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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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Editorial

# Moving forward together under the Hong Kong College of Obstetricians and Gynaecologists

Stepping into my third year of presidency, I am witnessing the 36th year of the Hong Kong College of Obstetricians and Gynaecologists (HKCOG) commitment to postgraduate training, maintenance of professional standards, and continuous medical education in Hong Kong. The years of the COVID pandemic were a harsh time for everyone, hindering travel and face-to-face contact. In 2023, the HKCOG family was pleased to gather again for knowledge exchange and fraternity building at the 35th anniversary events. It was a particularly memorable occasion when the HKCOG held its first international conference. Over 3 days, we were delighted to meet our local experts and international supporters. We were honoured to be joined by representatives from our sister colleges and professional societies from the United Kingdom, United States, Mainland China, Asia and Oceania Region, Singapore, and Malaysia. This was a testimonial to HKCOG's commitment to upholding professional knowledge and standards through international collaborations, and we look forward to organising more international conferences in future.

During the 3 years of my tenure, I started a few new initiatives in postgraduate training in obstetrics and gynaecology. First, we completed the curriculum review, an important task that would shape how our specialists are trained in the years ahead. The Royal College of Obstetricians and Gynaecologists (RCOG), our partner in postgraduate training and examinations, has revolutionised its training format. We recognised the need to review our own curriculum to cater for the demands of the changing medical world. In addition to holding conjoint examinations with the RCOG, we referenced the new RCOG curriculum and revised our own, considering our own needs and practicalities. I must thank the working group, led by Dr Daniel LW Chan, for bringing this important accomplishment to fruition. It was amazing to see young fellows making major contributions to the working group. As trainees not long ago and as new trainers who understand the curriculum best, young fellows are paramount to guide our specialist training on track to match local and international expectations. Meanwhile, the Information Technology Committee has worked closely to launch an electronic logbook that makes real-time logging easier and more environmentally friendly. Starting in 2024, the HKCOG has organised induction courses annually for new incoming trainees to familiarise them with the curriculum and the logbook.

In addition to dedicated trainees and an up-to-date curriculum, competent trainers are also key to the success of the training programme. In line with the RCOG, we pay extra attention to competence-based assessments in the workplace. As elaborated by Dr Kwok Keung Tang in a previous editorial of this journal, HKCOG has actively collaborated with other colleges to promote training in medical education and equip our trainers with modern-day training and assessment methods.

Going one step further, the HKCOG shared its expertise and experience in structured training with the Shenzhen-Hong Kong Medical Specialties Training Centre, a joint venture between the Hong Kong Academy of Medicine and the Shenzhen government. We have set up a training programme for specialists and subspecialists in Shenzhen, modelling that in Hong Kong. We piloted this at The University of Hong Kong–Shenzhen Hospital over the past few years, and it has now been officially extended to other hospitals in Shenzhen. I strongly hope and confidently believe that these new initiatives will shape our training system to cater to the needs and competence of our future specialists and to be compatible with international standards.

Obstetrics and gynaecology is a very meaningful and exciting, but stressful, speciality. To understand the psychosocial well-being of our doctors, we conducted a territory-wide survey, to which about a third of obstetricians and gynaecologists (including trainees) in Hong Kong responded. The results are being analysed and will be disseminated in due course. They will provide valuable insights to help lessen the stress that our colleagues face from work and training.

I am grateful to have been entrusted by the HKCOG over the years. I am sure that the HKCOG will continue to thrive and reach new heights with all our concerted efforts.

**Dr Karen Kar Loen CHAN**
President
Hong Kong College of Obstetricians and Gynaecologists

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# Urinary incontinence during pregnancy and postpartum pelvic floor muscle exercise: a prospective study

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***Objectives:*** To investigate the incidence of urinary incontinence (UI) during pregnancy and after delivery, perceptions of UI, effectiveness of pelvic floor muscle exercise (PFME) on UI, and risk factors for UI among pregnant women.
***Methods:*** Chinese women aged ≥18 years at 35 to 37 weeks of gestation were invited to participate. Perceptions of UI were assessed using a questionnaire that comprises seven statements. Urinary symptoms were assessed using the self-report six-item Urogenital Distress Inventory (UDI-6). Women were considered to have UI when they had positive scores on any of the incontinence items. Women who reported to have UI symptoms were assessed by a physiotherapist in the postnatal ward and were taught PFME. UI impact on quality of life was assessed using the self-report seven-item Incontinence Impact Questionnaire. Participants with UI during pregnancy who delivered in our hospital were followed up at 6 weeks postnatally through telephone. Their adherence to PFME was assessed in terms of the mean number of contractions performed per day.
***Results:*** Of 1134 participants, the incidence of UI was 73.0% during pregnancy and 21.9% after delivery. Predictors for UI during pregnancy were a history of UI before pregnancy (odds ratio [OR]=14.40, p<0.001), higher pre-pregnancy body mass index (OR=1.04, p=0.034), and previous vaginal delivery (OR=2.06, p=0.001), whereas predictors for UI after delivery were vaginal delivery in the index pregnancy (OR=3.86, p<0.001), older age (OR=1.12, p<0.001), a history of UI before pregnancy (OR=1.86, p=0.028), and total score of items 2 to 4 on the UDI-6 during pregnancy (OR=1.20, p=0.015). 86.4% of participants reported poor or no adherence to PFME. Adherence to postnatal PFME was not associated with UI after delivery (p=0.477). Women with higher education levels adhered more to PFME (p=0.008). Perceptions of UI were not associated with adherence to postnatal PFME.
***Conclusion:*** A history of pre-pregnancy UI is the main predictor for UI during pregnancy, whereas vaginal delivery is the main predictor for UI after delivery. The effect of postpartum PFME on UI after delivery is not significant, probably owing to the low rate of adherence to PFME.

*Keywords: Pelvic floor; Pregnant women; Urinary incontinence*

## Introduction

The incidence of urinary incontinence (UI) among pregnant women ranges from 32% to 64%[1]. UI can be caused by hormonal changes, increased abdominal pressure or weight gain and can lead to decreased quality of life (QoL), embarrassment, depression, and social isolation[2]. UI during pregnancy is underreported and undertreated[3]. In a study of Hong Kong Chinese women, 78.3% of respondents were not aware of UI being a disease entity[4]. Only 14.8% of pregnant women sought professional help for urinary symptoms[5]. Screening for UI is not routinely performed during antenatal care.

Pelvic floor muscle exercise (PFME) is effective in reducing the incidence of UI during pregnancy[6]. However, its effects in the postnatal period yield conflicting results[7-9]. This study aimed to investigate the incidence of UI during pregnancy and after delivery, perceptions of UI, effectiveness of PFME on UI, and risk factors for UI among pregnant women.

## Materials and methods

This prospective longitudinal observational study was carried out in the Princess Margaret Hospital in Hong Kong from June 2021 to April 2022. Chinese women aged ≥18 years who attended the antenatal group B streptococcus screening clinic at 35 to 37 weeks of gestation were invited to participate. Women who did not understand written Chinese were excluded.

Perceptions of UI were assessed using a questionnaire that comprises seven statements measured on a 4-point Likert scale (totally disagree, disagree, agree,

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totally agree). The questionnaire had been validated by nine obstetricians and gynaecologists in our hospital; both the item-level and scale-level content validity indices were 1.0, which meets Lynn's criteria[10]. Urinary symptoms were assessed using the self-report six-item Urogenital Distress Inventory (UDI-6). Women were considered to have UI when they had positive scores on any of the incontinence items, including leakage related to feeling of urgency (item 2), leakage related to activity (item 3), or coughing/sneezing small amounts of leakage (item 4). Women who reported to have UI symptoms were assessed by a physiotherapist in the postnatal ward and were taught PFME. UI impact on QoL was assessed using the self-report seven-item Incontinence Impact Questionnaire (IIQ-7). Both UDI-6 and IIQ-7 have been validated[11], and their Chinese versions have been validated in the Chinese population[12].

Participants with UI during pregnancy who delivered in our hospital were followed up at 6 weeks postnatally through telephone; they were asked to complete the UDI-6 and IIQ-7 again to assess any change in urinary symptoms and the impact on QoL. In addition, their adherence to PFME was assessed in terms of the mean number of contractions performed per day. The cut-off for high adherence to PFME was ≥60 contractions per day (≥420 contractions per week), based on a study that showed good results with 45 to 60 contractions per day[13]. Moderate adherence was defined as 210 to 419 contractions per week, and poor adherence was defined as <210 contractions per week.

The statistical analyses were performed using SPSS version 27. Women with or without UI during pregnancy and after delivery were compared using the Chi-squared test or Fisher's exact test for categorical variables and the Student's *t* tests or Mann-Whitney *U* test for continuous variables. Predictors for UI during pregnancy and after delivery were identified using multiple logistic regression with forward stepwise selection. Women with high, moderate, poor, or no adherence were compared using the one-way analysis of variance. A p value of <0.05 was considered statistically significant.

## Results

Of 1134 participants aged 18 to 46 (mean, 32.5) years who completed the questionnaire, 826 reported UI, 306 reported no UI, and two had missing values on the UDI-6. Of 580 participants with UI during pregnancy who delivered in our hospital, 470 (81%) completed the follow-up questionnaire at a mean of 57 (range, 36-96) days after delivery.

With regard to perceptions of UI, 94.8% of participants agreed or totally agreed that 'PFME can treat UI effectively'; 79.2% agreed or totally agreed that 'severity of UI increases with age'; 74.8% agreed or totally agreed that 'pregnancy causes UI'; 74.4% agreed or totally agreed that 'UI is a physiological change of ageing'; 56.8% agreed or totally agreed that 'UI is a disease entity'; 51.1% agreed or totally agreed that 'UI resolves after delivery'; and 17.8% agreed or totally agreed that 'UI is not curable' (Table 1). Perceptions of UI were not associated with adherence to postnatal PFME.

The incidence of UI during pregnancy was 73.0% (826/1132). Compared with women with no UI during pregnancy, women with UI during pregnancy tended to have higher pre-pregnancy body mass index (22.27 vs 21.55 kg/m$^2$, p=0.033), a history of UI before pregnancy (21.1% vs 1.6%, p<0.001), higher number of parities (1 vs 0, p=0.015), higher number of vaginal deliveries (0.56 vs 0.35, p<0.001), higher UDI-6 score (26.3 vs 8.99, p<0.001), and higher IIQ-7 score (9.21 vs 3.66, p<0.001) and subscale scores (p<0.001) [Table 2].

**Table 1. Women's perceptions of urinary incontinence (UI) [n=1134]**

| | No. (%) of participants | | | |
|---|---|---|---|---|
| | **Totally disagree** | **Disagree** | **Agree** | **Totally agree** |
| Q1: UI is a disease entity | 42 (3.7) | 448 (39.5) | 547 (48.2) | 97 (8.6) |
| Q2: Pregnancy causes UI | 14 (1.2) | 272 (24.0) | 785 (69.2) | 63 (5.6) |
| Q3: UI resolves after delivery | 30 (2.6) | 524 (46.2) | 532 (46.9) | 48 (4.2) |
| Q4: Pelvic floor muscle exercise can treat UI effectively | 6 (0.5) | 53 (4.7) | 872 (76.9) | 203 (17.9) |
| Q5: UI is a physiological change of ageing | 14 (1.2) | 276 (24.3) | 725 (63.9) | 119 (10.5) |
| Q6: Severity of UI increases with age | 13 (1.1) | 223 (19.7) | 762 (67.2) | 136 (12.0) |
| Q7: UI is not curable | 98 (8.6) | 834 (73.5) | 174 (15.3) | 28 (2.5) |

The incidence of UI after delivery was 21.9% (103/470). Compared with women with no UI after delivery, women with UI after delivery tended to be older (33.80 vs 31.98 years, p=0.002), have a history of UI before pregnancy (32% vs 21.3%, p=0.023), have an episiotomy (53.4% vs 36.5%, p=0.003), and have normal vaginal delivery (73.8% vs 67.8%, p=0.001) and assisted vaginal delivery (17.5% vs 9.3%, p=0.001) [Table 2].

In multiple logistic regression, predictors for UI during pregnancy were a history of UI before pregnancy (odds ratio [OR]=14.40, p<0.001), higher pre-pregnancy body mass index (OR=1.04, p=0.034), and previous vaginal delivery (OR=2.06, p=0.001), whereas predictors for UI after delivery were vaginal delivery in the index pregnancy (OR=3.86, p<0.001), older age (OR=1.12, p<0.001), a history of UI before pregnancy (OR=1.86, p=0.028), and

**Table 2. Comparisons of women with or without urinary incontinence (UI) during pregnancy (n=1132) and after delivery (n=470)**

| | UI during pregnancy* | | p Value | UI after delivery* | | p Value |
|---|---|---|---|---|---|---|
| | No (n=306) | Yes (n=826) | | No (n=367) | Yes (n=103) | |
| Age, y | 32.33±4.64 | 32.60±5.02 | 0.402 | 31.98±5.06 | 33.80±5.32 | 0.002 |
| Pre-pregnancy body mass index, kg/m$^2$ | 21.55±3.06 | 22.27±3.99 | 0.033 | 22.41±4.07 | 22.79±3.95 | 0.398 |
| Employed | 155 (50.7) | 439 (53.1) | 0.455 | 183 (49.9) | 48 (46.6) | 0.558 |
| Education level | | | 0.703 | | | 0.657 |
| Primary | 5 (1.6) | 14 (1.7) | | 8 (2.2) | 1 (1.0) | |
| Secondary | 142 (46.4) | 406 (49.2) | | 202 (55.0) | 60 (58.3) | |
| Tertiary | 159 (52.0) | 406 (49.2) | | 157 (42.8) | 42 (40.8) | |
| Smoking | 35 (11.4) | 103 (12.5) | 0.890 | 57 (15.6) | 12 (11.7) | 0.512 |
| Ex-smoker | 30 (9.8) | 89 (10.8) | | 48 (13.1) | 11 (10.7) | |
| Active smoker | 5 (1.6) | 14 (1.7) | | 9 (2.5) | 1 (1.0) | |
| History of UI before pregnancy | 5 (1.6) | 174 (21.1) | <0.001 | 78 (21.3) | 33 (32.0) | 0.023 |
| Parity | 0 (0-4) | 1 (0-4) | 0.015 | 1 (0-4) | 1 (0-2) | 0.183 |
| Multiple pregnancy | 5 (1.6) | 16 (1.9) | 0.737 | 8 (2.2) | 1 (1.0) | 0.691 |
| Nulliparous | 181 (59.2) | 399 (48.3) | 0.001 | - | - | - |
| No. of vaginal deliveries | 0.35±0.61 | 0.56±0.76 | <0.001 | - | - | - |
| Diabetes mellitus/gestational diabetes mellitus | 57 (18.6) | 127 (15.4) | 0.188 | - | - | - |
| Gestation at delivery, wk | - | - | - | 38.65±1.22 | 38.77±1.25 | 0.375 |
| Birth weight, g | - | - | - | 3155±422 | 3138±423 | 0.713 |
| Mode of delivery | | | | | | 0.001 |
| Normal vaginal delivery | - | - | - | 249 (67.8) | 76 (73.8) | |
| Assisted vaginal delivery | - | - | - | 34 (9.3) | 18 (17.5) | |
| Caesarean section | - | - | - | 84 (22.9) | 9 (8.7) | |
| Episiotomy | - | - | - | 134 (36.5) | 55 (53.4) | 0.003 |
| Shoulder dystocia | - | - | - | 3 (0.8) | 0 | 1.000 |
| Obstetric anal sphincter injury | - | - | - | 2 (0.5) | 0 | 1.000 |
| Urogenital Distress Inventory score | 8.99±6.66 | 26.30±13.78 | <0.001 | 0.29±1.59 | 10.68±7.45 | <0.001 |
| Incontinence Impact Questionnaire score | 3.66±11.57 | 9.21±15.57 | <0.001 | 0.08±1.49 | 1.85±5.82 | <0.001 |
| Physical subscale | 3.67±12.01 | 8.95±16.72 | <0.001 | 0 | 0.65±3.24 | <0.001 |
| Travel subscale | 3.62±12.30 | 8.34±16.38 | <0.001 | 0 | 1.46±6.64 | <0.001 |
| Social subscale | 3.39±12.74 | 8.89±18.41 | <0.001 | 0 | 0.97±5.63 | <0.001 |
| Emotional subscale | 3.84±14.16 | 10.48±19.44 | <0.001 | 0.27±5.22 | 3.88±15.16 | <0.001 |

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

total score of items 2 to 4 on the UDI-6 during pregnancy (OR=1.20, p=0.015) [Table 3].

With regard to adherence to postnatal PFME, 4.3% of participants reported high adherence, 9.4% reported moderate adherence, and 86.4% reported poor or no adherence. Adherence to postnatal PFME was not associated with UI after delivery (p=0.477, Table 4). Improvement in the UDI-6 score was highest (but not significantly) in women with high adherence (p=0.396). Women with higher education levels adhered more to PFME (p=0.008).

## Discussion

In the present study, the incidence of UI during pregnancy was 73.0%, which was higher than the 40% to 68.8% reported in other studies[14-16] and similar to the 73.2% in a cross-sectional study[17]. The higher incidence of

**Table 3. Predictors for urinary incontinence (UI) during pregnancy and after delivery**

| Variables | Odds ratio (95% confidence interval) | p Value |
|---|---|---|
| UI during pregnancy | | |
| History of UI before pregnancy | 14.40 (5.82-35.62) | <0.001 |
| Pre-pregnancy body mass index | 1.04 (1.00-1.09) | 0.034 |
| Previous vaginal delivery | 2.06 (1.34-3.17) | 0.001 |
| UI after delivery | | |
| Age | 1.12 (1.06-1.17) | <0.001 |
| History of UI before pregnancy | 1.86 (1.07-3.24) | 0.028 |
| Vaginal delivery | 3.86 (1.81-8.23) | <0.001 |
| Total score of items 2 to 4 on the six-item Urogenital Distress Inventory during pregnancy* | 1.20 (1.04-1.40) | 0.015 |

* Item 2: leakage related to feeling of urgency; item 3: leakage related to activity; item 4: coughing/sneezing small amounts of leakage

**Table 4. Adherence to pelvic floor muscle exercise after delivery (n=470)**

| Characteristic | Adherence to pelvic floor muscle exercise | | | | p Value |
|---|---|---|---|---|---|
| | No (n=135) | Poor (n=271) | Moderate (n=44) | High (n=20) | |
| Age, y | 32.29±5.61 | 32.40±5.05 | 32.55±4.31 | 32.40±5.80 | 0.999 |
| Pre-pregnancy body mass index, kg/m$^2$ | 21.74±3.96 | 22.96±3.95 | 21.95±4.64 | 22.47±3.86 | 0.027 |
| Employed | 56 (41.5) | 142 (52.4) | 21 (47.7) | 12 (60.0) | 0.151 |
| Education level | | | | | 0.008 |
| Primary | 5 (3.7) | 4 (1.5) | 0 | 0 | |
| Secondary | 90 (66.7) | 144 (53.1) | 19 (43.2) | 9 (45.0) | |
| Tertiary | 40 (29.6) | 123 (45.4) | 25 (56.8) | 11 (55.0) | |
| Days from delivery to follow-up | 56.78±8.41 | 57.46±10.11 | 58.09±8.90 | 53.55±6.53 | 0.277 |
| Urinary incontinence after delivery | 25 (18.5) | 63 (23.2) | 12 (27.3) | 3 (15.0) | 0.477 |
| Change in six-item Urogenital Distress Inventory score | -23.58±15.90 | -24.31±14.25 | -25.38±13.68 | -29.44±14.54 | 0.396 |
| Change in seven-item Incontinence Impact Questionnaire score | -7.62±14.17 | -8.52±16.53 | -10.39±16.95 | -11.90±18.05 | 0.590 |
| Physical subscale | -8.77±16.77 | -8.61±17.56 | -10.23±16.16 | -12.50±19.40 | 0.752 |
| Travel subscale | -7.16±14.76 | -8.18±18.08 | -9.47±19.15 | -9.17±16.64 | 0.860 |
| Social subscale | -7.65±18.18 | -8.49±19.61 | -9.09±19.51 | -15.00±27.52 | 0.479 |
| Emotional subscale | -6.91±20.20 | -8.79±20.53 | -12.12±19.48 | -12.50±21.54 | 0.396 |

UI may be the result of a selection bias, whereby women experiencing UI symptoms were more likely to participate in the study. Moreover, UI tends to worsen as pregnancy progresses and as the weight of the uterus increases[18]. Our participants were recruited during late pregnancy; this could result in the higher incidence of UI.

