ISSN 1608-9367 (Print)
ISSN 2225-904X (Online)

July 2023 • Volume 23 • Number 2

二零二三年七月 · 第廿三期 · 第二號

香港婦產助產科雜誌

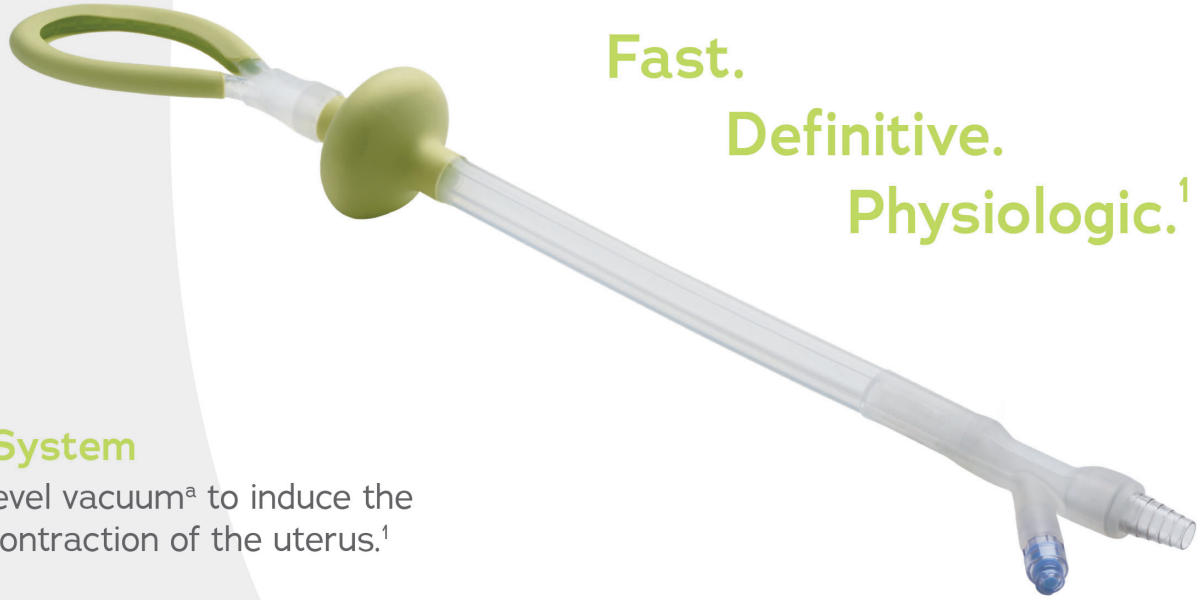
Hong Kong Journal of Gynaecology, Obstetrics and Midwifery

香港醫學專科學院出版社
HONG KONG ACADEMY OF MEDICINE PRESS

HONG KONG JOURNAL OF GYNAECOLOGY, OBSTETRICS AND MIDWIFERY
JULY 2023
VOLUME 23 NUMBER 2
PAGES 73–140

Jada

The Jada® System is intended to provide control and treatment of abnormal postpartum uterine bleeding or hemorrhage when conservative management is warranted.



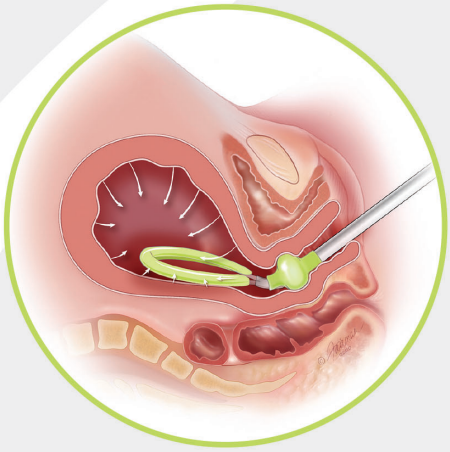
Fast. Definitive. Physiologic.[1]

The Jada System

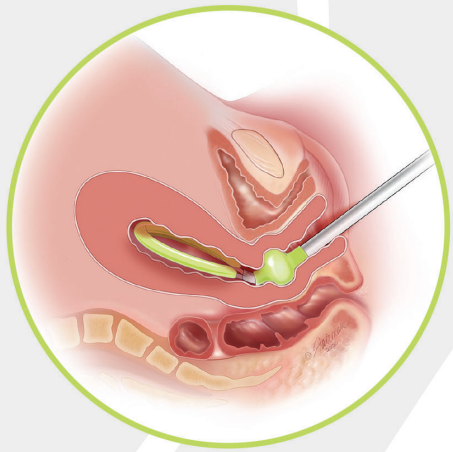
utilizes low-level vacuum[a] to induce the physiologic contraction of the uterus.[1]

94% Effectiveness

94% (n=100/106) of participants treated successfully in the PEARLE study with the Jada System (*P*<0.001).[1,b]



Low-level vacuum[a] induces collapse of the atonic postpartum uterus[1]



Contraction of the myometrium provides physiologic control of bleeding[1]

[a] 80 mm Hg +/- 10 mm Hg. The maximum vacuum pressure is 90 mm Hg. Do not increase the vacuum pressure higher than 90 mm Hg or tissue trauma may occur.

[b] Primary effectiveness was the control of postpartum hemorrhage, defined as the avoidance of non-surgical, second-line, or surgical intervention to control uterine hemorrhage.[1]

Reference: 1. D'Alton ME, Rood KM, Smid MC, et al. Intrauterine vacuum-induced hemorrhage-control device for rapid treatment of postpartum hemorrhage. *Obstet Gynecol.* 2020;136(5):882-891. doi:10.1097/AOG.0000000000004138

Please refer to the Jada System Instructions for Use for the indications, contraindications, warnings, precautions, and other important information at thejadasystem.com/ifu.

ORGANON
Here for her health

Organon Hong Kong Limited
Unit 48-136, 48/F Lee Garden One, 33 Hysan Avenue, Causeway Bay, Hong Kong
TEL: (852) 3427 8178 FAX: (852) 3427 8163

Scan this QR code to learn more about Jada

Tel: (852) 3427 8178
E-mail: seacomms@organon.com

HK-JDA-110000 Jul/2022

HONG KONG JOURNAL

OF

GYNAECOLOGY, OBSTETRICS & MIDWIFERY

July 2023, Volume 23, Number 2

EDITORIAL

Moving forward 80
Raymond HW LI

OBSTETRICS

Pregnancy and perinatal outcomes in women with pre-gestational diabetes before and during the COVID-19 pandemic 81
Wing Cheung PUN, Po Lam SO, Kar Hung SIONG

Effects of antenatal dexamethasone for maternal antepartum haemorrhage on term babies 88
Ka-Wai KONG, Kwok-Yin LEUNG

Conservative management for placenta accreta spectrum disorders: experience of a regional hospital from 2013 to 2021 93
Yiu Fai WONG, Tsz Kin LO, Viola Ying Tze CHAN, Vivian Kwun Sin NG, Wai Kuen YUNG, Hin Hung TSANG, Chi Hung KOO, Danny Hing Yan CHO, Wai Lam LAU, Wing Cheong LEUNG

Timing of elective Caesarean section at term on neonatal morbidities 101
Man Kee Teresa MA, Kwok-Yin LEUNG

Maternal near miss in three tertiary-level hospitals in Hong Kong 106
Shu Man Carmen NG, Po Lam SO, Wendy SHU, Tin Yan Mimi SETO, Ka Wang CHEUNG

GYNAECOLOGY

Patient acceptability and satisfaction for hysteroscopic morcellation 113
Cassie LEUNG, Lee Ting KWONG, Po Lam SO, Sai Fun WONG, Kam Ming CHOW

Safety and efficacy of ferric derisomaltose and its effect on blood transfusions in women with severe anaemia from heavy menstrual bleeding 120
Caryssa Ling YAN, Benjamin Ross YOUNG, Jade Wing Ngan SHEK, Po Lam SO

Levonorgestrel-releasing intrauterine system versus oral progestogens for non-atypical endometrial hyperplasia: predictors for treatment failure 127
James Yuen Jim LAW, Lee Ting KWONG, Po Lam SO

FEATURE

Tsan Yuk Hospital: a century of dedicated obstetrical service 135
Barry Ming-Chak LAW, Pui-Wah HUI

OBITUARY

In memory of Prof LEE Kin Hung 140
Karen KL CHAN, KK TANG

Duratocin®
CARBETOCIN

Protecting Mothers from Postpartum Haemorrhage due to Uterine Atony[1]

- Provide the balance between efficacy & safety amongst uterotonics[2]
- Heat-stable & does not need refrigeration[1,3]

References:

1. Hong Kong Product Package Insert of DURATOCIN (Date of revision: JAN 2020). 2. Gallos ID *et al* 2018. Uterotonic agents for preventing postpartum haemorrhage: a network meta-analysis. *Cochrane Database Syst Rev.* 12(12):CD011689. 3. Malm M *et al* 2018. Development and stability of a heat-stable formulation of carbetocin for the prevention of postpartum haemorrhage for use in low and middle-income countries. *J Pept Sci.* 24(6):e3082.

Abbreviated Prescribing Information of DURATOCIN

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.

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

Ferring Pharmaceuticals Ltd.
Suite 3301, 33/F, AIA Kowloon Tower, Landmark East,
100 How Ming Street, Kwun Tong, Kowloon, Hong Kong
Tel: +852 2622 8000 Fax: +852 2622 8001

FERRING
PHARMACEUTICALS

HK-DUR-2200003 Date of Production: Oct 2022

MIMS EDUCATION

Make a difference in your patient care

Advance your clinical skills with free online courses.

An expansive catalogue of medical modules.

Learn on-demand, anytime, and anywhere.

New courses added every month.

Improving HPV screening and triage in light of vaccination NEW Course

Obstetrics And Gynaecology | Family Medicine | General Practice

Learning outcomes

Upon completion of this module, participants will be able to:

- Identify factors necessitating HPV screening of increased sensitivity.
- Compare the risk of cervical disease in people screened HPV-negative or HPV-positive for HPV16/18 and 12 other HPVs.
- Evaluate the performance of dual staining versus cytology in risk stratification of HPV-positive cases.
- Explain the impact of shifting from cytology to dual staining on HPV management algorithms (including sensitivity, residual disease and number of colposcopies).

Enroll Now!

Please scan the QR code to access the module

HKJGOM

EDITORIAL BOARD

Address for Submission of Manuscripts and Correspondence to Editors:

(Gynaecology and Obstetrics Section)
c/o Department of Obstetrics and Gynaecology
Queen Mary Hospital, 102 Pokfulam Road, Hong Kong
Tel: 2255 4517 Fax: 2855 0947 E-mail: raymondli@hku.hk

(Midwifery Section)
Hong Kong Midwives Association
D1, 13/F, Hyde Centre, 223 Gloucester Road, Wanchai, Hong Kong
Tel: 2893 8800 Fax: 2572 5329 E-mail: midwives@netvigator.com

Address for Advertising & Subscription Enquiries:

The Obstetrical and Gynaecological Society of Hong Kong
Duke of Windsor Social Service Building, 4/F, 15 Hennessy Road, Hong Kong
Dr. KY Leung E-mail: leungky1@ha.org.hk
Dr. Danny TN Leung E-mail: dannytnleung@gmail.com
Dr. Dominic FH Li E-mail: dfhli@hkstar.com

Subscriptions

The *Hong Kong Journal of Gynaecology, Obstetrics & Midwifery* is distributed free to members of the Obstetrical & Gynaecological Society of Hong Kong and the Hong Kong Midwives Association as part of their membership. Subscription is HK$200/year for Hong Kong delivery and US$50/year for airmail delivery outside Hong Kong.

IF SHE RESPONDS TO CHEMOTHERAPY

YOU RESPOND WITH ZEJULA®

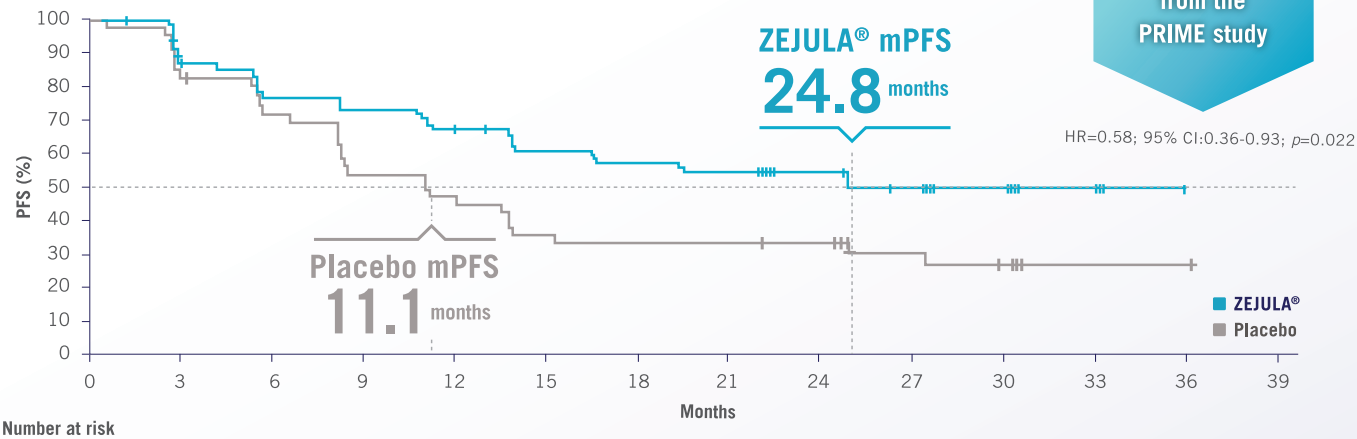
For your HRd BRCAwt patients:

Choose ZEJULA®

The only PARP inhibitor* that significantly improved mPFS in newly diagnosed advanced ovarian cancer patients with HRd BRCAwt tumors who responded to platinum-based chemotherapy.[1-3]

PFS in the BRCAwt, HRd subgroup populations[4]

New data from the PRIME study



Number at risk

ZEJULA®	85	71	63	60	54	48	45	42	36	25	13	6	0	0
Placebo	47	39	32	24	20	16	15	15	13	8	6	1	1	0

Figure adapted from Li N, 2022.

The efficacy with ZEJULA® was observed to be consistent across different patient subgroups, regardless of HRd or BRCA status.[4]

*as monotherapy

Abbreviations: BRCA: Breast cancer susceptibility gene; BRCAwt: Breast cancer susceptibility gene wild type; CI: Confidence interval; HR: Hazard ratio; HRd: Homologous recombination deficient; mPFS: Median progression-free survival; PARP: Poly ADP ribose polymerase; PFS: Progression-free survival

References: 1. ZEJULA® (niraparib). Prescribing information. Zai Lab; Aug 2021. 2. Lynparza® (Olaparib). Summary of Product Characteristics. Jan 2018. 4206580. 3. Rubraca® (Rucaparib). Summary of Product Characteristics. May 2020. 4609275. 4. Li N et al. Efficacy and Safety of Niraparib as Maintenance Treatment in Patients with Newly Diagnosed Advanced Ovarian Cancer Using an Individualized Starting Dose (PRIME Study): A Randomized, Double-blind, Placebo-controlled, Phase 3 Trial. Presented at: Society of Gynecologic Oncology Annual Meeting on Womens' Cancer 2022; 18-21 March 2022; Phoenix, Arizona, USA.

Zejula Capsules 100 mg – Abbreviated PI

Name of the Medicinal Product: Zejula Capsules 100 mg. Each hard capsule contains niraparib tosylate monohydrate equivalent to 100 mg niraparib. Therapeutic Indications: Zejula is indicated as monotherapy for the maintenance treatment of adult patients with: • advanced epithelial (FIGO Stages III and IV) high-grade ovarian, fallopian tube or primary peritoneal cancer who are in response (complete or partial) following completion of first-line platinum-based chemotherapy, • platinum-sensitive relapsed high grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in response (complete or partial) to platinum-based chemotherapy. Posology: *First-line ovarian cancer maintenance treatment*: 200mg once daily. *Recurrent ovarian cancer maintenance treatment*: 300mg once daily. Take the dose at approximately the same time each day. Bedtime administration may potentially help to manage nausea. Continued treatment is recommended until disease progression or toxicity. *Dose adjustments for adverse reactions*: In general, it is recommended to first interrupt the treatment (but no longer than 28 consecutive days) to allow the patient to recover from the adverse reaction and then restart at the same dose. In the case that the adverse reaction recurs, it is recommended to reduce the dose. If adverse reactions persist beyond a 28-day dose interruption, or are not manageable with this strategy of dose interruption and reduction, recommend to discontinue Zejula. Refer to the full prescribing information for detailed recommendations on dosage adjustments for adverse reactions, patients with higher/lower body weight and missed dose. No dose adjustment is needed for patients with mild to moderate renal impairment or mild hepatic impairment. Contraindications: Hypersensitivity. Breast-feeding. Warnings and Precautions: *Haematologic* - Haematologic adverse reactions (thrombocytopenia, anaemia, neutropenia) have been reported in patients treated with Zejula. Complete blood counts should be tested according to schedule. Discontinue Zejula if patient develops severe persistent haematologic toxicity including pancytopenia that does not resolve within 28 days following interruption. Anticoagulants and medicinal products known to reduce thrombocyte count should be used with caution. *Myelodysplastic syndrome/acute myeloid leukaemia* - Cases of MDS/AML have been observed in patients treated with Zejula monotherapy or combination therapy in clinical trials and postmarketing. If MDS and/or AML are confirmed while on treatment with Zejula, treatment should be discontinued and the patient treated appropriately. *Hypertension, including hypertensive crisis* – Hypertension, including hypertensive crisis, has been reported with the use of Zejula. Pre-existing hypertension should be adequately controlled before starting treatment and monitor blood pressure at least weekly for two months, monthly afterwards for the first year and periodically thereafter during treatment. Discontinue Zejula in case of hypertensive crisis or if medically significant hypertension cannot be adequately controlled with antihypertensive therapy. *Posterior Reversible Encephalopathy Syndrome (PRES)* – PRES has been reported in patients receiving Zejula. In case of PRES, discontinue Zejula and to treat specific symptoms including hypertension. *Hepatic impairment* – Carefully monitor in patients with moderate and severe hepatic impairment. Interaction with other medicinal products and other forms of interaction: Exercise caution when use in combination with vaccines, immunosuppressant agents or with other cytotoxic medicinal products; when niraparib is combined with active substances the metabolism of which is CYP3A4-dependent and, notably, those having a narrow therapeutic range (e.g. ciclosporin, tacrolimus, alfentanil, ergotamine, pimozide, quetiapine, and halofantrine), and metabolism of which is CYP1A2-dependent and, notably, those having a narrow therapeutic range (e.g. clozapine, theophylline, and ropinirole); when niraparib is combined with substrates of BCRP (irinotecan, rosuvastatin, simvastatin, atorvastatin, and methotrexate); and when combined with active substances that undergo an uptake transport by OCT1 such as metformin. Fertility, pregnancy and lactation: Women of childbearing potential should not become pregnant while on treatment and should not be pregnant at the beginning of treatment. A pregnancy test should be performed on all women of childbearing potential prior to treatment. Women of childbearing potential must use effective contraception during therapy and for 1 month after receiving the last dose of Zejula. Zejula should not be used during pregnancy. Breast-feeding is contraindicated during treatment and for 1 month after receiving the last dose. Undesirable Effects: ADRs of all grades occurring in ≥ 10% of patients in both PRIMA and NOVA trials were: nausea, anaemia, thrombocytopenia, fatigue, constipation, vomiting, headache, insomnia, platelet count decreased, neutropenia, abdominal pain, decreased appetite, diarrhoea, dyspnoea, hypertension, asthenia, dizziness, neutrophil count decreased, cough, arthralgia, back pain, white blood cell count decreased, and hot flush. The most common serious adverse reactions > 1 % (treatment-emergent frequencies) were thrombocytopenia and anaemia. Please refer to the full prescribing information before prescribing. Ref: HKPI version Aug 2021

Zai Lab (Hong Kong) Limited
Room 2301, 23/F, Island Place Tower, 510 King's Road North Point, Hong Kong, P.R. China
T: +852 3844 8100

HK-ZEJ-202206-01

Once-daily oral Zejula® niraparib capsules 100 mg

HKJGOM

INSTRUCTIONS TO AUTHORS

The *Hong Kong Journal of Gynaecology, Obstetrics & Midwifery* publishes peer-reviewed articles on all aspects of gynaecology, obstetrics, midwifery and related fields, including original basic and clinical studies, review articles, case reports, perspective, and abstracts or reports presented at scientific meetings or seminars.

Manuscripts submitted to this Journal must not be under simultaneous consideration by any other publication and should not have been published elsewhere in substantially similar form. A letter confirming the transfer of copyright to the Journal signed by all authors should accompany all submitted papers.

Manuscript Preparation

Manuscripts must be submitted in English or Chinese in an electronic format. This applies to all parts of the manuscript, i.e. references, legends, figures, illustrations etc. Liberal margins should be left at all edges. The manuscript should be submitted in the following order: Title Page, Abstract, Text, References, Tables, Legends, and Figures. Each page, beginning with the summary, should also include the senior author's surname in the upper left-hand corner. The author should not make any changes in the proofs except for the correction of editorial errors, if any, and/or correction of typesetter's errors. A commercial name should not be part of a manuscript title. If a trademark item is named, the name(s) and address(es) of the manufacturer(s) or supplier(s), in addition to the generic name, should be footnoted. Authors should make no claims of priority in their manuscripts.

Title Page

- Include full name(s), degree(s) and affiliations(s) of author(s): list under file
- Give a running title of 3 to 6 words
- At the bottom of the page, include information about grants, if applicable, and any conflicts of interest
- Add "Correspondence to: …", followed by full name, address, telephone and fax numbers, e-mail

Abstract

- The abstract should be after the title page and numbered page 1
- It should not exceed 250 words for major articles; case reports should have an abstract of no more than 100 words
- At the end of the abstract, provide a maximum of 6 key words suitable for indexing
- Abbreviations should be kept to a minimum and must be explained when they first appear; after first use, abbreviations alone may be used
- Standard abbreviations should be used for all measurements (SI units)

Text

- The text should follow the abstract and begin on a new page, as should references, tables and legends
- Abbreviations not defined in the abstract should be explained when they first appear in the text
- References should be cited in numerical order, as should tables and figures

References

- Number the references in the order they appear in the text
- Abbreviate titles of periodicals according to the style of *Index Medicus*. Follow the format (arrangement, punctuation) shown below:

Periodicals

1. Fuchs AR, Fuchs F, Husslein P, et al. Oxytocin receptors in the human uterus during pregnancy and parturition. *Am J Obstet Gynecol* 1984; 150:734-41.

Books edited by other authors of the article

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

Books edited by author

3. Varney H. Nurse Midwifery. *Boston: Blackwell Scientific Publications*; 1987: 23-32.

Abstract

4. Same as Periodicals and followed by (Abstract)

Tables

- Tables should supplement, but not duplicate, the text
- Tables should be numbered consecutively in their order of appearance in the text
- Each table must be given an Arabic numeral and a title, placed at the top of the page
- Abbreviations used in the table should be footnoted and explained in the order they appear in the table
- Any material which is not self-explanatory should be footnoted

Legends

- Be sure that legends and figures correspond
- Identify all abbreviations used in a figure at the end of each legend, if the abbreviation has not been used in the text
- Be sure abbreviations used for measurements are standard

Figures

- Submit written permission from publisher(s) for any figure which has been published elsewhere
- Do not send original art-work, X-rays, or CTGs
- Photographs in which a patient or other person is identifiable must have written permission from that person. The consent must state specifically what the person is consenting to and what restrictions, if any, the person has placed on the publication of the photograph; all restrictions must be strictly observed
- Colour illustrations will be charged to the author. Authors should inquire about cost from the publisher before submitting a colour illustration

Ethics

Published studies on humans should indicate the nature of consent and the approval of the institutional ethics committee. In reports of animal experiments, ethical approval must be enclosed.

Reprints

Reprints are available at authors' expense. Ordering information can be obtained from the Publisher.

Hong Kong J Gynaecol Obstet Midwifery 2023;23(2):80 | https://doi.org/10.12809/hkjgom.23.2.350

Editorial
Moving forward

Conceived in 2000, the *Hong Kong Journal of Gynaecology, Obstetrics and Midwifery* (HKJGOM) is the official publication of the Obstetrical and Gynaecological Society of Hong Kong and the Hong Kong Midwives Association. It has thrived, thanks to the capable leadership of past editors-in-chief. It is truly a great honour for me to succeed Dr William Wing-Kee To, who has recently retired from this position, and to continue the journal's mission, together with Dr Irene Lai-Yin Lee.

Our journal has been predominated by articles with a local flavour. Indeed, it is an important and popular platform for our trainees to publish their research. Additionally, it publishes articles related to history, evolution, new developments, and milestones of our specialty. Looking to the future, we welcome contributions from outside Hong Kong to foster the exchange of knowledge and experience.

While we are grateful that most of our editorial board members have agreed to continue serving our journal, we gladly welcome Dr Symphorosa Chan and Dr Kwok-Keung Tang as new editors on board to provide comprehensive coverage of all subspecialties. We thank Mr Kim Hinshaw, Dr Waldo Sepulveda, and Prof Paul Anthony Lewis for guiding us in their capacity as overseas editors. Following their retirement, we are very pleased to have Prof Kristina Gemzell-Danielsson, Prof Katie Morris, and Prof Dame Cathy Warwick joining us as new overseas editors.

It was amazing to read in the last issue's editorial how Dr William To single-handedly managed the vast majority of the editorial work in the obstetrics and gynaecology section. I very much agree with his vision that we should aim to further improve our articles in both quantitative and qualitative terms. To prepare for the increasing workload, we have introduced changes to the editorial process. The work of the editors-in-chief is now shared with three deputy editors: Dr Tsz-Kin Lo, Dr Ka-Yu Tse, and Ms Chit-Ying Lai. Each incoming manuscript is assigned to a handling editor who will manage the peer review process and make recommendations. With the help of the Hong Kong Academy of Medicine Press, we have established an online manuscript management system to facilitate the workflow. This is facilitated by the Open Journal Systems, an open-source journal management and publishing software, to which the electronic archive has been migrated as well. Accepted articles can be accessed online as soon as they are copyedited and proofread. Ultimately, our goal is to get HKJGOM indexed in MEDLINE and PubMed and to obtain an impact factor, but this takes time.

During the COVID-19 pandemic, our profession was immensely affected. Research activities were hampered by service interruptions, staff redeployment, sickness, and infection control measures. However, it was gratifying to see that many researchers, particularly trainees, persisted in conducting meaningful research projects and reporting their findings through our Journal. Now academic exchange and research activities are getting back on track, which is key to progress in this era of evidence-based medicine.

