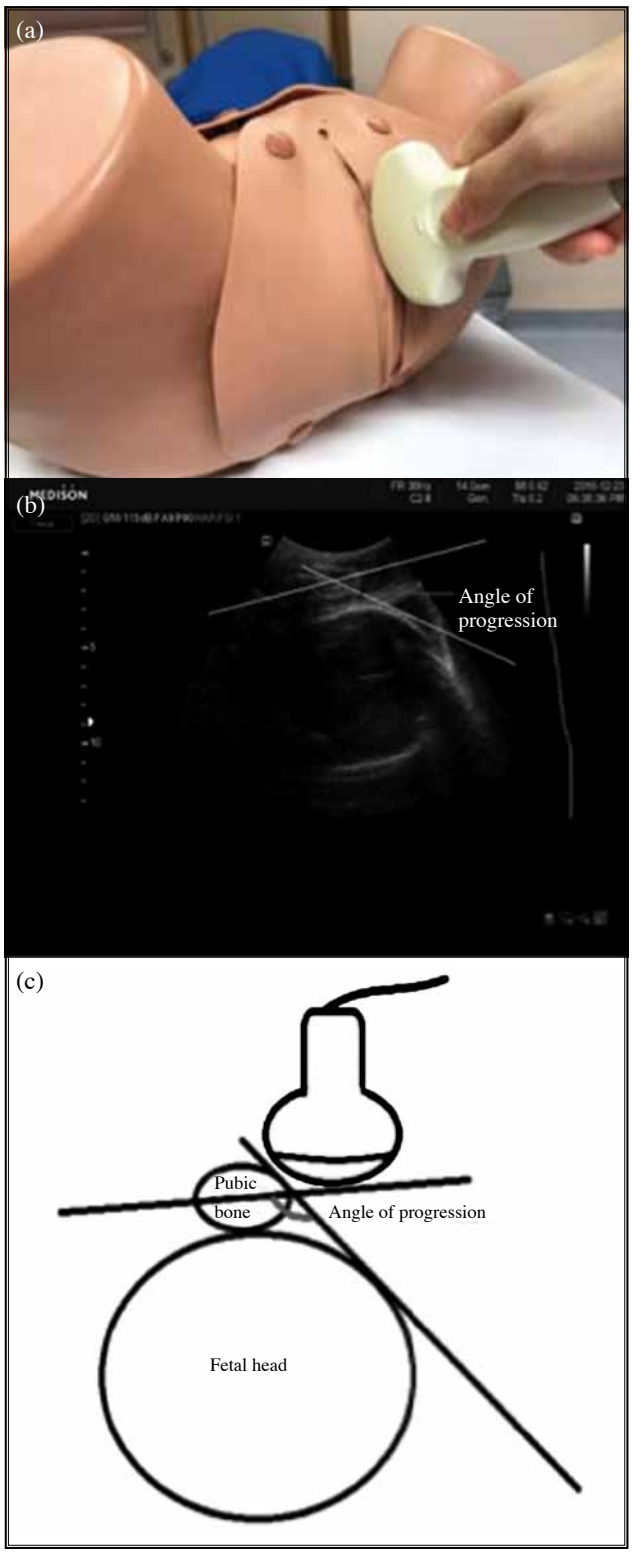

Figure 4. Placing the ultrasound probe sagittally on the maternal perineum to obtain the angle of progression: illustrated by (a) manikin, (b) ultrasound image, and (c) schematic diagram

Angle of Progression

AoP is the angle between the pubic symphysis and a line tangential to the fetal head contour[17] (Figure 4). Care must be taken to ensure both the long axis of the pubic symphysis and the fetal head contour can be ascertained on the sagittal image. The first line is drawn traversing two points identifying the long axis of the pubic symphysis, followed by a second line that extends from the most inferior portion of the pubic symphysis tangentially to the fetal skull contour (Figure 4). The angle can be measured directly on the screen or with a goniometer. In our previous study[15], AoP correlated linearly with clinical station (r=0.579, p<0.001); an AoP of about 120 degrees correlated with clinical head station 0, and echoes the findings of other groups[18,19]. Several studies suggested that a cutoff AoP of at least 120 degrees measured during the second stage of labour was associated with a higher chance of subsequent spontaneous vaginal delivery[17,20,21]. In our pilot study in 2009, using a cutoff of 150 degrees for AoP during contraction with pushing enabled us to predict 12 (80%) of the 15 successful vacuum extractions and all five Caesarean sections[22]. We postulated that the AoP during contraction with pushing probably reflects the combination of fetal head station as well as the dynamic change in fetal head descent against the birth canal. In a recent large single-centre prospective observational study of vacuum extraction at term by Bultez et al[23], AoP of >145.5 degrees was associated with a <5% vacuum extraction failure rate. The authors concluded that AoP may help to predict failure of vacuum extraction, especially among nulliparous women whose risk of failure is high.

Head Direction

Movement of the fetal head with pushing during uterine contractions can be visualised on real-time two-dimensional (2D) ultrasound in the sagittal view. Since the birth canal is curved, an upward head direction indicates the final stage of the fetal head descent. It has been shown that horizontal or downward head direction is associated with poor success of operative vaginal delivery[24,25]. Nonetheless the labour dynamic is different when the fetal head position is OP when absence of upward direction may be normal[26].