94.8% of the participants agreed that PFME can treat UI effectively, and 82.2% of participants agreed that UI can be cured. These findings indicated that most women were knowledgeable about the PFME to alleviate their UI symptoms. 51.1% of participants agreed that UI symptoms will resolve spontaneously after delivery; they tended to adhere less to postnatal PFME. 56.8% of the participants agreed that UI is a disease entity; this may explain the lack of help-seeking behaviour for UI symptoms in pregnancy[4].

UI during pregnancy was more common in multiparous than in nulliparous women. This could be due to pelvic structural changes after delivery. A higher number of previous vaginal deliveries was associated with UI during pregnancy. Vaginal delivery is a predictor for postpartum UI[19] and increases the risk of pelvic floor dysfunction secondary to damages to pelvic innervation and laceration of the pelvic musculature[20]. Instrumental delivery can result in more laceration and mechanical stress and thus further increases the risk of pelvic floor dystundtion[21].

A history of UI before pregnancy was a strong predictor for UI during pregnancy and after delivery. It is associated with both antepartum and postpartum UI[5,7,14]. Women with an episiotomy were associated with UI after delivery. A systemic review on the long-term effects of episiotomy concluded that episiotomy is not protective against UI symptoms[22]. This may be confounded by vaginal delivery, which is a risk factor for postpartum UI. The use of an episiotomy reflects the anticipation of a difficult delivery, which is also a risk factor for postpartum UI. In our study, multiple logistic regression analysis showed no significant association between episiotomy and postpartum UI. A higher total score of items 2 to 4 on the UDI-6 during pregnancy was associated with postpartum UI, consistent with a study[7].

Understanding the risk factors for UI helps in antenatal counselling and may increase women's adherence to PFME. Targeted interventions may be offered to high-risk women. Healthcare professionals can implement early intervention and prevention strategies such as PFME and healthy bladder habits for high-risk women.

In our study, postpartum PFME did not significantly reduce the incidence of postpartum UI or improve UI symptoms or QoL. This could be due to a lack of regular supervised instruction. Supervised PFME is more effective than unsupervised PFME[23], and intensive training with close follow-up is more likely to achieve beneficial effects[24]. Despite good adherence to PFME, women may inadvertently perform PFME incorrectly. Consistent input from healthcare professionals and close follow-up may help women to achieve effective PFME. Furthermore, the training period of 6 weeks (median, 56 days) may be too short to strengthen the pelvic floor muscles. Supervised training protocol lasting at least 8 weeks is recommended for effective PFME[6].

Although the effect of postpartum PFME was not significant, improvements in UDI-6 and IIQ-7 scores were associated with higher adherence to PFME. Only 13.7% of participants moderately or highly adhered to PFME; this may be due to inadequate promotion by medical staff[25]. Regular follow-up or training sessions can remind the participants of the importance of adherence to PFME. The proportion of pregnant women adhere to PFME increases from 5.8% to 37.2% after two sessions of education classes[25]. Physiotherapists may customise the PFME programme for each woman and integrate PFME into women's daily routines, particularly for women with lower education levels, which was associated with lower adherence.

There were limitations to this study. The study was not randomised or controlled owing to resource constraints and ethical concerns. There may be selection bias, as pregnant women with UI are more likely to participate in the study. Follow-up at 6 weeks after delivery may be too short to observe the effects of PFME. The lack of interval follow-ups or training sessions may result in the poor adherence to PFME.

## Conclusion

A history of pre-pregnancy UI is the main predictor for UI during pregnancy, whereas vaginal delivery is the main predictor for UI after delivery. The effect of postpartum PFME on UI after delivery is not significant, probably owing to the low rate of adherence to PFME.

## Contributors

SCW and YTL designed the study. SCW and LFH acquired the data. SCW analysed the data and drafted the manuscript. All authors critically revised the manuscript for important intellectual content. All authors had full

access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

## Conflicts of interest

All authors have no conflicts of interest to disclose.

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## Data availability

All data generated or analysed during the present study are available from the corresponding author on reasonable request.

## Ethics approval

The study was approved by the Kowloon West Cluster Research Ethics Committee (reference: EX-20-107(150-01)). The patients were treated in accordance with the tenets of the Declaration of Helsinki. The patients provided written informed consent for all treatments and procedures and for publication.

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# Alternative pathways to oral glucose tolerance test for Chinese pregnant women

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***Objectives:*** To compare the gold standard pathway of universal second-trimester oral glucose tolerance test (OGTT) with eight alternative pathways to determine the optimal pathway that can reduce the number of OGTTs performed but still maintains high sensitivity and specificity for gestational diabetes mellitus (GDM) diagnosis in the Chinese population.
***Methods:*** We retrospectively reviewed medical records of pregnant women who underwent an OGTT during 26+0 to 29+6 weeks of gestation between January 2021 and June 2021 at the Pamela Youde Nethersole Eastern Hospital. The gold standard pathway of universal second-trimester OGTT were compared with eight alternative pathways (which considered fasting glucose levels, a history of GDM, and/or any risk factors) in terms of the estimated percentage reduction in the number of OGTTs performed, sensitivity and specificity of detecting GDM, and estimated percentage of women with composite adverse outcomes (CAO).
***Results:*** Of 769 women who underwent the OGTT, 96 (12.5%) had GDM. The need for an OGTT was reduced 100% in pathway 3, 87.1% in pathway 9, 84.9% in pathway 5, 80.8% in pathway 8, 78.5% in pathway 4, 46.3% in pathway 7, 41.4% in pathway 2, 4.8% in pathway 6, and 0% in pathway 1. Specificity was high (97% to 100%) for all pathways, as were negative predictive values (90% to 100%). However, sensitivity was low (20% to 59%) for all pathways, except for pathways 1 and 6 (100%). In all pathways, the estimated percentage of women with CAO was higher in true-positive groups than in false-negative groups.
***Conclusion:*** In Chinese women, compared with the universal second-trimester OGTT, alternative pathways could reduce the number of OGTTs performed, but the detection rate of GDM was poor. Obstetricians should encourage pregnant women to undergo the OGTT to reduce maternal and neonatal complications, even in the event of pandemic. In situations when infection control measures are ineffective, pathway 3 can be considered because it detects the highest percentage of women with CAO and eliminates the need for OGTTs.

*Keywords: Diabetes, gestational; Glucose tolerance test; Infection control*

## Introduction

Gestational diabetes mellitus (GDM) affects both mothers and fetuses and can complicate 9.3% to 25.5% of pregnancies[1]. Poor glycaemic control increases the risks of preterm delivery, macrosomia, birth injury such as shoulder dystocia, neonatal hypoglycaemia, polycythaemia, and stillbirth. Maternal complications include hypertensive diseases and the need for labour induction and Caesarean sections. GDM is defined as a fasting plasma glucose level of ≥5.1 mmol/l and/or a 2-hour post-glucose load plasma glucose level of ≥8.5 mmol/l[2]. Oral glucose tolerance test (OGTT) at around 28 weeks of gestation is considered standard prenatal care[3]. At the beginning of the COVID-19 pandemic, the OGTT was considered to have a high infection risk when unvaccinated unmasked pregnant women grouped together in an enclosed area, and some might vomit after drinking the glucose solution. Some women declined to take the OGTT, taking the risks of undiagnosed GDM and maternal and perinatal complications.

Alternative pathways for the universal OGTT have been suggested, including measurement of the fasting glucose (FG) level alone, pre-screening of a history of GDM, and selective OGTTs for high-risk women[4-6]. However, these alternative pathways greatly reduce the detection rate of GDM[7] and may not be applicable to the Chinese population owing to their higher skeletal muscle insulin resistance. Only 26% of women with GDM have a raised FG level in Hong Kong (mainly Chinese ethnicity), whereas >70% of women with GDM have a raised FG level in Barbados (mainly Black population), Bellflower, California (mainly Hispanic population), and Providence, Rhode Island (mainly White population)[1].

We compared the gold standard pathway of universal second-trimester OGTT with eight alternative pathways to

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determine the optimal pathway that can reduce the number of OGTTs performed but still maintains high sensitivity and specificity for GDM diagnosis in the Chinese population.

## Methods

In accordance with the World Health Organization recommendations[2], pregnant women attending antenatal care in our hospital were screened for GDM using the OGTT. Women with a high risk of GDM would undergo an OGTT at the early second trimester, whereas women without a high risk of GDM and women with normal early OGTT results would undergo an OGTT at around 28 weeks of gestation. We retrospectively reviewed medical records of pregnant women who underwent an OGTT during 26+0 to 29+6 weeks of gestation between January 2021 and June 2021 at the Pamela Youde Nethersole Eastern Hospital. Women with multiple pregnancy, incomplete OGTT records, or non-Chinese ethnicity were excluded. Data collected included baseline characteristics, pre-existing risk factors, OGTT results, and delivery outcomes.

The gold standard pathway of universal second-trimester OGTT were compared with eight alternative pathways in terms of specificity and sensitivity, positive and negative predictive values, and the percentage reduction in the number of OGTTs performed. Pathway 1 is the gold standard universal second-trimester OGTT. Pathway 2 provides the OGTT only to women with any risk factors. Pathway 3 is the universal screening of the FG level alone. Pathway 4 is the universal screening of the FG level and then provides the OGTT only to women with an FG level of 4.5 to 5.1 mmol/l, based on the Australasian Diabetes in Pregnancy Society recommendations during the COVID-19 pandemic[6]. Pathway 5 is the universal screening of the FG level and then provides the OGTT only to women with an FG level of 4.5 to 5.1 mmol/l plus any risk factors. Pathways 6 to 9 assume that women with a history of GDM have GDM and provide the OGTT only to women with no history of GDM, women with no history of GDM plus any risk factors, women with no history of GDM plus an FG level of 4.5 to 5.1 mmol/l, and women with no history of GDM plus any risk factors plus an FG level of 4.5-5.1 mmol/l, respectively (Figure 1). The optimal pathway that can reduce the number of OGTTs performed but still maintains high sensitivity and specificity for GDM diagnosis was determined.

Similar pathways have been studied in a French population in 2021[8]. In accordance with the Hong Kong College of Obstetricians and Gynecologists[9], high-risk women were defined as those with any risk factors of maternal age ≥35 years, body mass index ≥25 kg/m$^2$ before

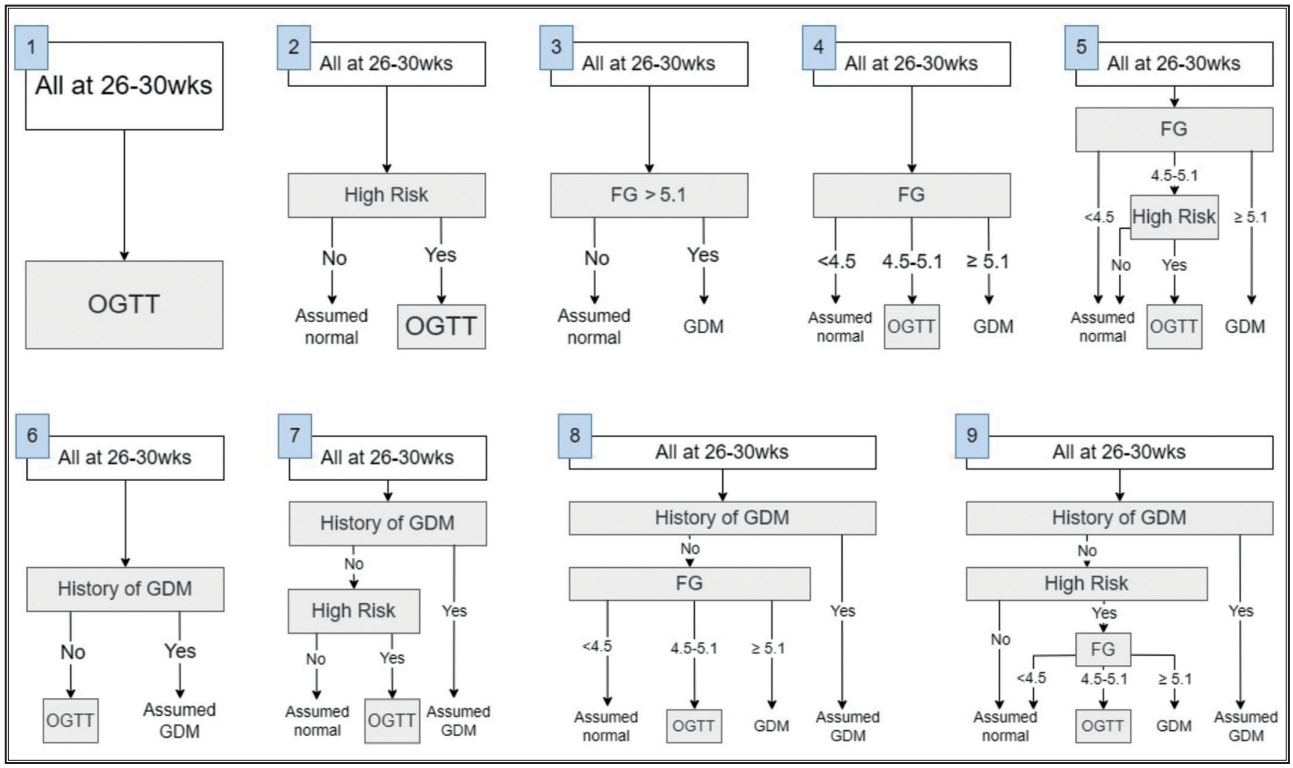


*Figure 1. The nine pathways of oral glucose tolerance test (OGTT) with or without consideration of fasting glucose (FG) levels, a history of gestational diabetes mellitus (GDM), and/or any risk factors*

pregnancy or in the first trimester, family history of diabetes in first-degree relatives, polycystic ovarian syndrome, autoimmune disease, chronic hypertension, long-term use of diabetogenic medications (such as corticosteroids), history of macrosomia (≥4 kg), and history of GDM. Although Asian ethnicity was considered a risk factor by the National Institute for Health and Care Excellence and the American College of Obstetricians and Gynecologists[10,11], we did not consider Asian ethnicity as a risk factor, because most of our population are Asian, and this makes it difficult to differentiate high- and low-risk groups.

Preterm delivery was defined as birth before 34 weeks. Birthweight was adjusted by gestational age according to Hong Kong specific reference ranges[12]. Appropriate for gestational age was defined as those within the 10th to 90th percentiles. Hypertensive diseases in pregnancy included eclampsia, pre-eclampsia, and pregnancy-induced hypertension. Shoulder dystocia was defined as the head-to-shoulder delivery time of >1 minute[13] and the use of an additional manoeuvre (eg, McRoberts manoeuvre, suprapubic pressure, rotational manoeuvres, removal of posterior arm)[14]. Neonatal complications included hypoglycaemia and clavicular fracture. Composite adverse outcomes (CAO) comprised preterm birth, large for gestational age, hypertensive diseases in pregnancy, shoulder dystocia, and neonatal complications.

Women with or without GDM were compared using the analysis of variance for continuous variables and Chi-squared test or Fisher's exact test for categorical variables. A p value of <0.05 was considered statistically significant.

## Results

Of 834 women who underwent an OGTT during the study period, 65 were excluded because of multiple pregnancies (n=12), non-Chinese ethnicity (n=52), or incompletion of OGTT owing to sepsis (n=1). Of 769 women included in analysis, 96 (12.5%) had GDM. Women with or without GDM were comparable in terms of all baseline characteristics and the rate of CAO, except that a higher proportion of women with GDM, as expected, had a higher body mass index at the first visit, a history of GDM, a history of macrosomia, a higher FG level, and a higher 2-hour plasma glucose level (Table 1).

The need for an OGTT was reduced 100% in pathway 3, 87.1% in pathway 9, 84.9% in pathway 5, 80.8% in pathway 8, 78.5% in pathway 4, 46.3% in pathway 7, 41.4% in pathway 2, 4.8% in pathway 6, and 0% in pathway 1 (Table 2). Specificity was high (97% to 100%) for all pathways, as were negative predictive values (90% to 100%). However, sensitivity was low (20% to 59%) for all pathways, except for pathways 1 and 6 (100%).

In total, 538 delivery records were available for analysis. Figure 2 shows the estimated rates of CAO in each pathway in terms of true-positive, false-negative, true-negative, and false-negative groups. The true-positive group of pathway 3 had the highest rate of CAO at 31.3%.

The sensitivity was almost 100% when the FG cutoff level of <3.7 mmol/l was used. The sensitivity reduced gradually as the FG cutoff level increased. The sensitivity was about 50% when the FG cutoff level was 4.5 mmol/l. The estimated percentage reduction in the number of OGTTs performed was 100% when the FG cutoff level was 5.1 mmol/l, which was the pathway 3 (Figure 3).

In future pandemics, pathway 3 can be used, because it completely eliminated the need for an OGTT and could detect the highest rate (31.3%) of CAO. However, if the risk of infection can be controlled, the universal OGTT (pathway 1) is still recommended, because alternative pathways had poor sensitivity in detecting GDM.

## Discussion

The prevalence of GDM in our patients was 12.5%. This is comparable to the 14.4% in a Hong Kong population[1] and the 11.9% in a pooled Chinese population[15]. The alternative pathways could reduce the number of OGTTs performed, but the sensitivity in detecting GDM decreased to 20% to 59%.