In this issue, we include a feature article commemorating Tsan Yuk Hospital's centenary. Established in 1922 as a maternity hospital, Tsan Yuk Hospital has played a leading role in the development of obstetric services in Hong Kong. Nowadays, while we recognise with pride the high-quality obstetric and midwifery care provided by obstetric units in Hong Kong, we cherish the legacy and foundation that Tsan Yuk Hospital has laid.

In the years to come, we hope to see contributions by authors from various backgrounds to enrich our Journal's scientific content. Constructive comments and suggestions to help our Journal reach new heights are welcome.

Raymond HW LI, MBBS, MD, FRCOG, FHKAM (O&G), Cert RCOG (Reproductive Medicine), Cert HKCOG (Reproductive Medicine)
Editor-in-Chief, *Hong Kong Journal of Gynaecology, Obstetrics and Midwifery*

Correspondence to: Dr Raymond HW LI
Email: raymondli@hku.hk

Hong Kong J Gynaecol Obstet Midwifery 2023;23(2):81-7 | https://doi.org/10.12809/hkjgom.23.2.340

Pregnancy and perinatal outcomes in women with pre-gestational diabetes before and during the COVID-19 pandemic

Wing Cheung PUN, MBBS, MRCOG
Po Lam SO, MBBS, MRCOG, FHKAM (O&G)
Kar Hung SIONG, MBBS, MRCOG, FHKAM (O&G)
Department of Obstetrics and Gynaecology, Tuen Mun Hospital, Hong Kong SAR, China

Objective: This study compared the compliance with scheduled antenatal visits as well as pregnancy and perinatal outcomes of pregnant women with pre-gestational diabetes before and during the COVID-19 pandemic.
Methods: Medical records of women with singleton pregnancies and pre-gestational type I or type II diabetes who attended antenatal care at Tuen Mun Hospital between 1 September 2017 and 31 March 2022 were retrieved. Modifiable and non-modifiable risk factors associated with adverse pregnancy outcomes were analysed, including glycated haemoglobin levels, body mass index, smoking status, attendance of antenatal follow-up, maternal age, parity, ethnicity, diabetes type, pre-pregnancy medical conditions, Caesarean section rate, hypertensive disorders complicating pregnancy, preterm birth (birth at <37 weeks of gestation), and large and small for gestational age.
Results: Of 152 women included in the analysis, 74 attended between 4 January 2020 and 31 March 2022 (the pandemic group) and 78 attended between 1 September 2017 and 3 January 2020 (the pre-pandemic group). The two groups were comparable in terms of compliance with their scheduled antenatal visits and all pregnancy and perinatal outcomes, except that the pandemic group had higher rates of emergency Caesarean sections (44.6% vs 23.5%, p=0.010) and neonatal hypoglycaemia (51.6% vs 34.3%, p=0.046). Both groups had good glycaemic control.
Conclusion: In women with pre-gestational diabetes, the rate of emergency Caesarean sections significantly increased during the pandemic, although compliance with scheduled antenatal visits and maternal and neonatal outcomes were similar before and during the pandemic. This suggests that the quality and accessibility of maternity care were not compromised by the pandemic.

Keywords: COVID-19; Pregnancy, high-risk; Pregnancy in diabetics; Pregnancy outcome

Introduction

In March 2020, the World Health Organization declared the emergence of the novel coronavirus SARS-CoV-2 (also known as COVID-19) a pandemic and major international health emergency, replete with the associated socio-economic, political, and emotional impacts[1]. This may have affected women's perception of the risk of catching COVID-19 in hospital and their health-seeking behaviour. For example, in the United Kingdom, pregnant women were reluctant to attend fetal monitoring appointments because of concerns about potential exposure to the virus while in hospital[2]. Similarly, the rate of loss to antenatal appointments increases from 18% to 51.9% during the pandemic in middle- and low-income countries due to fear of the virus, a lack of transportation, and the social pressure to isolate[3,4]. Likewise, in Hong Kong, 30.4% of the interviewed subjects reported avoiding medical consultation for fear of catching COVID-19[5]. Since Hong Kong government activated the 'serious response level', attendance at emergency departments decreased by 37%[6].

Pregnancy in women with pre-gestational diabetes is associated with an increased risk of adverse fetal and maternal outcomes, as fetal glucose uptake is directly related to maternal glucose concentration. Maternal hyperglycaemia stimulates fetal insulin secretion, which leads to hypertrophy of insulin-sensitive tissues (adipose tissue, skeletal muscle, and myocardium) and accelerated fetal growth[7,8]. In particular, women with type I diabetes and suboptimal glucose control have a higher risk of perinatal morbidity[9]. Maternal hyperglycaemia is associated with a greater likelihood of adverse pregnancy outcomes such as macrosomia, primary Caesarean section, clinical neonatal hypoglycaemia, shoulder dystocia or birth injury, preterm delivery, intensive neonatal care admission, hyperbilirubinemia, stillbirth, pre-eclampsia, and maternal mortality[10]. Therefore, pregnant women with pre-gestational diabetes require more intense care to improve their glycaemic control and pregnancy outcomes[11,12].

Correspondence to: Dr Wing Cheung PUN
Email: pwc574@ha.org.hk

During the COVID-19 pandemic, the general population was less physically active and more sedentary[13-15]. This lifestyle changes, together with the disruption to essential healthcare services, restrictions on social interaction, and changes to health-seeking behaviour particularly affect pregnant women with diabetes. Rates of maternal mortality and stillbirths are reported to increase in low- and middle-income countries during the pandemic[16]. This study compared the compliance with scheduled antenatal visits as well as pregnancy and perinatal outcomes of pregnant women with pre-gestational diabetes before and during the pandemic.

Materials and methods

Medical records of women with singleton pregnancies and pre-gestational type I or type II diabetes who attended antenatal care at Tuen Mun Hospital between 1 September 2017 and 31 March 2022 were retrieved through the Hospital Obstetrics Specialty Clinical Information System and the Antenatal Record System. Management for these women was standardised, involving early diabetic complication screening, shorter follow-up intervals, universal prescription of aspirin, and close monitoring of blood glucose levels.

Characteristics and pregnancy and perinatal outcomes of these women were collected. Pregnancy outcomes included any antepartum complications, hypertension, diabetes type, pre-eclampsia, induction of labour, and mode of delivery. Fetal and perinatal outcomes included premature birth, gestational age at birth, stillbirth, neonatal death, sex, birth weight, Apgar scores, and admission to a neonatal intensive care unit.

Modifiable and non-modifiable risk factors associated with adverse pregnancy outcomes were analysed. Modifiable risk factors included glycated haemoglobin (HbA1c) levels, body mass index, smoking status, and attendance at antenatal follow-ups. Good compliance was defined as >75% attendance at scheduled antenatal visits. Non-modifiable risk factors included maternal age, parity, ethnicity, diabetes type, and pre-pregnancy medical conditions. Adverse pregnancy outcomes included undergoing a Caesarean section, hypertensive disorders complicating pregnancy, preterm birth (birth at <37 weeks of gestation), large and small for gestational age (LGA and SGA) as defined by the local growth chart, neonatal intensive care unit admission, birth asphyxia, and stillbirth. The composite adverse neonatal outcome included LGA, SGA, preterm birth, and birth asphyxia at 5 minutes.

Data analysis was performed using SPSS (Windows version 22.0; IBM Corp, Armonk [NY], US). Continuous variables for the two groups (before and during the pandemic) were compared using the unpaired *t* test or Wilcoxon rank-sum test, whereas categorical variables were compared using the Chi-squared test or Fisher's exact test. A p value of <0.05 was considered statistically significant.

Results

Of 216 pregnant women with pre-gestational diabetes identified, 32 with duplicated entries, 30 with no diabetes before pregnancy, and two with twin pregnancies were excluded. The remaining 152 women were included in the analysis. Of them, 74 attended between 4 January 2020 and 31 March 2022 after the declaration of the serious response level (the pandemic group) and 78 attended between 1 September 2017 and 3 January 2020 (the pre-pandemic group).

The two groups were comparable in terms of compliance with their scheduled antenatal visits and all pregnancy and perinatal outcomes, except that the pandemic group had higher rates of emergency Caesarean sections (44.6% vs 23.5%, p=0.010) and neonatal hypoglycaemia (51.6% vs 34.3%, p=0.046) [Table 1]. Both groups had good glycaemic control as evidenced by a reduction in women with suboptimal HbA1c and an increase in insulin usage during pregnancy.

During the pandemic, there was a non-significant increasing trend in the number of emergency Caesarean sections performed for hypertensive disorder, refusal of a trial of scar during labour, and placenta praevia (Table 2). None of the Caesarean sections was performed because of maternal medical conditions related to COVID-19; indeed, only one patient developed a COVID-19 infection during pregnancy. There was no increase in hypertensive disorder complicating pregnancy during the pandemic.

Pregnancy preparation was considered adequate when the pre-pregnancy HbA1C was <6.5%; by this measure, only 28.8% and 35.8% of women were well prepared before and during the pandemic, respectively. The two groups were comparable in terms of pre-pregnancy HbA1c and the proportion of pre-pregnancy body mass index >25 kg/m^2. There was no significant reduction of SGA or prematurity during the pandemic. Cases of congenital anomalies in babies were few (Table 3).

Table 1. Baseline characteristics and pregnancy and perinatal outcomes of women with diabetes before and during the COVID-19 pandemic

	Pre-pandemic (n=78)*	Pandemic (n=74)*	p Value
Age, y	34.83±5.53	34.19±5.44	0.470
Smoker	8 (10.3)	8 (10.8)	0.911
In-vitro fertilisation	5 (6.4)	3 (4.1)	0.72
Nulliparous	42 (53.8)	36 (48.6)	0.522
Chinese	69 (89.6)	67 (90.5)	0.849
Diabetic mellitus			0.486
Type I	3 (3.8)	5 (6.8)	
Type II	75 (96.2)	69 (93.2)	
Readiness for pregnancy			
Pre-pregnancy body mass index >25 kg/m^2	57 (75)	52 (70.3)	0.584
Pre-pregnancy glycated haemoglobin (HbA1C) >6.5%	42 (71.2)	34 (64.2)	0.544
Pre-pregnancy HbA1c, %	7.55±1.61	7.70±2.23	0.680
Use of aspirin	43 (55.8)	51 (68.9)	0.098
Comorbidities			
Pre-existing hypertension	10 (12.8)	12 (16.2)	0.552
Retinopathy	10 (12.8)	9 (12.2)	0.902
Nephropathy	12 (15.4)	5 (6.8)	0.092
Weight gained during pregnancy, kg	10.81±6.84	9.63±5.19	0.251
HbA1c >6.5 % in the third trimester	25 (37.3)	25 (37.9)	0.946
Good compliance to scheduled antenatal visits	50 (70.4)	47 (67.1)	0.686
Glucose in range of <6 (fasting) to <8 (post meal) mmol/L	28 (40)	29 (42)	0.571
Insulin usage			
First trimester			
Short acting, unit/dose	6.68±6.65	5.50±5.03	0.233
Long acting, unit	8.34±10.86	7.96±9.48	0.822
Second trimester			
Short acting, unit/ dose	10.74±7.48	10.49±9.0	0.858
Long acting, unit	11.12±10.81	13.15±13.57	0.892
Third trimester			
Short acting, unit/dose	13.51±9.21	13.52±10.58	1.00
Long acting, unit	13.62±12.00	16.23±11.1	0.267
Pregnancy outcome		0.561	
Live birth	68 (87.2)	65 (87.8)	
Miscarriage	5 (6.4)	4 (5.4)	
Stillbirth	2 (2.6)	0	
Elective termination of pregnancy	3 (3.8)	2 (2.7)	
Induction of labour	27 (39.7)	28 (42.4)	0.861
Vaginal delivery	26 (36.6)	16 (23.5)	0.238
Assisted vaginal delivery	4 (5.6)	4 (5.9)	0.238
Emergency Caesarean section	16 (23.5)	29 (44.6)	0.010
Hypertensive disorder complicating pregnancy	24 (31.6)	25 (35.7)	0.085

* Data are presented as mean ± standard deviation or No. (%) of participants; total may not equal 100% because of missing data

Table 1. (cont'd)

	Pre-pandemic (n=78)*	Pandemic (n=74)*	p Value
Antepartum haemorrhage	4 (5.8)	8 (12.3)	0.187
Primary postpartum haemorrhage >500 ml	26 (33.3)	32 (43.2)	0.209
Baby sex	n=68	n=65	
Female	25 (36.8)	26 (40.0)	0.701
Male	43 (63.2)	39 (60.0)	0.701
Large for gestational age	33 (45.8)	37 (53.6)	0.225
Small for gestational age	9 (12.5)	5 (7.2)	0.248
Fetal anomaly	7 (10.1)	6 (9.2)	0.858
Prematurity (<37 weeks)	14 (17.9)	12 (16.2)	0.777
Birth asphyxia (Apgar score <3 at 5 mins)	2 (3.0)	0	0.164
Neonatal intensive care unit care (>24 hours)	18 (26.9)	22 (34.4)	0.427
Neonatal sepsis	10 (14.9)	17 (26.6)	0.100
Neonatal hypoglycaemia	23 (34.3)	33 (51.6)	0.046
Shoulder dystocia	0	2 (2.7)	0.230
Composite adverse neonatal outcome (small for gestational age, birth asphyxia, and preterm delivery <37 weeks)	19 (26)	15 (25.4)	0.539
Composite adverse neonatal outcome (large and small for gestational age, birth asphyxia, and preterm delivery <37 weeks)	44 (60.3)	47 (66.2)	0.287

Table 2. Indications for emergency Caesarean section

Indication	No. (%) of women with emergency Caesarean section		p Value
	Pre-pandemic (n=16)	Pandemic (n=29)	
Hypertensive disorder	3 (18.7)	8 (27.5)	0.720
Refused trial of scar during labour	2 (12.5)	7 (24.1)	0.456
Placenta praevia	1 (6.3)	5 (17.2)	0.399
Fetal distress/suboptimal cardiotocography	3 (18.7)	5 (17.2)	1.000
No progress	1 (6.3)	3 (10.3)	1.000

Table 3. Congenital anomalies of babies

Congenital anomaly	No. of babies with congenital anomaly	
	Pre-pandemic	Pandemic
Cardiac	4	3
Renal	0	2
Multiple	1	1
Talipes	1	0

Discussion

The pregnancy outcomes of women with pre-gestational diabetes were similar before and during the COVID-19 pandemic, except that the rate of emergency Caesarean sections increased from 23.5% to 44.6%, which concurs with a cohort study in England[17] and a preliminary report on singleton non-diabetic pregnancies in the United Kingdom[18], but the increase was 1.4% only in the English study, compared with 21.1% in our study. A higher rate of induced labour was observed in the English study. The centralisation of maternity services and potential delays due to virtual appointments noted in the Western world[19,20] are unlikely the attributable factors in Hong Kong as the structure of maternity services remained largely unchanged. There was no significant reduction in in-person attendance of antenatal services in Hong Kong during the pandemic. In our study, the rate of refusal of a trial of scar during labour increased from 12.5% to 24.1% during the pandemic. The

increased rate could be due to the patients' anxiety or the attending doctors' anticipation of difficulties in arranging emergency operations during the pandemic. Occupational stress and burnout during the pandemic among maternity staff could also have resulted in a lower threshold for interventions to expedite births and avoid emergencies[21].

In our study, the stillbirth rate remained similar before and during the pandemic. Interestingly, a study in Ireland observed an unprecedented reduction in infants born at a very low birth weight during the COVID-19 lockdown[22]. In our cohort, although there was a reduction in SGA babies from 11.4% before the pandemic to 5.9% during the pandemic, the impact of the pandemic is less evident because there was no lockdown in Hong Kong and the decrease in the antenatal attendance rate was not apparent. However, our sample was from a single centre in a short time frame; the findings may not be generalised to the entire population. For example, a significant increase in the stillbirth rate was observed at St George's University Hospital in London, but the stillbirth rate reached a record low of 3.8 stillbirths per 1000 births in 2020 in the United Kingdom[23].

During the pandemic, there was a reduction in both routine and unscheduled pregnancy care across different healthcare settings in high- and low-income countries[24-26]. Concern and anxiety about the risk of contracting COVID-19 in healthcare settings, lockdowns, and reduced public transport provision might have led to this reduction[24]. However, in our study, the antenatal attendance rate remained largely unchanged because there was no lockdown in Hong Kong. Moreover, women with high-risk pregnancies such as those with pre-gestational diabetes have no option but have to comply with the management from tertiary-level centres in public hospitals as the care provided by the private sector can be limited. Priority is also given to high-risk pregnancies. These women are followed up in a designated clinic with multidisciplinary inputs in accordance with protocols.

In our study, diabetic control in pregnant women with pre-gestational diabetes was not deteriorated during the pandemic, as evidenced by patients' in-range HbA1c and glucose levels. These findings align with those in studies of patients with diabetes during the pandemic[27,28]. Maintenance of diabetic control may be due to more time for self-care and diabetic management, including eating a balanced diet and exercising, during the pandemic.

In our study, the miscarriage rate was similar before and during the pandemic, in contrast to a review of women with pre-gestational diabetes in Ireland in 2021[29]. Compared with the Irish study, our study had much higher rates of SGA (9.9% vs 0.4%) and congenital anomalies (7.7% vs 4.8%). According to the 2014 territory-wide audit published by the Hong Kong College of Obstetricians and Gynaecologists, 6.6% of singletons were born with a low birth weight (<2500 g)[30]. Our study defined SGA as a birth weight less than the tenth percentile for gestational age instead of <2500 g, which can explain the apparently lower incidence of SGA in our cohort than in the general population of Hong Kong. In our study, most congenital anomalies involved non-life-threatening and surgically correctable conditions such as small atrial or ventricular septal defects, dilated renal pelvis, and talipes.

Limitations to our study include its retrospective nature, small sample size, and short time frame. In Hong Kong, most women with pre-gestational diabetes attend public hospitals for antenatal care. Thus, data for pre-gestational diabetic control were comprehensive and accessible despite the study being retrospective. The sample size during the COVID-19 pandemic was small. However, our sample is predominantly Chinese and is specifically relevant to Hong Kong. There were potential associations between changes in healthcare and society during the COVID-19 pandemic and the pregnancy outcomes of women with pre-gestational diabetes. A territory-wide prospective study to delineate healthcare needs in Hong Kong during the pandemic, for example to assess whether face-to-face care or telemedicine would better cater to pregnant women with pre-gestational diabetes, is warranted.

Conclusion

In women with pre-gestational diabetes, the rate of emergency Caesarean sections significantly increased during the pandemic, although compliance with scheduled antenatal visits and maternal and neonatal outcomes were similar before and during the pandemic. This suggests that the quality and accessibility of maternity care were not compromised by the pandemic.

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 disclosed no conflicts of interest.

Funding/support

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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 New Territories West Cluster Research Ethics Committee (reference: NTWC/REC/22022). 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.

References

1. Bogin B, Varea C. COVID-19, crisis, and emotional stress: a biocultural perspective of their impact on growth and development for the next generation. Am J Hum Biol 2020;32:e23474. Crossref
2. Karavadra B, Stockl A, Prosser-Snelling E, Simpson P, Morris E. Women's perceptions of COVID-19 and their healthcare experiences: a qualitative thematic analysis of a national survey of pregnant women in the United Kingdom. BMC Pregnancy Childbirth 2020;20:600. Crossref
3. Kotlar B, Gerson EM, Petrillo S, Langer A, Tiemeier H. The impact of the COVID-19 pandemic on maternal and perinatal health: a scoping review. Reprod Health 2021;18:10. Crossref
4. Landrian A, Mboya J, Golub G, Moucheraud C, Kepha S, Sudhinaraset M. Effects of the COVID-19 pandemic on antenatal care utilisation in Kenya: a cross-sectional study. BMJ Open 2022;12:e060185. Crossref
5. Hospital Authority Clinical Data Analysis and Reporting System, Hospital Authority, Hong Kong SAR.
6. Hung KK, Walline JH, Chan EYY, et al. Health service utilization in Hong Kong during the COVID-19 pandemic: a cross-sectional public survey. Int J Health Policy Manag 2022;11:508-13.
7. Hay WW Jr. Placental-fetal glucose exchange and fetal glucose metabolism. Trans Am Clin Climatol Assoc 2006;117:321-40.
8. Di Cianni G, Miccoli R, Volpe L, Lencioni C, Del Prato S. Intermediate metabolism in normal pregnancy and in gestational diabetes. Diabetes Metab Res Rev 2003;19:259-70. Crossref
9. Murphy HR, Howgate C, O'Keefe J, et al. Characteristics and outcomes of pregnant women with type 1 or type 2 diabetes: a 5-year national population-based cohort study. Lancet Diabetes Endocrinol 2021;9:153-64. Crossref
10. Evers IM, de Valk HW, Visser GH. Risk of complications of pregnancy in women with type 1 diabetes: nationwide prospective study in the Netherlands. BMJ 2004;328:915. Crossref
11. Malaza N, Masete M, Adam S, Dias S, Nyawo T, Pheiffer C. A systematic review to compare adverse pregnancy outcomes in women with pregestational diabetes and gestational diabetes. Int J Environ Res Public Health 2022;19:10846. Crossref
12. Negrato CA, Mattar R, Gomes MB. Adverse pregnancy outcomes in women with diabetes. Diabetol Metab Syndr 2012;4:41. Crossref
13. Ong JL, Lau TY, Massar SAA, et al. COVID-19-related mobility reduction: heterogenous effects on sleep and physical activity rhythms. Sleep 2021;44:zsaa179. Crossref
14. Clemente-Suárez VJ, Beltrán-Velasco AI, Ramos-Campo DJ, et al. Physical activity and COVID-19. The basis for an efficient intervention in times of COVID-19 pandemic. Physiol Behav 2022;244:113667. Crossref
15. Castañeda-Babarro A, Arbillaga-Etxarri A, Gutiérrez-Santamaría B, Coca A. Physical activity change during COVID-19 confinement. Int J Environ Res Public Health 2020;17:6878. Crossref
16. Chmielewska B, Barrett I, Townsend R, et al. Effects of the COVID-19 pandemic on maternal and perinatal outcomes: a systematic review and meta-analysis. Lancet Glob Health 2021;9:e759-72. Crossref
17. Gurol-Urganci I, Waite L, Webster K, et al. Obstetric interventions and pregnancy outcomes during the COVID-19 pandemic in England: a nationwide cohort study. PLoS Med 2022;19:e1003884. Crossref
18. Office for National Statistics. Provisional Births in England and Wales: 2020. Available at: https://wwwonsgovuk/peoplepopulationandcommunity/birthsdeathsandmarriages/livebirths/articles/ provisionalbirthsinenglandandwales/2020.
19. Birthplace in England Collaborative Group, Brocklehurst P, Hardy P, et al. Perinatal and maternal outcomes by planned place of birth for healthy women with low risk pregnancies: the Birthplace in England national prospective cohort study. BMJ 2011;343:d7400. Crossref
20. Jardine J, Relph S, Magee L, et al. Maternity services in the UK during the coronavirus disease 2019 pandemic: a national survey of modifications to standard care. BJOG 2021;128:880-9. Crossref
21. Bourne T, Shah H, Falconieri N, et al. Burnout, well- being and defensive medical practice among obstetricians and gynaecologists in the UK: cross-sectional survey study. BMJ Open 2019;9:e030968. Crossref

22. Philip RK, Purtill H, Reidy E, et al. Unprecedented reduction in births of very low birthweight (VLBW) and extremely low birthweight (ELBW) infants during the COVID-19 lockdown in Ireland: a 'natural experiment' allowing analysis of data from the prior two decades. BMJ Glob Health 2020;5:e003075. Crossref
23. Khalil A, von Dadelszen P, Draycott T, Ugwumadu A, O'Brien P, Magee L. Change in the incidence of stillbirth and preterm delivery during the COVID-19 pandemic. JAMA 2020;324:705-6. Crossref
24. Khalil A, von Dadelszen P, Kalafat E, et al. Change in obstetric attendance and activities during the COVID-19 pandemic. Lancet Infect Dis 2021;21:e115. Crossref
25. Goyal M, Singh P, Singh K, Shekhar S, Agrawal N, Misra S. The effect of the COVID-19 pandemic on maternal health due to delay in seeking health care: experience from a tertiary center. Int J Gynaecol Obstet 2021;152:231-5. Crossref
26. Justman N, Shahak G, Gutzeit O, et al. Lockdown with a price: the impact of the COVID-19 pandemic on prenatal care and perinatal outcomes in a tertiary care center. Isr Med Assoc J 2020;22:533-7.
27. Fernández E, Cortazar A, Bellido V. Impact of COVID-19 lockdown on glycemic control in patients with type 1 diabetes. Diabetes Res Clin Pract 2020;166:108348. Crossref
28. Eberle C, Stichling S. Impact of COVID-19 lockdown on glycemic control in patients with type 1 and type 2 diabetes mellitus: a systematic review. Diabetol Metab Syndr 2021;13:95. Crossref
29. Newman C, Egan AM, Ahern T, et al. Diabetes care and pregnancy outcomes for women with pregestational diabetes in Ireland. Diabetes Res Clin Pract 2021;173:108685. Crossref
30. Hong Kong College of Obstetricians and Gynaecologists. Territory-wide audit in obstetrics and gynecology 2014. Available at: https://www.hkcog.org.hk/hkcog/Download/Territory-wide_Audit_in_Obstetrics_Gynaecology_2014.pdf.

Hong Kong J Gynaecol Obstet Midwifery 2023;23(2):88-92 | https://doi.org/10.12809/hkjgom.23.2.341

Effects of antenatal dexamethasone for maternal antepartum haemorrhage on term babies

Ka-Wai Kong, MBChB, MRCOG
Kwok-Yin Leung, MBBS, MD, FRCOG, FHKAM (O&G), Cert HKCOG (MFM)
Department of Obstetrics and Gynaecology, Queen Elizabeth Hospital, Hong Kong

Objective: This study aims to compare the outcomes of term babies with or without in utero exposure to dexamethasone as a result of maternal antepartum haemorrhage (APH).
Methods: Medical records of women with antepartum haemorrhage who had a singleton livebirth delivered at ≥37 weeks of gestation in the Queen Elizabeth Hospital, Hong Kong, between 1 January 2019 and 31 December 2021 were retrospectively reviewed. Primary outcomes were the small-for-gestational-age (SGA) rate, the neonatal intensive care unit (NICU) admission rate, and low Apgar score at 5 minutes. Secondary outcomes were the Caesarean section rate and the operative vaginal delivery rate.
Results: A total of 898 women were included; 50 (5.6%) of them had completed a course of antenatal dexamethasone. Compared with women without antenatal dexamethasone, women with antenatal dexamethasone were associated with higher rates of gestational diabetes mellitus (22% vs 7.2%, p<0.001), operative vaginal delivery (16% vs 9.8%, p=0.005), earlier gestational week at delivery (38.2 vs 39.2 weeks, p<0.001), and lower neonatal birthweight (3001.4 vs 3149.6 g, p=0.004). In logistic regression analysis, antenatal exposure to dexamethasone was associated with an increased risk of having an operative vaginal delivery (adjusted odds ratio=2.98, p=0.016) and a reduced risk of having an SGA baby for every 1-week increase in pregnancy (adjusted odds ratio=0.69, p=0.002).
Conclusion: Antenatal dexamethasone for women with antepartum haemorrhage was not associated with SGA infants, NICU admission, or low Apgar score but was associated with earlier delivery, lower neonatal birthweight, and a higher rate of operative vaginal delivery. The latter remained significant in logistic regression analysis. More studies are needed to identify any potential effects on term babies exposed to antenatal corticosteroids.