Clinical Applications

Before Onset of Active Labour

Cervical dilatation during active labour can generally be 'predicted' by partogram[27], but it remains difficult to predict onset of active labour. A recent systematic review and meta-analysis showed that cervical length measured by transvaginal ultrasound at term had moderate predictive value for the onset of spontaneous labour[28]. A short HPD of <45 mm at the time of prelabour rupture of membranes has also been associated with a higher chance of successful vaginal delivery and fewer Caesarean

sections[14]. In addition, Levy et al[29] suggested that narrow AoP of <95 degrees in nulliparous women at term before onset of labour is associated with a higher rate of Caesarean delivery. This was echoed by Jin et al[30] who showed that an AoP of >99 degrees in nulliparous women at term before onset of labour was associated with a higher rate of vaginal delivery. Some studies have also suggested that ultrasound before induction of labour may help to predict success of vaginal delivery and offer an alternative to the modified Bishop score[31,32].

First Stage of Labour

As discussed in the previous section, fetal head and spine position determined by transabdominal ultrasound might help predict persistent OP position. In addition, serial ultrasound examination of fetal head station, cervical length and dilatation combined with digital vaginal examination might provide a more objective assessment of labour progress. Hassan et al[33] proposed the concept of a 'sonopartogram', an ultrasound-based assessment of labour progress. In the study, cervical dilatation and fetal head descent were measured using both vaginal and ultrasound examination. Ultrasound assessment of labour progress was feasible in most cases, and there was good agreement between digital vaginal examination and ultrasound examination for cervical dilatation and head rotation. In our previous study, we found that HPD and AoP measured during uterine contractions correlated with time to normal vaginal delivery in primiparous women[15]. In the multicentre trial conducted on prolonged first stage, if the HPD was <40 mm the likelihood of Caesarean section was 7% but this increased to 82% if the HPD was >50 mm[21]. In the same study, if the AoP was >110 degrees the likelihood of Caesarean section was 12% but increased to 62% if the AoP was <100 degrees[21]. Therefore, intrapartum ultrasound may play a role when there is slow or lack of progress during the first stage of labour.

Second Stage of Labour

Ultrasound assessment is most useful when the mode of delivery is not apparent, such as in a woman with prolonged second stage and large fetal caput succedaneum. In this scenario, ultrasound can be useful to (1) determine the fetal head and spine position; (2) assess objectively the fetal head station with transperineal parameters such as HPD, AoP, and head direction; (3) visualise objectively the degree of caput and moulding[33]; and (4) avoid misplacement of instrument if an instrumental delivery is needed. Malpresentation or asynclitism can also be determined[34,35].

Use of transabdominal scan alone has been shown to reduce the misdiagnosis of fetal head position prior to instrumental delivery but not maternal or neonatal morbidity[5]. Recent studies that focused on the transperineal scan examination show that successful instrumental delivery is generally associated with AoP of >120-146 degrees or HPD of <35 mm[16,20,23]. We are currently analysing our 5-year data from women with a prolonged second stage, with an aim of determining the best cut-off value for HPD and AoP in triaging operative vaginal delivery or direct second-stage Caesarean delivery. A combination of both transabdominal and transperineal ultrasound findings should be more informative. As shown from the recent multicentre trial, only 3/138 (2.2%) fetuses in occiput-anterior position and HPD of ≤35 mm vs. 6/17 (35.3%) with non–occiput-anterior position and HPD of >35 mm were delivered by Caesarean section[16]. Further studies are needed to identify the optimal cutoff value of HPD or AoP below which a Caesarean delivery is a safer mode of delivery than operative vaginal delivery.

Other Benefits of Intrapartum Ultrasound

As both the woman and her partner can see the ultrasound images on screen, intrapartum ultrasound has the potential for coaching during active pushing[36]. Transperineal ultrasound has been shown to be well-tolerated, with close to 75% of pregnant women reporting no pain[37].

Conclusion

Intrapartum ultrasound provides an objective assessment of labour progress. It is easy to learn, with negligible intra- and inter-observer differences. Moreover, most of the parameters can be captured by 2D ultrasound and measured on the spot. When the optimal cutoff for ultrasound parameters is supported by evidence, it will also aid decision-making, especially when the choice of delivery mode is not straightforward such as slow or lack of progress in the second stage and possibly in the first stage too. With proper training and standardisation of technique, intrapartum ultrasound assessment will be the future diagnostic tool in active labour. Our group is currently exploring the possibility of midwifery-led intrapartum ultrasound serial assessment of labour progress. Meanwhile, clinical assessment by digital vaginal palpation should not become obsolete, but applied alongside sonography. A new algorithm that combines both the clinical and intrapartum ultrasound parameters should be the way forward.

Declaration

The authors have disclosed no conflicts of interest.

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For Healthcare Professionals only

Important Notice:
Breast-feeding is the best form of nutrition for babies and provides many benefits to babies and mothers. It is important that, in preparation for and during breast-feeding, pregnant and lactating women eat a healthy, balanced diet. Combined breast and bottle-feeding in the first weeks of life may reduce the supply of their own breast-milk, and reversing the decision not to breast-feed is difficult. Always consult healthcare professional for advice about feeding baby. If infant formula is used, mothers / care givers should follow manufacturer's instructions for use carefully– failure to follow the instructions may make baby ill. The social and financial implications of using infant formula should be considered. Improper use of an infant formula or inappropriate foods or feeding methods may present a health hazard.

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