In pathway 3, when universal screening of FG level was used, OGTTs could be eliminated, but the sensitivity was poor at 20%, which is worse than the 49% reported in a French population[8]. In the Hyperglycemia and Adverse Pregnancy Outcome Study, the post-glucose load level had a higher detection rate of GDM, compared with the FG level, in Chinese populations[1]. In pathway 6, when an OGTT was provided only to women without a history of GDM, the sensitivity was 100%, but only 4.8% of OGTTs were avoided. Although the universal OGTT is recommended by the World Health Organization, some centres provide OGTTs to high-risk women only, probably owing to limited resources. Pathway 2 had a 59% sensitivity, meaning that 41% of women with GDM had no personal or family history risk factors of GDM. In pathways 4 and 5, when the FG cutoff level of 4.5-5.1 mmol/l was used to triage OGTTs, the sensitivity was poor (47% and 38%, respectively), although the estimated percentage reduction

**Table 1. Baseline characteristics of women with or without gestational diabetes mellitus (GDM)**

| Characteristic | GDM (n=96)* | No GDM (n=673)* | p Value |
|---|---|---|---|
| Age at delivery (estimated), y | 33.7±3.9 | 33.4±4.2 | 0.51 |
| No. of parities | 0.7±1.1 | 0.5±0.7 | 0.11 |
| First pregnancy | 50 (52.1) | 372 (55.3) | 0.59 |
| Chinese ethnicity | 96 (100) | 673 (100) | - |
| Body weight at first visit, kg | 57.9±9.4 | 56.3±8.5 | 0.09 |
| Body mass index at first visit, kg/m$^2$ | 22.9±3.4 | 22.2±3.0 | 0.05 |
| Relevant medical history | 5 (5.2) | 27 (4.0) | 0.58 |
| Family history of diabetes | 16 (16.7) | 133 (19.8) | 0.49 |
| Women with previous pregnancy | n=46 | n=301 | |
| History of GDM | 19 (41.3) | 19 (6.3) | <0.001 |
| History of macrosomia | 3 (6.5) | 2 (0.7) | 0.005 |
| History of hypertensive diseases in pregnancy | 0 | 10 (3.3) | 0.38 |
| High-risk group | 57 (59.4) | 393 (58.4) | 0.91 |
| Gestation at oral glucose tolerance test, wk | 27.7±0.6 | 27.7±0.6 | 0.44 |
| Fasting plasma glucose level, mmol/l | 4.6±0.6 | 4.2±0.3 | <0.001 |
| 2-hour plasma glucose level after oral glucose tolerance test, mmol/l | 9.2±1.2 | 6.5±1.0 | <0.001 |
| Women with delivery records available | n=69 | n=469 | |
| Gestation at delivery, wk | 38.4±1.2 | 38.6±1.6 | 0.11 |
| Preterm delivery <34 weeks | 0 | 5 (1.1) | 0.39 |
| Induction of labour | 24 (34.8) | 133 (28.4) | 0.32 |
| Mode of delivery | | | 0.93 |
| Normal vaginal delivery | 42 (60.9) | 300 (64) | |
| Vacuum extraction | 5 (7.3) | 40 (8.5) | |
| Forceps delivery | 1 (1.5) | 6 (1.3) | |
| Elective Caesarean section | 14 (20.3) | 75 (16.0) | |
| Emergency Caesarean section | 7 (10.1) | 48 (10.2) | |
| Birthweight, g | 3051.4±433.6 | 3069.6±421.8 | 0.74 |
| Small for gestational age | 9 (13.0) | 47 (10.0) | 0.34 |
| Appropriate for gestational age | 55 (79.7) | 403 (85.9) | |
| Large of gestational age | 5 (7.3) | 19 (4.1) | |
| Hypertensive disorders of pregnancy | 3 (4.4) | 18 (3.8) | 0.74 |
| Shoulder dystocia | 0 | 1 (0.3) | - |
| Neonatal complications | 3 (4.3) | 17 (3.6) | 0.73 |
| Intrauterine death/neonatal death | 0 | 3 (0.6) | - |
| Composite adverse outcome | 11 (15.9) | 50 (10.7) | 0.22 |

* Data are presented as mean±standard deviation or No. (%) of participants

in the number of OGTTs was high (78.5% and 84.9%, respectively). However, 15.1% to 21.5% of women would need to be tested twice: first for the FG level and second for an OGTT. This may lead to a higher non-compliance rate of OGTTs. In pathways 7 to 9, the OGTT was provided only to women with no history of GDM with or without reaching the FG cutoff level of 4.5-5.1 mmol/l and/or any risk factors. Triage based on the FG level of 4.5-5.1 mmol/l with or without any risk factor resulted in a higher percentage reduction in the number of OGTTs performed but a lower sensitivity; 2.5% of women with a history of GDM were falsely labelled as having GDM and received unnecessary intervention, although their OGTT result was actually normal.

**Table 2. Estimated percentage reduction in the number of oral glucose tolerance tests (OGTTs) performed and sensitivity in detecting gestational diabetes mellitus (GDM) in the nine pathways with or without consideration of fasting glucose (FG) levels, a history of GDM, and/or any risk factors**

| Pathway | No. of OGTTs performed | Estimated % reduction in the No. of OGTTs performed | Sensitivity, % |
|---|---|---|---|
| 1: Universal OGTT | 769 | 0 | 100 |
| 2: OGTT for high-risk group | 451 | 41.4 | 59 |
| 3: Universal FG alone | 0 | 100.0 | 20 |
| 4: Universal FG then OGTT for FG level of 4.5-5.1 mmol/l | 165 | 78.5 | 47 |
| 5: Universal FG then OGTT for FG level of 4.5-5.1 mmol/l + high risk | 116 | 84.9 | 38 |
| 6: OGTT for no history of GDM | 732 | 4.8 | 100 |
| 7: OGTT for no history of GDM + high risk | 413 | 46.3 | 59 |
| 8: OGTT for no history of GDM + FG level of 4.5-5.1 mmol/l | 148 | 80.8 | 54 |
| 9: OGTT for no history of GDM + high risk + FG level of 4.5-5.1 mmol/l | 99 | 87.1 | 42 |

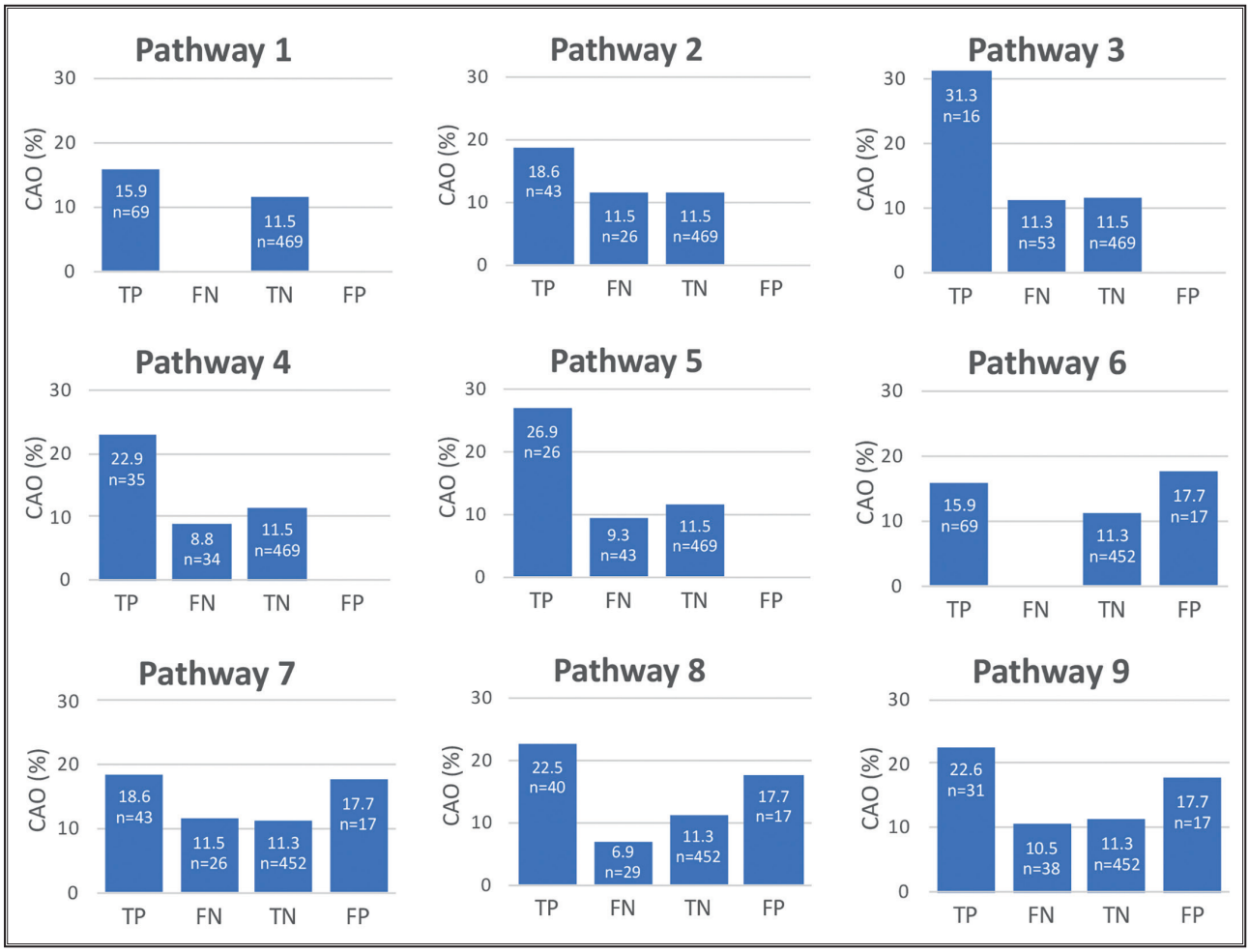


*Figure 2. Estimated percentages of women with composite adverse outcome (CAO) in terms of the true-positive (TP), false-negative (FN), true-negative (TN), and false-positive (FP) groups in the nine pathways*

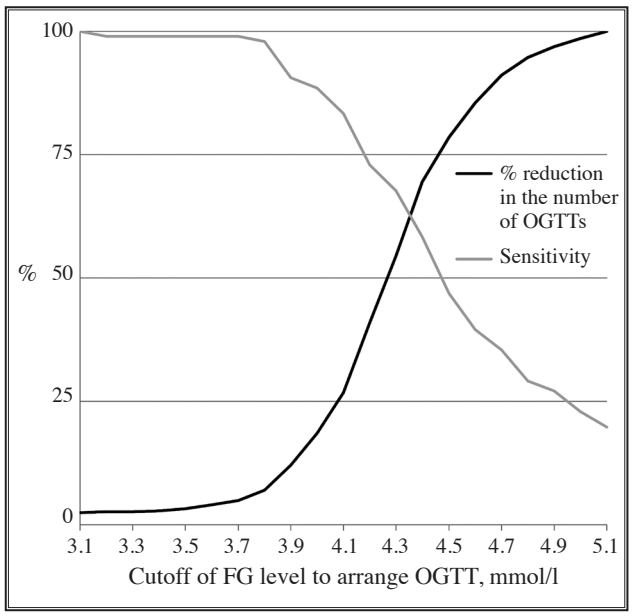


*Figure 3. Relationship of estimated percentage reduction in the number of oral glucose tolerance tests (OGTTs) performed and sensitivity of fasting glucose (FG) level in detection of gestational diabetes mellitus*

In the Hyperglycemia and Adverse Pregnancy Outcome Study, only 24% of patients with GDM had an abnormal FG level in a Bangkok population. A Japanese study[16] presented similar problems based on the Japanese COVID guideline, which was adapted from the guidelines of The Royal College of Obstetricians and Gynaecologists and the Australasian Diabetes in Pregnancy Society[4,6]. At an FG cutoff level of 5.1 mmol/l, most GDM diagnoses were made based on postprandial plasma glucose levels. The Japanese COVID guideline missed 60% of GDM cases. This difference in ethnicity is important for provision of optimal clinical care in various ethnic groups, especially during a pandemic with strict infection control measures.

When the universal OGTT is non-expendable, different logistics may be applied during a pandemic. Ideally, each pregnant woman should undergo the OGTT individually in a negative-pressure room with disinfection before and after use. If the single-room setting is not feasible, seating with replaceable plastic sheeting, anti-virus coating, and an ultraviolet-C disinfection unit that integrates a portable pump and a high-efficiency particulate air filter should be used[17]. Social distancing can be improved by reducing the number of bookings in each time slot and by increasing the number of time slots throughout the week. In our centre, a negative rapid test result on the morning before arrival to hospital for the OGTT was necessary. Straws were provided for the women to take the glucose load with the mask on. Women were asked to raise their hands and be escorted to isolated areas when there was a need to vomit.

All alternative pathways were able to identify women at the highest risk of GDM. The estimated rate of CAO in all pathways were higher in the true-positive groups than in the false-negative groups. This suggests that the selection criteria (any high-risk factor, higher FG level, and a history of GDM) individually and jointly prognosticate adverse outcomes of GDM. Pathway 3 (using the FG level alone) could detect the highest percentage of women with CAO, suggesting that, although the FG level was not sensitive for diagnosis of GDM in a Chinese population, elevated FG levels could be associated with higher maternal and neonatal complications.

For pathways 6 to 9, 2.5% of women with a history of GDM were falsely labelled as having GDM and received unnecessary monitoring and intervention, although their OGTT results were normal. The rate of CAO in these women was 17%, which was higher than that in the true negative groups (ie, women without GDM), consistent with one study[8]. It is postulated that higher FG levels (although not beyond the cutoff) might correlate with more adverse outcomes, and that women with a history of GDM might have hidden risk factors that could result in the higher rate of CAO.

Our study had several limitations. Although the sample size was 769, about 30% of the delivery records were not available for analysis because of delivery in private hospitals. Subgroup analysis was not possible because there were few cases of complications such as shoulder dystocia, intrauterine fetal demise, or neonatal death. Only historical risk factors and FG levels were collected for analysis. The Royal College of Obstetricians and Gynaecologists advocated using the glycated haemoglobin (HbA1c) level of 5.7% as a substitute for the second-trimester OGTT during the COVID-19 pandemic[4]. Measurement of HbA1c levels requires no fasting or consumption of a glucose load. Although the HbA1c level was not used for diagnosis of GDM in our study, all women with GDM had their HbA1c level checked a few days after diagnosis. If a HbA1c level of 5.7% were used, we would have missed 88% of GDM cases. In a study of 19 000 pregnant women who underwent second-trimester OGTT and HbA1c measurement together, the HbA1c level was only weakly correlated with OGTT results; a cutoff of 5.0% yielded a sensitivity of 60%[18]. Other alternative pathways such as random measurement

of glucose levels, personalised risk calculators, and a combination of these parameters may be assessed in future studies.

Women with the highest risk of GDM who had already been diagnosed in an early OGTT were not included in the analysis. This reduced the sensitivity in all pathways tested. The false-negative groups were actually managed as having GDM in real life. Hence, the estimated rate of CAO would underestimate the true rate of CAO if the women did not receive treatment. However, the estimated rate of CAO for false-negative groups in pathways 2 to 9 was similar to that for true-negative groups. This suggests that interventions such as advice from a dietitian, regular self-monitoring of blood glucose levels, and additional counselling and monitoring can help reduce the rate of CAO to the level similar to true-negative groups. The false-negative groups were at lower risk than the true-positive groups, because both groups received the same intervention, but the false-negative groups had a consistently lower rate of CAO. Our cohort was affected by the COVID-19 pandemic; the prevalence of GDM and adverse outcomes were reported to increase during the pandemic. A historical cohort without the effects of the COVID-19 pandemic may be used to compare with our cohort to detect any differences.

## Conclusion

In Chinese women, compared with the universal second-trimester OGTT, alternative pathways could reduce the number of OGTTs performed, but the detection rate of GDM was poor. Obstetricians should encourage pregnant women to undergo the OGTT to reduce maternal and neonatal complications, even in the event of pandemic. In situations when infection control measures are ineffective, pathway 3 can be considered because it could detect the highest rate of CAO and eliminated the need for OGTTs.

## Contributors

All authors designed the study, acquired the data, analysed the data, drafted the manuscript, and critically revised the manuscript for important intellectual content. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

## Conflicts of interest

All authors have no conflicts of interest to disclose.

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## Data availability

All data generated or analysed during the present study are available from the corresponding author on reasonable request.

## Ethics approval

The study was approved by the Central Institutional Review Board of the Hospital Authority (reference: CIRB-2023-072-1). The patients were treated in accordance with the tenets of the Declaration of Helsinki. The patients provided written informed consent for all treatments and procedures and for publication.

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# Predictors for adverse pregnancy outcomes in women with pre-gestational diabetes: a retrospective study

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***Objective:*** To identify predictors for adverse pregnancy outcomes among women with pre-gestational diabetes.
***Methods:*** We retrospectively reviewed medical records of women with pre-gestational diabetes who attended the Tuen Mun Hospital between 1 January 2012 and 30 December 2022 for antenatal care and delivery. Composite adverse early perinatal outcomes included spontaneous fetal loss before 24 weeks and congenital malformations. Composite adverse maternal outcomes included pre-eclampsia and Caesarean section. Composite adverse neonatal outcomes included preterm delivery <37 weeks, small and large for gestational age, shoulder dystocia, hypoglycaemia, Apgar score <7 at 5 minutes, arterial cord blood pH <7.0, admission to a neonatal intensive care unit, stillbirth, and death within 28 days of life. Factors associated with adverse pregnancy outcomes were identified.
***Results:*** Among 245 women included in analysis, there were 10 spontaneous pregnancy losses before 24 weeks, four stillbirths, and 41 congenital malformations, which resulted in four terminations of pregnancy. The glycated haemoglobin (HbA1c) level at the first antenatal visit was a predictor for composite adverse early perinatal outcomes (adjusted odds ratio [aOR]=1.27, p=0.013). The rate of congenital anomaly increased threefold from 10% when the HbA1c level was <5.6% to 37.1% when the HbA1c level was >9.1% (p=0.003). Predictors for composite adverse maternal outcomes were a pre-pregnancy body mass index ≥25 kg/m$^2$ (aOR=2.04, p=0.033) and chronic hypertension (aOR=3.59, p=0.009), whereas the predictor for composite adverse neonatal outcomes were the HbA1c level before delivery (aOR=1.57, p=0.025). Pre-pregnancy medical care was associated with a lower maternal HbA1c level at the first antenatal visit (6.8% vs 8.2%, p=0.002) and earlier gestational age at the first antenatal visit (8 vs 12 weeks, p<0.001), compared with no pre-pregnancy medical care.
***Conclusion:*** Maternal glycaemic control and body mass index are the major modifiable risk factors for adverse pregnancy outcomes in women with pre-gestational diabetes. Pre-pregnancy medical care should emphasise lowering the HbA1c level and bodyweight at early pregnancy to avoid adverse pregnancy outcomes.

*Keywords: Congenital abnormalities; Diabetes mellitus; Glycated hemoglobin; Pregnancy complications*

## Introduction

The worldwide prevalence of pre-gestational diabetes has increased from 0.5% to 1% during the period 1990 to 2020 and ranges from 0.5% to 2.4% among different populations[1]. Factors associated with pre-gestational diabetes include obesity, type 2 diabetes, and advanced maternal age[1]. Pregnancies with pre-gestational diabetes are associated with an increased risk of adverse pregnancy outcomes including spontaneous abortion, congenital anomalies (cardiac malformations, neural tube defect, sacral agenesis, and caudal regression syndrome[2,3]), pre-eclampsia, Caesarean section, preterm delivery, macrosomia, low Apgar score at 5 minutes, neonatal hypoglycaemia, hyperbilirubinaemia, neonatal respiratory distress syndrome, stillbirth, neonatal death, and admission to a neonatal intensive care unit[4-8]. Pregnancy care for women with pre-gestational diabetes improves the maternal and perinatal outcomes[9,10].

Risk factors for adverse pregnancy outcomes in women with pre-gestational diabetes include a high glycated haemoglobin (HbA1c) level at the periconceptional period and in late pregnancy, a high pre-pregnancy body mass index (BMI), excessive gestational weight gain, lack of preconception care, nulliparity, low socioeconomic status, smoking, and the presence of microvascular disease (including diabetic nephropathy and retinopathy)[10-14]. We aimed to identify predictors associated with adverse

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pregnancy outcomes among women with pre-gestational diabetes in Hong Kong.

## Materials and methods

We retrospectively reviewed medical records of women with pre-gestational type 1 or type 2 diabetes who attended the Tuen Mun Hospital between 1 January 2012 and 30 December 2022 for antenatal care and delivery. Women with more than one pregnancy during the study period were analysed independently. Women were excluded if they had incomplete clinical data, diabetes first recognised during pregnancy, multiple pregnancies, or delivery in other hospitals.