Keywords: Apgar score; Dexamethasone; Infant, small for gestational age; Intensive care units, neonatal

Introduction

Antenatal corticosteroids given to pregnant women within 7 days of preterm delivery can reduce the risks of fetal prematurity including respiratory distress syndrome, intraventricular haemorrhage, necrotising enterocolitis, and even neonatal death[1,2]. Antepartum haemorrhage (APH) is associated with preterm delivery; unexplained APH carries a threefold higher risk of preterm delivery[3], notwithstanding placenta abruptio or heavy bleeding associated with placenta praevia. APH may also be an early sign of preterm labour. Patients with spotting, even if the most likely cause is lower genital tract bleeding, may consider taking antenatal corticosteroids[4], but the optimal regimen and the effects of corticosteroids on term infants are unclear[5]. In utero exposure to betamethasone is associated with a higher risk of having a small-for-gestational-age (SGA) infant and neonatal intensive care unit (NICU) admission[6]. This study aimed to compare the outcomes of term babies with or without in utero exposure to dexamethasone as a result of maternal APH.

Materials and methods

Medical records of women with APH who had a singleton livebirth delivered at ≥37 weeks of gestation in the Queen Elizabeth Hospital, Hong Kong, between 1 January 2019 and 31 December 2021 were retrieved from the Clinical Data Analysis and Reporting System and retrospectively reviewed. Those who did not receive a complete course of dexamethasone or had preterm premature rupture of membranes were excluded.

The diagnosis and management of APH were based on history taking, physical examination, ultrasonography, and speculum examination, with reference to guidelines from the Royal College of Obstetricians and Gynaecologists[4]. Cardiotocography was used to assess fetuses at ≥26 weeks of gestation. Delivery was considered in patients with severe vaginal bleeding, evidence of fetal compromise, or pregnancy at term. Antenatal corticosteroids were given to women with major vaginal bleeding between a gestational age of 24+0 and 33+6 weeks. The dexamethasone regimen was decided by the attending obstetrician: either three intramuscular doses of dexamethasone 8 mg every 8 hours

Correspondence to: Ka-Wai KONG
Email: kkw013@ha.org.hk

or two intramuscular doses of dexamethasone 12 mg every 12 hours. A repeated course of dexamethasone was only given by specialist obstetricians for women who had a recurring threat of preterm birth within 7 days of 33 weeks' gestation with an interval of >14 days after completing the first course.

Maternal variables collected included age at delivery, race, mode of delivery, antenatal complications (ie, APH, gestational diabetes mellitus [GDM], hypertensive disorder), estimated date of confinement, and date of dexamethasone administration. Neonatal variables collected included gestational age at birth, birth weight, sex, date of birth, Apgar score at 5 minutes, and NICU admission within 24 hours of delivery.

Primary outcomes were the SGA rate, the NICU admission rate, and low Apgar score (<7) at 5 minutes. Birthweights were compared against the World Health Organization estimated fetal weight chart based on the Hadlock formula, using a cut-off of the <10th percentile at the corresponding gestational age at birth[7]. Secondary outcomes were the Caesarean section rate and the operative vaginal delivery rate (ie, ventouse or forceps delivery).

Assuming one-third of patients with APH were prescribed with antenatal corticosteroids[8,9], the proportion of SGA infants was expected to increase from 5% to 10% after exposure to in utero dexamethasone. To achieve alpha of 0.05 and 80% power, the sample size required was 1085. In our hospital, about 300 to 400 patients delivering at term each year have a history of APH, and thus 3 years of records were retrieved. Statistical analysis was performed using SPSS (Windows version 28.0; IBM Corp, Armonk [NY], USA). The dexamethasone and control groups were compared using Chi-squared and *t* tests. Continuous variables were compared using two-sample independent *t* tests. Binary logistic regression analysis was used to determine associations of in utero exposure to dexamethasone with the SGA rate, the NICU admission rate, the Caesarean section rate, and the operative vaginal delivery rate.

Results

A total of 898 women were included in analysis; 50 (5.6%) of them had completed a course of antenatal dexamethasone (Table 1). The mean gestation age at the time of exposure to dexamethasone was 30.95±2.27 weeks, and the mean interval from completion of dexamethasone to delivery was 7.2±2.47 weeks. No patient had a repeated course of corticosteroids.

Compared with women without antenatal dexamethasone (n=848), women with antenatal dexamethasone (n=50) were associated with higher rates of gestational diabetes mellitus (22% vs 7.2%, p<0.001), operative vaginal delivery (16% vs 9.8%, p=0.005), earlier gestational week at delivery (38.2 vs 39.2 weeks, p<0.001), and lower neonatal birthweight (3001.4 vs 3149.6 g, p=0.004) but was not associated with SGA infants, NICU admission, or low Apgar score (Table 1).

In logistic regression analysis, antenatal exposure to dexamethasone was associated with an increased risk of having an operative vaginal delivery (adjusted odds ratio [aOR]=2.98, p=0.016) and a reduced risk of having an SGA baby for every 1-week increase in gestational age at delivery (aOR=0.69, p=0.002) [Table 2]. Every 1-week increase in gestational age at delivery was associated with a reduced odds of having a Caesarean section (aOR=0.59, p<0.001) and an increased odds in having an operative vaginal delivery (aOR=1.47, p=0.003). Women with GDM were two times more likely to have a Caesarean section (aOR=2.09, p=0.005).

Discussion

Antenatal corticosteroids for APH did not increase the risks of having an SGA infant, NICU admission, or low Apgar score. This is in contrast to the findings of a study that reported an increase in the rates of NICU admission and SGA among babies delivered at term after antenatal exposure to betamethasone[6]. This may be due to differences in case selection criteria, as in the present study only patients with a clinically significant episode of APH were given antenatal dexamethasone. Nonetheless, another study reported no difference in neonatal morbidities after in utero exposure to corticosteroids[10].

Exposure to antenatal corticosteroids has been reported to be associated with lower neonatal birthweight[11], which was related to earlier delivery in the present study, although the clinical significance may be limited to a 1-week difference at term. Besides, the odds of operative vaginal delivery increased in women with antenatal dexamethasone. Further studies are needed to establish the underlying cause.

The inverse associations of gestational age with SGA infants and with Caesarean section rates may provide support for expectant management at term for patients with a history of APH, unless there is evidence of fetal compromise such as sonographic features of fetal growth restriction or abnormal cardiotocography.

Table 1. Maternal and fetal characteristics and outcomes in women with or without antenatal dexamethasone

	Antenatal dexamethasone		
	Yes (n=50)*	No (n=848)*	p Value
Maternal age, y	32.8±4.2	32.4±4.2	0.475
Advanced maternal age (>35 y)	15 (30)	242 (28.5)	0.824
Race			0.159
Chinese	44 (88)	790 (93.2)	
Non-Chinese Asian	6 (12)	43 (5.1)	
Caucasian	0	2 (0.2)	
Others/unknown	0	13 (1.5)	
Gestational diabetes mellitus	11 (22)	61 (7.2)	<0.001
Hypertensive disorder in pregnancy	0	1 (0.1)	0.808
Maternal asthma	2 (4)	15 (1.8)	0.261
Mode of delivery			0.005
Normal vaginal delivery	25 (50)	540 (63.7)	
Operative vaginal delivery	8 (16)	83 (9.8)	
Caesarean section	17 (34)	225 (26.5)	
Cause of antepartum haemorrhage			0.472
Unknown origin	44 (88)	745 (87.9)	
Placenta praevia	6 (12)	82 (9.7)	
Other	0	21 (2.5)	
Fetal characteristics			
Gestational week at delivery	38.2±0.97	39.2±1.1	<0.001
Birthweight, g	3001.4±353.2	3149.6±351.9	0.004
Apgar score at 5 min	8.34±0.59	8.23±0.57	0.179
Sex of baby			0.722
Male	26 (52)	419 (49.4)	
Female	24 (48)	429 (50.6)	
Small for gestational age	3 (6)	66 (7.8)	0.453
Neonatal intensive care unit admission	5 (10)	89 (10.5)	0.911
Low Apgar score (<7) at 5 min	1 (2)	5 (0.6)	0.292
Caesarean section	17 (34)	225 (26.5)	0.248
Indication for Caesarean section			0.057
Placenta praevia	5 (29.4)	71 (31.7)	
Previous uterine scar	5 (29.4)	14 (6.3)	
Failed induction	4 (23.5)	87 (38.7)	
Malpresentation	0	10 (4.4)	
Cephalopelvic disproportion	2 (11.8)	16 (7.1)	
Abnormal cardiotocograph	0	16 (7.1)	
Other	1 (5.9)	10 (4.4)	
Operative vaginal delivery	8 (16)	83 (9.8)	0.077
Indication for operative vaginal delivery			0.297
Abnormal cardiotocograph	3 (37.5)	40 (48.2)	
Prolonged second stage	4 (50)	41 (49.4)	
Other	1 (12.5)	2 (2.4)	

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

Table 2. Logistic regression analysis of outcomes adjusted for covariates

	Small-for-gestational-age baby*	p Value	Neonatal intensive care unit admission*	p Value	Caesarean section*	p Value	Operative vaginal delivery*	p Value
Dexamethasone (exposed vs non-exposed)	0.54 (0.16-1.82)	0.318	1.00 (0.38-2.66)	0.997	0.74 (0.39-1.43)	0.37	2.98 (1.23-7.26)	0.016
Maternal age (1-year increase)	0.97 (0.92-1.03)	0.313	1.02 (0.97-1.07)	0.537	1.03 (0.99-1.07)	0.104	0.99 (0.94-1.05)	0.78
Gestational age at delivery (1-week increase)	0.69 (0.55-0.87)	0.002	1.00 (0.82-1.22)	1.00	0.59 (0.51-0.69)	<0.001	1.47 (1.14-1.90)	0.003
Gestational diabetes mellitus (yes vs no)	0.96 (0.39-2.38)	0.925	0.59 (0.22-1.53)	0.276	2.09 (1.25-3.52)	0.005	2.04 (0.82-5.12)	0.127
Maternal asthma (yes vs no)	0.67 (0.09-5.22)	0.705	1.17 (0.26-5.21)	0.84	0.95 (0.31-2.87)	0.95	-	-

* Data are presented as adjusted odds ratio (95% confidence interval)

The presence of GDM has been reported to be associated with a higher Caesarean section rate[12]. Although the present study found that GDM was associated with dexamethasone use, 64% (n=7) of patients were diagnosed to have GDM before they were given dexamethasone. In the remaining 36% (n=4) of patients, the mean gestational age at the time of exposure to dexamethasone was 27.32±0.94 weeks and the time from dexamethasone completion to diagnosis of GDM was 12 to 46 days. Thus, the effect of dexamethasone on GDM was minimal, as the interval from dexamethasone completion to diagnosis of GDM was >72 hours[13]. As an oral glucose tolerance test was not routinely performed after dexamethasone administration, the actual prevalence of GDM in both groups may be underestimated.

The use of antenatal corticosteroids has well-established benefits for preterm babies, whereas the evidence for adverse effects in term babies is inconsistent. Antenatal corticosteroids should be given if there is a high chance of preterm delivery. The fibronectin test[14], transvaginal ultrasound measurement of cervical length[15], and uterine contractions[16] are useful predictors of preterm labour. The timing of the single course of antenatal corticosteroid should be carefully planned[17]. Repeated courses of corticosteroids should be avoided, as the long-term benefits and harms are not well understood.

Our study population consisted of mainly Chinese women, so the findings can be used as a reference for clinical practice in Hong Kong and China. However, the present study was prone to bias because of its retrospective nature. The small proportion of patients exposed to dexamethasone (5.6%) could be an indicator of reliable clinical experience among obstetricians in predicting preterm birth in those presenting with APH. Even so, the power of the study is limited by the small sample size in the exposed group. Furthermore, the severity of APH was not studied. The clinical judgement of significant APH or risk of preterm delivery may be subject to interobserver differences. In addition, the underlying cause of earlier deliveries was not investigated. Our findings might be attributed to different severities of APH or underlying pathologies, rather than the effects of dexamethasone. Hence, further observational studies are warranted to determine whether in utero exposure to dexamethasone is associated with earlier spontaneous onset of labour and a higher proportion of iatrogenic deliveries. There were no data on respiratory distress or long-term outcomes such as neurological deficits in the newborn. Maternal smoking was not assessed, but the effect was expected to be insignificant given active smoking in pregnancy is rare in Hong Kong[18]. Further studies are warranted to identify the underlying cause of the association between dexamethasone use and operative vaginal delivery.

Conclusions

Antenatal dexamethasone for APH was not associated with SGA infants, NICU admission, or low Apgar score but was associated with earlier delivery, lower neonatal birthweight, and a higher rate of operative vaginal delivery. The latter remained significant in logistic regression analysis. More studies are needed to identify any potential effects on term babies exposed to antenatal corticosteroids.

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

As an editor of the journal, KYL was not involved in the peer review process of this article. All other authors have disclosed no conflicts of interest.

Funding/support

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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-22-0092/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.

References

1. Stock SJ, Thomson AJ, Papworth S; Royal College of Obstetricians and Gynaecologists. Antenatal corticosteroids to reduce neonatal morbidity and mortality: Green-top Guideline No. 74. BJOG 2022;129:e35-60. Crossref
2. McGoldrick E, Stewart F, Parker R, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database Syst Rev 2020;12:CD004454. Crossref
3. Magann EF, Cummings JE, Niederhauser A, Rodriguez-Thompson D, McCormack R, Chauhan SP. Antepartum bleeding of unknown origin in the second half of pregnancy: a review. Obstet Gynecol Surv 2005;60:741-5. Crossref
4. Antepartum haemorrhage. Green-top Guideline No. 63. London: Royal College of Obstetricians and Gynaecologists; 2011.
5. Williams MJ, Ramson JA, Brownfoot FC. Different corticosteroids and regimens for accelerating fetal lung maturation for babies at risk of preterm birth. Cochrane Database Syst Rev 2022;8:CD006764. Crossref
6. McKinzie A, Yang Z, Teal E, et al. Are newborn outcomes different for term babies who were exposed to antenatal corticosteroids? Am J Obstet Gynecol 2021;225:536.e1-7. Crossref
7. Cheng YKY, Lu J, Leung TY, Chan YM, Sahota DS. Prospective assessment of INTERGROWTH-21st and World Health Organization estimated fetal weight reference curves. Ultrasound Obstet Gynecol 2018;51:792-8. Crossref
8. Sarid EB, Stoopler ML, Morency AM, Garfinkle J. Neurological implications of antenatal corticosteroids on late preterm and term infants: a scoping review. Pediatr Res 2022;92:1225-39. Crossref
9. Osteen SJ, Yang Z, McKinzie AH, et al. Long-term childhood outcomes for babies born at term who were exposed to antenatal corticosteroids. Am J Obstet Gynecol 2023;228:80.e1-6. Crossref
10. Muche AA, Olayemi OO, Gete YK. Effects of gestational diabetes mellitus on risk of adverse maternal outcomes: a prospective cohort study in Northwest Ethiopia. BMC Pregnancy Childbirth 2020;20:73. Crossref
11. Taleghani AA, Bhriguvanshi A, Kamath-Rayne BD, Liu C, Narendran V. Timing of antenatal steroid administration and effects on the newborn infant: a retrospective study. Am J Perinatol 2022;39:1065-73. Crossref
12. Gorgal R, Gonçalves E, Barros M, et al. Gestational diabetes mellitus: a risk factor for non-elective cesarean section. J Obstet Gynaecol Res 2012;38:154-9. Crossref
13. Jian Yun X, Zhaoxia L, Yun C, Qin F, Yuanyuan C, Danqing C. Changes in maternal glucose metabolism after the administration of dexamethasone for fetal lung development. Int J Endocrinol 2012;2012:652806. Crossref
14. Berghella V, Saccone G. Fetal fibronectin testing for reducing the risk of preterm birth. Cochrane Database Syst Rev 2019;7:CD006843. Crossref
15. Sotiriadis A, Papatheodorou S, Kavvadias A, Makrydimas G. Transvaginal cervical length measurement for prediction of preterm birth in women with threatened preterm labor: a meta-analysis. Ultrasound Obstet Gynecol 2010;35:54-64. Crossref
16. Leung TY, Chan LW, Tam WH, Leung TN, Lau TK. Risk and prediction of preterm delivery in pregnancies complicated by antepartum hemorrhage of unknown origin before 34 weeks. Gynecol Obstet Invest 2001;52:227-31. Crossref
17. Walters A, McKinlay C, Middleton P, Harding JE, Crowther CA. Repeat doses of prenatal corticosteroids for women at risk of preterm birth for improving neonatal health outcomes. Cochrane Database Syst Rev 2022;4:CD003935. Crossref
18. Kong GW, Tam WH, Sahota DS, Nelson EA. Smoking pattern during pregnancy in Hong Kong Chinese. Aust N Z J Obstet Gynaecol 2008;48:280-5. Crossref

Hong Kong J Gynaecol Obstet Midwifery 2023;23(2):93-100 | https://doi.org/10.12809/hkjgom.23.2.342

Conservative management for placenta accreta spectrum disorders: experience of a regional hospital from 2013 to 2021

Yiu Fai WONG[1], MBBS, MRCOG
Tsz Kin LO[2], MBBS, MRCOG, FHKAM (O&G)
Viola Ying Tze CHAN[1], MBBS, MRCOG, FHKAM (O&G), FHKCOG
Vivian Kwun Sin NG[1], MBChB, MSc in Medical Genetics, MRCOG, FHKCOG, FHKAM (O&G), Cert HKCOG (Maternal and Fetal Medicine)
Wai Kuen YUNG[1], MBBS, MRCOG, FHKAM (O&G), FHKCOG, Cert HKCOG (Maternal and Fetal Medicine)
Hin Hung TSANG[3], MBBS, MRCP, FHKAM (Medicine)
Chi Hung KOO[4], MBBS, FHKCA, FHKAM (Anaesthesiology), FANZCA
Danny Hing Yan CHO[5], MBBS, FRCR, HKCR, FHKAM (Radiology)
Wai Lam LAU[1], MBBS, FRCOG, FHKAM (O&G), FHKCOG, Cert HKCOG (Maternal and Fetal Medicine)
Wing Cheong LEUNG[1], MBBS, MD, FRCOG, FHKAM (O&G), FHKCOG, Cert RCOG (Maternal and Fetal Medicine), Cert HKCOG (Maternal and Fetal Medicine)
[1] Department of Obstetrics and Gynaecology, Kwong Wah Hospital, Hong Kong
[2] Department of Obstetrics and Gynaecology, Princess Margaret Hospital, Hong Kong
[3] Department of Intensive Care Unit, Kwong Wah Hospital, Hong Kong
[4] Department of Anaesthesiology & OT Services, Kwong Wah Hospital, Hong Kong
[5] Department of Diagnostic and Interventional Radiology, Kwong Wah Hospital, Hong Kong

Introduction: Conservative management by leaving the placenta in situ for placenta accreta spectrum (PAS) disorders can preserve the uterus with reduced surgical complications. This study aims to review the outcomes of planned conservative management for PAS disorders between January 2013 and December 2021.
Methods: The medical records of patients with clinically and/or histopathologically confirmed PAS disorders who underwent conservative management by leaving the placenta in situ between 1 January 2013 and 31 December 2021 at Kwong Wah Hospital, Hong Kong, were retrospectively reviewed. Uterine artery embolisation and various haemostatic methods were used to control bleeding.
Results: A total of 17 patients with PAS disorders were conservatively treated by leaving the placenta in situ. Of these, 15 patients had major placenta praevia; 16 patients had a history of Caesarean delivery; and 10 patients presented with sonographic features of PAS disorders. Intraoperatively, eight patients had partial placenta left in situ, whereas five patients had the entire placenta left in situ. All patients had good maternal outcomes and recovery, except for four patients who had major complications during the immediate postpartum period. Two patients eventually required a hysterectomy.
Conclusion: Planned conservative management for PAS disorders can achieve good clinical outcomes in a regional hospital with a multidisciplinary team.

Keywords: Conservative treatment; Hysterectomy; Placenta; Placenta accreta; Postpartum haemorrhage

Introduction

Placenta accreta spectrum (PAS) disorders, ranging from abnormally adherent to deeply invasive placental tissue, can significantly affect deliveries[1]. The prevalence of PAS disorders is on a rising trend. In Hong Kong, the prevalence of PAS disorders increased from 0.17 per 1000 births in 1999-2003 to 0.79 per 1000 births in 2009-2013[2]. Caesarean hysterectomy is the recommended treatment[3] but is associated with risks of massive intraoperative haemorrhage, injury to other pelvic organs, and loss of fertility. Thus, conservative management is advocated for selected patients[4], including the extirpative technique (manual removal of the placenta), the expectant approach (leaving the placenta in situ), the one-step conservative surgery (removal of the accreta area), and the triple-P procedure (perioperative localisation of the upper placental

Correspondence to: Dr Yiu Fai WONG
Email: matthewwong007@hotmail.com

edge, pelvic devascularisation, placental non-separation with myometrial excision, and uterine repair)[5].

Leaving the placenta in situ is the primary management plan in our hospital. In 2013, we reported on 12 cases of PAS treated with this method, and the results supported its use in hospitals with interventional radiology facilities[6]. This study aimed to review the outcomes of planned conservative management for PAS disorders between January 2013 and December 2021, with use of various haemostatic measures.

Materials and methods

The medical records of patients with clinically and/or histopathologically confirmed PAS disorders who underwent conservative management by leaving the placenta in situ between 1 January 2013 and 31 December 2021 at Kwong Wah Hospital, Hong Kong, were retrospectively identified through the Clinical Data Analysis and Reporting System using diagnosis codes for adherent placenta, placenta accreta, placenta increta, placenta percreta, and morbidly adherent placenta. Patients in whom PAS was not suspected antenatally but was detected incidentally during delivery were excluded. To ensure no cases of PAS were missed, another hospital database, OBSCIS, was cross-checked using the keywords 'primary post-partum haemorrhage due to accreta/percreta' and 'Caesarean section for morbidly adherent placenta'.

Since 2008, our hospital has adopted a protocol for uterine conservation for patients with PAS who wish to retain their uterus. Patients with risk factors for PAS (including major placenta praevia in previous Caesarean deliveries, multiple uterine surgeries such as surgical termination of pregnancies and uterine curettage, and a previous history of PAS) were reviewed by maternal-fetal medicine specialists in the third trimester. Detailed ultrasound scanning was performed to identify features of PAS (such as abnormal placental lacunae, myometrial thinning), as described by FIGO (The International Federation of Gynecology and Obstetrics)[7]. For patients with clinical and/or sonographic features suspicious of PAS, detailed counselling on intrapartum management, potential complications, and follow-up with diagram illustrations were provided, taking into account the patient's wish for uterine conservation.

Caesarean delivery was scheduled at around 37 weeks, with bilateral tubal ligation offered at same setting. A multidisciplinary approach was initiated, involving the blood bank, paediatricians, an anaesthetic team, an intensive care unit team for postoperative support, a radiology team for uterine artery embolisation (UAE), and a urology team on standby in case of bladder injury. Steroid prophylaxis was given if delivery was scheduled before 37 weeks of gestation.

Delivery by Caesarean section was performed under general anaesthesia in a lead-shielded operating room equipped with facilities for interventional radiology. Patient haemodynamics were monitored intra- and post-operatively. Large-bore intravenous cannulae and rapid fluid infusion and warming devices were used for fluid resuscitation and to prevent hypothermia. A 5-Fr femoral arterial sheath was inserted by the interventional radiologist via the groin before Caesarean section. The operation was attended by operating surgeons and one or two consultant obstetricians. A vertical skin incision was made to avoid cutting through the vascular lower segment and placenta. After delivery of the baby, the edge of the uterine wound was clamped using Green-Armytage forceps. Time was allowed for spontaneous separation of the placenta, usually within 30 minutes. Forceful manual removal of the adherent placental part was prohibited, while any spontaneously separated part was trimmed away. The remaining morbidly adherent placenta tissue was left in situ unless there was active bleeding or haemodynamic instability. The proportion of placenta left in situ was estimated visually. After uterine wound closure, UAE was then performed with absorbable gelatin-based microparticles injected under fluoroscopic screening to embolise engorged arteries. An angiogram was performed to confirm sluggish flow of bilateral uterine arteries and beyond. A speculum examination was performed before and after UAE and at the end of the operation to check for excessive bleeding from the cervical os.

After surgery, prophylactic broad-spectrum antibiotics with amoxicillin/clavulanic acid were given for at least 1 week. Patients were transferred to the intensive care unit for close monitoring for at least 1 day and then returned to general ward once they had stabilised. After discharge, patients were followed up in a special postnatal clinic. Early signs of sepsis and delayed haemorrhage were sought, with regular monitoring of markers including the haemoglobin level, white blood cell count, C-reactive protein, and genital swabs. Serial ultrasounds were performed to monitor placental resorption. Methotrexate was not given as adjuvant therapy.

Owing to the rare occurrence of PAS disorders, the sample size was expected to be small. Statistical analysis was performed using SPSS (version 26.0; IBM Corp, Armonk

[NY], United States of America). Nominal variables were summarised by frequencies and percentages and tested with the Fisher's exact test. Quantitative variables were summarised by median and range and were tested with the Wilcoxon rank-sum test. Statistical significance was set at $p<0.05$.

Results

A total of 17 patients with PAS disorders were managed conservatively in our unit between 2013 and 2021. With a total delivery number of around 38 700, the rate of PAS disorders was 0.44 per 1000 births, which was similar to the 0.4 per 1000 births reported in our unit between 2008 and 2012[6] (Table 1).

Of the 17 patients, 13 were aged ≥35 years at the time of delivery. Only one patient did not have a history of Caesarean delivery. All diagnoses of placenta praevia were made antenatally by ultrasound. 15 patients had major praevia (type III-IV); 10 patients presented with sonographic features of PAS disorders, and four of them had more than one marker. All patients underwent classical Caesarean section, except for one who had a lower segment transverse uterine incision in view of the well-formed and relatively avascular lower uterine segment. Patient 17 required a Caesarean hysterectomy because of uncontrolled massive bleeding despite multiple medical treatments. After delivery, all patients (except the patient with a lower segment Caesarean section) were transferred to the intensive care unit.

All patients had good maternal outcomes and recovery, except for four patients who had major complications during the immediate postpartum period (Table 2). Patient 3 underwent re-laparotomy for haemorrhagic shock due to bleeding from raw areas, which was controlled with stitches. Patient 7 had sepsis and severe anaemia after passing 5-cm placental tissue on day 10; the complication was controlled with blood transfusion, intravenous antibiotics, and an intrauterine balloon. Patient 15 had a burst abdomen on day 8 after removal of skin stitches, which was re-sutured using tension sutures. Patient 16 had persistent vaginal bleeding with fever despite broad-spectrum intravenous antibiotics; she underwent emergency suction evacuation under ultrasound guidance to remove intrauterine septic foci on day 15. Six (35%) patients required re-admission; all were treated conservatively, except for patient 9 who required a hysterectomy at 2 months after delivery for uncontrolled postpartum haemorrhage despite repeated UAE. The patient had haemoperitoneum 1 day after hysterectomy, requiring re-laparotomy to control bleeding from the peritoneal edge at the left pelvic sidewall.

The 17 patients with PAS disorders in 2013-2021 were compared with the 12 patients with PAS disorders in 2008-2012 (Table 1). All patients had placenta praevia. The proportion of patients with placenta adherent and left behind was lower in the present cohort than in the past cohort (median [range], 30% [0%-100%] vs 90% [20%-100%], p=0.03). The proportion of patients with postpartum haemorrhage requiring treatment was also lower in the present cohort than in the past cohort (29% vs 75%, p=0.025), as was the proportion of patients with paralytic ileus after delivery despite not significantly (24% vs 42%, p=0.422). However, two patients in the present cohort required a hysterectomy, compared with no patient in the past cohort required a hysterectomy.

Discussion

The success rate of uterine conservation using the expectant approach for PAS disorders has been reported to range from 62% to 90%[4,8-10]. In the present study, the success rate of uterine conservation was nearly 90%. Thus, this study supports the use of an expectant approach for managing PAS disorders.

Antenatal diagnosis of PAS disorders is crucial. In our unit, both clinical risk factors and sonographic features are assessed to identify patients antenatally. In our patients, sonographic features of PAS disorders, as described by FIGO[7], were absent in >40% of patients; this shows the limitations of ultrasonography for the prenatal diagnosis of PAS disorders. The median gestation at delivery in our patients was 37 weeks, which is recommended by the Royal College of Obstetricians and Gynaecologists[3]. In 2019, FIGO proposed a new classification system for the clinical diagnosis of PAS disorders[11]. We reclassified our patients using this system to better differentiate between accreta, increta, and percreta. Although four of our patients had no placental tissue left in situ after Caesarean delivery, they were classified as PAS (grade 1) under the new classification system, as the adherent placental tissue was manually removed secondary to excessive bleeding from the placental bed and required extra haemostatic procedures to control bleeding. Patients with a higher clinical grade required a more complicated operation for a deeper and larger adherent area and a longer follow-up duration and had more postpartum complications and a lower success rate of uterine conservation.

Table 1. Baseline, antepartum, intrapartum, and postpartum characteristics of patients with placenta accreta spectrum (PAS) disorders in 2013-2021 and 2008-2012

Characteristic	2013-2021 (n=17)*	2008-2012 (n=12)*	p Value
Maternal age, y	37 (31-43)	35 (33-40)	0.211
Advanced maternal age (≥35 y)	13 (76)	8 (67)	0.683
Parity	2 (1-9)	1 (1-2)	0.152
History of Caesarean delivery	16 (94)	12 (100)	1.00
For placenta praevia	2 (12.5)	2 (17)	1.00
History of PAS	0	-	-
History of surgical termination of pregnancy / dilation and curettage	9 (53)	8 (73) of 11	0.435
No. of previous surgical termination of pregnancy / dilation and curettage	2 (1-6)	1 (1-3)	0.236
Placenta praevia			-
Type I	1 (6)	0	
Type II	1 (6)	0	
Type III anterior	6 (35)	2 (17)	
Type III posterior	5 (29)	2 (17)	
Type IV	4 (24)	8 (67)	
History of antepartum haemorrhage	8 (47)	5 (42)	1.00
Sonographic features of PAS disorders	10 (59)	9 (75)	0.449
>1 sonographic marker	4 (24)	6 (50)	-
Steroid given before delivery	10 (59)	-	-
Total operative time, min	176 (68-438)	153 (91-254)	0.419
Gestation at delivery, wk	37 (33-38)	37 (33-38)	0.394
Emergency Caesarean section	4 (24)	4 (33)	0.683
Type of skin incision, midline	17 (100)	12 (100)	-
Classical Caesarean section	16 (94)	11 (92)	1.00
Placenta removal			
Adherent but removed completely	4 (24)	0	-
Left partially in situ	8 (47)	7 (58)	-
Left completely in situ	5 (29)	5 (42)	-
Duration of observation to confirm absence of placental separation, min	20 (0-30) [6 not documented]	17.5 (10-59)	0.913
% of placenta adherent and left in situ	30 (0-100)	90 (20-100)	0.03
Intraoperative blood loss, ml	1100 (300-7600)	1200 (500-3300)	0.845
No. of patients requiring transfusion	9 (53)	6 (50)	1.00
No. of pack cells transfused	2 (0-15)	1 (0-10)	0.879
Additional haemostatic measures			
Tranexamic acid	9 (53)	-	-
Additional uterotonics besides oxytocin	4 (24)	6 (50)	-
Balloon tamponade	6 (35)	-	-
Uterine artery embolisation	16 (94)	12 (100)	-
Ligation of uterine vessels	0	-	-
Compression sutures	5 (29)	4 (33)	-
Hysterectomy	1 (6)	0	-

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

Table 1. (cont'd)

Characteristic	2013-2021 (n=17)*	2008-2012 (n=12)*	p Value
FIGO classification			
Grade 1 (placenta accreta)	11 (all clinical)	-	-
Grade 2 (placenta increta)	6 (5 clinical + 1 histological)	-	-
Grade 3 (placenta percreta)	0	-	-
Hospital stay after delivery, d	8 (5-29)	7.5 (5-13)	0.303
Intensive care unit admission after delivery	16 (94)	11 (92)	1.00
Paralytic ileus	4 (24)	5 (42)	0.422
Major complications	4 (24)	0	0.121
Re-admission	6 (35)	8 (67)	0.139
Total episodes of re-admission	9	13	-
Secondary postpartum haemorrhage	5 (29)	9 (75)	0.025
Transfusion required	3 (18)	1 (8)	-
Managed conservatively	4 (24)	9 (75)	-
Passage of tissue	8 (47)	8 (67)	0.338
Interval from Caesarean delivery, mo	2.3 (0.3-4)	3.3 (1-7)	0.232
Sepsis	2 (12)	0	0.498
Return of menstruation	11 (65); 4 lost to follow-up; 2 had hysterectomy	12 (100)	-
Interval from Caesarean delivery, mo	3 (1-12)	3.6 (1.5-7.5)	0.519
Sonographic resolution of retained placenta, mo	4 (0.3-14)	6.6 (2-13)	0.408
Fertility	1 Caesarean hysterectomy, 1 elective hysterectomy 2 mo later	No hysterectomy	-
Bilateral tubal ligation at Caesarean delivery on maternal request	9 (53)	6 (50)	-
Declined bilateral tubal ligation but no plan for future pregnancy	6 (38); 1 not discussed	6 (50)	-
Pregnancy after delivery	0	-	-

Haemostatic measures during delivery have changed over the years. First, the early prophylactic use of tranexamic acid at skin incision has increased, whereas the prophylactic use of tranexamic acid during Caesarean delivery has mixed results in preventing massive obstetric haemorrhage. The additional use of tranexamic acid is effective in reducing intraoperative blood loss and intraoperative and postoperative transfusion of blood and blood products[12,13]. Second, the use of misoprostol has reduced over the years, because oxytocin is superior to misoprostol in controlling bleeding and misoprostol has a delayed clinical effect on uterine tone[14,15]. Third, there is wider use of mechanical methods to control bleeding such as Hwu's compression sutures for lower uterine segment placental bed bleeding, balloon tamponade for local compression, and temporary tourniquet around the lower segment of the uterus to locally compress the uterine vessels; the choice of method depends on the surgeon's intraoperative judgement. Fourth, there has been limited use of carbetocin, as it can lead to earlier separation of the adherent placental part, causing excessive bleeding. UAE is routinely performed after closing the uterine wound to arrest bleeding in patients with PAS[16].

In our patients, resolution of retained placental tissue took weeks to >1 year. The prevalence of postpartum bleeding and sepsis was low, and most patients with these complications were treated conservatively and made a good recovery. Nevertheless, clinicians should actively monitor patients for signs and symptoms of these complications to enable early intervention. Two of our patients had a hysterectomy. This suggests that conservative management

Table 2. Management of the 17 patients during Caesarean delivery and postpartum re-admission

Patient	Year admitted	Extent of placenta retained, %	Additional haemostatic measures besides oxytocin and uterine artery embolisation	Blood loss, ml	Postpartum major complications	Re-admission interval from delivery, mo	Reason for re-admission	Treatment
1	2013	10	Tourniquet around lower segment with tube or gauze, Hwu's sutures, B-Lynch compression sutures	2200	-	-	-	-
2	2013	100	-	1800	-	1, 2, 3	Postpartum haemorrhage, urethral pain, urethral pain	Repeated uterine artery embolisation, transfusion, conservative treatment
3	2013	0	Balloon tamponade	2000	Re-laparotomy for haemorrhagic shock, with 3000 ml haemoperitoneum due to bleeding from raw areas, controlled with stitches	-	-	-
4	2013	100	-	300	-	3	Abdominal pain	Manual removal at bedside with no anaesthesia (of dislodging placental tissue through cervix)
5	2015	0	Tourniquet around lower segment with tube or gauze, balloon tamponade, Hemabate, B-Lynch compression sutures, Transamin	3500	-	-	-	-
6	2016	30	Tourniquet around lower segment with tube or gauze, B-Lynch compression sutures, repeated uterine artery embolisation, balloon tamponade, Hemabate	2700	-	1	Postpartum haemorrhage, *Escherichia coli* bacteraemia	Conservative treatment
7	2016	50	-	1600	Passed 5-cm placental tissue on postdelivery day 10, complicated with sepsis and severe anaemia, controlled with blood transfusion, intravenous antibiotics, and intrauterine balloon	-	-	-
8	2017	0	Hwu's sutures, B-Lynch compression sutures	1000	-	-	-	-
9	2017	100	Transamin	400	-	2, 2.5	Endometritis, massive postpartum haemorrhage	Conservative treatment, repeated uterine artery embolisation, then total abdominal hysterectomy owing to persistent significant per-vaginal bleeding
10	2018	25	Transamin, carbetocin	1100	-	-	-	-
11	2019	0	Transamin, balloon tamponade	1800	-	-	-	-
12	2019	100	Transamin	1000	-	-	-	-
13	2019	100	-	1000	-	-	-	-

Table 2. (cont'd)

Patient	Year admitted	Extent of placenta retained, %	Additional haemostatic measures besides oxytocin and uterine artery embolisation	Blood loss, ml	Postpartum major complications	Re-admission interval from delivery, mo	Reason for re-admission	Treatment
14	2019	30	Transamin	500	-	2.5	Endometritis	Manual removal at bedside with no anaesthesia (of dislodging placental tissue through cervix)
15	2019	5	Transamin	500	Burst abdomen on postdelivery day 8 after removal of skin stitches, re-sutured using tension sutures	-	-	-
16	2019	10	Transamin, balloon tamponade	500	Persistent vaginal bleeding with fever despite broad-spectrum intravenous antibiotics; emergency suction evacuation under ultrasound guidance to remove intrauterine septic foci on postdelivery day 15	3	Urinary tract infection due to *Candida glabrata* cystitis	Antifungal, cystoscopy
17	2021	30	Transamin, balloon tamponade, Hemabate, B-Lynch compression sutures, NovoSeven, total abdominal hysterectomy	7600 (Caesarean hysterectomy for uncontrolled bleeding)	-	-	-	-

for PAS disorders can result in significant morbidities and is not necessarily successful. Both patients had a good recovery after hysterectomy; early resort to hysterectomy is important to avoid delays in controlling the life-threatening bleeding. Good clinical outcomes after conservative management are also possible in PAS disorders of higher clinical grades (increta).

There are several limitations to the present study. First, morbidly adherent placental tissue was not coded as PAS in the system and such patients were not included. Second, the sample size was small, owing to the rare incidence of PAS disorders worldwide. Third, outcomes of subsequent pregnancies were not assessed, as no patient had another pregnancy after the index delivery. Fourth, three patients were lost to long-term follow-up, and there were a few missing data in the documentation. Fifth, all 17 patients opted for uterine preservation; therefore, no patient underwent primary Caesarean hysterectomy for comparison.

Conclusion

Uterine preservation for PAS disorders by leaving the placenta in situ followed by UAE and various haemostatic measures has good clinical outcomes. Nonetheless, early resort to hysterectomy is important in case of uncontrolled life-threatening bleeding to avoid maternal mortality and morbidity.

Contributors

Concept or design: YF Wong, TK Lo, WC Leung
Acquisition of data: YF Wong, TK Lo
Analysis or interpretation of data: All authors
Drafting of the article: YF Wong, WC Leung
Critical revision for important intellectual content: All authors
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

As editors of the journal, TKL and WLL were not involved in the peer review process of this article. All other authors have disclosed no conflicts of interest.

Acknowledgement

We thank Mr Steven Lau of the Kwong Wah

Hospital Clinical Research Centre for statistical support during data analysis.

Funding/support

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Ethics approval

The study was approved by the Kowloon Central / Kowloon East Cluster Research Ethics Committee (reference: KC/KE-22-0088/ER-1).

References

1. Jauniaux E, Jurkovic D. Placenta accreta: pathogenesis of a 20th century iatrogenic uterine disease. Placenta 2012;33:244-51. Crossref
2. Cheng KK, Lee MM. Rising incidence of morbidly adherent placenta and its association with previous caesarean section: a 15-year analysis in a tertiary hospital in Hong Kong. Hong Kong Med J 2015;21:511-7. Crossref
3. Jauniaux E, Alfirevic Z, Bhide AG, et al. Placenta praevia and placenta accreta: diagnosis and management. Green-top Guideline No. 27a. BJOG 2019;126:e1-48. Crossref
4. Sentilhes L, Seco A, Azria E, et al. Conservative management or cesarean hysterectomy for placenta accreta spectrum: the PACCRETA prospective study. Am J Obstet Gynecol 2022;226:839.e1-24.
5. Sentilhes L, Kayem G, Chandraharan E, Palacios-Jaraquemada J, Jauniaux E; FIGO Placenta Accreta Diagnosis and Management Expert Consensus Panel. FIGO consensus guidelines on placenta accreta spectrum disorders: conservative management. Int J Gynaecol Obstet 2018;140:291-8. Crossref
6. Lo TK, Yung WK, Lau WL, Law B, Lau S, Leung WC. Planned conservative management of placenta accreta — experience of a regional general hospital. J Matern Fetal Neonatal Med 2014;27:291-6. Crossref
7. Jauniaux E, Bhide A, Kennedy A, et al. FIGO consensus guidelines on placenta accreta spectrum disorders: prenatal diagnosis and screening. Int J Gynaecol Obstet 2018;140:274-80. Crossref
8. Kutuk MS, Ak M, Ozgun MT. Leaving the placenta in situ versus conservative and radical surgery in the treatment of placenta accreta spectrum disorders. Int J Gynaecol Obstet 2018;140:338-44. Crossref
9. Huang KL, Leung-Chit Tsang L, Cheng YF, et al. Planned conservative management of placenta increta and percreta with prophylactic transcatheter arterial embolization and leaving placenta in situ for women who desire fertility preservation. Placenta 2020;97:51-7. Crossref
10. Schwickert A, van Beekhuizen HJ, Bertholdt C, et al. Association of peripartum management and high maternal blood loss at cesarean delivery for placenta accreta spectrum (PAS): a multinational database study. Acta Obstet Gynecol Scand 2021;100(Suppl 1):29-40. Crossref
11. Jauniaux E, Ayres-de-Campos D, Langhoff-Roos J, Fox KA, Collins S; FIGO Placenta Accreta Diagnosis and Management Expert Consensus Panel. FIGO classification for the clinical diagnosis of placenta accreta spectrum disorders. Int J Gynaecol Obstet 2019;146:20-4. Crossref
12. Ibrahim TH. Efficacy of tranexamic acid in reducing blood loss, blood and blood products requirements in cesarian sections for patients with placenta accreta. Ain-Shams J Anesthesiol 2019;11:31. Crossref
13. Sentilhes L, Sénat MV, Le Lous M, et al. Tranexamic acid for the prevention of blood loss after cesarean delivery. N Engl J Med 2021;384:1623-34. Crossref
14. Gizzo S, Patrelli TS, Gangi SD, et al. Which uterotonic is better to prevent the postpartum hemorrhage? Latest news in terms of clinical efficacy, side effects, and contraindications: a systematic review. Reprod Sci 2013;20:1011-9. Crossref
15. Meckstroth KR, Whitaker AK, Bertisch S, Goldberg AB, Darney PD. Misoprostol administered by epithelial routes: drug absorption and uterine response. Obstet Gynecol 2006;108:582-90. Crossref
16. D'Souza DL, Kingdom JC, Amsalem H, Beecroft JR, Windrim RC, Kachura JR. Conservative management of invasive placenta using combined prophylactic internal iliac artery balloon occlusion and immediate postoperative uterine artery embolization. Can Assoc Radiol J 2015;66:179-84. Crossref

Hong Kong J Gynaecol Obstet Midwifery 2023;23(2):101-5 | https://doi.org/10.12809/hkjgom.23.2.343

Timing of elective Caesarean section at term on neonatal morbidities

Man Kee Teresa MA, MBChB, MRCOG
Kwok-Yin LEUNG, MBBS, FRCOG, FHKAM (Obstetrics and Gynaecology)
Department of Obstetrics and Gynaecology, Queen Elizabeth Hospital, Hong Kong

Objective: To compare the incidence of neonatal morbidities with elective Caesarean sections at different weeks of gestation in Hong Kong.
Methods: Medical records of all women with an elective Caesarean section performed at gestational age ≥37 weeks in Queen Elizabeth Hospital, Hong Kong, between 1 January 2016 and 31 December 2018 were retrospectively reviewed. Adverse neonatal outcomes collected included respiratory distress syndrome, transient tachypnoea, persistent pulmonary hypertension, sepsis, and neonatal intensive care unit admission.
Results: A total of 1576 records were analysed. Overall, 74.68% of babies were delivered at 38 weeks' gestation. The most common adverse neonatal outcome was transient tachypnoea (6.66%), followed by neonatal intensive care unit admission (5.90%), respiratory distress syndrome (5.26%), and sepsis (4.69%). Compared with babies born at 39 weeks' gestation, those born at 37 weeks' gestation were at increased risk of respiratory distress syndrome (odds ratio [OR]=5.348, p=0.024), neonatal intensive care unit admission (OR=3.938, p=0.027), a composite respiratory outcome (OR=3.402, p=0.007), and an overall composite outcome (OR=3.397, p=0.002).
Conclusion: Elective Caesarean delivery at 37 weeks' gestation is associated with higher risks of respiratory distress syndrome and neonatal intensive care unit admission, compared with elective Caesarean delivery at 39 weeks' gestation.

Keywords: Cesarean section; Infant, newborn; Intensive care units, neonatal; Neonatal sepsis; Respiratory distress syndrome, newborn

Introduction

According to the World Health Organization, a Caesarean section rate of >10% at the population level is not associated with reductions in maternal and newborn mortality rates[1]. In Hong Kong, the overall Caesarean section rate is around 30% to 40%. In the most recent audit in Hong Kong in 2014, the Caesarean section rate increased from 30.4% in 2004 to 42.1% in 2009 and decreased to 37.3% in 2014; 60% of Caesarean sections were elective[2]. The most common indication for Caesarean section was a previous uterine scar (32.3%), followed by social reasons (15.1%) and fetal malpresentation or abnormal lie (9.2%)[2].

The incidence of neonatal morbidities, especially respiratory complications, significantly increased following Caesarean section, compared with vaginal delivery. In a meta-analysis of 16 studies with 327 272 neonates born by vaginal delivery and 55 246 neonates born by elective Caesarean section, the risk of neonatal respiratory morbidity increased by 95% in those delivered by elective Caesarean section[3]. In a study in the United States, elective repeated Caesarean delivery before 39 weeks was associated with respiratory and other adverse neonatal outcomes such as newborn sepsis, transient hypoglycaemia, and neonatal intensive care unit admission[4]. In a multicentre retrospective cohort study in Lebanon, Caesarean delivery before 39 weeks' gestation was associated with respiratory and other adverse neonatal outcomes, and delaying birth by 1 to 2 weeks (until 39 weeks) could prevent 64% to 77% of adverse respiratory outcomes[5]. In a prospective cohort study in Iran, compared with Caesarean section after 39 weeks' gestation, Caesarean section at 38 to 39 weeks was associated with a higher rate of transient tachypnoea of the newborn (adjusted odds ratio [OR]=2.91, p=0.032) and neonatal intensive care unit admission (adjusted OR=2.59, p=0.02)[6]. Therefore, the National Institute for Health and Care Excellence[7], the Royal College of Obstetricians and Gynaecologists[8], the American College of Obstetricians and Gynecologists[9], and the Royal Australian and New Zealand College of Obstetricians and Gynaecologists[10] all recommend against routinely performing elective Caesarean sections before 39 weeks because of the increased risk of respiratory morbidity in the newborn.

In a retrospective study in Hong Kong in 2012, a significantly increased risk of transient tachypnoea was found for babies delivered by elective Caesarean section

Correspondence to: Man Kee Teresa MA
Email: mmk166@ha.org.hk

at 37 and 38 weeks[11], which may be due to differences in the timing of lung maturation between Chinese and non-Chinese babies. This aim of this study was to investigate associations between gestational age and neonatal outcomes in term babies born by elective Caesarean section in Hong Kong.

Materials and methods

Medical records of all women with an elective Caesarean section performed at gestational age ≥37 weeks in Queen Elizabeth Hospital, Hong Kong, between 1 January 2016 and 31 December 2018 were retrieved from the Clinical Management System and Obstetric Specialty Clinical Information System and retrospectively reviewed. Those with multiple pregnancies, major fetal congenital abnormality, gestational diabetes mellitus, known diabetes mellitus, intrauterine death, preterm delivery, small-for-gestational-age foetus or intrauterine growth restriction were excluded. Maternal characteristics retrieved included parity, age, ethnicity, gestation, antenatal risk factors, and indication for Caesarean section. The gestational age was determined according to the last menstrual period and early ultrasound at 11 to 14 weeks' gestation. However, if the date of the last menstrual period was unknown, or if the gestational age determined by early ultrasound was inconsistent with that calculated by the last menstrual period by >1 week, then the gestational age was adjusted according to the early ultrasound. Diagnosis of neonatal morbidities was made by paediatricians after clinical assessment, blood tests, and radiological examinations. Neonatal characteristics (sex and birth weight) and outcomes (respiratory distress syndrome, transient tachypnoea, persistent pulmonary hypertension, sepsis, and neonatal intensive care unit admission) were collected. A composite respiratory outcome for newborns included the first three outcomes, whereas an overall composite outcome included all five outcomes.

Data analysis was performed using SPSS (Windows version 24.0; IBM Corp, Armonk [NY], US). Descriptive analyses were used for the frequency and distribution of data for categorical variables. For all analyses, 39 weeks' gestation was used as the reference because it is the recommended gestational age for Caesarean section delivery. Logistic regression analyses were used to determine the risk of neonatal outcomes, the composite respiratory outcome, and an overall composite outcome in relation to the gestational week of delivery. Odds ratio with 95% confidence intervals were calculated after adjusting for confounders such as ethnicity to determine associations between gestational week of delivery and neonatal morbidities. A p value of <0.05 was considered statistically significant.

Results

Of 2204 patients who underwent an elective Caesarean section during the study period, 628 were excluded because they did not meet the eligibility criteria and the remaining 1576 were included in the analysis (Table 1). The mean maternal age was 33.44 years; 72.4% of patients were multiparous; 90.23% of patients were Chinese; and 60.53% of patients had a previous Caesarean section. Most (74.68%) of elective Caesarean sections were performed at 38 completed weeks' gestation.

The most common adverse neonatal outcome was transient tachypnoea (n=105, 6.66%), followed by neonatal intensive care unit admission (n=93, 5.90%), respiratory distress syndrome (n=83, 5.26%), and sepsis (n=74, 4.69%) [Table 2].

Table 1. Maternal, pregnancy, and neonatal characteristics of participants with elective Caesarean sections

Characteristic	No. (%) of participants (n=1576)
Maternal age, y	
<18	1 (0.06)
18-35	948 (60.15)
≥35	627 (39.78)
Parity	
Primipara	435 (27.60)
Multipara	1141 (72.40)
Ethnicity	
Chinese	1422 (90.23)
Non-Chinese	154 (9.77)
Baby sex	
Male	822 (52.16)
Female	754 (47.84)
Birth weight, g	
<2500	37 (2.35)
2500-4000	1517 (96.26)
>4000	22 (1.40)
Gestational age, wk	
37	271 (17.20)
38	1177 (74.68)
39	97 (6.15)
40	22 (1.40)
≥41	9 (0.57)

Compared with babies born at 39 weeks' gestation, babies born at 37 weeks' gestation were at increased risk of respiratory distress syndrome (OR=5.348, p=0.024), neonatal intensive care unit admission (OR=3.938, p=0.027), the composite respiratory outcome (OR=3.402, p=0.007), and the overall composite outcome (OR=3.397, p=0.002) [Table 3]. Compared with babies born at 39 weeks' gestation, babies born at 38 weeks' gestation and 40 weeks' gestation were also at increased risks but not significantly, except for the overall composite outcome in babies born at 40 weeks' gestation (p=0.018).