According to our protocol, combined antenatal and diabetic care was provided weekly to fortnightly throughout the pregnancy by a multidisciplinary team that comprises obstetricians, endocrinologists, diabetes midwife specialists, and dietitians. Women were educated on the importance of good glycaemic control, proper techniques of capillary blood glucose monitoring (and insulin injection if required), and dietary advice. Diabetic control was assessed by daily self-monitoring of capillary blood glucose and the 3-monthly HbA1c level. Fetal outcomes were assessed using morphology scans, serial growth scans, and cardiotocography. Women were offered delivery from 38 weeks onward.

Pregnancy outcomes included spontaneous pregnancy loss before 24 weeks, termination of pregnancy, congenital malformations, and stillbirth. Maternal outcomes included polyhydramnios, pre-eclampsia, gestation, mode of delivery, primary postpartum haemorrhage, and admission to an intensive care unit. Neonatal outcomes included sex, birthweight, large and small for gestational age[15,16], Apgar scores, umbilical cord arterial blood pH, admission to a neonatal intensive care unit, shoulder dystocia, birth trauma (including brachial plexus injury and bone fracture), neonatal hypoglycaemia, neonatal hyperbilirubinaemia requiring phototherapy, transient tachypnoea, respiratory distress syndrome, cerebral palsy, and death within 28 days of life.

Composite adverse early perinatal outcomes included spontaneous fetal loss before 24 weeks and congenital malformations. Composite adverse maternal outcomes included pre-eclampsia and Caesarean section. Composite adverse neonatal outcomes included preterm delivery <37 weeks, small and large for gestational age, shoulder dystocia, hypoglycaemia, Apgar score <7 at 5 minutes, arterial cord blood pH <7.0, admission to a neonatal intensive care unit, stillbirth, and death within 28 days of life.

Women with or without composite adverse pregnancy outcomes were compared using the Student's *t* test or Mann-Whitney *U* test for continuous variables and the Chi-squared test or Fisher's exact test for categorical variables. Univariate and multivariate logistic regression analyses were performed to determine predictors for adverse pregnancy outcomes. Data analysis was performed using SPSS (Windows version 26.0; IBM Corp, Armonk [NY], United States). A p value of <0.05 was considered statistically significant.

## Results

Over the 11 years, the number of pre-gestational diabetes cases has increased from 4.05 to 5.83 per 1000 deliveries per year (Table 1). Of 389 women with pre-gestational diabetes managed in our unit, 144 were excluded because of diabetes first recognised during pregnancy (n=111), incomplete clinical data (n=11), unknown pregnancy outcomes (n=3), delivery in other hospitals (n=13), and multiple pregnancies (n=6). The remaining 245 women were included in the analysis.

Most (92.2%) of the women were Chinese. The median maternal age at delivery was 34 (interquartile range [IQR]=30-37) years (Table 2). Most (96.3%) pregnancies were conceived naturally; 45.3% were nulliparous. The median interval from diagnosis of diabetes to pregnancy was 4 (IQR=2-7) years; 91.0% had type 2 diabetes and

**Table 1. Numbers of pregnant women with pre-gestational diabetes per 1000 deliveries from 2012 to 2022**

| Year | No. of pregnant women with pre-gestational diabetes per 1000 deliveries | | |
|---|---|---|---|
| | Type 1 diabetes | Type 2 diabetes | Total |
| 2012 | 0.35 | 3.69 | 4.05 |
| 2013 | 0.59 | 3.74 | 4.34 |
| 2014 | 0.37 | 3.67 | 4.03 |
| 2015 | 0.18 | 3.87 | 4.05 |
| 2016 | 0.35 | 2.46 | 2.81 |
| 2017 | 0.38 | 3.23 | 3.61 |
| 2018 | 0.19 | 4.28 | 4.48 |
| 2019 | 0.41 | 4.31 | 4.72 |
| 2020 | 0.99 | 5.43 | 6.42 |
| 2021 | 0 | 5.66 | 5.66 |
| 2022 | 1.03 | 4.8 | 5.83 |

9.0% had type 1 diabetes. In addition, 65.3% had a BMI ≥25 kg/m$^2$ (33.9% overweight, 31.4% obese); 84.5% received pre-conception diabetic care; 11% had diabetic retinopathy; 13.5% had diabetic nephropathy; 0.4% had diabetic neuropathy; and 22.9% had chronic hypertension. Only 4.5% of the women were taking pre-conception folic acid. The median gestational age at booking visit was 8 (IQR=7-12) weeks. Dietary control was practised by 10.2% and 12.2% of women before and during pregnancy, respectively. Insulin use increased from 14.3% before pregnancy to 86.9% during pregnancy. At the first antenatal visit, the median HbA1c level was 7.0% (IQR=6.1-8.4%); 80 (32.7%) women had a HbA1c level <6.5%. At delivery, the median HbA1c level was 6.3% (IQR=5.9%-7.0%); 60 (26.0%) women had a HbA1c level <6.0%.

Among the 245 women, there were 10 (4.1%) spontaneous pregnancy losses before 24 weeks, four (1.6%) stillbirths, and 41 (16.7%) congenital malformations, which resulted in four (1.6%) terminations of pregnancy (Table 3). Details of the four stillbirths and one death within 28 days of life are shown in Table 4, whereas details of the 41 cases of congenital malformations are shown in Table 5. In women with pregnancy beyond 24 weeks (n=231), the median gestational age at delivery was 37 (IQR=36-38) weeks; 59 (25.5%) women had preterm delivery; 44 (19.0%) had pre-eclampsia; and 145 (62.8%) had a Caesarean section. With regard to neonates, the median birthweight was 3180 (IQR=2750-3620) g; 93 (40.3%) were large for gestational age; 19 (8.2%) were macrosomic (birthweight ≥4000 g); one (0.4%) had an Apgar score <7 at 5 minutes; one (0.4%) had umbilical cord arterial pH <7.0; one (0.4%) had shoulder dystocia; 61 (26.9%) had hypoglycaemia; 31 (13.7%) required admission to a neonatal intensive care unit; and one (0.4%) died within 28 days of life.

The HbA1c level at the first antenatal visit was a predictor for composite adverse early perinatal outcomes (adjusted odds ratio [aOR]=1.27, p=0.013, Table 6). The rate of congenital anomaly increased threefold from 10% when the HbA1c level was <5.6% to 37.1% when the HbA1c level was >9.1% (p=0.003, Table 7). Predictors for composite adverse maternal outcomes were a pre-pregnancy BMI ≥25 kg/m$^2$ (aOR=2.04, p=0.033) and chronic hypertension (aOR=3.59, p=0.009), whereas the predictor for composite adverse neonatal outcomes were the HbA1c level before delivery (aOR=1.57, p=0.025) [Table 6].

Pre-pregnancy medical care was associated with a lower maternal HbA1c level at the first antenatal visit (6.8% vs 8.2%, p=0.002) and earlier gestational age at the first antenatal visit (8 vs 12 weeks, p<0.001), compared with no pre-pregnancy medical care.

## Discussion

In the present study, predictors for adverse pregnancy outcomes were the HbA1c level at the first antenatal visit, pre-pregnancy BMI, chronic hypertension, and the HbA1c level before delivery. The rate of congenital anomaly was associated with the HbA1c level at the first antenatal visit, whereas pre-pregnancy medical care was associated with a lower HbA1c level and an earlier gestational age at the first antenatal visit.

The rate of congenital anomalies in our cohort was 16.7%, which is similar to the 14.4% reported in a study in Canada in 2021, which includes major and minor anomalies identified according to the International Classification of Diseases, 10th revision. In our cohort, 32.7% of women had a HbA1c level <6.5% during the periconceptional period; periconceptional HbA1c level was associated with congenital anomalies.

Women with pre-gestational diabetes are at four- to five-fold increased risk of stillbirth[17]. Maternal hyperglycaemia causes fetal hyperinsulinaemia, acidosis, and hyperlacticaemia leading to fetal distress[18]. Maternal and fetal hyperglycaemia may cause angiopathy that affects the uteroplacental blood vessels and leads to fetal hypoxia[19]. The rate of stillbirth in our cohort was 1.6%, which is similar to the rate reported in other studies[20,21]. Maternal blood glucose control is an important modifiable risk factors for stillbirth in mothers with diabetes. In our three cases of stillbirth (presumably related to poor glycaemic control), the HbA1c level at the first antenatal visit ranged from 7.1% to 8.8%, and the HbA1c level at delivery ranged from 6.2% to 8.1%. This highlights the importance of glycaemic control.

In our study, the HbA1c level at the first antenatal visit was associated with early pregnancy loss and congenital anomalies; the findings are consistent with those reported in studies in 1980s[22] and in Japan[23] and the United States[24]. High maternal HbA1c level is a major teratogenic agent, which affects the signalling pathways involved in organogenesis and fetal development. These results highlight the importance of periconceptional glycaemic control and pre-pregnancy medical care in reducing adverse pregnancy outcomes, as recommended by the American Diabetes Association[8].

**Table 2. Characteristics of women with pre-gestational diabetes (n=245)**

| Characteristic | Value* |
|---|---|
| Maternal age at delivery, y | 34 (30-37) |
| Ethnicity | |
| Chinese | 226 (92.2) |
| Southeast Asian | 17 (6.9) |
| African | 2 (0.8) |
| Education level | |
| Primary | 10 (4.1) |
| Secondary | 176 (71.8) |
| Tertiary | 59 (24.1) |
| Nulliparity | 111 (45.3) |
| Previous Caesarean section | 71 (29.0) |
| Type 1 diabetes | 22 (9.0) |
| Type 2 diabetes | 223 (91.0) |
| Smoking | 18 (7.3) |
| Drinking | 2 (0.8) |
| Natural conception | 236 (96.3) |
| Planned pregnancy | 125 (51.0) |
| Duration of diabetes, y | 4 (2-7) |
| Pre-pregnancy body mass index, kg/m$^2$ | 26.9 (23.6-31.3) |
| 25-29.9 (overweight) | 83 (33.9) |
| ≥30 (obese) | 77 (31.4) |
| Pre-conception medical care | 207 (84.5) |
| Pre-pregnancy diabetic treatment | |
| Dietary control alone | 25 (10.2) |
| Oral medication | 122 (49.8) |
| Insulin | 35 (14.3) |
| Oral medication and insulin | 27 (11.0) |
| Pre-conception folic acid | 11 (4.5) |
| Diabetic retinopathy | 27 (11.0) |
| Diabetic nephropathy | 33 (13.5) |
| Diabetic neuropathy | 1 (0.4) |
| Chronic hypertension | 56 (22.9) |
| Gestational age at first antenatal visit, wk | 8 (7-12) |
| Glycated haemoglobin at first antenatal visit, % | 7.0 (6.1-8.4) |
| <6.5 | 80 (32.7) |
| ≥6.5 | 165 (67.3) |
| Glycated haemoglobin at delivery, % (excluding cases of miscarriage and pregnancy termination) | 6.3 (5.9-7.0) |
| <6.0 | 60 (26.0) |
| ≥6.0 | 171 (74.0) |
| Diabetic treatment during pregnancy | |
| Dietary control only | 30 (12.2) |
| Oral medication | 1 (0.4) |
| Insulin | 213 (86.9) |
| Oral medication and insulin | 1 (0.4) |
| Increment in insulin during pregnancy, units/day | 22 (7-42) |

* Data are expressed as median (interquartile range) or No. (%) of patients

**Table 3. Pregnancy, maternal, and neonatal outcomes of women with pre-gestational diabetes**

| Outcome | Value* |
|---|---|
| **Pregnancy outcome** | **n=245** |
| Spontaneous pregnancy loss before 24 weeks | 10 (4.1) |
| Termination of pregnancy | 4 (1.6) |
| Stillbirth | 4 (1.6) |
| Livebirth | 227 (92.7) |
| Pregnancy with congenital malformation | 41 (16.7) |
| **Maternal outcome** | **n=231** |
| Polyhydramnios | 14 (6.1) |
| Pre-eclampsia | 44 (19.0) |
| Gestational age at delivery, wk | 37 (36-38) |
| Preterm delivery <37 weeks | 59 (25.5) |
| Preterm delivery <34 weeks | 21 (9.1) |
| Mode of delivery | |
| Normal vaginal delivery | 73 (31.6) |
| Instrumental delivery | 13 (5.6) |
| Caesarean section | 145 (62.8) |
| Primary Caesarean section | 84 (36.4) |
| Primary postpartum haemorrhage (≥500 ml) | 64 (27.7) |
| Intensive care unit admission | 4 (1.7) |
| **Neonatal outcome** | **n=231** |
| Male sex | 139 (60.2) |
| Birthweight, g | 3180 (2750-3620) |
| Macrosomia (≥4000 g) | 19 (8.2) |
| Birthweight percentiles | |
| Large for gestational age | 93 (40.3) |
| Small for gestational age | 11 (4.8) |
| Apgar score | **n=227** |
| 1 minute | 8 (8-8) |
| 5 minutes | 9 (9-9) |
| Low Apgar score <7 at 5 minutes | 1 (0.4) |
| Umbilical cord arterial pH <7.0 | 1 (0.4) |
| Admission to neonatal intensive care unit | 31 (13.7) |
| Shoulder dystocia | 1 (0.4) |
| Birth trauma (brachial plexus injury, bone fracture) | 0 |
| Neonatal hypoglycaemia | 61 (26.9) |
| Neonatal hyperbilirubinaemia requiring phototherapy | 86 (37.9) |
| Transient tachypnoea of the newborn | 7 (3.1) |
| Respiratory distress syndrome | 18 (7.9) |
| Cerebral palsy | 1 (0.4) |
| Neonatal death within 28 days | 1 (0.4) |

* Data are expressed as median (interquartile range) or No. (%) of patients

**Table 4. Details of four stillbirths and one neonatal death**

| Characteristic | Case 1 | Case 2 | Case 3 | Case 4 | Case 5 |
|---|---|---|---|---|---|
| Age at delivery, y | 34 | 31 | 38 | 27 | 43 |
| Race | Chinese | Chinese | Chinese | Southeast Asian | Chinese |
| Education level | Secondary | Secondary | Secondary | Secondary | Secondary |
| Smoker | No | No | No | No | No |
| Gravidity | 2 | 1 | 2 | 3 | 3 |
| Parity | 1 | 0 | 1 | 2 | 0 |
| History of pregnancy loss | No | No | No | No | Two (2nd trimester) |
| Consanguineous relationship | No | No | No | No | No |
| Previous Caesarean section | Yes | No | Yes | No | No |
| Type of diabetes | 2 | 1 | 2 | 2 | 2 |
| Duration of diabetes, y | 3 | 13 | 3 | 0.5 | 2 |
| Planned pregnancy | No | No | No | Yes | No |
| Method of conception | Natural | Natural | Natural | Natural | Natural |
| Pre-pregnancy body mass index, kg/m$^2$ | 28.6 | 17.3 | 32.8 | 35.7 | 26.0 |
| Pre-pregnancy medical care | No | Yes | Yes | Yes | Yes |
| Comorbidity | Chronic hypertension, hyperlipidaemia, nephropathy, polycystic ovarian syndrome | No | Chronic hypertension, hyperlipidaemia | Chronic hypertension | History of loop electrosurgical excision procedure for cervical intraepithelial neoplasia III, cervical incompetence (cerclage performed), polycystic ovarian syndrome |
| Gestational age at first antenatal visit, wk | 17 | 6 | 10 | 11 | 9 |
| Glycated haemoglobin, % | | | | | |
| Pre-pregnancy | - | 11.1 | 6.2 | 10.1 | - |
| First trimester | - | 8.8 | 7.1 | 7.9 | 5.8 |
| Second trimester | 7.5 | 7.1 | 6 | 6.9 | 5.7 |
| Third trimester | 6.2 | 8.1 | 5.9 | 8.1 | - |
| Diabetic treatment before conception | No | Insulin | Oral hypoglycaemic agent | Oral hypoglycaemic agent | Oral hypoglycaemic agent |
| Presence of folate supplementation | No | No | No | No | No |
| Aspirin use | Yes | No | No | No | No |
| Diabetic treatment during pregnancy | | | | | |
| At first trimester | No | Insulin | Oral hypoglycaemic agent | Insulin | Insulin |
| At second trimester | Insulin | Insulin | Oral hypoglycaemic agent | Insulin | Insulin |
| At third trimester | Insulin | Insulin | Oral hypoglycaemic agent | Insulin | - |
| Compliance to antenatal follow-up/treatment | Poor, occasional hyperglycaemia | Poor, occasional hypoglycaemia | Good | Poor, occasional hyperglycaemia | Good |

**Table 4. (cont'd)**

| Characteristic | Case 1 | Case 2 | Case 3 | Case 4 | Case 5 |
|---|---|---|---|---|---|
| Antenatal ultrasound finding | Polyhydramnios | Large for gestational age | Large for gestational age | Large for gestational age | Normal |
| Antenatal complication | No | Threatened preterm labour at 28 weeks | No | No | Antepartum haemorrhage, preterm premature rupture of the membranes, intrauterine infection |
| Mode of delivery (indication) | Vaginal delivery | Vaginal delivery | Caesarean section (previous Caesarean section) | Caesarean section (macrosomia) | Vaginal delivery |
| Gestational age at stillbirth/delivery, wk | 30 | 35 | 34 | 36 | 25 |
| Birthweight at delivery, g | 1486 (50th-90th centile) | 2600 (50th-90th centile) | 2940 (>90th centile) | 4220 (>90th centile) | 670 (10th-50th centile) |
| Perinatal/neonatal outcome | Stillbirth | Stillbirth | Stillbirth | Stillbirth | Neonatal death |
| Likely cause of stillbirth/ neonatal death | Suboptimal glycaemic control | Suboptimal glycaemic control | Congenital leukaemia | Suboptimal glycaemic control | Prematurity, respiratory distress syndrome, necrotising enterocolitis, sepsis, disseminated intravascular coagulation, neonatal death at day 14 |
| Postmortem examination | Right microtia, aortopulmonary window, 11 pairs of ribs | No | Placental histopathology: B-lymphoblastic leukaemia | No | No |

**Table 5. Details of the 41 cases of congenital malformations**

| Classification by the International Classification of Diseases, 10th revision | No. (%) of cases |
|---|---|
| Q00-07: Congenital malformations of the nervous system | 1 (2.4) |
| Q05: Spina bifida | 1 (2.4) |
| Q10-Q18: Congenital malformations of eye, ear, face, and neck | 2 (4.9) |
| Q17: Other congenital malformations of ear | 2 (4.9) |
| Q17.2: Microtia | 1 (2.4) |
| Q17.4: Misplaced ear | 1 (2.4) |
| Q20-Q28: Congenital malformations of the circulatory system | 36 (87.8) |
| Q21: Congenital malformations of cardiac septa | 23 (56.1) |
| Q21.0: Ventricular septal defect | 7 (17.1) |
| Q21.1: Atrial septal defect | 14 (34.1) |
| Q21.3: Tetralogy of Fallot | 1 (2.4) |
| Q21.4: Aortopulmonary septal defect | 1 (2.4) |
| Q25: Congenital malformations of great arteries | 9 (22.0) |
| Q25.0: Patent ductus arteriosus | 6 (14.6) |
| Q25.4: Other congenital malformations of aorta | 1 (2.4) |
| Q25.5: Atresia of pulmonary artery | 1 (2.4) |
| Q25.6: Stenosis of pulmonary artery | 1 (2.4) |
| Q26: Congenital malformations of great veins | 1 (2.4) |
| Q26.1: Persistent left superior vena cava | 1 (2.4) |
| Q27: Other congenital malformations of peripheral vascular system | 3 (7.3) |
| Q27.0: Congenital absence and hypoplasia of umbilical artery | 3 (7.3) |