Discussion

In the present study, the risks of respiratory distress syndrome and neonatal intensive care unit admission significantly increased in babies born at 37 weeks' gestation, compared with 39 weeks' gestation. Similarly, in a retrospective cohort study in the Netherlands, the risks of neonatal mortality and morbidity increased in babies born before 39 weeks, compared with at 39 weeks[12]. In a multicentre study in Lebanon, Caesarean delivery prior to 39 weeks was associated with respiratory and other adverse neonatal outcomes[5]. In a retrospective cohort study in Turkey, babies born at 37 weeks to 37 weeks plus 6 days of gestation had a higher rate of respiratory distress syndrome[13]. In the United States, the Consortium on Safe Labor reported that the risk of developing respiratory distress syndrome was threefold greater at 37 weeks than at 39 to 40 weeks of gestation[14].

In the present study, the incidence of adverse neonatal outcomes was also higher (but not significantly) in

Table 2. Incidence of adverse neonatal outcomes at different gestation age

Adverse neonatal outcome	No. (%) of neonates				
	37 weeks' gestation (n=271)	38 weeks' gestation (n=1177)	39 weeks' gestation (n=97)	40 weeks' gestation (n=22)	≥41 weeks' gestation (n=9)
Respiratory distress syndrome	27 (9.96)	53 (4.50)	2 (2.06)	1 (4.55)	0
Transient tachypnoea	26 (9.59)	72 (6.12)	4 (4.12)	3 (13.64)	0
Persistent pulmonary hypertension	0	1 (0.08)	0	0	0
Sepsis	14 (5.17)	54 (4.59)	3 (3.09)	3 (13.64)	0
Neonatal intensive care unit admission	30 (11.07)	59 (5.01)	3 (3.09)	1 (4.55)	0
Composite respiratory outcomes	49 (18.08)	123 (10.45)	6 (6.19)	4 (18.18)	0
Overall composite outcomes	63 (23.25)	172 (14.61)	8 (8.25)	6 (27.27)	0

Table 3. Comparison of adverse neonatal outcomes at different gestational ages, with 39 weeks' gestation as the reference

Neonatal outcome	37 weeks' gestation		38 weeks' gestation		40 weeks' gestation	
	Odds ratio (95% confidence interval)	p Value	Odds ratio (95% confidence interval)	p Value	Odds ratio (95% confidence interval)	p Value
Respiratory distress syndrome	5.348 (1.245-22.965)	0.024	2.372 (0.567-9.921)	0.237	2.25 (0.193-26.183)	0.517
Transient tachypnoea	2.475 (0.841-7.289)	0.1	1.548 (0.552-4.339)	0.406	3.703 (0.755-18.168)	0.107
Persistent pulmonary hypertension	-	-	-	-	-	-
Sepsis	1.659 (0.465-5.925)	0.436	1.485 (0.455-4.846)	0.512	5 (0.925-27.041)	0.062
Neonatal intensive care unit admission	3.938 (1.173-13.225)	0.027	1.704 (0.523-5.55)	0.377	1.481 (0.146-15.078)	0.74
Composite respiratory outcomes	3.402 (1.406-8.233)	0.007	1.845 (0.789-4.316)	0.158	3.422 (0.86-13.614)	0.081
Overall composite outcomes	3.397 (1.56-7.383)	0.002	1.94 (0.923-4.077)	0.08	4.327 (1.289-14.529)	0.018

babies born at 38 or 40 weeks' gestation, compared with 39 weeks. The non-significance may be due to the small sample size for babies delivered at 39 weeks (n=97) and 40 weeks (n=22), compared 38 weeks (n=1177). In a retrospective cohort study in Shanghai, babies born at 38 or ≥40 weeks also had an increased risk of neonatal respiratory disease[15]. However, in a randomised control study in Denmark, no significant reduction in the neonatal admission rate was reported for babies delivered by elective Caesarean section at 39 weeks gestation, compared with 38 weeks' gestation[16].

The use of antenatal corticosteroids to induce maturation of the surfactant system has been reported to reduce the incidence of respiratory morbidities in babies[8]. However, a Cochrane systemic review concluded that there is insufficient evidence to draw any definite conclusions regarding antenatal corticosteroid administration before elective Caesarean section at term, and that higher-quality studies with large sample sizes are needed[17]. In addition, antenatal corticosteroids may increase the risk of neonatal hypoglycaemia[18] in term neonates and the risk of mental and behavioural disorders in children[19].

When counselling patients on the gestational week of delivery, obstetricians should consider the risk of stillbirth and the risk of emergency Caesarean section when patients go into labour before the scheduled date. The rate of stillbirth after 24 weeks' gestation is around 1 in 200[20]. In a 10-year retrospective cohort study in California, the risk of stillbirth at term was found to increase with gestational age from 2.1 per 10 000 pregnancies at 37 weeks' gestation to 10.8 per 10 000 pregnancies at 42 weeks' gestation[21]. Similarly, at each later gestational week after 38 weeks, the mortality risk of expectant management was higher than the risk of delivery; thus, delivery at 39 weeks may reduce the risk of stillbirth. Therefore, it is not advised to delay delivery after 39 weeks.

As for the risk of going into labour before the scheduled date of an elective Caesarean section, emergency Caesarean sections have higher maternal and fetal complication rates. In a cross-sectional study in Nepal, emergency Caesarean section increased the risks of adverse maternal outcomes (wound infection, postpartum haemorrhage, fever, and maternal intensive care unit admission) and fetal outcomes (birth asphyxia, meconium-stained liquor, and neonatal intensive care unit admission)[22]. A systemic review and meta-analysis also reported a higher risk of maternal complications (infection, fever, and wound dehiscence) and fetal complications after emergency Caesarean section[23].

When counselling patients on the timing of delivery for elective Caesarean section, the risks of adverse maternal and fetal outcomes should be balanced with those of stillbirth, going into spontaneous onset of labour, and neonatal morbidities.

Limitations of the present study include the small sample size for babies born at 39 weeks' gestation, which was used as the reference. A larger sample size may reveal any associations of neonatal outcomes in babies born at 39 weeks. In addition, records from only a single hospital were reviewed; there are eight public hospitals in Hong Kong providing obstetric care. A territory-wide study of all hospitals is warranted to obtain a more representative picture of the risks associated with the timing of elective Caesarean section.

Conclusion

Elective Caesarean delivery at 37 weeks' gestation is associated with higher risks of respiratory distress syndrome and neonatal intensive care unit admission, compared with elective Caesarean delivery at 39 weeks' gestation.

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

As an editor of the journal, KYL was not involved in the peer review process of this article. All other authors have disclosed no conflicts of interest.

Funding/support

This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Data availability

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

Ethics approval

The study was approved by the Kowloon Central Cluster Research Ethics Committee (reference: KC/KE-22-0149/ER-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.

References

1. World Health Organization. Statement on Caesarean Section Rates. Available from: https://apps.who.int/iris/rest/bitstreams/714841/retrieve.
2. Hong Kong College of Obstetricians and Gynaecologists. Territory-Wide Audit in Obstetrics and Gynaecology 2014. Available from: https://www.hkcog.org.hk/hkcog/Download/Territory-wide_Audit_in_Obstetrics_Gynaecology_2014.pdf.
3. Tefera M, Assefa N, Mengistie B, Abrham A, Teji K, Worku T. Elective cesarean section on term pregnancies has a high risk for neonatal respiratory morbidity in developed countries: a systematic review and meta-analysis. Front Pediatr 2020;8:286. Crossref
4. Tita AT, Landon MB, Spong CY, et al. Timing of elective repeat cesarean delivery at term and neonatal outcomes. N Engl J Med 2009;360:111-20. Crossref
5. Al Bizri A, Boghossian NS, Nassar A, et al. Timing of term elective cesarean section and adverse neonatal outcomes: a multi-center retrospective cohort study. PLoS One 2021;16:e0249557. Crossref
6. Pirjani R, Afrakhteh M, Sepidarkish M, et al. Elective Caesarean section at 38–39 weeks gestation compared to >39 weeks on neonatal outcomes: a prospective cohort study. BMC Pregnancy Childbirth 2018;18:140. Crossref
7. National Institute for Health and Care Excellence. Caesarean Birth. Available from: https://www.nice.org.uk/guidance/ng192.
8. Stock SJ, Thomson AJ, Papworth S; the Royal College of Obstetricians and Gynaecologists. Antenatal corticosteroids to reduce neonatal morbidity and mortality: Green-top Guideline No. 74. BJOG 2022;129:e35-60. Crossref
9. American College of Obstetricians and Gynecologists. Cesarean Delivery on Maternal Request. Available from: https://www.acog.org/clinical/clinical-guidance/committee-opinion/articles/2019/01/cesarean-delivery-on-maternal-request.
10. Royal Australian and New Zealand College of Obstetricians and Gynaecologists. Timing of planned Caesarean section at term. Available from: https://www1.health.nsw.gov.au/pds/ActivePDSDocuments/GL2016_015.pdf.
11. Tse HM, Au Yeung KC, Lee HC, Yong SPY. The timing of elective Caesarean section on neonatal respiratory outcome in Hong Kong. Hong Kong J Gynaecol Obstet Midwifery 2012;12:13-20.
12. Wilmink FA, Hukkelhoven CW, Lunshof S, Mol BW, van der Post JA, Papatsonis DN. Neonatal outcome following elective cesarean section beyond 37 weeks of gestation: a 7-year retrospective analysis of a national registry. Am J Obstet Gynecol 2010;202:250.e1-8. Crossref
13. Ongun H, Ongun EA, Yolcular BO. Evaluation of respiratory problems according to week of delivery: a comparative analysis in infants of gestational age 37 weeks. Iran J Pediatr 2018;28:e59488. Crossref
14. Consortium on Safe Labor; Hibbard JU, Wilkins I, et al. Respiratory morbidity in late preterm births. JAMA 2010;304:419-25. Crossref
15. Hu Y, Shen H, Landon MB, Cheng W, Liu X. Optimal timing for elective caesarean delivery in a Chinese population: a large hospital-based retrospective cohort study in Shanghai. BMJ Open 2017;7:e014659. Crossref
16. Glavind J, Kindberg SF, Uldbjerg N, et al. Elective Caesarean section at 38 weeks versus 39 weeks: neonatal and maternal outcomes in a randomised controlled trial. BJOG 2013;120:1123-32. Crossref
17. Sotiriadis A, McGoldrick E, Makrydimas G, et al. Antenatal corticosteroids prior to planned caesarean at term for improving neonatal outcomes. Cochrane Database Syst Rev 2021;12:CD006614. Crossref
18. Gupta K, Rajagopal R, King F, Simmons D. Complications of antenatal corticosteroids in infants born by early term scheduled cesarean section. Diabetes Care 2020;43:906-8. Crossref
19. Räikkönen K, Gissler M, Kajantie E. Associations between maternal antenatal corticosteroid treatment and mental and behavioral disorders in children. JAMA 2020;323:1924-33. Crossref
20. Royal College of Obstetricians and Gynaecologists. Late Intrauterine Fetal Death and Stillbirth. Green-top Guideline No.55. Available from: https://www.rcog.org.uk/media/0fefdrk4/gtg_55.pdf.
21. Rosenstein MG, Cheng YW, Snowden JM, Nicholson JM, Caughey AB. Risk of stillbirth and infant death stratified by gestational age. Obstet Gynecol 2012;120:76-82. Crossref
22. Darnal N, Dangal G. Maternal and fetal outcome in emergency versus elective Caesarean section. J Nepal Health Res Counc 2020;18:186-9. Crossref
23. Yang XJ, Sun SS. Comparison of maternal and fetal complications in elective and emergency cesarean section: a systematic review and meta-analysis. Arch Gynecol Obstet 2017;296:503-12. Crossref

Hong Kong J Gynaecol Obstet Midwifery 2023;23(2):106-12 | https://doi.org/10.12809/hkjgom.23.2.337

Maternal near miss in three tertiary-level hospitals in Hong Kong

Shu Man Carmen NG[1], MBBS, MRCOG
Po Lam SO[2], MBBS (HK), MMedSc (Genetic Counselling), MSc (Medical Genetics), FHKCOG, FHKAM (O&G)
Wendy SHU[3], MBBCh, MRCOG, FHKAM (O&G)
Tin Yan Mimi SETO[1], MBBS, MRCOG, FHKAM (O&G)
Ka Wang CHEUNG[1], MBBS, MRCOG, FHKCOG, FHKAM (O&G), Cert RCOG (MFM), MD
[1] Department of Obstetrics and Gynaecology, Queen Mary Hospital, Hong Kong SAR, China
[2] Department of Obstetrics and Gynaecology, Tuen Mun Hospital, Hong Kong SAR, China
[3] Department of Obstetrics and Gynaecology, Pamela Youde Nethersole Eastern Hospital, Hong Kong SAR, China

Background: Maternal near miss refers to women who nearly died from a complication during pregnancy. We applied the World Health Organization near miss criteria to determine the incidence and aetiologies of maternal near miss in Hong Kong.
Methods: Medical records of women in three tertiary-level maternity centres in Hong Kong in 2019 who met any of the clinical, laboratory, or management criteria for maternal near miss were retrospectively reviewed. The maternal-near-miss ratio was calculated by the number of maternal-near-miss cases per 1000 livebirths. Women who were admitted to an intensive care unit were compared with women who were not in terms of obstetric characteristics, aetiologies, and organ dysfunctions.
Results: There were 11 075 livebirths in the three hospitals in 2019. 61 maternal-near-miss cases were identified. 29 of these were admitted to an ICU; the median length of stay was 2 days. The maternal-near-miss ratio was 5.51 per 1000 livebirths. The most common cause of maternal near miss was postpartum haemorrhage (52.5%), followed by severe complications of abortion or early pregnancy (24.6%). The most common organ dysfunction was coagulation/haematological dysfunction (45.9%), followed by cardiovascular dysfunction (42.6%), and uterine dysfunction (16.4%). 11.5% of women had more than one organ dysfunction. 73.1% of women with cardiovascular dysfunction did not require ICU admission (p=0.05). Women with uterine dysfunction resulting in a hysterectomy were more likely to be admitted to an ICU (p=0.037). Interventional radiology was more commonly performed on those who were admitted to an ICU than those who were not (24.1% vs 3.1%, p=0.022).
Conclusion: Most maternal-near-miss cases were attributed to postpartum haemorrhage and early pregnancy complications. Early identification and close monitoring are effective in improving maternal healthcare.

Keywords: Intensive care units; Maternal mortality; Postpartum hemorrhage; Pregnancy complications

Background

Hong Kong boasts one of the lowest maternal mortality rates in the world, with 0.10 maternal death per 100 000 livebirths between 2008 and 2017, a dramatic reduction from 4.43 maternal deaths per 100 000 livebirths between 1946 and 1977[1]. However, the number of maternal mortalities may be under-reported due to the lack of a confidential enquiry system to record maternal-near-miss morbidities. Between 2000 and 2019, suicide and hypertensive disorders were the leading causes of maternal death in Hong Kong[2].

Maternal near miss refers to women who nearly die from a complication during pregnancy, childbirth, or within 42 days of pregnancy termination[3]. Maternal near miss and maternal mortality share similar characteristics and pathological processes. The World Health Organization (WHO) maternal-near-miss criteria are a standardised tool to identify maternal-near-miss cases (Appendix)[3]. The criteria are widely used to assess both maternal morbidity and standards of maternity care.

Data on maternal-near-miss cases in Hong Kong are lacking. Investigation of maternal mortality and near miss may help address deficiencies in maternal care and facilitate changes in healthcare strategies to prevent potentially life-threatening events. This study aimed to determine the incidence and aetiologies of maternal near miss across three tertiary-level hospitals in Hong Kong,

Correspondence to: Dr Shu Man Carmen NG
Email: ngsmcarmen@gmail.com

using the WHO criteria. Characteristics of maternal-near-miss cases with or without admission to an intensive care unit (ICU) were compared.

Materials and methods

This was an observational study conducted in three tertiary-level maternity centres in Hong Kong, namely Queen Mary Hospital, Pamela Youde Nethersole Eastern Hospital, and Tuen Mun Hospital.

Medical records of women admitted in the three hospitals between 1 January 2019 and 31 December 2019 who met any of the WHO clinical, laboratory, or management criteria for maternal near miss were retrospectively reviewed. Data collected included duration of hospital stay, mode of delivery, and pathology of near miss. The maternal-near-miss ratio (MNMR) was calculated by the number of maternal-near-miss cases per 1000 livebirths.[3]

Data were analysed using SPSS (Windows version 26; IBM Corp, Armonk [NY], US). Characteristics of maternal-near-miss cases with or without admission to an ICU were compared using the Chi-square test or Fisher's exact test for categorical data. Associations between ICU admission and risk factors were presented as odds ratios and 95% confidence intervals. A p value of <0.05 was considered statistically significant.

Results

There were 11 075 livebirths in the three hospitals in 2019. Of 343 women identified to have severe maternal complications, critical interventions, or admission to an ICU, 61 who had severe maternal outcomes with organ dysfunction met the near-miss criteria. 29 out of these 61 patients were admitted to an ICU; the median length of stay was 2 days. There was no case of maternal mortality in our cohort. The MNMR was 5.51 per 1000 livebirths. The mean MNMR for women admitted to an ICU was 2.62 per 1000 livebirths.

Maternal near miss most commonly occurred at term (≥37 weeks) [39.3%], followed by during the first trimester (29.5%) and at 24 to 36 weeks of gestation (21.3%) [Table 1]. Not being admitted to an ICU was associated with non-booking status for maternal check-up (p=0.026) and a gestational age of <12 weeks at presentation (p=0.003).

The most common cause of maternal near miss was severe postpartum haemorrhage (52.5%), followed by severe complications of abortion or early pregnancy (24.6%) [Table 2]. The most common organ dysfunction was coagulation/haematological dysfunction (45.9%), followed by cardiovascular dysfunction (42.6%), and uterine dysfunction (16.4%) [Table 2]. 11.5% of women had more than one organ dysfunction. 73.1% of women with cardiovascular dysfunction did not require ICU admission (p=0.05). 65.6% of women received ≥5 units of blood product transfusion, which included packed cells, platelet concentrates, and fresh frozen plasma. Women with uterine dysfunction resulting in a hysterectomy were more likely to be admitted to an ICU (p=0.037). Interventional radiology was more commonly performed on those who were admitted to an ICU than those who were not (24.1% vs 3.1%, p=0.022, Table 2).

Discussion

In the present study, the MNMR was 5.51 per 1000 livebirths, which is comparable to MNMRs in other developed countries[4] and lower than that reported by the WHO[3]. There was no case of maternal mortality in our cohort.

Severe postpartum haemorrhage was the leading cause of maternal near miss, which is in line with the existing evidence[4]. Two-thirds of the maternal-near-miss cases who developed postpartum haemorrhage underwent Caesarean sections. Placenta praevia and placenta accreta spectrum were the most prevalent causes, resulting in 40% of the Caesarean sections in our cohort. In an Italian study, Caesarean section delivery carries a five-fold increased risk of maternal near miss, compared with vaginal delivery[5]. However, this association may be confounded, as Caesarean sections can result from underlying maternal and obstetrical conditions rather than being a standalone risk factor. Nonetheless, undergoing a Caesarean section has been shown to be an independent risk factor for maternal morbidity and mortality[6].

Physicians should be vigilant to prevent postpartum haemorrhages and be prepared to manage such situations should they occur. Early identification of patients with risk factors for postpartum haemorrhage and thorough planning can help reduce maternal mortality and morbidity. The use of tranexamic acid as a therapeutic adjunct to control postpartum haemorrhage is recommended, with early administration preferred[7]. In the present study, 84.4% of patients with postpartum haemorrhage were given tranexamic acid, and 10% of patients were given carbetocin. Oxytocin has long been used as a prophylactic measure to prevent postpartum haemorrhage; carbetocin is a newer long-acting synthetic analogue of oxytocin, with agonist

Table 1. Obstetric characteristics of maternal-near-miss cases with or without admission to an intensive care unit (ICU)

	ICU admission (n=29)*	No ICU admission (n=32)*	Odds ratio (95% confidence interval)	p Value
Age, y				0.614
<18	0	0	-	
18-34	9 (31.0)	12 (37.5)	Reference	
35-39	11 (37.9)	14 (43.8)	1.05 (0.32-3.38)	
≥40	9 (31.0)	6 (18.8)	2.00 (0.52-7.69)	
Ethnicity				0.307
Chinese	26 (89.7)	25 (78.1)	Reference	
Other Asian countries	3 (10.3)	7 (21.9)	0.41 (0.10-1.77)	
Caucasians and others	0	0	-	
Education level				0.174
Secondary or below	15 (51.7)	10 (31.3)	1.69 (0.49-5.85)	
Tertiary or above	8 (27.6)	9 (28.1)	Reference	
Unknown	6 (20.7)	13 (40.6)	0.52 (0.13-2.02)	
Body mass index at booking, kg/m^2				0.095
<18.5	2 (6.9)	0	3.57 (0.11-111.71)	
18.5-22.9	3 (10.3)	2 (6.3)	Reference	
23-24.9	5 (17.2)	5 (15.6)	0.67 (0.08-5.88)	
25-29.9	13 (44.8)	12 (37.5)	0.72 (0.10-5.10)	
≥30	4 (13.8)	2 (6.3)	1.33 (0.11-15.70)	
Unknown	2 (6.9)	11 (34.4)	0.12 (0.01-1.26)	
Parity				0.574
0	7 (24.1)	11 (34.4)	Reference	
1	15 (52.7)	16 (50.0)	1.47 (0.45-4.80)	
≥2	7 (24.1)	5 (15.6)	2.20 (0.50-9.75)	
Booking status				0.026
Booked	24 (82.8)	18 (56.3)	Reference	
Non-booked	5 (17.2)	14 (43.8)	0.27 (0.08-0.88)	
Gestational age at presentation				0.003
<12 weeks	3 (10.3)	15 (46.9)	0.17 (0.04-0.74)	
12-23 weeks	2 (6.9)	2 (6.3)	0.85 (0.10-7.04)	
24-36 weeks	11 (37.9)	3 (9.4)	3.10 (0.69-14.02)	
≥37 weeks	13 (44.8)	11 (34.3)	Reference	
Postpartum	0	1 (3.1)	0.28 (0.01-7.67)	
Timing of delivery				0.432
Preterm (24w0d-33w6d)	2 (6.9)	1 (3.1)	1.69 (0.14-21.27)	
Late preterm (34w0d-36w6d)	8 (27.6)	2 (6.3)	3.38 (0.50-19.38)	
Term (37w0d-39w6d)	13 (44.8)	11 (34.4)	Reference	
Past term (beyond 40w)	2 (6.9)	3 (9.4)	0.56 (0.079-4.01)	

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

Table 1. (cont'd)

	ICU admission (n=29)*	No ICU admission (n=32)*	Odds ratio (95% confidence interval)	p Value
Medical comorbidities				-
Cardiac disease	1 (3.4)	1 (3.1)		
Hypertension	2 (6.9)	0		
Psychiatric disorder	1 (3.4)	0		
Diabetes	0	1 (3.1)		
Haematological disease	0	3 (9.4)		
Respiratory disease	1 (3.4)	0		
Others	1 (3.4)	0		
Obstetric risk factors				
Fibroid	1 (3.4)	0		
Multiple pregnancy	0	2 (6.3)		
Gestational diabetes	7 (24.1)	3 (9.4)		
Hypertensive disorders in pregnancy	1 (3.4)	1 (3.1)		
Placenta praevia / placenta accreta spectrum	10 (34.5)	2 (6.3)		
Length of hospital stay				0.001
≤7 days	10 (34.5)	25 (78.1)		
>7 days	19 (65.5)	7 (21.9)		
Mode of delivery				0.058
Normal vaginal delivery	3 (10.3)	6 (18.8)	Reference	
Instrumental delivery	1 (3.4)	1 (3.1)	2.00 (0.09-44.4)	
Caesarean section	22 (75.9)	8 (25.0)	5.50 (1.11-27.37)	
Status of infant at birth				
Alive (one born at 23 weeks at peri-viability gestation)	26	15		
Dead	0	0		
Status of infant at hospital discharge or 7th day of life if still in hospital				0.524
Alive	24 (92.3)	15 (100)		
Dead	2 (7.7)	0		
Admission to ICU				-
1-3 days	25 (86.2)	-		
≥4 days	4 (13.8)	-		
Maternal death	0	0		-

properties that are more effective than oxytocin's[8] and a similar adverse effect profile. Nonetheless, larger trials of carbetocin are in progress, and cost-effectiveness of carbetocin has been inconclusive. In addition, radiological intervention such as arterial balloon catheter placement and uterine artery embolisation has effectively decreased the hysterectomy rate[9], which in turn minimises maternal near miss and mortality.

24.6% of maternal-near-miss cases were caused by severe abortion or early pregnancy complications. More than half of these patients required a laparotomy, but most patients did not require admission to an ICU, likely owing to the low risk of further bleeding. Blood transfusion to

Table 2. Causes of maternal near miss, types of organ dysfunction, and critical interventions in women with or without admission to an intensive care unit (ICU)

	ICU admission (n=29)*	No ICU admission (n=32)*	p Value
Cause			
Severe postpartum haemorrhage	17 (58.6)	15 (46.9%)	0.013
Severe pre-eclampsia	1 (3.4)	0	
Eclampsia	0	0	
Sepsis or severe systemic infection	2 (6.9)	1 (3.1)	
Ruptured uterus	1 (3.4)	1 (3.1)	
Severe complications of abortion or early pregnancy complications caused by ectopic pregnancy (n=11), scar pregnancy (n=3), and septic abortion (n=1)	2 (6.9)	13 (40.6)	
Others (acute liver failure, peripartum cardiomyopathy, pulmonary embolism, maternal congenital cardiac disease, metastatic carcinoma, postpartum stroke, and asthma)	6 (20.7)	2 (6.3)	
Organ dysfunction			
Cardiovascular	7 (24.1)	19 (59.4)	0.005
Respiratory	5 (17.2)	0	0.020
Renal	2 (6.9)	0	0.222
Coagulation/haematological	16 (55.2)	12 (37.5)	0.167
Hepatic	2 (6.9)	0	0.222
Neurological	1 (3.4)	1 (3.1)	>0.99
Uterine	8 (27.6)	2 (6.3)	0.037
Critical intervention			
Admission to intensive care unit	29 (100.0)	-	-
Interventional radiology	7 (24.1)	1 (3.1)	0.022
Laparotomy	6 (20.7)	7 (21.9)	0.910
Use of blood products	17 (58.6)	23 (71.9)	0.277

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

correct their haemodynamic status on a general ward was sufficient. Although non-booking status for maternal check-up and early gestational age at presentation appeared to be protective factors against ICU admission, most such patients were diagnosed with ruptured ectopic pregnancy at first presentation, which may have led to a skewed result. In a Korean study, low socioeconomic status was associated with a higher risk of ectopic pregnancy[10]. In our cohort, there were 14 cases of ectopic pregnancy, 73.3% of which occurred in those who were unemployed or worked as domestic helpers. Lower socioeconomic status may restrict access to early medical care, thus delaying referrals and leading to adverse outcomes.