* Data are presented as No. (%) of pregnancies

**Table 5. (cont'd)**

| Classification by the International Classification of Diseases, 10th revision | No. (%) of cases |
|---|---|
| Q30-Q34: Congenital malformations of the respiratory system | 0 |
| Q35-37: Cleft lip and cleft palate | 1 (2.4) |
| Q36: Cleft lip | 1 (2.4) |
| Q36.9: Cleft lip, unilateral | 1 (2.4) |
| Q38-Q45: Other congenital malformations of the digestive system | 1 (2.4) |
| Q42: Congenital absence, atresia, and stenosis of large intestine | 1 (2.4) |
| Q42.2: Congenital absence, atresia, and stenosis of anus with fistula | 1 (2.4) |
| Q50-Q56: Congenital malformations of genital organs | 3 (7.3) |
| Q53: Undescended testicle | 2 (4.9) |
| Q53.1: Undescended testicle, unilateral | 1 (2.4) |
| Q53.2: Undescended testicle, bilateral | 1 (2.4) |
| Q55: Other congenital malformations of male genital organs | 1 (2.4) |
| Q55.4: Other congenital malformations of vas deferens, epididymis, seminal vesicles, and prostate | 1 (2.4) |
| Q60-Q64: Congenital malformations of the urinary system | 8 (19.5) |
| Q60: Renal agenesis and other reduction defects of kidney | 1 (2.4) |
| Q60.3: Renal hypoplasia, unilateral | 1 (2.4) |
| Q61: Cystic kidney disease | 1 (2.4) |
| Q61.0: Congenital single renal cyst | 1 (2.4) |
| Q62: Congenital obstructive defects of renal pelvis and congenital malformations of ureter | 4 (9.8) |
| Q62.0: Congenital hydronephrosis | 4 (9.8) |
| Q63: Other congenital malformations of kidney | 2 (4.9) |
| Q63.1: Lobulated, fused, and horseshoe kidney | 1 (2.4) |
| Q63.2: Ectopic kidney | 1 (2.4) |
| Q65-Q79: Congenital malformations and deformations of the musculoskeletal system | 15 (36.6) |
| Q66: Congenital deformities of feet | 2 (4.9) |
| Q66.4: Talipes calcaneovalgus | 1 (2.4) |
| Q66.8: Other congenital deformities of feet | 1 (2.4) |
| Q67: Congenital musculoskeletal deformities of head, face, spine, and chest | 1 (2.4) |
| Q67.5: Congenital deformity of spine | 1 (2.4) |
| Q69: Polydactyly | 8 (19.5) |
| Q69.1: Accessory thumb(s) | 6 (14.6) |
| Q69.2: Accessory toe(s) | 2 (4.9) |
| Q72: Reduction defects of lower limb | 2 (4.9) |
| Q72.3: Congenital absence of foot and toe(s) | 1 (2.4) |
| Q72.4: Longitudinal reduction defect of femur | 1 (2.4) |
| Q76: Congenital malformations of spine and bony thorax | 2 (4.9) |
| Q76.6: Other congenital malformations of ribs | 2 (4.9) |
| Q80-Q89: Other congenital malformations | 2 (4.9) |
| Q85: Phacomatoses, not elsewhere classified | 1 (2.4) |
| Q85.0: Neurofibromatosis (non-malignant) | 1 (2.4) |
| Q89: Other congenital malformations, not elsewhere classified | 1 (2.4) |
| Q89.2: Congenital malformations of other endocrine glands | 1 (2.4) |
| Q90-Q99: Chromosomal abnormalities, not elsewhere classified | 0 |

**Table 6. Predictors for adverse pregnancy outcome in women with pre-gestational diabetes**

| Outcome | With adverse outcome* | Without adverse outcome* | Odds ratio (95% confidence interval) | p Value | Adjusted odds ratio (95% confidence interval) | p Value |
|---|---|---|---|---|---|---|
| Composite adverse early perinatal outcome | n=51 | n=194 | | | | |
| Advanced maternal age | 22 (43.1) | 86 (44.3) | 0.953 (0.51-1.78) | 0.879 | 1.01 (0.52-1.96) | 0.981 |
| Type 1 diabetes | 4 (7.8) | 18 (9.3) | 0.832 (0.27-2.58) | >0.99 | 0.79 (0.23-2.80) | 0.720 |
| Pre-pregnancy overweight/obesity | 34 (66.7) | 126 (64.9) | 1.08 (0.56-2.1) | 0.819 | 1.15 (0.55-2.40) | 0.705 |
| Pre-conceptional folic acid | 21 (41.2) | 82 (42.3) | 0.96 (0.51-1.79) | 0.888 | 1.08 (0.22-5.31) | 0.927 |
| Glycated haemoglobin at first antenatal visit | 7.3 (6.6-9.2) | 6.9 (6.1-8.1) | 1.25 (1.05-1.50) | 0.015 | 1.27 (1.05-1.53) | 0.013 |
| Composite adverse maternal outcome | n=153 | n=78 | | | | |
| Advanced maternal age | 71 (46.4) | 29 (37.2) | 1.46 (0.84-2.56) | 0.181 | 1.16 (0.62-2.18) | 0.647 |
| Type 1 diabetes | 10 (6.5) | 11 (14.1) | 0.43 (0.17-1.05) | 0.059 | 0.66 (0.22-1.99) | 0.457 |
| Pre-pregnancy overweight/obesity | 111 (72.5) | 39 (50.0) | 2.64 (1.50-4.67) | 0.001 | 2.04 (1.06-3.94) | 0.033 |
| Nulliparity | 69 (45.1) | 36 (46.2) | 0.96 (0.55-1.66) | 0.879 | 1.04 (0.56-1.94) | 0.907 |
| Chronic hypertension | 47 (30.7) | 6 (7.7) | 5.32 (2.16-13.10) | <0.001 | 3.59 (1.38-9.31) | 0.009 |
| Use of aspirin | 72 (47.1) | 30 (38.5) | 1.42 (0.82-2.48) | 0.213 | 1.28 (0.69-2.38) | 0.439 |
| Glycated haemoglobin at first antenatal visit | 7.2 (6.3-8.6) | 6.7 (5.9-7.7) | 1.16 (0.97-1.39) | 0.099 | 1.19 (0.96-1.49) | 0.120 |
| Glycated haemoglobin before delivery | 6.3 (6.0-7.1) | 6.2 (5.9-6.8) | 1.14 (0.87-1.50) | 0.338 | 1.07 (0.76-1.51) | 0.684 |
| Composite adverse neonatal outcome | n=155 | n=76 | | | | |
| Advanced maternal age | 62 (40.0) | 38 (50.0) | 0.67 (0.38-1.16) | 0.150 | 0.65 (0.36-1.20) | 0.166 |
| Type 1 diabetes | 14 (9.0) | 7 (9.2) | 0.98 (0.38-2.54) | 0.965 | 0.85 (0.28-2.58) | 0.772 |
| Pre-pregnancy overweight/obesity | 105 (67.7) | 45 (59.2) | 1.45 (0.82-2.55) | 0.202 | 1.66 (0.85-3.25) | 0.137 |
| Chronic hypertension | 40 (25.8) | 13 (17.1) | 1.69 (0.84-3.39) | 0.139 | 1.47 (0.69-3.12) | 0.324 |
| Glycated haemoglobin at first antenatal visit | 7.2 (6.2-8.8) | 6.8 (6.0-7.6) | 1.32 (1.09-1.60) | 0.005 | 1.15 (0.91-1.43) | 0.238 |
| Glycated haemoglobin before delivery | 6.4 (6.0-7.3) | 6.1 (5.8-6.5) | 1.75 (1.25-2.46) | 0.001 | 1.57 (1.06-2.33) | 0.025 |

* Data are presented as No. (%) of participants or median (interquartile range)

**Table 7. Association of congenital anomaly with maternal glycated haemoglobin at first antenatal visit in women with pre-gestational diabetes**

| Glycated haemoglobin at first antenatal visit, % | % of congenital anomaly |
|---|---|
| <5.6 | 10 |
| 5.7-6.5 | 10.1 |
| 6.6-7.8 | 16.7 |
| 7.9-9.1 | 14 |
| >9.1 | 37.1 |

In our study, maternal pre-pregnancy BMI and chronic hypertension were predictors for adverse maternal outcomes. Maternal obesity is associated with hypertensive disorders and Caesarean sections in mothers with diabetes[25]. Chronic hypertension is a well-established risk factor for pre-eclampsia. Although chronic hypertension is considered a non-modifiable risk factor, optimising pre-pregnancy BMI and strict compliance with low-dose aspirin for pre-eclampsia prevention are recommended for reduction of maternal complications.

The HbA1c level at delivery was a predictor of adverse neonatal outcomes. Hyperinsulinaemia causes excessive fetal growth and macrosomia and is associated with shoulder dystocia, birth trauma, respiratory distress syndrome, neonatal hypoglycaemia, hyperbilirubinaemia, and polycythaemia[26]. In our study, the median HbA1c level at delivery was 6.3%. In our cohort, 40.3% of neonates had excessive growth; 8.2% had macrosomia; 26.9% had neonatal hypoglycaemia; and 37.9% had jaundice requiring phototherapy. There was room for improvement in glycaemic control because only 26.0% of women could reduce their HbA1c level to <6.0% at delivery, which was the optimal level recommended by the American Diabetes Association[8].

We recommend that women of reproductive age with diabetes should be educated about the importance of periconceptional folate intake, optimisation of BMI, and glycaemic control to the HbA1c level of <6.5% before conception. Effective contraception should be conducted until the general health condition and the HbA1c level are optimised[8]. Compliance with pre-pregnancy medical care can reduce congenital malformations, early HbA1c level, and adverse maternal and fetal outcomes[9,10,27,28]. Pregnant women with pre-gestational diabetes should be managed by a multidisciplinary team to facilitate timely and personalised care in dietetic counselling, insulin injection technique and titration, early dating by ultrasound for timely start of low-dose aspirin regimen for pre-eclampsia prevention, and routine obstetric care. In hindsight, more aggressive glycaemic control should have been aimed, and women should have been made aware of the HbA1c target of <6.0%. Daily self-monitoring of blood glucose should be emphasised to women with pre-gestational diabetes[29].

To the best of our knowledge, this is the first study to identify predictors of adverse pregnancy outcomes in women with pre-gestational diabetes in Hong Kong. Nonetheless, there were limitations to our study. It was a retrospective cohort study, and some data were missing. The pre-pregnancy BMI was self-reported. Analyses for each adverse outcome were not performed because of the small sample sizes; this can be overcome by inclusion of women from multiple centres. The presence of maternal hypoglycaemia was not recorded, although it could lead to adverse outcomes.

## Conclusion

Predictors for adverse pregnancy outcomes were HbA1c level, pre-pregnancy BMI, and chronic hypertension. Women should be educated about the pre-pregnancy medical care for diabetes and the aggressive glycaemic control throughout pregnancy to optimise maternal, fetal, and neonatal outcomes.

## Contributors

TCL, PLS, and LTK designed the study. TCL, PLS, and DYC acquired and analysed the data. TCL drafted the manuscript. All authors critically revised the manuscript for important intellectual content. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

## Conflicts of interest

All authors have no conflicts of interest to disclose.

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## Data availability

All data generated or analysed during the present study are available from the corresponding author on reasonable request.

## Ethics approval

The study was approved by the Central Institutional Review Board of Hospital Authority (reference: CIRB-2023-052-1). The patients were treated in accordance with the tenets of the Declaration of Helsinki. The patients provided written informed consent for all treatments and procedures and for publication.

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# Uterine artery ligation as the first-line surgical treatment for postpartum haemorrhage during Caesarean section: a retrospective study

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***Objective:*** To examine the efficacy of uterine artery ligation (UAL) with or without subsequent haemostatic procedures in management of postpartum haemorrhage (PPH) during Caesarean section.
***Methods:*** Women who underwent UAL with or without subsequent haemostatic procedures were compared in terms of maternal demographics, antenatal risk factors, delivery details, causes of PPH, sequence of treatment modalities used, and short-term complications.
***Results:*** A total of 173 women underwent UAL with or without subsequent haemostatic procedures. The success rate of haemostasis was 96.5% (167/173) after UAL with or without subsequent haemostatic procedures; it was 81.5% (141/173) after UAL alone. Multivariate analysis revealed that women with prior PPH had a higher risk for haemostasis failure after UAL alone (adjusted odds ratio [aOR]=10.35, p=0.027), whereas women with placenta praevia had a lower risk for haemostasis failure after UAL alone (aOR=0.05, p=0.001). Compared with UAL alone, UAL followed by haemostatic procedures resulted in a higher risk of postoperative complications including haemorrhagic shock (p=0.012), disseminated intravascular coagulopathy (p<0.001), and intensive care unit admission (p<0.001). There were five cases of bowel injury and one case of pelvic vessel injury.
***Conclusion:*** UAL is an effective and safe first-line surgical procedure for management of PPH during Caesarean section, especially for women with placenta praevia.

*Keywords: Postpartum hemorrhage; Treatment outcome; Uterine artery*

## Introduction

Postpartum haemorrhage (PPH) is defined as blood loss ≥500 ml after delivery; it accounts for 27% of maternal deaths worldwide each year[1,2]. Common causes of primary PPH include uterine atony, genital tract trauma, retained products of conception, and coagulopathy.

In the event of failed haemostasis after medical treatment, in haemodynamically stable women, various uterine-sparing procedures (including intrauterine balloon tamponade, compression sutures, uterine artery ligation [UAL], stepwise uterine devascularisation, and pelvic artery embolisation) should be considered before a hysterectomy is performed[3]. Specifically, UAL, the first step in stepwise uterine devascularisation, can reduce 90% of blood flow to the uterus. It is a simple surgical procedure and has a haemostasis success rate ranging from 42% to 97%[3]. UAL is safe and associated with a few short-term complications such as retroperitoneal haematoma and arteriovenous malformation secondary to vessel injury[4,5]. Therefore, UAL is proposed as the first-line surgical procedure for PPH refractory to medical treatment[6]. Combinations of various uterine-sparing techniques have also been reported[7]. This study aimed to evaluate the efficacy of UAL with or without subsequent haemostatic procedures for management of PPH during Caesarean section.

## Materials and methods

We retrospectively reviewed medical records of women who underwent UAL with or without subsequent haemostatic procedures for management of primary PPH during Caesarean section at Tuen Mun Hospital between 1 January 2008 and 31 December 2023. Patients with an antenatal diagnosis of placenta accreta were excluded because they opted for a Caesarean hysterectomy if the placenta failed to separate spontaneously. Data collected included demographics, antenatal risk factors, delivery details, causes of PPH, sequence of treatment modalities used, and complications.

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Before delivery of placenta during Caesarean section, routine prophylactic uterotonics of synthetic intravenous oxytocin was administered, and intravenous carbetocin and 40 IU of oxytocin infusion were given to women with risk factors for haemorrhage. Routine prophylactic antibiotics were administered before Caesarean section (1 g of intravenous cefazolin) and after uterine-sparing treatment (750 mg of intravenous cefuroxime and 500 mg of intravenous metronidazole).

UAL was performed unilaterally or bilaterally, depending on the degree of haemostasis and disease pathology. The uterus was exteriorised, and the bladder was reflected until 3 to 4 cm below the uterine incision site. Ligation was made with no. 1 Vicryl (polyglactin 910) and placed 2 to 3 cm below the level of the uterine incision through the myometrium (but not into the uterine cavity) and exited at the avascular area of the broad ligament. If UAL failed, subsequent haemostatic procedures and their sequence were decided on by senior obstetricians. For compression sutures, both the B-Lynch suture and the Hayman suture were performed with no. 1 Monocryl (polyglecaprone 25), whereas the Cho suture was performed with no. 1 Vicryl (polyglactin 910). Pelvic artery embolisation with gelatine sponges was performed by an interventional radiologist. Postnatally, pelvic examination and ultrasound were performed to assess short-term complications.

Data were analysed using SPSS (Windows version 21.0; IBM Corp, Armonk [NY], United States). Women who underwent UAL with or without subsequent haemostatic procedures were compared using the Student's *t* test or Mann-Whitney *U* test for continuous variables and the Chi-squared test or Fisher's exact test for categorical variables. Univariate and multivariate analyses were performed to identify factors associated with successful haemostasis after UAL alone. A p value of <0.05 was considered statistically significant.

## Results

Over the 16 years, 173 women underwent UAL with or without subsequent haemostatic procedures for management of PPH during Caesarean section. Of these, 141 (81.5%) achieved haemostasis after UAL alone and 32 (18.5%) required subsequent haemostatic procedures. Of the latter, 30 underwent compression suture with the B-Lynch suture (n=15), Hayman suture (n=13) or Cho suture (n=2), and two underwent hysterectomy. After the compression suture, one woman required pelvic embolisation and four women required hysterectomy. The primary causes of PPH in the six women who required hysterectomy were uterine atony (n=2), placenta praevia (n=2), and placenta accreta (n=2). All the six women experienced persistent uterine atony, coagulopathy, or unstable haemodynamics.

In terms of the primary cause of PPH, UAL alone could achieve haemostasis in 92.5% (74/80) of women with placenta praevia, 87.5% (21/24) of women with tears over the uterine incision during Caesarean section, 86.2% (25/29) of women with placenta accreta, 66.7% (2/3) of women with coagulopathy, and 51.4% (19/37) of women with uterine atony.

Compared with women who required subsequent haemostatic procedures, women with UAL alone were associated with a higher rate of regional anaesthesia (38.3% vs 15.6%, p=0.015) and a lower rate of conversion to general anaesthesia (9.2% vs 25.0%, p=0.030). More women with placenta praevia underwent UAL alone (52.5% vs 18.8%, p=0.001), whereas more women with uterine atony required subsequent haemostatic procedures (56.3% vs 13.5%, p<0.001). More women who required subsequent haemostatic procedures received bilateral UAL (100% vs 85.8%, p=0.027), had longer surgical time (149 vs 83 minutes, p<0.001), more total blood loss (3800 vs 1900 ml, p<0.001), and lower intra-/post-operative haemoglobin level (7.2 vs 8.3 g/dl, p<0.001), and required more units of blood product transfusion (red blood cells: 5 vs 2, p<0.001; platelets: 4 vs 0, p<0.001; fresh frozen plasma: 4 vs 0, p<0.001) and additional medical treatment (recombinant factor VIIa: 12.5% vs 0.7%, p=0.004; carboprost: 93.8% vs 75.2%, p=0.021).

Compared with women with UAL alone, women who required subsequent haemostatic procedures had higher rates of haemorrhagic shock (15.6% vs 2.8%, p=0.012), disseminated intravascular coagulopathy (46.9% vs 9.9%, p<0.001), re-laparotomy (15.6% vs 1.4%, p=0.003), paralytic ileus (18.8% vs 4.3%, p=0.010), inotropic support (34.4% vs 2.8%, p <0.001), and admission to an intensive care unit (78.1% vs 23.4%, p<0.001), as well as longer duration of hospitalisation (median, 5.5 vs 4 days, p<0.001).

Multivariate analysis showed that prior PPH was a predictor for UAL failure (adjusted odds ratio [aOR]=10.35, 95% confidence interval [CI]=1.30-82.29, p=0.027), whereas placenta praevia was a predictor for successful haemostasis after UAL alone (aOR=0.05, 95% CI=0.01-0.32, p=0.001) [Table].