Improving transition of care by establishing special maternity care units may reduce the number of ICU admissions and length of ICU stay. Such units serve as an interim between general wards and the ICU so that high-risk obstetric conditions can be expertly monitored by a multidisciplinary team of obstetricians, obstetric anaesthetists, and specialised midwives with critical care training. Such units are expected to play a greater role in managing maternal morbidities.

Our study has some limitations. The lack of controls and the small sample size resulted in a broad 95% CI and less precision to estimate the effect. Longitudinal studies with an extended study period are warranted. Moreover, our data did not include neonatal characteristics; inclusion of the newborn characteristics is helpful when evaluating neonatal and maternal outcomes.

Suicide is the leading cause of maternal mortality in Hong Kong[2], but the WHO near miss criteria neglect

to address psychiatric conditions of patients. Further refinement of the criteria to include psychiatric conditions may improve the criteria's application and validity in the Hong Kong context.

Conclusion

Most maternal-near-miss cases were attributed to postpartum haemorrhage and early pregnancy complications. Early identification and close monitoring are effective in improving maternal healthcare.

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 disclosed no conflicts of interest.

Funding/support

This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Data availability

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

Ethics approval

The study was approved by the Institutional Review Board of The University of Hong Kong / Hospital Authority Hong Kong West Cluster (reference: UW18-595), Hong Kong East Cluster Research Ethics Committee (reference: HKECREC-2018-099), and New Territories West Cluster Research Ethics Committee (reference: NTWC/REC/19022). Patients were treated in accordance with the tenets of the Declaration of Helsinki. Each patient provided written informed consent for all treatments, procedures, and publication.

References

1. Cheung KW, Seto MTY, Wang W, Ng CT, To WWK, Ng EHY. Trend and causes of maternal death, stillbirth and neonatal death over seven decades in Hong Kong. Lancet Reg Health West Pac 2022;26:100523. Crossref
2. Cheung KW, Seto MTY, Wang W, et al. Characteristics of maternal mortality missed by vital statistics in Hong Kong, 2000-2019. JAMA Netw Open 2023;6:e230429. Crossref
3. World Health Organization. Evaluating the quality of care for severe pregnancy complications: the WHO near-miss approach for maternal health. Geneva: WHO; 2011.
4. De Silva M, Panisi L, Lindquist A, et al. Severe maternal morbidity in the Asia Pacific: a systematic review and meta-analysis. Lancet Reg Health West Pac 2021;14:100217. Crossref
5. Donati S, Senatore S, Ronconi A; Regional Maternal Mortality Working Group. Obstetric near-miss cases among women admitted to intensive care units in Italy. Acta Obstet Gynecol Scand 2012;91:452-7. Crossref
6. Deneux-Tharaux C, Carmona E, Bouvier-Colle MH, Bréart G. Postpartum maternal mortality and cesarean delivery. Obstet Gynecol 2006;108:541-8. Crossref
7. Shander A, Javidroozi M, Sentilhes L. Tranexamic acid and obstetric hemorrhage: give empirically or selectively? Int J Obstet Anesth 2021;48:103206. Crossref
8. Gallos ID, Williams HM, Price MJ, et al. Uterotonic agents for preventing postpartum haemorrhage: a network meta-analysis. Cochrane Database Syst Rev 2018;4:CD011689. Crossref
9. Maraschini A, Lega I, D'Aloja P, et al. Women undergoing peripartum hysterectomy due to obstetric hemorrhage: a prospective population-based study. Acta Obstet Gynecol Scand 2019;99:274-82. Crossref
10. Yuk JS, Kim YJ, Hur JY, Shin JH. Association between socioeconomic status and ectopic pregnancy rate in the Republic of Korea. Int J Gynecol Obstet 2013;122:104-7. Crossref

Appendix.
Inclusion criteria for maternal near miss[3]

Severe maternal complications

- Severe postpartum haemorrhage
- Severe pre-eclampsia
- Eclampsia
- Sepsis or severe systemic infection
- Ruptured uterus
- Severe complications of abortion

Critical interventions or intensive care unit use

- Admission to intensive care unit
- Interventional radiology
- Laparotomy (includes hysterectomy, excludes Caesarean section)
- Use of blood products

Life-threatening conditions (near miss criteria)

- Cardiovascular dysfunction
  - Shock, cardiac arrest (absence of pulse/heartbeat and loss of consciousness), use of continuous vasoactive drugs, cardiopulmonary resuscitation, severe hypoperfusion (lactate >5 mmol/l or >45 mg/dl), severe acidosis (pH <7.1)
- Respiratory dysfunction
  - Acute cyanosis, gasping, severe tachypnoea (respiratory rate >40 breaths per minute), severe bradypnoea (respiratory rate <6 breaths per minute), intubation and ventilation not related to anaesthesia, severe hypoxemia (O2 saturation <90% for ≥60 minutes or PAO_2/ FiO_2 <200)
- Renal dysfunction
  - Oliguria non-responsive to fluids or diuretics, dialysis for acute renal failure, severe acute azotaemia (creatinine ≥300 μmol/ml or ≥3.5 mg/dl)
- Coagulation/haematological dysfunction
  - Failure to form clots, massive transfusion of blood or red cells (≥5 units), severe acute thrombocytopenia (<50 000 platelets/ml)
- Hepatic dysfunction
  - Jaundice in the presence of pre-eclampsia, severe acute hyperbilirubinemia (bilirubin >100 μmol/l or >6.0 mg/dl)
- Neurological dysfunction
  - Prolonged unconsciousness (lasting ≥12 hours)/coma (including metabolic coma), stroke, uncontrollable fits/status epilepticus, total paralysis
- Uterine dysfunction
  - Uterine haemorrhage or infection leading to hysterectomy

Maternal vital status

- Maternal death

Hong Kong J Gynaecol Obstet Midwifery 2023;23(2):113-9 | https://doi.org/10.12809/hkjgom.23.2.344

Patient acceptability and satisfaction for hysteroscopic morcellation

Cassie LEUNG[1,2], Lee Ting KWONG[1,2], Po Lam SO[1,2], Sai Fun WONG[1,2], Kam Ming CHOW[1,2]

[1] Department of Obstetrics and Gynaecology, Tuen Mun Hospital, Hong Kong SAR, China

[2] Department of Obstetrics and Gynaecology, Pok Oi Hospital, Hong Kong SAR, China

Objective: To evaluate patients' pain scores and satisfaction with hysteroscopic morcellation service in two hospitals in Hong Kong.

Methods: Medical records of women who underwent hysteroscopic morcellation as a day procedure using the Intrauterine Bigatti Shaver between 1 November 2018 and 31 October 2022 at Tuen Mun Hospital or Pok Oi Hospital were retrospectively reviewed.

Results: 242 patients who underwent hysteroscopic morcellation were included. The mean patient age was 54.1 years. Postmenopausal bleeding was the commonest presenting symptom (48.8%), followed by abnormal menstrual bleeding (42.6%). 43.8% of patients had one lesion; 87.2% of patients had endometrial polyps. There were 523 endometrial polyps and 29 myomas; 99.4% of endometrial polyps and 79.3% of myomas were removed. The complete resection rate was higher for patients with endometrial polyps than for patients with myomas (98.7% vs 77.8%, p<0.001). Most patients reported mild pain intraoperatively (57.4%), immediately after the procedure (72.3%), and upon discharge (95.0%). 98.8% of patients were satisfied with the procedure; 94.2% would undergo the same operation again if clinically indicated; and 95.5% would recommend this procedure to others. Premenopausal women reported more pain immediately after the procedure (2 vs 1, p=0.020) and upon discharge (0 vs 0, p=0.040) than postmenopausal women. Patients with an operative time of >20 minutes reported more pain immediately after the procedure (3 vs 1, p=0.007) than patients with an operative time of ≤20 minutes.

Conclusion: Almost all patients were satisfied with hysteroscopic morcellation. Most patients experienced only mild pain during and immediately after the procedure and upon discharge. Premenopausal status and operative time of >20 minutes were associated with higher pain scores. Further optimisation of pain-relief methods should be considered.

Keywords: Hysteroscopy; Morcellation; Patient satisfaction; Safety; Treatment outcome

Introduction

Abnormal uterine bleeding is a common problem for both premenopausal and postmenopausal women and can be caused by polyps and myomas[1,2]. Removal of these intrauterine lesions may help improve symptoms and aid diagnosis and malignancy detection. Hysteroscopy enables a minimally invasive approach to this problem, together with instruments such as grasping forceps, microscissors, resectoscope, bipolar electrosurgical probe, and morcellator. Conventionally, the bipolar resectoscope was considered the instrument of choice for technically more difficult lesions. However, electrosurgery may cause collateral thermal damage and increase the risk of uterine perforation[3]; repeated manual removal of tissue causes cervical trauma[4]; and larger lesions are associated with longer operative times.

A hybrid system of morcellation, irrigation, and suction under direct vision facilitates the effective removal of intrauterine lesions[5]. Compared with resectoscopy, hysteroscopic morcellation is associated with a higher success rate, shorter operative time, and better patient acceptability[6,7]. For residents in training, hysteroscopic morcellation takes less time to learn and is associated with higher levels of confidence and satisfaction[8-10]. The mechanical cutting mechanism causes no collateral electrical or thermal damage near the intrauterine lesions. Because no gas bubbles are generated when the device is activated, hysteroscopic morcellation enables better visibility of the operative field and possibly a lower risk of complications such as gas embolism[11]. In addition, continuous aspiration of the tissue fragments further ensures a clear field of view, and the fragments can be directly collected for histological examination[4].

In our hospitals, hysteroscopic morcellation is performed as a day procedure using the Intrauterine Bigatti Shaver (Karl Storz, Tuttlingen, Germany). It avoids the

Correspondence to: Dr Po Lam SO
Email: so_pauline@yahoo.com.hk

risks associated with general anaesthesia and enables a shorter recovery time and a faster return to mobility. It is also economical, decreasing costs related to dedicated personnel and operating room use as well as reducing waiting times for major surgery by freeing up the operating room[12]. However, only a few studies have examined patient acceptability and satisfaction with hysteroscopic morcellation[13,14]. Therefore, we aimed to evaluate patient pain scores and their associated factors and patient satisfaction with hysteroscopic morcellation.

Materials and methods

Medical records of women who underwent hysteroscopic morcellation as a day procedure using the Intrauterine Bigatti Shaver between 1 November 2018 and 31 October 2022 at Tuen Mun Hospital or Pok Oi Hospital were retrospectively reviewed. Women were excluded if the uterine cavity was not entered.

All women received prior diagnostic hysteroscopy. Hysteroscopic morcellation was performed by trained gynaecologists in a dedicated hysteroscopy suite. Patients' height, weight, and blood pressure were recorded, and a urine pregnancy test was performed. In accordance with our analgesia protocol, all women received 1 g paracetamol 1 hour before the procedure, and paracervical block (lignocaine hydrochloride 2% with 1:80 000 adrenaline, 1.8 ml) intraoperatively, unless there was a known history of allergy. In addition, 400 μg buccal misoprostol was prescribed for premenopausal and nulliparous women to facilitate cervical dilatation. Cervices were dilated to 6 mm with Hegar dilators to facilitate entry of the instrument. Hysteroscopic morcellation was performed with the Intrauterine Bigatti Shaver Fr 19, which consists of a 6.3 mm diameter rod-lens telescope and a 4 mm diameter rotational cutting device with an automatic window closure activated by a footswitch. Normal saline was used as the distension medium. Fluid balance was monitored with the Hysteromat system (Karl Storz, Tuttlingen, Germany). Intrauterine pressure was set as the patient's diastolic blood pressure. All morcellated tissues were sent for histopathological examination.

Operative time was defined as the total duration of the procedure excluding instrument preparation time. Patients were asked to rate their pain on a visual analogue scale (VAS) from 0 (no pain) to 10 (worst possible pain) during, immediately after, and 1 hour after the procedure. Pain scores were then categorised as mild (0-3), moderate (4-6), and severe (7-10). Patients were asked yes/no questions on whether they were satisfied with the procedure, whether they would be willing to undergo the procedure again if clinically indicated, and whether they would recommend the procedure to others.

Baseline characteristics, clinical details, and final diagnoses were retrieved from the clinical case notes and electronic medical record system. Details of the hysteroscopic morcellation procedure were retrieved from the standard proforma. The nature, size, and location of the intracavitary lesions were collected, as were procedure duration, completeness of resection, procedural difficulties, and intraoperative complications (bleeding, infection, cervical trauma, and uterine perforation). Shaver speed, suction rate, irrigation pump pressure, and flow rate were also recorded.

Analyses were performed using SPSS (Windows version 27.0; IBM Corp, Armonk [NY], US). Parametric continuous data were presented as means with standard deviations and analysed using the Student's *t* test. Nonparametric continuous data were presented as medians with interquartile ranges and analysed using the Mann-Whitney *U* test. Categorical variables were presented as frequencies and percentages and analysed using the Pearson's Chi-squared test or Fisher's exact test. A value of $p<0.05$ was considered statistically significant. The STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines were followed in the preparation of this article.

Results

Over the 4-year period, 247 patients underwent hysteroscopic morcellations. Five of them were excluded because of having a non-intracavitary lesion (n=3) or a procedural failure owing to a tight cervical os (n=2). The remaining 242 patients were included in analysis (Table 1). The mean patient age was 54.1 years, and the median body mass index was 24.7 kg/m^2. 167 (69.0%) of patients had previous vaginal deliveries, and 133 (55.0%) were postmenopausal. The commonest presenting symptom was postmenopausal bleeding (48.8%), followed by abnormal menstrual bleeding (42.6%) and suspected intracavitary lesion (8.7%). 43.8% of patients had one lesion; 87.2% of patients had endometrial polyps. There were 523 endometrial polyps, which were evenly distributed within the uterine cavity, and the median size was 1 (range, 0.1-8.0) cm. There were 29 myomas; 93.1% were solitary; 75.9% were type 0; the median size was 2 (range, 1-5) cm; and 31.0% were located at the fundal region. 96.3% and 95.5% of patients received oral paracetamol and paracervical block, respectively. 99.4% of endometrial polyps and

Table 1. Characteristics of patients who underwent hysteroscopic morcellation for intracavitary lesions (n=242)

Characteristic	Value*
Age, y	54.1±10.1
Ethnicity	
Chinese	239 (98.8)
Southeast Asian: Thai, Indonesian	2 (0.8)
South Asian: Nepalese	1 (0.4)
Weight, kg	59.1 (38.5-102.8)
Body mass index, kg/m^2	24.7 (16.4-42.6)
Ambulatory	240 (99.2)
Medical problems	
Hypertension	78 (32.2)
Diabetes mellitus	41 (16.9)
Cardiac disease	8 (3.3)
Breast cancer with history of tamoxifen use	44 (18.2)
Polycystic ovarian syndrome	1 (0.4)
Nulliparous	38 (15.7)
Previous vaginal delivery	167 (69.0)
Postmenopausal	133 (55.0)
Presenting symptom	
Abnormal menstrual bleeding	103 (42.6)
Postmenopausal bleeding	118 (48.8)
Incidental sonographic finding	21 (8.7)
No. of intracavitary lesions	
1	106 (43.8)
2	55 (22.7)
3	21 (8.7)
4	28 (11.6)
5	28 (11.6)
6	2 (0.8)
7	2 (0.8)
Type of intrauterine pathology	
Endometrial polyp	211 (87.2)
Myoma	11 (4.5)
Endometrial polyp and myoma	16 (6.6)
Endocervical polyp and endometrial polyp	3 (1.2)
Endocervical polyp, endometrial polyp, and myoma	1 (0.4)
Patients with endometrial polyps (n=231)	
1 lesion	107 (46.3)
>1 lesions	124 (53.7)
Diameter, cm	1 (0.1-8.0)
Location of endometrial polyps (n=523)	
Fundal	103 (19.7)
Anterior	105 (20.1)
Posterior	125 (23.9)
Right	98 (18.7)
Left	92 (17.6)
Complete resection	228 (98.7)
Total number of endometrial polyps removed	520/523 (99.4)
Patients with myomas (n=27)	
1 lesion	25 (92.6)
>1 lesions	2 (7.4)
Diameter, cm	2.0 (1.0-5.0)
Location of myomas (n=29)	
Fundal	9 (31.0)
Anterior	4 (13.8)
Posterior	5 (17.2)
Right	8 (27.6)
Left	3 (10.3)
Type of submucosal myomas (n=29)	
Type 0 (pedunculated intracavitary)	22 (75.9)
Type 1 (<50% intramural)	2 (6.9)
Type 2 (≥50% intramural)	5 (17.2)
Complete resection	21 (77.8)
Total number of myomas removed	23/29 (79.3)
Surgeon experience	
Specialist	78 (32.2)
Resident	17 (7.0)
Both	147 (60.7)
Antibiotic cover	10 (4.1)
Analgesia	
Oral paracetamol	233 (96.3)
Cervical block	231 (95.5)
Buccal misoprostol	86 (35.5)
Instrumental preparation time, min	15 (2-31)
Operative time, min	20 (7-78)
Fluid used, ml	1400 (200-11 000)
Fluid deficit, ml	0 (–300 to 700)
Shaver speed, rpm	2100 (800-4000)
Suction rate, ml/min	240 (200-400)
Histological diagnosis	
Benign endometrial polyp	189 (78.1)
Myoma	24 (9.9)
Normal endometrium	13 (5.4)
Endometrial polyp and myoma	8 (3.3)
Endocervical polyp and endometrial polyp	2 (0.8)
Endometrial hyperplasia without atypia	3 (1.2)
Endometrial hyperplasia with atypia	1 (0.4)
Malignant cells suggestive of metastatic breast cancer	1 (0.4)
Insufficient tissue for diagnosis	1 (0.4)

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

79.3% of myomas were removed. The complete resection rate was higher for patients with endometrial polyps than for patients with myomas (98.7% vs 77.8%, p<0.001). There were complications of bleeding (n=2) and endometritis (n=1) but no cervical trauma or uterine perforation. All histological diagnoses matched the hysteroscopic findings, except for five cases of endometrial hyperplasia and one case of malignancy suggestive of metastatic breast cancer.

Most patients reported mild pain intraoperatively (57.4%), immediately after the procedure (72.3%), and upon discharge (95.0%) [Table 2]. 98.8% of patients were satisfied with the procedure; 94.2% would undergo the same operation again if clinically indicated; and 95.5% would recommend this procedure to others. Premenopausal women reported more pain immediately after the procedure (2 vs 1, p=0.020) and upon discharge (0 vs 0, p=0.040) than postmenopausal women (Table 3). Patients with an operative time of >20 minutes reported more pain immediately after the procedure (3 vs 1, p=0.007) than patients with an operative time of ≤20 minutes. Surprisingly, satisfaction was not correlated with pain during the procedure (3 vs 3, p=0.782), after the procedure (2 vs 3, p=0.518), and before discharge (0 vs 0, p=0.340).

Table 2. Patients' pain levels and satisfaction with hysteroscopic morcellation (n=242)

Outcome	Value*
Visual analogue scale for pain	
During procedure	
Mild (≤3)	139 (57.4)
Moderate (4-6)	73 (30.2)
Severe (≥7)	30 (12.4)
Immediately after procedure	
Mild (≤3)	175 (72.3)
Moderate (4-6)	54 (22.3)
Severe (≥7)	13 (5.4)
Upon discharge	
Mild (≤3)	230 (95.0)
Moderate (4-6)	10 (4.1)
Severe (≥7)	2 (0.8)
Are you satisfied with the service you have received?	
Yes	239 (98.8)
No	3 (1.2)
Are you willing to undergo this operation again if clinically indicated?	
Yes	228 (94.2)
No	14 (5.8)
Will you recommend this operation to others?	
Yes	231 (95.5)
No	11 (4.5)

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

Discussion

Almost all patients were satisfied with the procedure, would undergo the procedure again if needed, and would recommend the procedure to others. Most patients experienced only mild pain (VAS score 0-3) during and immediately after the procedure and upon discharge. For 30 patients who reported severe pain (VAS score ≥7) during the procedure, only two reported severe pain upon discharge.

Premenopausal women reported higher pain scores than postmenopausal women immediately after the procedure (p=0.020) and upon discharge (p=0.040). This is in contrast to most findings that suggest that postmenopausal status is related to a higher pain score in hysteroscopy, which is attributed to a tighter cervical os and vaginal dryness from a hypo-oestrogenic state[15]. However, our results are in line with those in a study that reported significantly higher pain scores in premenopausal women than in postmenopausal women (3.2 vs 2.5, p=0.047) who underwent removal of endometrial polyps in an outpatient setting using the MyoSure morcellation device[16]. One explanation for this observation may be that pain receptors in the cervix or uterus are more sensitive in premenopausal women, and that the co-existence of adenomyosis, fibroids, and chronic inflammatory pelvic conditions is more common in premenopausal women[17].

An operating time of >20 minutes was associated with higher pain scores immediately after the procedure. This may be explained by the surgeon expertise, distension pressure and duration, and procedural difficulty.

To improve pain relief, the Royal College of Obstetricians and Gynaecologists suggests replacing pre-procedural paracetamol with sustained-release nonsteroidal anti-inflammatory drugs and adding post-procedural paracetamol[18]. Non-pharmacological strategies to minimise pain include the 'vocal local' approach, the vaginoscopic approach, the use of miniaturised instruments, and playing music to reduce patient anxiety[19-21].

Patient satisfaction was not associated with pain scores during the procedure (p=0.782), immediately after the procedure (p=0.518), or upon discharge (p=0.340).

Table 3. Predictors for pain during and immediately after hysteroscopic morcellation and upon discharge

	Pain score during procedure*	p Value	Pain score immediately after procedure*	p Value	Pain score upon discharge*	p Value
Menopausal status		0.644		0.020		0.040
Premenopausal	3 (1-5)		2 (0-4)		0 (0-1)	
Postmenopausal	3 (1-5)		1 (0-3)		0 (0-0)	
Previous vaginal delivery		0.943		0.636		0.385
Yes	3 (1-5)		2 (0-3)		0 (0-0)	
No	3 (1-5)		2 (0-4)		0 (0-1)	
Operative time		0.358		0.007		0.465
≤20min	3 (0-5)		1 (0-3)		0 (0-0)	
>20min	3 (1-5)		3 (0-4)		0 (0-1)	
Paracetamol before procedure		0.756		0.645		0.385
Yes	3 (1-5)		2 (0-4)		0 (0-0)	
No	3 (0.5-4.5)		3 (0.5-3)		0 (0-0)	
Paracervical block		0.444		0.463		0.063
Yes	3 (1-5)		2 (0-4)		0 (0-0)	
No	3 (1-4)		2 (0-3)		0 (0-0)	
Buccal misoprostol		0.273		0.126		0.063
Yes	3 (1-5)		2 (0-4)		0 (0-1)	
No	3 (0.5-5)		2 (0-3)		0 (0-0)	
Lesion		0.817		0.489		0.093
Solitary	3 (0-5)		2 (0-3)		0 (0-1)	
Multiple (>1)	3 (1-5)		2 (0-4)		0 (0-0)	
Presence of myoma		0.825		0.273		0.733
Yes	3 (1-6)		3 (1-4)		0 (0-0)	
No	3 (1-5)		2 (0-4)		0 (0-0)	
Satisfaction		0.782		0.518		0.340
Yes	3 (1-5)		2 (1-5)		0 (0-0)	
No	3 (0-5)		3 (0-5)		0 (0-0)	

* Data are presented as median (interquartile range)

This suggests that patient satisfaction/acceptability may be attributed to the quality of preoperative counselling and information-giving[13] and differences in the pain experienced and the pain expected[12]. Therefore, optimising expectations with pre-procedural counselling and close communication may further increase patient satisfaction.

Hysteroscopic morcellation is a good alternative to conventional resectoscopy because of higher rates of resection of polyps and myomas[5,6,22]. The complete resection rate was higher for patients with endometrial polyps than for patients with myomas (98.7% vs 77.8%, p<0.001), which may be attributed to the difference in tissue consistency. In seven patients with myomas >3.5 cm, the resection was incomplete. Of them, two underwent a second hysteroscopic resectoscopy, one underwent resection under general anaesthesia, and four opted for observation only. Endometrial polyps were incompletely resected in four women. Two of these women subsequently underwent bipolar resectoscopy under general anaesthesia, and the remaining two underwent hysterectomies because they had concurrent multiple fibroids.

Two patients were complicated by intraoperative bleeding, which resolved spontaneously. The hysteroscopic morcellation system cannot coagulate bleeding vessels

during surgery. Introducing a bipolar probe through the operative channel for focal haemostasis may be a solution.

There are limitations to our study. First, patient selection may be biased, because women who preferred the procedure performed in other settings or who had intracavitary lesions deemed difficult to be resected by hysteroscopic morcellation were excluded at the outset. Therefore, satisfaction could be affected by preconceived acceptance and might be overestimated. Second, confounding factors such as patient preoperative anxiety level and any concomitant uterine pathologies (adenomyosis, endometriosis, chronic pelvic pain, or pelvic congestion syndrome) that might have affected patient pain perception were not taken into account. Third, rating scores for satisfaction should have been used rather than yes/no questions. Fourth, long-term outcomes of this procedure including the extent of symptom improvement, recurrence of lesions, quality of life, and cost-effectiveness were not addressed. Nonetheless, the present study included details of the procedure, reasons for procedure failure, patient pain scores at different time intervals, and patient satisfaction. The present study also included more patients with large endometrial polyps and various types of myomas than other studies; this may enable better generalisation of our results across populations.

Conclusion

Almost all patients were satisfied with hysteroscopic morcellation. Most patients experienced only mild pain during and immediately after the procedure and upon discharge. Premenopausal status and operative time of >20 minutes were associated with higher pain scores. Further optimisation of pain-relief methods should be considered.

Contributors

Concept or design: PL So, SF Wong, KM Chow
Acquisition of data: C Leung, LT Kwong, PL So
Analysis or interpretation of data: C Leung, LT Kwong, PL So
Drafting of the manuscript: C Leung, LT Kwong, PL So
Critical revision of the manuscript for important intellectual content: All authors

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 disclosed no conflicts of interest.

Funding/support

This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Data availability

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

Ethics approval

This study was approved by the Hospital Authority Central Institutional Review Board (reference: CIRB-2023-023-4).