**Table. Characteristics and outcomes of women who underwent uterine artery ligation (UAL) with or without subsequent haemostatic procedures for postpartum haemorrhage (PPH) during Caesarean section**

| Characteristic | UAL alone (n=141)* | UAL with subsequent haemostatic procedures (n=32)* | Odds ratio (95% confidence interval) | p Value | Adjusted odds ratio (95% confidence interval) | p Value |
|---|---|---|---|---|---|---|
| Maternal age ≥35 y | 67 (47.5) | 13 (40.6) | 0.76 (0.35-1.65) | 0.480 | 1.12 (0.36-3.50) | 0.851 |
| Body mass index ≥25 kg/m$^2$ | 32 (22.7) | 5 (15.6) | 0.63 (0.23-1.77) | 0.379 | 0.32 (0.07-1.45) | 0.138 |
| Nulliparity | 46 (32.6) | 19 (59.4) | 3.02 (1.37-6.64) | 0.005 | 3.35 (0.86-13.05) | 0.081 |
| Previous Caesarean section | 44 (31.2) | 7 (21.9) | 0.62 (0.25-1.54) | 0.296 | 0.22 (0.04-1.21) | 0.081 |
| Prior PPH | 5 (3.5) | 4 (12.5) | 3.89 (0.98-15.39) | 0.062 | 10.35 (1.30-82.29) | 0.027 |
| Assisted conception | 14 (9.9) | 6 (18.8) | 2.09 (0.74-5.95) | 0.216 | 2.45 (0.38-15.77) | 0.346 |
| Multiple pregnancy | 6 (4.3) | 6 (18.8) | 5.19 (1.55-17.36) | 0.010 | 2.70 (0.34-21.26) | 0.347 |
| Polyhydramnios | 1 (0.7) | 0 | - | >0.99 | - | >0.99 |
| Uterine fibroid/adenomyosis | 13 (9.2) | 5 (15.6) | 1.82 (0.60-5.54) | 0.334 | 2.18 (0.40-11.88) | 0.369 |
| History of antepartum haemorrhage | 68 (48.2) | 12 (37.5) | 0.64 (0.29-1.42) | 0.272 | 0.73 (0.16-3.42) | 0.690 |
| Hypertensive disorders of pregnancy | 4 (2.8) | 5 (15.6) | 6.34 (1.60-25.16) | 0.012 | 4.81 (0.52-44.60) | 0.167 |
| Fetal macrosomia | 8 (5.7) | 1 (3.1) | 0.54 (0.07-4.45) | >0.99 | 0.42 (0.03-5.26) | 0.502 |
| Preterm delivery | 64 (45.4) | 10 (31.3) | 0.55 (0.24-1.24) | 0.144 | 1.03 (0.23-4.65) | 0.974 |
| Preoperative haemoglobin <10.5 g/dl | 26 (18.4) | 5 (15.6) | 0.82 (0.29-2.33) | 0.708 | 0.73 (0.15-3.63) | 0.701 |
| Reason for Caesarean section | | | | | | |
| Placenta praevia | 98 (69.5) | 7 (21.9) | 0.12 (0.05-0.31) | <0.001 | 0.05 (0.01-0.32) | 0.001 |
| Abruptio placentae | 2 (1.4) | 6 (18.8) | 16.04 (3.07-83.86) | 0.001 | 5.67 (0.37-88.00) | 0.215 |
| Intrauterine infection | 3 (2.1) | 0 | - | >0.99 | - | >0.99 |
| Labour progress failure | 6 (4.3) | 4 (12.5) | 3.21 (0.85-12.14) | 0.090 | 0.59 (0.08-4.63) | 0.619 |
| Non-reassuring fetal status | 6 (4.3) | 4 (12.5) | 3.21 (0.85-12.14) | 0.090 | 1.11 (0.15-8.15) | 0.922 |
| Anaesthesia | | | | | | |
| Regional | 54 (38.3) | 5 (15.6) | - | 0.015 | - | - |
| General | 74 (52.5) | 19 (59.4) | - | 0.480 | - | - |
| Conversion from regional to general | 13 (9.2) | 8 (25.0) | - | 0.030 | - | - |
| Type of Caesarean section | | | | | | |
| Elective lower segment | 44 (31.2) | 8 (25.0) | - | 0.489 | - | - |
| Emergency lower segment | 93 (66.0) | 23 (71.9) | - | 0.520 | - | - |
| Emergency classical | 4 (2.8) | 1 (3.1) | - | >0.99 | - | - |
| Primary cause of postpartum haemorrhage | | | | | | |
| Uterine atony | 19 (13.5) | 18 (56.3) | - | <0.001 | - | - |
| Uterine tear | 21 (14.9) | 3 (9.4) | - | 0.575 | - | - |
| Placenta praevia | 74 (52.5) | 6 (18.8) | - | 0.001 | - | - |
| Placenta accreta | 25 (17.7) | 4 (12.5) | - | 0.475 | - | - |
| Coagulopathy | 2 (1.4) | 1 (3.1) | - | 0.461 | - | - |
| Laterality of UAL | | | | 0.027 | | - |
| Bilateral | 121 (85.8) | 32 (100) | - | | - | - |
| Unilateral | 20 (14.2) | 0 (0) | - | | - | - |

* Data are presented as No. (%) of patients or median (range)

**Table. (cont'd)**

| Characteristic | UAL alone (n=141)* | UAL with subsequent haemostatic procedures (n=32)* | Odds ratio (95% confidence interval) | p Value | Adjusted odds ratio (95% confidence interval) | p Value |
|---|---|---|---|---|---|---|
| Haemostatic procedure | | | | - | | - |
| Compression suture | - | 30 (93.8) | - | | - | |
| Pelvic embolisation | - | 1 (3.1) | - | | - | |
| Hysterectomy | - | 6 (18.8) | - | | - | |
| Duration of surgery, min | 83 (38-235) | 149 (66-339) | - | <0.001 | - | - |
| Estimated blood loss, ml | 1900 (400-6350) | 3800 (1400-12000) | - | <0.001 | - | - |
| Blood product used | | | | | | |
| Red blood cells, units | 2 (0-9) | 5 (1-22) | - | <0.001 | - | - |
| Platelets, units | 0 (0-8) | 4 (0-16) | - | <0.001 | - | - |
| Fresh frozen plasma, units | 0 (0-10) | 4 (0-18) | - | <0.001 | - | - |
| Cryoprecipitate, units | 0 (0-10) | 0 (0-6) | - | 0.935 | - | - |
| Fibrinogen | 9 (6.4) | 5 (15.6) | - | 0.141 | - | - |
| Recombinant factor VIIa | 1 (0.7) | 4 (12.5) | - | 0.004 | - | - |
| Use of uterotonics | | | | | | |
| Oxytocin/ergometrine | 88 (62.4) | 22 (68.8) | - | 0.501 | - | - |
| Carboprost | 106 (75.2) | 30 (93.8) | - | 0.021 | - | - |
| Use of tranexamic acid | 63 (44.7) | 20 (62.5) | - | 0.069 | - | - |
| Preoperative haemoglobin, g/dl | 11.7 (8.9-14.2) | 11.4 (8.6-15.6) | - | 0.539 | - | - |
| Lowest intra-/post-operative haemoglobin, g/dl | 8.3 (3.3-12.8) | 7.2 (4.7-9.7) | - | <0.001 | - | - |
| Maternal mortality | 0 | 0 | - | - | - | - |
| Haemorrhagic shock | 4 (2.8) | 5 (15.6) | - | 0.012 | - | - |
| Disseminated intravascular coagulopathy | 14 (9.9) | 15 (46.9) | - | <0.001 | - | - |
| Re-laparotomy | 2 (1.4) | 5 (15.6) | - | 0.003 | - | - |
| Inotropic support | 4 (2.8) | 11 (34.4) | - | <0.001 | - | - |
| Admission to intensive care unit | 33 (23.4) | 25 (78.1) | - | <0.001 | - | - |
| Paralytic ileus | 6 (4.3) | 6 (18.8) | - | 0.010 | - | - |
| Puerperal pyrexia | 15 (10.6) | 5 (15.6) | - | 0.539 | - | - |
| Wound infection | 6 (4.3) | 1 (3.1) | - | >0.99 | - | - |
| Venous thromboembolism | 0 | 0 | - | - | - | - |
| Bowel injury | 4 (2.8) | 1 (3.1) | - | >0.99 | - | - |
| Bladder injury | 0 | 0 | - | - | - | - |
| Ureteric injury | 0 | 0 | - | - | - | - |
| Broad ligament haematoma | 0 | 0 | - | - | - | - |
| Pelvic vessel injury | 1 (0.7) | 0 | - | >0.99 | - | - |
| Duration of hospitalisation, d | 4 (1-18) | 5.5 (2-19) | - | <0.001 | - | - |
| Re-admission within 90 days of discharge | 6 (4.3) | 1 (3.1) | - | >0.99 | - | - |
| Attendance to 6-week follow-up | 135 (95.7) | 31 (96.9) | - | >0.99 | - | - |
| Women without hysterectomy | n=141 | n=26 | | | | |
| Secondary PPH | 4 (2.8) | 1 (3.8) | - | 0.576 | - | - |
| Retained products of conception | 4 (2.8) | 1 (3.8) | - | 0.576 | - | - |
| Endometritis | 0 | 0 | - | - | - | - |
| Haematometra | 0 | 0 | - | - | - | - |
| Pyometra | 0 | 0 | - | - | - | - |
| Uterine necrosis | 0 | 0 | - | - | - | - |
| Uterine erosion | 0 | 0 | - | - | - | - |

There were five cases of bowel injury (full-thickness puncture of the sigmoid colon [n=2], serosal tear of the sigmoid colon during dissection for pelvic endometriosis [n=2], and serosal tear of the large bowel during dissection from the posterior uterine wall during hysterectomy [n=1]) and one case of uterine artery pseudoaneurysm injury, which was asymptomatic and was managed conservatively. At week 6, ultrasonography and computed tomography of the pelvis showed a 1.9-cm left adnexal vascular shadow with turbulent flow (Figure). There was no bladder injury, ureteric injury, broad ligament haematoma, mortality, endometritis, haematometra, pyometra, uterine necrosis, or erosion. At postnatal follow-up, five women had secondary PPH attributable to retained products of conception.

## Discussion

UAL is an effective and safe first-line surgical treatment for PPH during Caesarean section; 81.5% of women achieved haemostasis after UAL alone. Prior PPH was a predictor for haemostatic failure after UAL alone, whereas placenta praevia was a predictor for successful haemostasis after UAL alone.

In a study of 265 women with UAL (10 of them required additional therapy) in 1995, only six hysterectomies were performed and thus the efficacy of UAL was 97.7%[4], which was comparable to the 96.5% in our study. However, a higher proportion of women in our study required subsequent haemostatic procedures (mostly compression sutures). This could be due to a larger proportion of women with uterine atony as the primary cause of PPH. Since the introduction of compression sutures in 1997[8], obstetricians are more inclined to perform compression sutures when bleeding is not effectively controlled after UAL with suboptimal uterine contraction. Although both UAL and compression suture have similar haemostatic potential in atonic uterus[9], various international guidelines recommend compression sutures as the first surgical approach, followed by UAL[2,10-12]. In the International Federation of Gynaecology and Obstetrics guidelines, compression sutures are regarded as an effortless, fast, and conservative surgical procedure for uterine atony; UAL can decrease bleeding and allow additional time for compression sutures[13]. However, compression sutures can be complicated by uterine synechiae, necrosis, and haematometra, despite low overall incidence[14-16]. Prompt and effective uterine compression can reduce blood loss and the need for blood product transfusion, shorten the surgical time, and avoid the use of other immediate and short-term morbidities. Heavy bleeding leads to hypocalcaemia, which is associated with uterine atony and coagulopathy, which in turn exacerbate bleeding and may result in hysterectomy[17,18]. Therefore, UAL may not be the best option as a first-line surgical procedure in women with uterine atony. However, when compression sutures are technically difficult in cases of dense upper segment visceral adhesion, Müllerian anomaly, distorting fibroid, or adenomyoma, upfront UAL for haemostasis is recommended.

In our study, UAL alone could achieve haemostasis

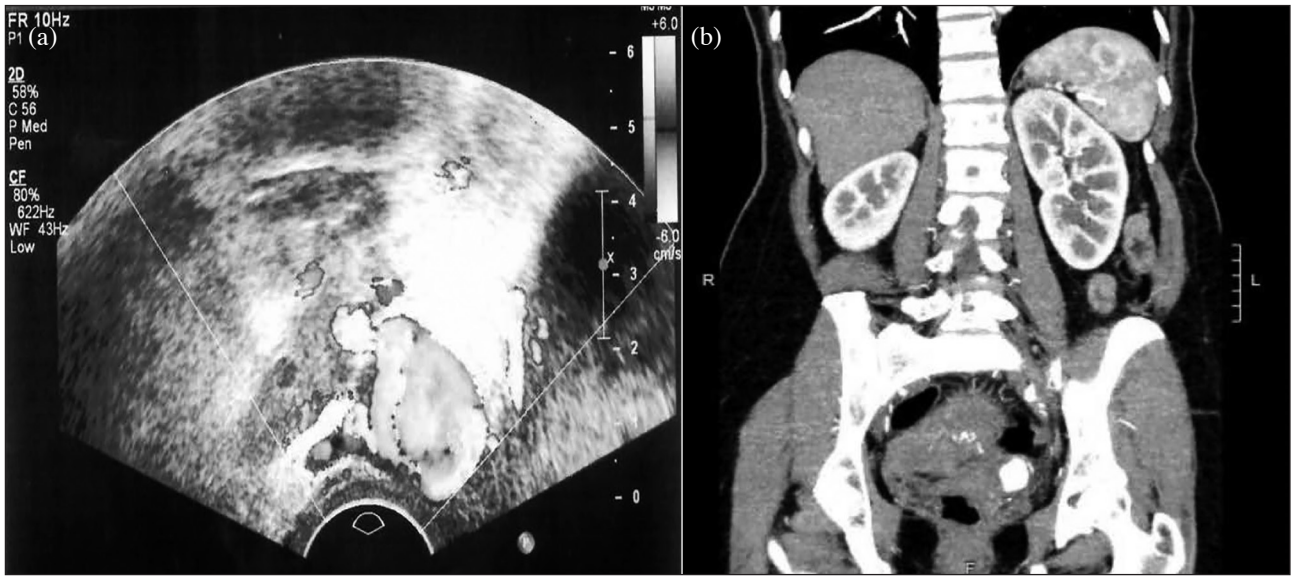


*Figure. At 6 weeks after uterine artery ligation in a patient with a pseudoaneurysm at the left uterine artery: (a) ultrasonography showing a blood flow signal at the adnexa and (b) computed tomography showing an arterial-enhancing lesion measuring 1.9 cm in size at the left adnexa, arising from a branch of the left internal iliac artery.*

in 92.5% of women with PPH secondary to placenta praevia. Two women with placenta praevia required hysterectomy: one after failure of the second ligatures caudal to the first one and another after failure of the Hayman sutures with complications of atony and coagulopathy. In hindsight, the failures could be associated with major placenta praevia, in which some of the arterial supply came from the cervical and vaginal arteries. In such a case, hypogastric artery ligation should be considered, although it is more time consuming and technically challenging. Alternatively, intrauterine balloons can be used for placental bed bleeding, especially in women with extensive adhesion across the lower uterine segment, bladder, or bowel, in women with diffuse vascularity at the site of needle entry, or in women with unusual uterine arteries secondary to concurrent pathology. However, it is more time-consuming to perform balloon placement, uterine wound closure, and then balloon inflation to achieve haemostasis. In cases of torrential bleeding from the placental bed, generalised devascularisation by UAL, which can be completed within 2 to 5 minutes in experienced hands, can enable more secure haemostasis by reducing uterine blood flow, compared with balloon tamponade.

In our study, UAL alone could achieve haemostasis in 86.2% of women with PPH secondary to placenta accreta. This can be explained by a mild degree of morbid adherent placenta. However, placenta accreta is associated with a higher rate of haemostasis failure when managing with UAL alone[17]. In a meta-analysis, haemostasis and uterine preservation were more likely to achieve when UAL was combined with other modalities[7]. This is probably related to the extensive collateral vasculature of the abnormal placentation hindering the success rate of UAL alone. Importantly, in cases of placenta percreta invading laterally, torrential bleeding can occur if the needle accidentally punctures through the abnormal placentation, especially in a bloody surgical field with active haemorrhage.

To prevent bladder injury, the bladder should be reflected at least 3 to 4 cm below the uterine incision. The bladder blade should be well placed to avoid accidental puncture of the bladder. To prevent ureteric injury, traction to the contralateral side and fenestration of the broad ligament can keep the ureter out of the way. After achieving haemostasis, the course of the ipsilateral ureter should be checked to ensure no ligation. To prevent bowel injury, abdominal packing with warm pads and passage of the suture from posterior to anterior can prevent direct puncture. In cases of dense visceral adhesion not amenable to dissection within a short time, intrauterine balloon tamponade should be considered. To prevent pelvic vessel injury, repeated needle entry and the figure-of-eight suture should be avoided, and a substantial amount of the myometrium with entry directly perpendicular to the uterine axis should be included in the ligature. The needle should exit through the avascular area of the broad ligament to prevent a haematoma.

Prophylactic UAL before placental delivery is suggested to reduce the incidence of PPH in high-risk women[19] such as women with placenta accreta[20]. Nonetheless, further studies on its long-term morbidity, menstrual return, and reproductive potential should be conducted to determine its effectiveness.

One limitation of our study was its retrospective nature; causal relationship cannot be established. In addition, women with placenta accreta detected antenatally were excluded; the sample size of women with placenta accreta was too small to make any conclusion.

## Conclusion

UAL is an effective and safe first-line surgical procedure for management of PPH during Caesarean section, especially in women with placenta praevia. UAL combined with subsequent haemostatic procedures may be required in women with prior PPH.

## Contributors

All authors designed the study, acquired the data, analysed the data, and critically revised the manuscript for important intellectual content. MSY drafted the manuscript. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

## Conflicts of interest

All authors have no conflicts of interest to disclose.

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## Data availability

All data generated or analysed during the present study are available from the corresponding author on reasonable request.

## Ethics approval

The study was approved by the Central Institutional

Review Board of Hospital Authority, Hong Kong SAR, China (reference: CIRB-2023-053-1). The patients were treated in accordance with the tenets of the Declaration of Helsinki. The patients provided written informed consent for all treatments and procedures and for publication.

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# Endometrial carcinoma in Chinese postmenopausal women with atypical endometrial hyperplasia

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***Objectives:*** To determine the risk factors and the rate of endometrial carcinoma (EC) among Chinese postmenopausal women with atypical endometrial hyperplasia (AEH).
***Methods:*** We retrospectively reviewed medical records of Chinese postmenopausal women with AEH who underwent endometrial biopsy (using pipelle) or curettage between 1 January 2012 and 31 December 2023 at the Queen Elizabeth Hospital. Postmenopausal women with a final diagnosis of AEH or EC were compared to determine the risk factors for EC.
***Results:*** In total, 45 Chinese postmenopausal women with AEH underwent hysterectomy and bilateral salpingo-oophorectomy. Of these, 15 (33.3%) underwent additional pelvic lymph node dissection with or without para-aortic lymph node dissection or subdiaphragmatic scraping, based on preoperative imaging findings (n=10) or intra-operative findings (n=5). All these 15 patients had a histopathological diagnosis of EC. Of the 45 patients, 11 and 34 had a histopathological diagnosis of AEH and EC, respectively. The final diagnosis of EC was not associated with age, body mass index, parity, hypertension, diabetes, or hyperlipidaemia in postmenopausal women with AEH.
***Conclusion:*** Of 45 Chinese postmenopausal women with AEH, 75.6% had a final diagnosis of EC and 24.4% required lymph node dissection in addition to hysterectomy and bilateral salpingo-oophorectomy. In selected patients, preoperative imaging and referral to a gynaecological oncologist for tumour staging may be necessary for optimal treatment outcomes.