Acknowledgement

The authors thank nursing staff Stella NL Fong, CK Poon, Pauline KL Wong, YK Wong, CY Cheung, and Damien LY Lau for organisational and clinical support in the office-based hysteroscopic morcellation clinic.

References

1. Stewart EA. Uterine fibroids. Lancet 2001;357:293-8. Crossref
2. American Association of Gynecologic Laparoscopists. AAGL practice report: practice guidelines for the diagnosis and management of endometrial polyps. J Minim Invasive Gynecol 2012;19:3-10. Crossref
3. Touboul C, Fernandez H, Deffieux X, Berry R, Frydman R, Gervaise A. Uterine synechiae after bipolar hysteroscopic resection of submucosal myomas in patients with infertility. Fertil Steril 2009;92:1690-3. Crossref
4. Hamerlynck TW, Schoot BC, van Vliet HA, Weyers S. Removal of endometrial polyps: hysteroscopic morcellation versus bipolar resectoscopy: a randomized trial. J Minim Invasive Gynecol 2015;22:1237-43. Crossref
5. Hamerlynck TW, Dietz V, Schoot BC. Clinical implementation of the hysteroscopic morcellator for removal of intrauterine myomas and polyps. A retrospective descriptive study. Gynecol Surg 2011;8:193-6. Crossref
6. Li C, Dai Z, Gong Y, Xie B, Wang B. A systematic review and meta-analysis of randomized controlled trials comparing hysteroscopic morcellation with resectoscopy for patients with endometrial lesions. Int J Gynaecol Obstet 2017;136:6-12. Crossref

7. Shazly SA, Laughlin-Tommaso SK, Breitkopf DM, et al. Hysteroscopic morcellation versus resection for the treatment of uterine cavitary lesions: a systematic review and meta-analysis. J Minim Invasive Gynecol 2016;23:867-77. Crossref
8. Scheiber MD, Chen SH. A prospective multicenter registry of patients undergoing hysteroscopic morcellation of uterine polyps and myomas. J Gynecol Surg 2016;32:318-23. Crossref
9. Pampalona JR, Bastos MD, Moreno GM, et al. A comparison of hysteroscopic mechanical tissue removal with bipolar electrical resection for the management of endometrial polyps in an ambulatory care setting: preliminary results. J Minim Invasive Gynecol 2015;22:439-45. Crossref
10. Emanuel MH, Wamsteker K. The intra uterine morcellator: a new hysteroscopic operating technique to remove intrauterine polyps and myomas. J Minim Invasive Gynecol 2005;12:62-6. Crossref
11. Murakami T, Tamura M, Ozawa Y, Suzuki H, Terada Y, Okamura K. Safe techniques in surgery for hysteroscopic myomectomy. J Obstet Gynaecol Res 2005;31:216-23. Crossref
12. Ma T, Readman E, Hicks L, et al. Is outpatient hysteroscopy the new gold standard? Results from an 11 year prospective observational study. Aust N Z J Obstet Gynaecol 2017;57:74-80. Crossref
13. Pervaiz Z, Korrapati S, Ghoubara A, Ewies A. Office hysteroscopic morcellation service: evaluation of women experience and factors affecting satisfaction. Eur J Obstet Gynecol Reprod Biol 2021;264:294-8. Crossref
14. Wortman M, Daggett A, Ball C. Operative hysteroscopy in an office-based surgical setting: review of patient safety and satisfaction in 414 cases. J Minim Invasive Gynecol 2013;20:56-63. Crossref
15. Agostini A, Bretelle F, Cravello L, Maisonneuve AS, Roger V, Blanc B. Acceptance of outpatient flexible hysteroscopy by premenopausal and postmenopausal women. J Reprod Med 2003;48:441-3.
16. McIlwaine P, McElhinney B, Karthigasu KA, Hart R. A prospective study of the use of the Myosure resectoscope to manage endometrial polyps in an outpatient setting. Aust N Z J Obstet Gynaecol 2015;55:482-6. Crossref
17. Di Spiezio Sardo A, Florio P, Fernandez LM, et al. The potential role of endometrial nerve fibers in the pathogenesis of pain during endometrial biopsy at office hysteroscopy. Reprod Sci 2015;22:124-31. Crossref
18. Hysteroscopy, Best Practice in Outpatient (Green Top Guideline No. 59). Available at: https://www.rcog.org.uk/guidance/browse-all-guidance/green-top-guidelines/hysteroscopy-best-practice-in-outpatient-green-top-guideline-no-59/
19. Law HY, Ng DYT, Chung CD. Use of music in reducing pain during outpatient hysteroscopy: prospective randomized trial. J Obstet Gynaecol Res 2021;47:904-12. Crossref
20. Sorrentino F, Petito A, Angioni S, et al. Impact of anxiety levels on the perception of pain in patients undergoing office hysteroscopy. Arch Gynecol Obstet 2021;303:999-1007. Crossref
21. Keogh SC, Fry K, Mbugua E, et al. Vocal local versus pharmacological treatments for pain management in tubal ligation procedures in rural Kenya: a non-inferiority trial. BMC Womens Health 2014;14:21. Crossref
22. Georgiou D, Tranoulis A, Jackson TL. Hysteroscopic tissue removal system (MyoSure) for the resection of polyps, sub-mucosal leiomyomas and retained products of conception in an out-patient setting: a single UK institution experience. Eur J Obstet Gynecol Reprod Biol 2018;231:147-51. Crossref

Hong Kong J Gynaecol Obstet Midwifery 2023;23(2):120-6 | https://doi.org/10.12809/hkjgom.23.2.338

Safety and efficacy of ferric derisomaltose and its effect on blood transfusions in women with severe anaemia from heavy menstrual bleeding

Caryssa Ling YAN[1], Benjamin Ross YOUNG[2], Jade Wing Ngan SHEK[1], Po Lam SO[1]

[1] Department of Obstetrics and Gynaecology, Tuen Mun Hospital, Hong Kong SAR, China

[2] WHO Collaborating Centre for Infectious Disease Epidemiology and Control, School of Public Health, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong SAR, China

Objective: This study investigates the safety and efficacy of ferric derisomaltose (FDI) and its effect on blood transfusion requirements in women with severe anaemia secondary to heavy menstrual bleeding (HMB).

Methods: Medical records of women aged ≥18 years who were admitted to Tuen Mun Hospital with severe iron deficiency anaemia (a haemoglobin level of <8.0 g/dL and a mean corpuscular volume of <80 fL) secondary to HMB in the periods before (1 July 2014 to 30 June 2018) and after (1 July 2018 to 30 June 2022) the introduction of FDI were retrospectively reviewed.

Results: In total, 1373 and 983 patients were admitted before and after the introduction of FDI, respectively. The mean number of blood units transfused per patient decreased from the pre-FDI period to the post-FDI period (2.02 vs 1.19, p<0.001). The decrease remained significant after adjusting for age, ethnicity, baseline haemoglobin, and leiomyoma. In 384 patients who received FDI, 55 (14.3%) had a hypersensitivity reaction (HSR), 41 of which were mild. There were no cases of cardiac or respiratory arrest or allergic reaction necessitating adrenaline administration. The occurrence of an HSR was not associated with the number of known drug allergies (p=0.076), ethnicity (p=0.563), or age (p=0.06). After FDI administration, the mean haemoglobin level increased from 6.2 g/dL to 10.6 g/dL (p<0.001), whereas the mean ferritin increased from 22.5 μg/L to 149 μg/L (p<0.001) at 3 to 4 weeks.

Conclusion: Intravenous FDI is safe and effective for treating severe iron deficiency anaemia secondary to HMB. FDI significantly reduces the requirement for blood transfusions. 14.3% of patients had an HSR. FDI mitigates the burden on blood transfusion services and supports patient blood management principles.

Keywords: Anemia, iron deficiency; Blood transfusion; Ferric derisomaltose; Iron isomaltoside 1000; Menorrhagia

Introduction

Heavy menstrual bleeding (HMB) is defined as regular excessive menstrual blood loss that affects the physical, social, emotional, or material quality of life of patients[1]. It affects approximately 18% to 38% of women of reproductive age[2,3]. Iron deficiency anaemia (IDA) is a common complication of HMB, present in up to 63% of HMB cases[3].

Severe anaemia is defined by the World Health Organization as a serum haemoglobin level of <8.0 g/dL in non-pregnant women aged >15 years[4]. Blood transfusions are commonly used to rapidly raise haemoglobin levels and can be lifesaving in acutely haemorrhagic, haemodynamically unstable patients. However, blood transfusions are associated with potentially serious morbidities such as anaphylaxis, sepsis, transfusion-related acute lung injury, transfusion-associated circulatory overload, and even mortality[5]. Nonetheless, the demand for blood has increased in the past decade owing to an ageing population[6], while the supply of blood products has decreased to critical levels amidst the COVID-19 pandemic that reduces social activities and blood donations[7].

In patients with chronic well-compensated anaemia, intravenous iron therapy is safe and effective and avoids the risks associated with blood transfusions[8-10]. Compared with the oral route, the intravenous route raises haemoglobin levels more quickly and reduces the rate of IDA recurrence[10]. Intravenous iron therapy is recommended in clinical guidelines across multiple specialities including gastroenterology[11], oncology[12], cardiology[13], and for pregnant women[14]. However, its use for HMB is poorly established, and the treatment and screening for IDA are inconsistent. In clinical guidelines for HMB worldwide, approximately one-third offer guidance on iron therapy and one-fifth recommend intravenous iron therapy[15].

Correspondence to: Dr Caryssa YAN
Email: caryssa.yan@gmail.com

Several formulations of intravenous iron therapy are available in Hong Kong. Iron sucrose (Venofer; Vifor, St Gallen, Switzerland) is safe and effective for severe anaemia secondary to HMB[16]. However, iron sucrose is limited by its multiple-dosage regimen and the use of the Ganzoni formula, which is shown to underestimate iron requirements[17]. Ferric derisomaltose (FDI), also known as iron isomaltoside 1000 (Monofer; Pharmacosmos, Holbaek, Denmark), is taken in a single dose and requires a simple calculation based on weight and can elevate haemoglobin levels more rapidly and effectively than iron sucrose[18].

On 1 July 2018, FDI was introduced in the gynaecology ward of Tuen Mun Hospital in Hong Kong. We aimed to evaluate the effect of FDI's introduction on blood transfusion requirements in patients with HMB as well as FDI's safety and efficacy.

Materials and methods

We performed a retrospective study to compare periods before (1 July 2014 to 30 June 2018) and after (1 July 2018 to 30 June 2022) the introduction of FDI at the gynaecology ward of Tuen Mun Hospital in Hong Kong. Through the clinical data analyses and reporting system, data of women aged ≥18 years admitted with severe IDA (defined as a haemoglobin level of <8.0 g/dL and a mean corpuscular volume of <80 fL) secondary to HMB were extracted. Patients with anaemia resulting from other causes (such as ruptured ectopic pregnancies, autoimmune or bone marrow diseases, drug-induced anaemia, and haemodynamic instability) were excluded, as were those with contraindications to intravenous iron (such as anaphylaxis to intravenous iron, iron storage disorders, chronic liver disease, first-trimester pregnancy, and active infections). Data collected included age, ethnicity, duration of admission, type of admission (emergency or clinical), cause of HMB, and baseline haemoglobin and ferritin levels. The proportions of women who received blood only, FDI only, both, or neither were calculated. Additionally, the number of blood units transfused were recorded. Patients were stratified by their haemoglobin levels in g/dL (7.0-7.9, 6.0-6.9, 5.0-5.9, 4.0-4.9, and ≤3.9).

Before the introduction of FDI, patients with HMB and severe IDA were managed with blood transfusion alone or without any blood transfusion. After the introduction of FDI, patients were given the option of intravenous iron therapy if they had a haemoglobin level of <8.0 g/dL or had anaemic symptoms in the absence of contraindications and were haemodynamically stable, with or without a previous blood transfusion. Patients could receive more than one management modality. A single dose of FDI at 20 mg per kg of the patient weight (maximum of 1000 mg) was administered as an intravenous infusion diluted in 500 ml 0.9% sodium chloride solution over 60 minutes. Patients were monitored at regular 15-minute intervals up to 1 hour after the transfusion for any hypersensitivity reaction (HSR) or adverse reactions. HSRs were treated according to international guidelines[19,20]. HSRs were categorised based on their timing (acute [within 30 minutes of FDI administration] and delayed) and severity (mild, moderate, and severe) [Table 1]. Patients with asthma or allergies to ≥2 drugs were administered 125 mg intravenous methylprednisolone before FDI administration to reduce the risk of HSR. Similarly, patients with inflammatory arthritis were given the same dose of methylprednisolone, followed by a short oral course of prednisolone (1 mg/kg per day) for 4 days.

Patients' levels of haemoglobin, mean corpuscular volume, ferritin, iron, iron saturation, and total iron binding capacity were assessed before FDI administration and 3 to 4 weeks later. The primary outcome was the difference in the mean number of units of red blood cells or whole blood transfused per patient between the pre-FDI and post-FDI periods. Secondary outcomes included changes in haemoglobin and iron panels 3 to 4 weeks after FDI administration, the incidence of HSRs and their management, and the association between HSRs and the number of known drug allergies.

Table 1. Severity of hypersensitivity reactions (adapted from Rampton et al[19])

Severity	Symptoms
Mild	Itching, flushing, urticaria, sensation of heat, slight chest tightness, hypertension, back/joint pains
Moderate	As in mild reaction + transient cough, flushing, chest tightness, nausea, shortness of breath, tachycardia, hypotension
Severe	Sudden onset and rapid aggravation of symptoms + wheezing/stridor, periorbital oedema, cyanosis, loss of consciousness, cardiac/respiratory arrest

Univariate analysis was performed using the Chi-squared test or the Mann-Whitney *U* test to assess the distribution of descriptive variables and the crude difference in the number of units of blood products transfused between the two study periods. To adjust for potential confounders, multivariate linear regression analysis was conducted with the study period as the predictor. Within-group comparisons were made using the paired *t* test. A p value of <0.05 was considered statistically significant. R (version 4.2.2) was used for the statistical analyses.

Table 2. Patient characteristics before and after the introduction of ferric derisomaltose (FDI) for heavy menstrual bleeding

	Pre-FDI (n=1373)*	Post-FDI (n=983)*	p Value
Age, y	44.1±6.9	43.8±6.7	0.278
Ethnicity			<0.001
Chinese	1252 (91.2)	838 (85.2)	
Southeast Asian	81 (5.9)	99 (10.1)	
South Asian	36 (2.6)	41 (4.2)	
Caucasian	4 (0.3)	5 (0.5)	
Type of admission			0.002
Emergency	909 (66.2)	709 (72.1)	
Clinical	464 (33.8)	274 (27.9)	
Duration of admission, d	1.5±4.3	1.4±1.7	0.962
Cause of heavy menstrual bleeding			
Leiomyoma	618 (45.0)	404 (41.1)	0.058
Adenomyosis	151 (11.0)	127 (12.9)	0.080
Cervical cancer	26 (1.9)	18 (1.8)	1.000
Endometrial polyp	22 (1.6)	20 (2.0)	0.392
Endometrial hyperplasia	16 (1.2)	3 (0.3)	0.042
Endometrial cancer	2 (0.1)	12 (1.2)	0.002
Not yet classified	190 (13.8)	166 (16.9)	0.048
Haemoglobin, g/dL	6.4±1.1	6.1±1.2	<0.001
7.0-7.9	508 (37.0)	263 (26.8)	
6.0-6.9	428 (31.2)	330 (33.6)	
5.0-5.9	270 (19.7)	226 (23.0)	
4.0-4.9	105 (7.6)	119 (12.1)	
≤3.9	62 (4.5)	45 (4.6)	
Ferritin, µg/L	21.6±61.9	23.1±125.9	0.800
Units of blood transfused per patient			
0	186 (13.5)	326 (33.2)	
1	66 (4.8)	276 (28.1)	
2	754 (54.9)	269 (27.4)	
3	295 (21.5)	95 (9.7)	
4	54 (3.9)	13 (1.3)	
5	18 (1.3)	3 (0.3)	
Management			
Blood transfusion alone	86.5	45.4	
No blood transfusion or intravenous iron therapy	13.5	15.6	
Intravenous iron therapy alone	-	17.7	
Blood transfusion and intravenous iron therapy	-	21.4	

* Data are presented as mean ± standard deviation, No. (%) of patients, or % of patients. Total may not equal to 100% because of missing data.

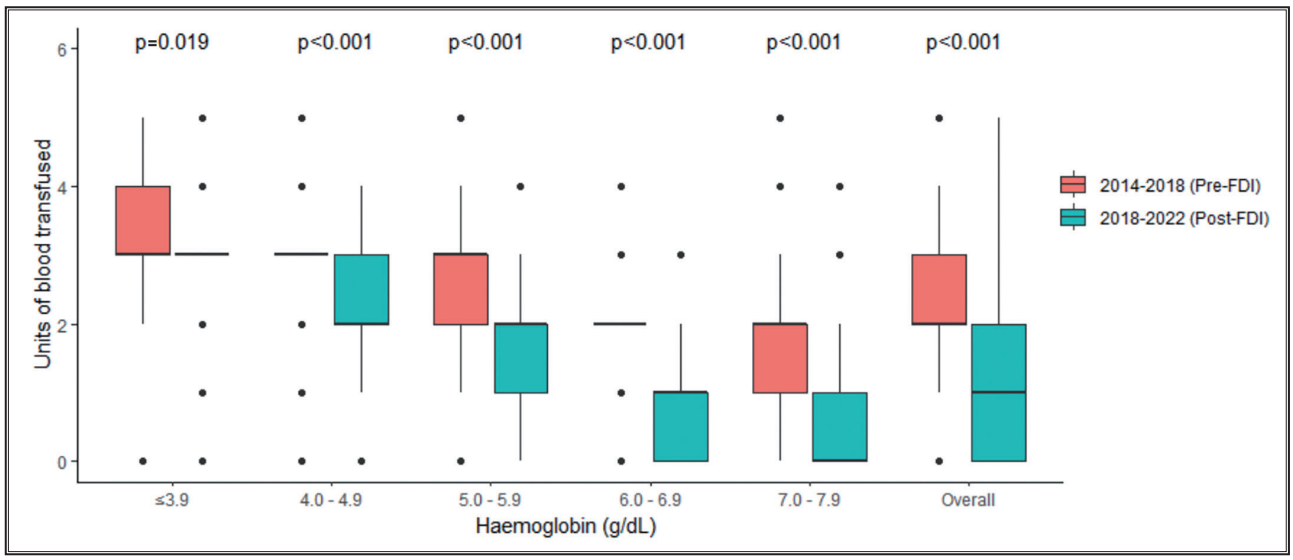


Figure 1. Medians and interquartile ranges of units of blood transfused per patient in each category of haemoglobin level before and after the introduction of ferric derisomaltose (FDI).

Results

In total, 1373 and 983 patients were admitted before and after the introduction of FDI, respectively. The two groups were comparable in terms of baseline characteristics, except for Chinese ethnicity, type of admission, and cause of HMB involving endometrial hyperplasia and endometrial cancer (Table 2).

The mean number of blood units transfused per patient decreased from the pre-FDI period to the post-FDI period (2.02 [95% confidence interval (CI)=1.96-2.07] vs 1.19 [95% CI=1.12-1.25], p<0.001). The decrease remained significant in the multivariate linear regression analysis, with a mean decrease of 1.07 (95% CI=0.97-1.16) units of blood transfused, after controlling for age, ethnicity, baseline haemoglobin, and leiomyoma. 55% of patients in the pre-FDI group received two units of blood, whereas 33.3% of patients in the post-FDI group did not receive any blood transfusion, and 28.1% received one unit of blood (Table 2). The proportions of patients with blood transfusions in every category of haemoglobin level also decreased in the post-FDI period (Figure 1).

Of the 983 patients in the post-FDI group, 446 (45.4%) received blood transfusion alone, 174 (17.7%) received FDI alone, 210 (21.4%) received both treatments, and 153 (15.6%) received neither (Table 2). The proportion of patients managed with blood transfusion alone decreased from 86.5% in the pre-FDI period to 45.4% in the post-FDI period.

Table 3. Hypersensitivity reactions after ferric derisomaltose administration in 55 patients

Hypersensitivity reactions	Value*
Severity	
Mild	41 (10.7)
Moderate	11 (2.9)
Severe	3 (0.8)
Type	
Acute	24 (43.6)
Delayed	31 (56.4)
Onset time, min	31.3±46.1
Development during the 60-min transfusion period	32 (58.2)
Management	
Discontinued if occurred during transfusion	24 (75.0)
No actions needed	20 (36.3)
Resumed at half rate	4 (7.2)
Topical crotamiton	2 (3.6)
Oral chlorphenamine	3 (5.5)
Intravenous chlorphenamine	1 (1.8)
Intravenous hydrocortisone	11 (20.0)
Inhaled salbutamol	1 (1.8)
Oxygen supplementation	2 (3.6)

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

Of the 384 patients who received FDI with or without a blood transfusion, 22 (5.7%) had drug allergies. Only one (0.3%) patient required methylprednisolone prior to FDI administration. 55 (14.3%) patients had an HSR, 41 of which were mild (Table 3). When HSRs occurred within 60 minutes of FDI administration, 75.0% of cases were managed by stopping the infusion and 7.2% of cases by resuming infusion at half the rate. The most common medication for HSRs was intravenous hydrocortisone (20.0%). There were no cases of cardiac or respiratory arrest or allergic reaction necessitating adrenaline administration. The occurrence of a HSR was not associated with the number of known drug allergies (p=0.076), ethnicity (p=0.563), or age (p=0.06).

In the 384 patients who received FDI with or without a blood transfusion, the mean haemoglobin level increased from 6.2 (95% CI=6.11-6.20) g/dL to 10.6 (95% CI=10.6-10.7) g/dL (p<0.001) and the mean ferritin increased from 22.5 (95% CI=16.9-28.2) µg/L to 149 (95% CI=126-172) µg/L (p<0.001) at 3 to 4 weeks after FDI administration (Figure 2).

Discussion

To the best of our knowledge, this is the first study to evaluate the real-world effect of intravenous iron therapy on blood transfusion requirements for severe IDA secondary to HMB. Before the availability of intravenous iron, there was a substantial reliance on blood transfusions to manage severe anaemia. Since the introduction of FDI, blood transfusion requirements have reduced overall and in each category of haemoglobin level. Notably, this reduction persisted even when the mean baseline haemoglobin level was significantly lower in the post-FDI group than in the pre-FDI group (6.1 vs 6.4 g/dL). Previous studies also reported a significant reduction in the number of blood transfusions given after the introduction of FDI in peri-operative patients[10] and emergency department patients[21].

Our study supports the three-pillar approach to patient blood management, which comprises reducing blood product usage, improving patient outcomes, and minimising costs[22]. Since 2010, the World Health Assembly has advocated these principles to its 193 member states[23].

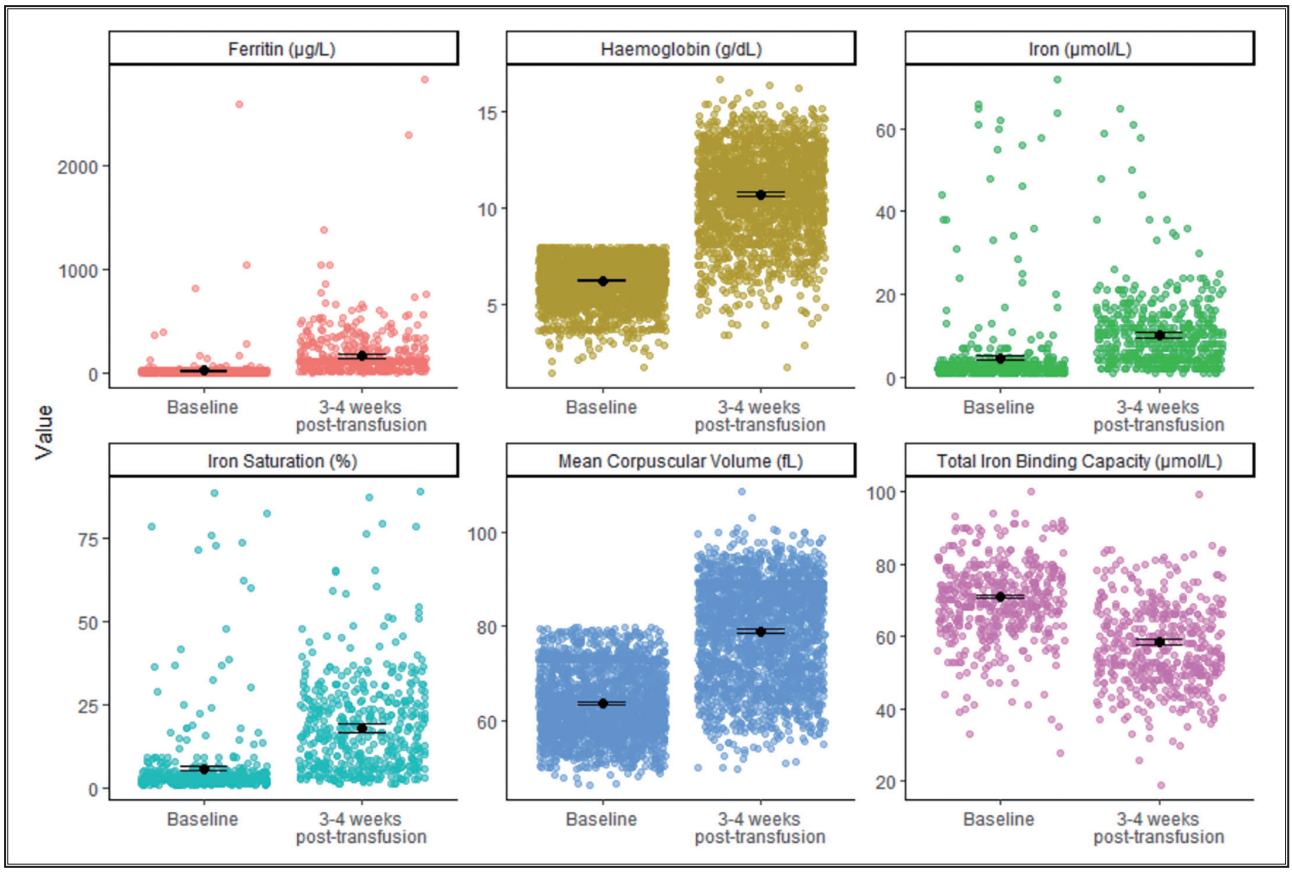


Figure 2. Scatterplots showing changes in means and 95% confidence intervals of haemoglobin, mean corpuscular volume, ferritin, iron, iron saturation, and total iron binding capacity from baseline to 3 to 4 weeks after transfusion of ferric derisomaltose.