*Keywords: Endometrial hyperplasia; Endometrial neoplasms; Lymph node excision; Menopause; Neoplasm staging*

## Background

Endometrial carcinoma (EC) is the fourth most common cancer among women in Hong Kong[1]. Its most common form is endometrioid EC, which typically develops from endometrial hyperplasia. Atypical endometrial hyperplasia (AEH) is characterised by abnormal cellular changes; the cells within the glands exhibit varying degrees of atypia including nuclear enlargement, pleomorphism, and increased mitotic activity. As the disease progresses, the cells may resist the normal hormonal regulatory mechanisms. This leads to uncontrolled cellular proliferation and differentiation and carcinoma development. In EC, the malignant cells acquire invasive properties and infiltrate the basement membrane and surrounding tissues. Lymphovascular invasion can occur, resulting in the spread of cancer cells to regional lymph nodes and distant sites.

Risk factors associated with the development of EC and AEH include age, body mass index, parity, hypertension, and diabetes, regardless of menopausal status. Nonetheless, postmenopausal status is a predictor for postoperative diagnosis of EC; 33.5 to 85% of postmenopausal women with AEH have a postoperative diagnosis of EC.[2-8]. In women with AEH, the risk of progression to malignancy is 30% and the risk of concomitant EC is 40% to 50%[3].

The Royal College of Obstetricians and Gynaecologists/British Gynaecological Cancer Society[9] and Hong Kong College of Obstetricians and Gynaecologists[10] guidelines suggest total hysterectomy as the first-line treatment for endometrial hyperplasia. In postmenopausal women, bilateral salpingo-oophorectomy is recommended. Routine lymphadenectomy is not necessary because the risk of concomitant advanced-stage cancer of the uterine corpus is extremely low. However, the risk of advanced-stage EC in postmenopausal patients with AEH was higher than expected (Table 1)[2-8]. Therefore, we aimed to determine the

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**Table 1. Studies of women with atypical endometrial hyperplasia and the rate of endometrial carcinoma (EC)**

| Study | No. of patients | % of patients with EC | No. of postmenopausal women | % of postmenopausal women with EC |
|---|---|---|---|---|
| Non-Asian population | | | | |
| Xie et al,[2] 2002 | 86 | 38.0 | 19 | 58.0 |
| Trimble et al,[3] 2012 | 289 | 43.0 | - | |
| Kadirogullari et al,[4] 2015 | 40 | 33.0 | 23 | 56.5 |
| Giannella et al,[5] 2023 | 629 | 30.7 | 427 | 33.5 |
| Asian population | | | | |
| Kimura et al,[6] 2003 | 33 | 27.0 | 10 | 50.0 |
| Yau et al,[7] 2010 | 62 | 45.0 | 13 | 85.0 |
| Lou et al,[8] 2021 | 624 | 30.4 | 118 | 49.0 |

risk factors and the rate of EC in postmenopausal Chinese women with AEH.

## Methods

We retrospectively reviewed medical records of Chinese postmenopausal women with AEH who underwent endometrial biopsy (using pipelle) or curettage between 1 January 2012 and 31 December 2023 at the Queen Elizabeth Hospital. Patients who were lost to follow-up or refused surgery were excluded.

Data collected included age at diagnosis, body mass index, parity, menopausal status, drinking and smoking habits, family history, hypertension, diabetes, hyperlipidaemia, history of polycystic ovarian syndrome, use of exogenous hormones, and use of tamoxifen.

Ultrasonography of the pelvis was performed through the transabdominal, transvaginal, or transrectal route. Magnetic resonance imaging of the pelvis was routinely advised. Hysterectomy with bilateral salpingo-oophorectomy was performed using the laparotomy or laparoscopic approach. Additional surgical procedures (pelvic and para-aortic lymph node dissection, peritoneal biopsy, and subdiaphragmatic scraping) were performed in selected patients, based on preoperative imaging or intra-operative findings of myometrial invasion of >50% and suspected lymph node and peritoneal involvement. Histopathological features were recorded, including the histology type, tumour grading, presence of lymphovascular space invasion, depth of myometrial invasion, cervical stromal involvement, and adnexal involvement. The International Federation of Gynecology and Obstetrics staging was used, based on imaging, intra-operative, and histopathological findings.

Data were analysed using SPSS (Windows version 22.0; IBM Corp, Armonk [NY], Unites States). The incidence of EC in postmenopausal women with AEH was calculated. Postmenopausal women with a final diagnosis of AEH or EC were compared using the Chi-squared test for categorical variables and the Fisher's exact test for continuous variables to determine the risk factors for EC.

## Results

Of 112 patients diagnosed with AEH during the study period, 54 were postmenopausal. Of these, nine were excluded because of they were non-Chinese (n=2), lost to follow-up or refused surgery (n=4), or refused surgery owing to advanced age and medical comorbidities (n=3).

Among 45 patients who underwent hysterectomy and bilateral salpingo-oophorectomy, the mean duration from diagnosis to operation was 11 (range, 4-20) weeks. The diagnosis was made based on curettage (n=13) or bedside endometrial aspirate (n=32). All patients underwent an ultrasound examination; 39 (87%) of patients underwent additional magnetic resonance imaging (n=35) or computed tomography/positron emission tomography (n=4). Of these 39 patients, six had myometrial invasion of >50% and four had lymph node involvement; the remaining 29 patients had no or <50% myometrial invasion.

Of the 45 patients, 15 (33.3%) underwent additional pelvic lymph node dissection. Of these, five also underwent

para-aortic lymph node dissection and two also underwent subdiaphragmatic scraping. Indications for additional surgical procedures were based on preoperative imaging findings of myometrial invasion of >50% or suspected lymph node involvement (n=10) or intra-operative findings of myometrial invasion of >50% (n=4) or omental nodule (n=1). All these 15 patients had a histopathological diagnosis of EC. Postoperatively, 13 of these patients received adjuvant therapy. Of these, two had grade IAG1 tumour, one had lymphovascular invasion, and one had double primary of poorly differentiated Sertoli-Leydig cell tumour. No patients required a second surgery.

Of the 45 patients, 11 and 34 had a histopathological diagnosis of AEH and EC, respectively. The grades of the 34 cases of EC were IA (n=22), IB (n=6) [both were defined as <5% of non-squamous or non-morular solid growth pattern], II (n=1), IIIC1 (n=2), IIIC2 (n=1), IVB (n=1), and missing data (n=1).

The final diagnosis of EC was not associated with age, body mass index, parity, hypertension, diabetes, or hyperlipidaemia in postmenopausal women with AEH (Table 2).

## Discussion

Among 45 postmenopausal women with AEH, 34 (75.6%) had a final diagnosis of EC. The tumour grade of 11 (24.4%) patients was at least grade IB, for which additional lymph node dissection was needed. Considering the higher rate of occult EC in postmenopausal women, the current guidelines on the management of AEH might not be adequate for these high-risk patients.

Postmenopausal status is a predictor for EC[5,8], because of the shift of the balance of hormones towards more oestrogen. Postmenopausal status is a hypo-oestrogenic condition. Oestrogen from the adipose tissue has greater impact after menopause, as production of oestrogen and progesterone from the ovaries stops. Hypo-oestrogenic status is a protective factor for endometrial pathology. However, in postmenopausal women with AEH, the grade

**Table 2. Risk factors associated with endometrial carcinoma in postmenopausal women with atypical endometrial hyperplasia**

| Variable | No. (%) of patients with a final diagnosis of | | 95% confidence interval | p Value |
|---|---|---|---|---|
| | Atypical endometrial hyperplasia | Endometrial cancer | | |
| Age, y | | | | |
| ≤60 (n=25) | 8 (32.0) | 17 (68.0) | Reference | |
| 61-70 (n=15) | 1 (6.7) | 14 (93.3) | 0.73-59.2 | 0.117 |
| >71 (n=5) | 2 (40.0) | 3 (60.0) | 0.1-5.1 | 1.0 |
| Body mass index, kg/m$^2$ | | | | |
| <23 (n=7) | 3 (42.9) | 4 (57.1) | Reference | |
| 23-25 (n=13) | 1 (7.7) | 12 (92.3) | 0.7-113.0 | 0.10 |
| >25 (n=25) | 7 (28.0) | 18 (72.0) | 0.34-10.9 | 0.648 |
| Parity | | | | |
| Nulliparous (n=14) | 3 (21.4) | 11 (78.6) | Reference | |
| Multiparous (n=31) | 8 (25.8) | 23 (74.2) | 0.17-3.5 | 1.0 |
| Hypertension | | | | |
| Yes (n=23) | 6 (26.1) | 17 (73.9) | 0.2-3.3 | 1.0 |
| No (n=22) | 5 (22.7) | 17 (77.3) | Reference | |
| Diabetes | | | | |
| Yes (n=9) | 0 | 9 (100.0) | 0.56-0.86 | 0.087 |
| No (n=36) | 11 (30.6) | 25 (69.4) | Reference | |
| Hyperlipidaemia | | | | |
| Yes (n=20) | 5 (25.0) | 15 (75.0) | 0.24-3.71 | 0.94 |
| No (n=25) | 6 (24.0) | 19 (76.0) | Reference | |

of EC was more invasive. Grade I endometrioid carcinoma in older women is more aggressive than that in younger women; old age is a predictor for shorter progression-free survival[11]. The underlying pathophysiology is unclear; confounding factors such as age, obesity, and medical comorbidities (metabolic syndrome) may be involved. In our postmenopausal women with AEH, EC was not associated with age, body mass index, parity, hypertension, diabetes, or hyperlipidaemia, probably owing to the small sample size.

According to the guidelines of The Royal College of Obstetricians and Gynaecologists/British Gynaecological Cancer Society and Hong Kong College of Obstetricians and Gynaecologists, in patients with AEH or early EC, routine pelvic and para-aortic lymphadenectomy is not recommended because only 10% of patients with AEH have myometrial invasion of >50% (ie, grade IB tumour) and no patient has grade II, III, or IV EC[3]. However, our study showed a higher rate of advanced-stage EC in postmenopausal women with AEH. Of the 45 patients, 11 (24.4%) had at least grade IB tumour. In one study, 28% of women with grade III EC and stage I outer myometrial invasion have lymph node involvement[9]. According to the International Federation of Gynecology and Obstetrics staging guidelines, patients with more than grade IA EC should undergo imaging for distant metastases and surgical staging such as lymph node dissection.

Complications associated with lymphadenectomy include lymphocoele formation, lymphoedema, and vascular, nerve, and ureteric injuries. Routine lymphadenectomy may lead to over-treatment and unnecessary surgical risks. A second surgery for tumour staging introduces additional risks associated with anaesthesia, surgery, and delay in initiating adjuvant therapy, particularly in public hospitals. Therefore, patient selection is important to minimise the need for a second surgery for tumour staging.

To reduce over-staging or under-staging of EC, preoperative imaging and intra-operative frozen section analysis are viable tools to guide surgical decision for additional lymphadenectomy and help minimise the risks associated with unnecessary surgical procedures. Re-sampling or hysteroscopically targeted biopsy should be considered in cases of preoperative imaging suspicious of invasive carcinoma.

In postmenopausal women with AEH, we recommend performing preoperative imaging to identify a suspected advanced-stage EC, for which input from gynaecological oncologists is needed. Comprehensive evaluation enables informed decision making and counselling, outcome optimisation, and reduction of the need for a second surgery for staging.

One limitation of our study was the small sample size from a single hospital. Chinese postmenopausal women with AEH are at higher risk of EC, which might be under-treated and under-staged in a primary surgery, given that the current guidelines are not specifically for Chinese postmenopausal women with AEH.

## Conclusion

Of 45 Chinese postmenopausal women with AEH, 75.6% had a final diagnosis of EC and 24.4% required lymph node dissection in addition to hysterectomy and bilateral salpingo-oophorectomy. In selected patients, preoperative imaging and referral to a gynaecological oncologist for tumour staging may be necessary for optimal treatment outcomes.

## Contributors

All authors designed the study, acquired the data, analysed the data, drafted the manuscript, and critically revised the manuscript for important intellectual content. The authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

## Conflicts of interest

All authors have no conflicts of interest to disclose.

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## Data availability

All data generated or analysed during the present study are available from the corresponding author on reasonable request.

## Ethics approval

The study was approved by the Kowloon Central/Kowloon East Cluster Research Ethics Committee (reference: KC/KE-23-0073/ER-2). The patients were treated in accordance with the tenets of the Declaration of Helsinki. The patients provided written informed consent for all treatments and procedures and for publication.

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# Sexual health of women from a gynaecology clinic in Hong Kong

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***Objectives:*** To identify factors associated with female sexual dysfunction (FSD) among Hong Kong Chinese women in a gynaecology outpatient clinic.
***Methods:*** Chinese women aged 18 to 65 years who had been sexually active in the past 4 weeks before recruitment and attended the gynaecology clinic of Kwong Wah Hospital between October 2020 and July 2021 were invited to participate in a sexual health survey. Participant demographics were collected through the clinical management system. Sexual function in the previous 4 weeks was assessed using the Female Sexual Function Index (FSFI).
***Results:*** 206 women (mean age, 43.6 years) were included in the analysis. The mean total FSFI score was 23.44; 42% of participants were at risk of FSD, with a total FSFI score of ≤23.45. The score was lowest in the sexual desire domain (2.88) and highest in the coital pain domain (4.51). Participants were divided into three age groups based on their reproductive age status: 18 to 35 years (n=44), 36 to 50 years (n=116), and 51 to 65 years (n=46). Although older age groups tended to have higher risks of FSD, the differences between groups were not significant. Specifically, only the satisfaction domain score was lower in the age group of 36 to 50 years than in the age group of 18 to 35 years (4.16 vs 4.61, p=0.01). The coital pain domain score was lower in menopausal women than in premenopausal women (3.76 vs 4.51, p=0.03). Parous women had a lower sexual desire domain score (2.78 vs 3.04, p=0.04) and higher vaginal lubrication domain score (4.42 vs 3.74, p=0.02) than nulliparous women. Women using contraception had a higher vaginal lubrication domain score than women not using contraception (4.47 vs 3.91, p=0.02). Women with distress related to sexual function had a lower total FSFI score (19.74 vs 23.78, p=0.01), lower satisfaction domain score (3.80 vs 4.42, p=0.02), and lower coital pain domain score (3.38 vs 4.51, p=0.01), compared with women without distress related to sexual function.
***Conclusion:*** Although older women tend to be at higher risk of FSD, the correlation between age and FSFI score was not significant. Menopausal women had a lower coital pain domain score; women not using contraception had a lower vaginal lubrication domain score.

*Keywords: Risk factors; Sexual dysfunction, physiological; Sexual dysfunctions, psychological; Sexual health; Sexuality; Surveys and questionnaires*

## Introduction

Sexual health is defined as a state of physical, emotional, mental, and social well-being in relation to sexuality; it is not merely the absence of disease, dysfunction, or infirmity[1]. Female sexual function plays a crucial role in the well-being and quality of life of women. Female sexual response involves neurovascular, endocrine, and psychosocial factors[2,3].

Sexual health among Chinese women is underexplored[4,5]. The prevalence of female sexual dysfunction (FSD) has been estimated to be 30% to 55%[6-8]. Differences in the prevalence were due to differences in FSD definitions and assessment tools. In an epidemiological survey in mainland China involving 25 446 women aged 20 to 70 years, the prevalence of FSD was 29.7%[6]. In Hong Kong, the prevalence was 25.6%

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to 37.9% among married or cohabiting Chinese women aged <49 years[9,10] and 77.2% among women aged 40 to 60 years[11]. Of 159 infertile women from two subfertility clinics in Hong Kong, 32.5% were at risk of FSD[12]. Of 431 Chinese unmarried young women aged <26 years from sexual health clinics in Hong Kong, 17.6% were at risk of FSD[13]. Of 540 women aged ≥40 years from a community women's centre in Hong Kong, 85.1% (91.2% among postmenopausal women) were at risk of FSD, which is associated with depression, and vaginal dryness and low sexual desire are the most common problems[14]. In Hong Kong, among couples undergoing assisted reproductive technologies, 22.6% of wives were at risk of FSD[15].

Age, menopausal status, and sociodemographic factors are risk factors for FSD[6,16,17]. In mainland Chinese women, being single or divorced, childbearing, and with lower educational attainment are associated with an increased risk of FSD, whereas higher educational attainment and urban residency are associated with a decreased risk of FSD[6]. In Turkish women, FSD is associated with smoking and marital status but not with educational status or contraceptive drug use[13]. The partner's age is negatively associated with the Female Sexual Function Index (FSFI) score[18]. Results are mixed with regard to the use of hormonal contraception on FSD, but non-use of contraception is associated with FSD[19-21]. Diabetes and non-gynaecological cancers negatively affect sexual function, and pelvic inflammatory disease and pelvic organ prolapse increase the risk of FSD[6]. FSD occurs more frequently in women with diabetes or hypertension[22,23]. Chronic pain also negatively affects sexual function[24], as do depression, anxiety disorders, and schizophrenia[25-28]. We aimed to identify factors associated with FSD among Hong Kong Chinese women seeking medical care for gynaecological conditions.

## Methods

Chinese women aged 18 to 65 years who had been sexually active in the past 4 weeks before recruitment and attended the gynaecology clinic of Kwong Wah Hospital between October 2020 and July 2021 were invited to participate in a sexual health survey. Those who could not read Chinese or were of non-Chinese ethnicity were excluded.

Participant demographics were collected through the clinical management system, including age, menopausal status, marital status, education level, employment status, religious belief, partner's age, and parity, as well as gynaecological conditions (menstrual disorders, chronic pelvic pain or dysmenorrhoea, pelvic mass, urinary or prolapse symptoms, vaginal discharge, and post-coital bleeding), hormonal treatments, medical comorbidities (hypertension, diabetes, chronic pain, and non-gynaecological cancers), and psychiatric history (depression, anxiety disorders, and schizophrenia). Sexuality issues were assessed using yes-or-no questions, including current contraception use, perceived distress related to sexual function, communication dynamics within relationships, and a history of seeking medical care for sexual dysfunction.

Sexual function in the previous 4 weeks was assessed using the FSFI, which comprises 19 questions in six domains: sexual desire, arousal, vaginal lubrication, orgasm, satisfaction, and coital pain[29]. Each item is scored from 0 to 5. Individual domain scores are the sum of scores of questions under the same domain multiplied by a factor ranging from 0.3 to 0.6. Total FSFI scores range from 2 to 36; higher scores indicate less risk of FSD. The FSFI has been validated in an urban Chinese population in Taiwan with high reliability (Cronbach's $\alpha$=0.96) and validity (87.1%)[30]. Different FSFI cut-off scores have been used to identify FSD among women in different ethnic groups or geographical regions[31,32]. The cut-off score of 23.45 had 66.9% sensitivity and 72.7% specificity for identifying FSD among urban Chinese women[33]. For the FSFI domains of sexual desire, arousal, vaginal lubrication, orgasm, and coital pain, the cut-off scores were ≤2.7, ≤3.15, ≤4.05, ≤3.8, and ≤3.8, respectively[33]. A cut-off score for the satisfaction domain was not established owing to a lack of data based on DSM-IV. The above cut-offs were used in our study, because of similar urban and cultural backgrounds of the sample.

Sample size was calculated based on a previous territory-wide survey in Hong Kong involving 1510 women[9], of whom 37.9% had FSD based on the DSM-IV. Assuming that 37.9% of women are at risk of FSD, with an estimated precision of 10% (d=0.1) at two-tailed 5% significance (z=1.96), the estimated sample size was 92 using the Cochran's sample size formula[34]. Assuming a response rate of 60% and an incomplete questionnaire rate of 20% owing to the COVID pandemic, the estimated sample size was 192.

FSFI score of ≤23.45 was defined as at risk of FSD. Women at risk and not at risk of FSD were compared using the Student's *t* test or Chi-squared test. Analysis of

variance was performed. A p value of <0.05 was considered statistically significant. Multiple regression analysis was performed to identify factors associated with FSD. Pearson's correlation was used to determine whether the woman's age or the partner's age affected female sexual function. Levene's test for equality of variances and Student's *t* test were used to detect any difference in FSFI total score and domain scores across different groups. Analyses were performed using the SPSS (Windows version 24.0; IBM Corp, Armonk [NY], United States).

## Results

Of 244 women recruited, 227 (93%) responded. Of these, 21 were excluded owing to not being sexually active in the past 4 weeks (n=1), invalid consent (n=3), and incomplete questionnaires (n=17). The remaining 206 women (mean age, 43.6±8.9 years) were included in the analysis (Table 1). The mean age of their partners was 47.0±10.3 years. The mean follow-up duration in the gynaecology clinic was 42.7±42.2 months. Reasons for attending the gynaecology clinic included menstrual disorder (n=134), dysmenorrhoea or chronic pelvic pain (n=32), a pelvic mass (n=111), genital prolapse (n=4), vaginal discharge (n=4), post-coital bleeding (n=12), and other reasons (n=77), for example intra-uterine contraceptive device removal, abnormal pap smear, and vulval conditions. Participants could have multiple reasons for attending the gynaecology clinic.

The total FSFI score ranged from 2.8 to 33.6 (mean, 23.44±6.18); 42% of participants were at risk of FSD, with a total FSFI score of ≤23.45. The score was lowest in the sexual desire domain (2.88) and highest in the coital pain domain (4.51).

Participants were divided into three age groups based on their reproductive age status: 18 to 35 years (n=44), 36 to 50 years (n=116), and 51 to 65 years (n=46). Although older age groups tended to have higher risks of FSD, the differences between groups were not significant (Table 2). Specifically, only the satisfaction domain score was lower in the age group of 36 to 50 years than in the age group of 18 to 35 years (4.16 vs 4.61, p=0.01, Table 3). The coital pain domain score was lower in menopausal women than in premenopausal women (3.76 vs 4.51, p=0.03). Parous women had a lower sexual desire domain score (2.78 vs 3.04, p=0.04) and higher vaginal lubrication domain score (4.42 vs 3.74, p=0.02) than nulliparous women. Women using contraception had a higher vaginal lubrication domain score than women not using contraception (4.47 vs 3.91, p=0.02). Women with distress related to sexual function had a lower total FSFI score (19.74 vs 23.78, p=0.01), lower satisfaction domain score (3.80 vs 4.42, p=0.02), and lower coital pain domain score (3.38 vs 4.51, p=0.01), compared with women without distress related to sexual function.

The FSFI total and subscale scores were not associated with communication dynamics within relationships, underlying gynaecological conditions, follow-up duration, or medical comorbidities. The number of women with psychiatric conditions (depression, anxiety neurosis, and schizophrenia) was too small for comparison.

## Discussion

In Asian populations (China, Turkey, India, Japan), the prevalence of FSD has been reported to be 26.1% to 73.2%[33,35-37], consistent with the 42% (29.5% among the age group of 18 to 35 years, 44.8% among the age group of 36 to 50 years, and 47.8% among the age group of 51 to 65 years) reported in the present study. Discrepancies in the prevalence of FSD among studies can be explained by differences in recruitment, assessment, and cut-off scores. Our sample was recruited from a gynaecology clinic during the COVID pandemic. Women who had not been sexually active in the past 4 weeks were excluded; this may underestimate the prevalence of FSD. The FSFI questionnaire is merely an assessment tool for female sexual function, rather than a diagnostic tool for FSD. Thus, it cannot be used to determine the prevalence of FSD. The Taiwan version of the FSFI questionnaire has not been validated in Hong Kong women.

In the present study, 21.4% and 56.3% of participants were in the age groups of 18 to 35 years and 36 to 50 years, respectively, and 29.5% and 44.8% of them were at risk of FSD, respectively. Of these women, 40.6% were at risk of FSD. This rate was higher than that reported in a previous Hong Kong study. The discrepancy can be explained by our specific recruitment of women seeking medical care for gynaecological conditions. These women are potentially at higher risk of FSD. In addition, the higher rate of FSD among reproductive age groups can be explained by the gynaecology clinic settings, which are characterised by more frequent interactions, closer doctor-patient relationships, better rapport, and increased openness in discussing sexual problems. Moreover, the recruitment was conducted during the COVID pandemic. The increased societal stress during the pandemic is associated with lower FSFI scores on sexual functioning and activity[38].

**Table 1. Comparisons of women at risk or not at risk of female sexual dysfunction (FSD) based on the Female Sexual Function Index (FSFI)**

| Variable | No. (%) of participants | No. (%) of participants | | p Value |
|---|---|---|---|---|
| | | At risk of FSD (FSFI score ≤23.45) [n=87] | Not at risk of FSD (FSFI score >23.45) [n=119] | |
| Age group, y | | | | 0.15 |
| 18-35 | 44 (21.4) | 13 (29.5) | 31 (70.5) | |
| 36-50 | 116 (56.3) | 52 (44.8) | 64 (55.2) | |
| 51-65 | 46 (22.3) | 22 (47.8) | 24 (52.2) | |
| Menopausal status | | | | 0.06 |
| Premenopausal | 179 (86.9) | 71 (39.7) | 108 (60.3) | |
| Menopausal | 27 (13.1) | 16 (59.3) | 11 (40.7) | |
| Marital status | | | | 0.90 |
| Married | 176 (85.4) | 74 (42.0) | 102 (58.0) | |
| Single | 30 (14.6) | 13 (43.3) | 17 (56.7) | |
| Education level | | | | 0.04 |
| Primary or below | 12 (5.8) | 9 (75.0) | 3 (25.0) | |
| Secondary | 136 (66.0) | 55 (40.4) | 81 (59.6) | |
| Tertiary or above | 58 (28.2) | 21 (36.2) | 37 (63.8) | |
| Occupation | | | | 0.75 |
| Employed | 142 (68.9) | 61 (43.0) | 81 (57.0) | |
| Unemployed | 64 (31.1) | 26 (40.6) | 38 (59.4) | |
| Religious belief | | | | 0.24 |
| Yes | 53 (25.7) | 25 (47.2) | 28 (52.8) | |
| No | 153 (74.3) | 62 (40.5) | 91 (59.5) | |
| Parity | | | | 0.29 |
| Parous | 150 (72.8) | 60 (40.0) | 90 (60.0) | |
| Nulliparous | 56 (27.2) | 27 (48.2) | 29 (51.8) | |
| Distress related to sexual function issues | | | | 0.09 |
| Yes | 19 (9.2) | 11 (57.9) | 8 (42.1) | |
| No | 187 (90.8) | 74 (39.6) | 113 (60.4) | |
| Talked with partner about sexual function issues | | | | 0.27 |
| Yes | 67 (32.5) | 32 (47.8) | 35 (52.2) | |
| No | 139 (67.5) | 55 (39.6) | 84 (60.4) | |
| Had medical consultation for sexual function issues | | | | 1 |
| Yes | 7 (3.4) | 3 (42.9) | 4 (57.1) | |
| No | 199 (96.6) | 84 (42.2) | 115 (57.8) | |
| Used contraception | | | | 0.11 |
| Yes | 122 (59.2) | 46 (37.7) | 76 (62.3) | |
| No | 84 (40.8) | 41 (48.8) | 43 (51.2) | |
| Medical comorbidity | | | | 0.84 |
| Yes | 112 (54.4) | 48 (42.9) | 64 (57.1) | |
| No | 94 (45.6) | 39 (41.5) | 55 (58.5) | |
| Psychiatric history | | | | 0.15 |
| Yes | 13 (6.3) | 3 (23.1) | 10 (76.9) | |
| No | 193 (93.7) | 84 (43.5) | 109 (56.5) | |
| Hormone treatment | | | | 0.70 |
| Yes | 38 (18.4) | 15 (39.5) | 23 (60.5) | |
| No | 168 (81.6) | 72 (42.9) | 96 (57.1) | |

**Table 2. Proportions of participants at risk of female sexual dysfunction (FSD) in each domain of the Female Sexual Function Index (FSFI)**

| Age group, y | No. (%) of participants at risk of FSD in each domain of the FSFI | | | | | | |
|---|---|---|---|---|---|---|---|
| | Sexual desire (cut-off score, ≤2.7) | Arousal (cut-off score, ≤3.15) | Vaginal lubrication (cut-off score, ≤4.05) | Orgasm (cut-off score, ≤3.8) | Satisfaction | Coital pain (cut-off score, ≤3.8) | Overall |
| 18-35 (n=44) | 17 (38.6) | 11 (25.0) | 12 (27.3) | 16 (36.4) | - | 9 (20.5) | 13 (29.5) |
| 36-50 (n=116) | 58 (50.0) | 39 (33.6) | 39 (33.6) | 40 (34.5) | - | 21 (18.1) | 52 (44.8) |
| 51-65 (n=46) | 23 (50.0) | 17 (37.0) | 18 (39.1) | 14 (30.4) | - | 19 (41.3) | 22 (47.8) |
| **Overall** | **98 (47.6)** | **67 (32.5)** | **69 (33.5)** | **70 (34.0)** | **-** | **49 (23.8)** | **87 (42.2)** |

**Table 3. Female Sexual Function Index (FSFI) domain scores in different comparison groups**

| | Mean±standard deviation FSFI score | | | | | | |
|---|---|---|---|---|---|---|---|
| | Sexual desire | Arousal | Vaginal lubrication | Orgasm | Satisfaction | Coital pain | Overall |
| All participants (n=206) | 2.88±0.82 | 3.41±1.20 | 4.32±1.65 | 3.98±1.37 | 4.35±1.10 | 4.51±1.56 | 23.44±6.18 |
| Age group, y | | | | | | | |
| 18-35 (n=44) | 3.00±0.95 | 3.65±1.23 | 4.54±1.40 | 4.12±1.32 | 4.61±0.95 | 4.68±1.52 | 24.60±5.94 |
| 36-50 (n=116) | 2.87±0.80 | 3.65±1.24 | 4.34±1.84 | 3.92±1.43 | 4.16±1.11 | 4.57±1.56 | 23.20±6.37 |
| 51-65 (n=46) | 2.78±0.73 | 3.32±1.05 | 4.04±1.30 | 3.99±1.29 | 4.60±1.12 | 4.21±1.57 | 22.90±5.91 |
| p Value | 0.44 | 0.32 | 0.35 | 0.71 | 0.01 | 0.30 | 0.37 |
| Menopausal status | | | | | | | |
| Premenopausal (n=179) | 2.90±0.85 | 3.43±1.24 | 4.38±1.68 | 4.00±1.40 | 4.34±1.09 | 4.51±1.71 | 23.68±6.29 |
| Menopausal (n=27) | 2.76±0.63 | 3.24±0.86 | 3.87±1.35 | 3.81±1.15 | 4.44±1.15 | 3.76±1.37 | 21.9±5.20 |
| p Value | 0.41 | 0.46 | 0.13 | 0.49 | 0.64 | 0.03 | 0.16 |
| Parity | | | | | | | |
| Parous (n=150) | 2.78±0.79 | 1.13±0.90 | 4.42±1.60 | 3.99±1.32 | 4.43±1.09 | 4.57±1.53 | 23.98±5.40 |
| Nulliparous (n=56) | 3.04±0.91 | 1.58±0.21 | 3.74±1.93 | 3.59±1.81 | 4.21±1.14 | 4.01±2.00 | 22.00±7.77 |
| p Value | 0.04 | 0.26 | 0.02 | 0.08 | 0.20 | 0.06 | 0.08 |
| Used contraception | | | | | | | |
| Yes (n=122) | 2.90±0.82 | 3.52±1.16 | 4.47±1.22 | 4.07±1.31 | 4.47±1.53 | 4.60±1.53 | 24.10±5.88 |
| No (n=84) | 2.85±0.82 | 3.24±1.23 | 3.91±1.43 | 3.85±1.45 | 4.19±1.20 | 4.39±1.59 | 22.50±6.51 |
| p Value | 0.69 | 0.09 | 0.02 | 0.26 | 0.07 | 0.34 | 0.07 |
| Distress related to sexual function issues | | | | | | | |
| Yes (n=19) | 2.72±1.12 | 2.80±1.28 | 3.55±1.50 | 3.44±1.57 | 3.80±1.30 | 3.38±1.87 | 19.74±6.86 |
| No (n=187) | 2.86±0.80 | 3.38±1.25 | 4.30±1.73 | 3.92±1.46 | 4.42±1.07 | 4.51±1.64 | 23.78±6.02 |
| p Value | 0.48 | 0.06 | 0.08 | 0.19 | 0.02 | 0.01 | 0.01 |

In the present study, despite lower FSFI scores tended to be associated with increasing age, correlation was not significant between age and FSFI scores in all domains, except for satisfaction. Specifically, only the satisfaction domain score was lower in the age group of 36 to 50 years than in the age group of 18 to 35 years. Although sexual function may decline with age, women aged 51 to 65 years may have more stable relationships or a better understanding of their own sexual needs, thereby having a higher satisfaction domain score than women

aged 36 to 50 years. In contrast, in a survey of female sexual function in a Dutch population, increasing age was significantly associated with lower FSFI total and subscale scores, except for the satisfaction domain[39].

In the present study, premenopausal and menopausal women were comparable in terms of the FSFI total score, although menopausal women scored significantly lower in the coital pain domain. However, menopause is a risk factor for FSD[6,16,17]. Menopausal women are more likely to experience FSD secondary to vaginal dryness and pain, compared with premenopausal women[14]. In the present study, premenopausal women were of greater heterogeneity because of a wider age range and a larger number, whereas the number of menopausal women was small. This may decrease the statistical power for assessing the effect of menopause on FSFI scores.

In the present study, women not using contraception had a higher risk of lubrication problems. Non-use of contraception is associated with FSD and dissatisfaction, possibly owing to concerns of unintended pregnancy[19]. In an Italian study, a lower total FSFI score was associated with women not using contraceptives[20]. Caution should be exercised when interpreting the association between lower lubrication domain score and non-use of contraception, owing to confounders (eg, age).

In the present study, 9.2% of women reported distress related to sexual function, but only 3.4% of them had sought medical consultations. In Chinese culture, sex is generally a taboo topic and perceived as a private matter[5]. Women with FSD are reluctant to seek treatment, resulting in underdiagnosis and undertreatment. Distress related to sexual function should have been evaluated using validated psychometric tools (such as the Female Sexual Distress Scale[40]), rather than yes-or-no questions.

In the present study, the FSFI total and subscale scores were not associated with underlying gynaecological conditions or medical comorbidities. In contrast, FSD has been reported to be associated with gynaecological diseases (pelvic inflammatory disease and pelvic organ prolapse), medical conditions (hypertension and diabetes), and psychiatric conditions[6,22-28]. The differences can be explained by cultural differences and the small sample size in our study.

FSD can negatively impact the women's quality of life. Gynaecologists can be the first point of contact for women at risk of sexual dysfunction. The use of FSFI to screen women at risk of FSD may facilitate timely referral to sexual health specialists. A multidisciplinary approach involving psychiatrists, endocrinologists, psychologists, and sex therapists is imperative for holistic care. The Family Planning Association of Hong Kong offers a wide range of services for female sexual health, including talks on sex and intimacy, sex coaching, and sexual dysfunction therapy. The Community Rehabilitation Service Support Centre in Queen Elizabeth Hospital receives referrals from doctors, nurses, allied health professionals, and medical social workers, and provides specialised services including occupational therapy and physiotherapy on sexuality counselling and rehabilitation.

The present study has limitations. Although the sample size was adequate for determining factors associated with FSD, the sample size may be inadequate for subgroup analyses. The sample was recruited from a gynaecology clinic. The findings may not be generalised to the general population. The distribution of the three age groups was uneven and the number of participants was smaller in the age groups of 18 to 35 years and 51 to 65 years. Distress related to sexual function should have been evaluated using validated psychometric tools (such as the Female Sexual Distress Scale[40]), rather than yes-or-no questions. Communication dynamics and health-seeking behaviours should have been evaluated using open-ended questions, rather than yes-or-no questions. Open-ended questions should also have been used to evaluate types of contraception use, specific gynaecological diseases, and types of hormones used. There may have been selection bias during recruitment, as sexual function is a sensitive issue, especially for Chinese women. The Taiwan version of the FSFI has not been validated in Hong Kong women; cut-off scores for Hong Kong women have not been established.

## Conclusion

Of Hong Kong gynaecology patients, 42% are at risk of FSD. Although older women tend to be at higher risk of FSD, the correlation between age and FSFI score was not significant. Menopausal women had a lower coital pain domain score; women not using contraception had a lower vaginal lubrication domain score.

## Contributors

WCL, TWL, JCPW and SSWN designed the study. AMHC, WKYY and PW acquired the data. AMHC and WKYY analysed the data. PW and KKWH drafted the manuscript. WCL and TWL critically revised the manuscript for important intellectual content. All authors had full

access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

## Conflicts of interest

All authors have no conflicts of interest to disclose.


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## Data availability

All data generated or analysed during the present study are available from the corresponding author on reasonable request.

## Ethics approval

The study was approved by the Kowloon Central/ Kowloon East Cluster Research Ethics Committee (reference: KC/KE-2019-0248/ER-3). The patients provided written informed consent for participating in the questionnaire study and for publication.


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**Active Ingredient:** Carbetocin. **Indications:** Prevention of postpartum haemorrhage due to uterine atony. **Dosage & Administration:** *Caesarean section under epidural or spinal anaesthesia* 100 mcg (1mL) IV slowly over 1 min. *Vaginal delivery* 100 mcg (1mL) IV slowly over 1 min or IM. **Contraindications:** Hypersensitivity. During pregnancy & labour before delivery. For induction of labour. Hepatic or renal disease. Serious CVD. Epilepsy. **Special Warnings and Precautions**: Must only be administered after delivery of infant & ASAP, preferably before delivery of placenta. Intended for single administration only. No data on additional doses of carbetocin or the use of carbetocin following persisting uterine atony after oxytocin. Monitor early signs of hyponatraemia e.g. drowsiness, listlessness & headache, particularly in patients receiving large vol of IV fluids. Use with caution in migraine, asthma, CVD or any state in which a rapid addition to extracellular water may produce hazard for an already overburdened system. Carefully monitor patients with eclampsia & pre-eclampsia. No studies on gestational DM. No established safety & efficacy, and dosage recommendation on adolescents. **Side Effects:** *IV* Headache, tremor, hypotension, flushing, nausea, abdominal pain, pruritus, feeling of warmth. *IM* Anaemia, headache, dizziness, tachycardia, hypotension, chest pain, nausea, abdominal pain, vomiting, back pain, muscular weakness, chills, pyrexia, pain. **Interactions:** Concomitant use w/ vasoconstrictors in conjunction w/ caudal block anaesthesia may lead to severe HTN. May enhance BP enhancing effect of ergot-alkaloids e.g. methylergometrine. Prostaglandins may potentiate effect of carbetocin. Some inhalation-anesthetics e.g. halothane & cyclopropane may enhance hypotensive effect of carbetocin, weaken effect of carbetocin & cause arrhythmias.

**References:** 1. Hong Kong Product Package Insert of DURATOCIN (Date of revision: JAN 2020)

**For additional information, please consult the product package insert before prescribing.**



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