The Hong Kong Society of Clinical Blood Management recommends single-unit transfusion and transfusing the minimum amount necessary to achieve clinical stability[6]. FDI does not increase the length of hospital stay, therefore requiring no additional hospitalisation costs.

The proportion of Chinese patients was significantly lower in the post-FDI group than in the pre-FDI group (85.2% vs 91.2%). This may be because the travel restrictions during the COVID-19 pandemic reduced medical tourism from Mainland China, which comprises a large proportion of admissions. Moreover, the post-FDI group involved a smaller sample size, a higher proportion of emergency admissions, a lower mean haemoglobin level, and more cases of endometrial cancer. Again, this may again be attributable to the COVID-19 pandemic, which reduced health-seeking behaviours, delayed disease presentation, and reduced hospital admissions by up to 21%[24].

The efficacy of FDI has been reported in both trial and real-world settings[8-10,25]. The rate of HSRs was higher in our study, compared with others (14.3% vs 0.3%-4.7%)[9,26]. This may be due to differences in the definition and classification of HSRs and the method of reporting. In the largest study of real-world FDI use involving 7342 patients from the United Kingdom in 2022, the incidence of HSRs was lower in the anaemic group than in the non-anaemic group (0.3% vs 0.9%)[9]. Our patients were severely anaemic and had a much higher incidence of HSRs. In a study of 126 postpartum women (88% were Chinese) with a mean age of 33 years treated with FDI, the incidence of HSR was 3.2%[27]. The mean age of our patients treated with FDI was 43.8 years; older age is a known risk factor for HSR[19,20].

Future research to evaluate the association of the Chinese ethnicity and HSRs secondary to FDI is warranted. Other formulations that are associated with fewer HSRs such as ferric carboxymaltose can be considered[25,28]. In addition, the wider use of methylprednisolone as a premedication warrants further investigation. Nonetheless, severe HSRs are uncommon and can be minimised with adequate and timely management.

One limitation of this study was the involvement of a single formulation in a single centre only. However, the sample size was large, and the FDI dosage and administration protocol were standardised. The study was not designed to investigate the incidence of HSRs or their associations. The period before the introduction of FDI reflects the real-world clinical practice and hence was chosen for comparison; patients who refused blood transfusions for personal or religious reasons, or who were contraindicated for blood transfusions were included.

Conclusion

Intravenous FDI is safe and effective for treating severe iron deficiency anaemia secondary to HMB. FDI significantly reduces the requirement for blood transfusions. 14.3% of patients had an HSR. FDI mitigates the burden on blood transfusion services and supports patient blood management principles.

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 disclosed no conflicts of interest.

Funding/support

This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Data availability

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

Ethics approval

This study was approved by the Hospital Authority Central Institutional Review Board (reference: CIRB-2023-014-3). 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.

Acknowledgements

We thank Mr Alvin Yip from the blood bank at the Department of Clinical Pathology, Tuen Mun Hospital and Dr Charing Szeto for their contributions to the data collection.

References

1. National Institute for Health and Care Excellence. NICE guideline [NG88]. Heavy menstrual bleeding: assessment and management. Available from: https://www.nice.org.uk/guidance/ng88.
2. Ding C, Wang J, Cao Y, et al. Heavy menstrual bleeding among women aged 18-50 years living in Beijing, China: prevalence, risk factors, and impact on daily life. BMC Womens Health 2019;19:27. Crossref
3. Kocaoz S, Cirpan R, Degirmencioglu AZ. The prevalence and impacts heavy menstrual bleeding on anemia, fatigue and quality of life in women of reproductive age. Pak J Med Sci 2019;35:365-70. Crossref
4. World Health Organization. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. Vitamin and Mineral Nutrition Information System (WHO/NMH/NHD/MNM/11.1). Available from: http://www.who.int/vmnis/indicators/haemoglobin.
5. Despotis GJ, Zhang L, Lublin DM. Transfusion risks and transfusion-related pro-inflammatory responses. Hematol Oncol Clin North Am 2007;21:147-61. Crossref
6. Chow YF, Cheng BCP, Cheng HK, et al. Hong Kong Society of Clinical Blood Management recommendations for implementation of patient blood management. Hong Kong Med J 2020;26:331-8. Crossref
7. The Government of the Hong Kong Special Administrative Region. Press Releases. Public urged to donate blood as inventories run low amid COVID-19 epidemic. Available from: https://www.info.gov.hk/gia/general/202203/18/P2022031800505.htm.
8. Litton E, Xiao J, Ho KM. Safety and efficacy of intravenous iron therapy in reducing requirement for allogeneic blood transfusion: systematic review and meta-analysis of randomised clinical trials. BMJ 2013;347:f4822. Crossref
9. Sinclair RCF, Nadaraja S, Kennedy NA, Wakatsuki M, Bhandari S. Real-world experience of intravenous ferric derisomaltose evaluated through safety and efficacy reporting in the UK. Sci Rep 2022;12:18859. Crossref
10. Ionescu A, Sharma A, Kundnani NR, et al. Intravenous iron infusion as an alternative to minimize blood transfusion in peri-operative patients. Sci Rep 2020;10:18403. Crossref
11. Kumar A, Brookes MJ. Iron therapy in inflammatory bowel disease. Nutrients 2020;12:3478. Crossref
12. Gemici C, Yetmen O, Yaprak G, et al. Is there any role of intravenous iron for the treatment of anemia in cancer? BMC Cancer 2016;16:661. Crossref
13. McDonagh TA, Metra M, Adamo M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J 2021;42:3599-726. Crossref
14. Pavord S, Daru J, Prasannan N, et al. UK guidelines on the management of iron deficiency in pregnancy. Br J Haematol 2020;188:819-30. Crossref
15. Mansour D, Hofmann A, Gemzell-Danielsson K. A review of clinical guidelines on the management of iron deficiency and iron-deficiency anemia in women with heavy menstrual bleeding. Adv Ther 2021;38:201-25. Crossref
16. Lau SCH, Hung CMW, Leung WC, Leung TW. Intravenous iron therapy for menorrhagic patients with severe iron-deficiency anaemia: a retrospective cohort study. Hong Kong J Gynaecol Obstet Midwifery 2019;19:103-9. Crossref
17. Reinisch W, Staun M, Tandon RK, et al. A randomized, open-label, non-inferiority study of intravenous iron isomaltoside 1,000 (Monofer) compared with oral iron for treatment of anemia in IBD (PROCEED). Am J Gastroenterol 2013;108:1877-88. Crossref
18. Derman R, Roman E, Modiano MR, Achebe MM, Thomsen LL, Auerbach M. A randomized trial of iron isomaltoside versus iron sucrose in patients with iron deficiency anemia. Am J Hematol 2017;92:286-91. Crossref
19. Rampton D, Folkersen J, Fishbane S, et al. Hypersensitivity reactions to intravenous iron: guidance for risk minimization and management. Haematologica 2014;99:1671-6. Crossref
20. Lim W, Afif W, Knowles S, et al. Canadian expert consensus: management of hypersensitivity reactions to intravenous iron in adults. Vox Sang 2019;114:363-73. Crossref
21. Beverina I, Razionale G, Ranzini M, Aloni A, Finazzi S, Brando B. Early intravenous iron administration in the Emergency Department reduces red blood cell unit transfusion, hospitalisation, re-transfusion, length of stay and costs. Blood Transfus 2020;18:106-16.
22. Farmer SL, Trentino K, Hofmann A, et al. A programmatic approach to patient blood management: reducing transfusions and improving patient outcomes. Open Anesth J 2015;9:9-16. Crossref
23. World Health Organization. Sixty-Third World Health Assembly. Resolutions and Decisions Anneses. WHA63.12: availability, safety and quality of blood products. Available from: https://apps.who.int/gb/ebwha/pdf_files/WHA63-REC1/WHA63_REC1-en.pdf.
24. Kalanj K, Marshall R, Karol K, Tiljak MK, Orešković S. The impact of COVID-19 on hospital admissions in Croatia. Front Public Health 2021;9:720948. Crossref
25. Aksan A, Işık H, Radeke HH, Dignass A, Stein J. Systematic review with network meta-analysis: comparative efficacy and tolerability of different intravenous iron formulations for the treatment of iron deficiency anaemia in patients with inflammatory bowel disease. Aliment Pharmacol Ther 2017;45:1303-18. Crossref
26. Kalra PA, Bhandari S, Spyridon M, et al. NIMO-CKD-UK: a real-world, observational study of iron isomaltoside in patients with iron deficiency anaemia and chronic kidney disease. BMC Nephrol 2020;21:539. Crossref
27. Lee LLT, Shu W. Efficacy and safety of intravenous iron isomaltoside in postpartum anaemia. Hong Kong J Gynaecol Obstet Midwifery 2022;22:16-20. Crossref
28. Arastu AH, Elstrott BK, Martens KL, et al. Analysis of adverse events and intravenous iron infusion formulations in adults with and without prior infusion reactions. JAMA Netw Open 2022;5:e224488. Crossref

Original Article

Hong Kong J Gynaecol Obstet Midwifery 2023;23(2):127-34 | https://doi.org/10.12809/hkjgom.23.2.339

Levonorgestrel-releasing intrauterine system versus oral progestogens for non-atypical endometrial hyperplasia: predictors for treatment failure

James Yuen Jim LAW, MBBS (HK), MRCOG
Lee Ting KWONG, MBBS (HK), FRCOG, FHKAM (O&G)
Po Lam SO, MBBS (HK), MMedSc (Genetic Counselling), MSc (Medical Genetics), FHKCOG, FHKAM (O&G)
Department of Obstetrics and Gynaecology, Tuen Mun Hospital, Hong Kong SAR, China

Objective: This study aims to compare treatment outcomes of a levonorgestrel-releasing intrauterine system (LNG-IUS) or oral progestogens in women with non-atypical endometrial hyperplasia (EH). Additionally, the predictors for EH non-regression were determined.
Methods: Medical records of women diagnosed with non-atypical EH between April 2016 and March 2022 at Tuen Mun Hospital were retrieved. These patients were offered LNG-IUS as the first-line option or oral progestogens if they refused or had LNG-IUS contraindications such as submucosal fibroid distorting endometrial cavity. The rate of EH non-regression at 12 months and the rate of EH relapse at 24 and 36 months between groups were compared. Univariate and multivariate analyses were conducted to identify predictors for EH non-regression.
Results: The median follow-up duration was 24 months for the LNG-IUS group and 19 months for the oral progestogens group. The rate of EH regression at 12 months was higher in the LNG-IUS group (93.9% vs 71.2%, p<0.001). The rate of EH relapse was higher in the oral progestogens group at 24 months (21.1% vs 1.1%, p=0.003) and 36 months (33.3% vs 2.3%, p=0.014). The incidence of hysterectomy for treatment failure was higher in the oral progestogens group (13.7% vs 4.2%, p=0.005). No EH relapse occurred in either group after 36 months post-treatment. Predictors for EH non-regression were postmenopausal status (odds ratio=5.80, p=0.022) and oral progestogens treatment (odds ratio=7.51, p<0.001).
Conclusion: In women with non-atypical EH, treatment with LNG-IUS leads to a higher regression rate at 12 months, a lower relapse rate within 36 months, and a lower rate of hysterectomy due to treatment failure, compared with treatment with oral progestogens. Postmenopausal status and treatment with oral progestogens are risk factors for treatment failure. Regular endometrial surveillance should be provided to women at risk. Hysterectomy is recommended for postmenopausal women.

Keywords: Endometrial hyperplasia; Levonorgestrel; Medroxyprogesterone; Metrorrhagia; Norethisterone; Recurrence

Introduction

Endometrial hyperplasia (EH) is the precursor to endometrial cancer (EC), which is the most common gynaecological malignancy in the developed world[1]. The incidence of EH is 133 per 100 000 women and peaks in women in their early 50s and 60s[2]. The main symptom of EH is abnormal uterine bleeding[3]. Early diagnosis and treatment of EH can prevent progression to EC.

Non-atypical EH accounts for about 90% of all EH, whereas atypical EH accounts for the remaining 10%[2]. For women with non-atypical EH, the cumulative long-term risk for progression to EC is <5%[4]. Although spontaneous regression of EH can occur[5], progestogen treatment leads to higher regression rates than observation alone and reduces the need for a hysterectomy and progression to EC[6,7]. Hence, treatments with progestogens are recommended. In particular, the levonorgestrel-releasing intrauterine system (LNG-IUS) is recommended as the first-line medical treatment for EH because it leads to a higher disease regression rate, more favourable bleeding profile, and fewer adverse effects, compared with oral progestogens[8-12].

We aimed to compare the clinical outcomes of women treated with LNG-IUS or oral progestogens, particularly the rate of disease non-regression at 12 months and the rate of disease relapse at 24 and 36 months. Additionally, the predictive factors for disease non-regression were determined.

Correspondence to: Dr James Yuen Jim LAW
Email: jameslaw1213@gmail.com

Materials and methods

Medical records of women diagnosed with non-atypical EH (according to the World Health Organization's 1994 classification[1]) between April 2016 and March 2022 at Tuen Mun Hospital, Hong Kong, were retrieved from the clinical notes and electronic patient record system. These patients were offered LNG-IUS as the first-line option or oral progestogens if they refused or had LNG-IUS contraindications such as submucosal fibroid distorting endometrial cavity. The LNG-IUS (Mirena; Bayer HealthCare Pharmaceuticals) has a steroid reservoir containing 52 mg levonorgestrel, with a release rate of 21 μg/day for the first 24 days and 11 μg/day for 5 years. The LNG-IUS should be kept in place for at least 6 months and to 5 years if tolerable. The oral progestogen options were either medroxyprogesterone or norethisterone 10 mg oral daily for 6 months. Treatment compliance was checked in follow-up sessions; non-compliant women were excluded.

Patients underwent endometrial biopsies at 6 and 12 months with LNG-IUS in situ. Patients were cleared from surveillance if these two biopsy results showed disease regression. For patients with a body mass index (BMI) ≥30 kg/m^2, with or without a history of chronic anovulation, endometrial biopsies were repeated annually thereafter. Patients were counselled for a hysterectomy if EH persisted after 12 months of LNG-IUS or 6 months of oral progestogens plus 6 months of LNG-IUS, or if the disease progressed or relapsed, or if patients had persistent bleeding, declined endometrial surveillance, or were non-compliant to medical treatment.

Primary outcomes were rates of disease regression and relapse after treatment. Disease regression was defined as the absence of endometrial hyperplasia at 12 months. Disease relapse was defined as the presence of non-atypical EH, atypical EH, or EC after the initial regression at 12 months. Secondary outcomes were predictors for disease non-regression at 12 months.

The sample size was calculated based on a study of regression rates after LNG-IUS or oral progestogen treatment.[6] A minimum of 172 women was required to have 80% power to detect statistical significance. The LNG-IUS and oral progestogen groups were compared using Pearson's Chi-squared test or Fisher's exact test for categorical data and Mann-Whitney *U* tests for non-parametric data. Continuous skewed variables were presented as median and interquartile ranges. Binary logistic regression analysis was performed. Among women whose treatment was successful, relapse rates were compared using time-to-failure methods with Kaplan–Meier plots and log-rank tests. Data analysis was performed using SPSS (Windows version 26.0; IBM Corp, Armonk [NY], US). A p value of <0.05 was considered statistically significant.

Results

Over the 6-year study period, 381 women were diagnosed with non-atypical EH and 285 of them completed 6 months' treatment with LNG-IUS (n=212) or oral progestogens (n=73), specifically medroxyprogesterone (n=63) and norethisterone (n=10) [Figure 1]. We excluded 96 women who were lost to follow-up after the initial diagnosis of EH (n=12), opted for observation (n=14) or hysterectomy (n=40), did not complete the 6-month treatment (n=20), or had changed treatment method within the first 6 months (n=10).

The median duration from diagnosis to the last histological follow-up was 24 months for the LNG-IUS group and 19 months for the oral progestogen group. The two groups were comparable in terms of demographics and uterine conditions, except that women treated with LNG-IUS were more likely to be multiparous (66.5% vs 47.9%, p=0.005) and absent of fibroids or adenomyosis (58.5% vs 45.2%, p=0.049), compared with those treated with oral progestogens (Table 1).

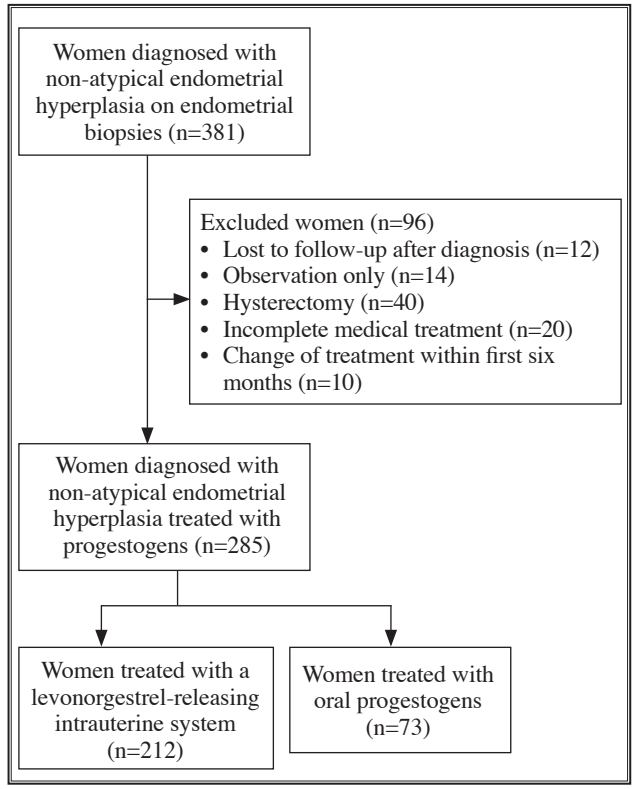


Figure 1. Flowchart of inclusion of patients.

Table 1. Baseline characteristics of women with non-atypical endometrial hyperplasia treated with a levonorgestrel-releasing intrauterine system (LNG-IUS) or oral progestogens

Characteristic	LNG-IUS (n=212)*	Oral progestogen (n=73)*	p Value
Age, y	46±9	43±12	0.166
Menopausal status			>0.99
Premenopausal	203 (95.8)	70 (95.9)	
Postmenopausal	9 (4.2)	3 (4.1)	
Presence of fibroids and/or adenomyosis			0.049
Yes	88 (41.5)	40 (54.8)	
No	124 (58.5)	33 (45.2)	
Uterine size			0.096
Normal size	142 (67.0)	41 (56.2)	
Enlarged	70 (33.0)	32 (43.8)	
Endometrial cavity length, cm	8.0±1.0	8.0±1.8	0.192
≤10	199 (93.9)	65 (89.0)	
>10	13 (6.1)	8 (11.0)	
Time from diagnosis to treatment, d	41±38	36±21	0.305
≤4 weeks	51 (24.1)	22 (30.1)	
>4 weeks	161 (75.9)	51 (69.9)	
Smoking status			0.573
Smoker	14 (6.6)	3 (4.1)	
Non-smoker	198 (93.4)	70 (95.9)	
Parity			0.005
Nulliparous	71 (33.5)	38 (52.1)	
Multiparous	141 (66.5)	35 (47.9)	
Body mass index, kg/m^2	26.5±7.8	25.9±7.6	0.819
<30	148 (69.8)	52 (71.2)	
≥30	64 (30.2)	21 (28.8)	
Ethnicity			0.526
Chinese	201 (94.8)	71 (97.3)	
Filipino	3 (1.4)	2 (2.7)	
Pakistani	3 (1.4)	0	
Indonesian	3 (1.4)	0	
Indian	1 (0.5)	0	
Vietnamese	1 (0.5)	0	
Concurrent use of Tamoxifen			>0.99
Yes	2 (0.9)	0	
No	210 (99.1)	73 (100)	
Concurrent use of hormonal replacement therapy			>0.99
Yes	1 (0.5)	0	
No	211 (99.5)	73 (100)	
Diabetes mellitus			0.634
Yes	30 (14.2)	12 (16.4)	
No	182 (85.8)	61 (83.6)	
Hypertension			0.686
Yes	39 (18.4)	15 (20.5)	
No	173 (81.6)	58 (79.5)	
Polycystic ovary syndrome			0.143
Yes	19 (9.0)	11 (15.1)	
No	193 (91.0)	62 (84.9)	
Family history of endometrial, ovarian, breast, or colorectal malignancy			0.551
Yes	16 (7.5)	4 (5.5)	
No	196 (92.5)	69 (94.5)	
Carrier of hereditary nonpolyposis colorectal cancer genes			>0.99
Confirmed	2 (0.9)	0	
Unknown	210 (99.1)	73 (100)	

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

At 12-month post-treatment, more women had achieved disease regression in the LNG-IUS group than in the oral progestogens group (93.9% vs 71.2%, p<0.001, Figure 2). Among the 251 women achieving disease regression, 137 had further endometrial biopsies beyond the initial 12 months. At 24 months, five (4.4%) of 114 women who had endometrial biopsies were diagnosed with EH relapse. At 36 months, four (7.7%) of 52 women who had endometrial biopsies were diagnosed with EH relapse. The risk of EH relapse was higher in the oral progestogens group than in the LNG-IUS group at 24 months (21.1% vs 1.1%, p=0.003) and 36 months (33.3% vs 2.3%, p=0.014). Figure 3 shows the Kaplan–Meier curves for EH relapse; the difference in EH relapse between the two groups was significant (p<0.001). The oral progestogens group had a higher rate of hysterectomy (13.7% vs 4.2%, p=0.005) performed for non-regression, relapse, or progression, compared with the LNG-IUS group. The incidence of EC was similar between groups (2.8% vs 4.1%, p=0.698, Figure 2).

Women with EH non-regression were more likely to be postmenopausal (41.7% vs 10.6%, p=0.008) and in the oral progestogens group (28.8% vs 6.1%, p<0.001) [Table 2]. In a multivariate analysis, postmenopausal status (odds ratio [OR]=5.80, 95% confidence interval [CI]=1.28-26.18, p=0.022) and treatment with oral progestogens (OR=7.51, 95% CI=3.28-17.20, p<0.001) were identified as predictors for EH non-regression at 12-month post-treatment.

Discussion

In the present study, women in the LNG-IUS group had a higher rate of EH regression at 12 months and a lower rate of EH relapse at 24 and 36 months and fewer hysterectomy performed due to treatment failure, compared with women in the oral progestogens group. Postmenopausal status and treatment with oral progestogens were significant risk factors for EH non-regression at 12-month post-treatment. These findings are consistent with those in other studies[6,7,13,14]. Nonetheless, the optimal type, dosage, and duration of progestogens have not been

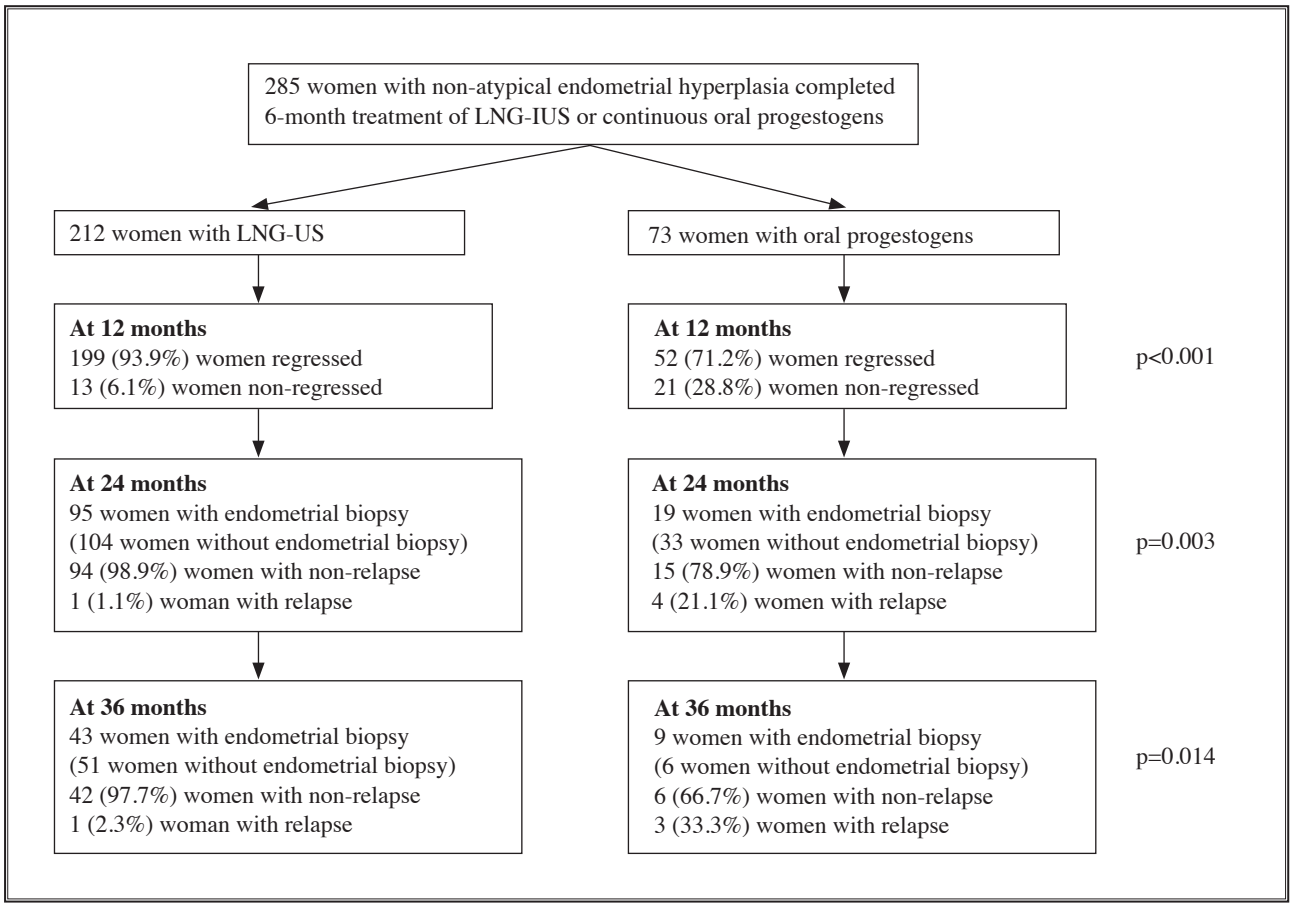


Figure 2. Flowchart of outcomes of women treated with a levonorgestrel-releasing intrauterine system (LNG-IUS) or oral progestogens.

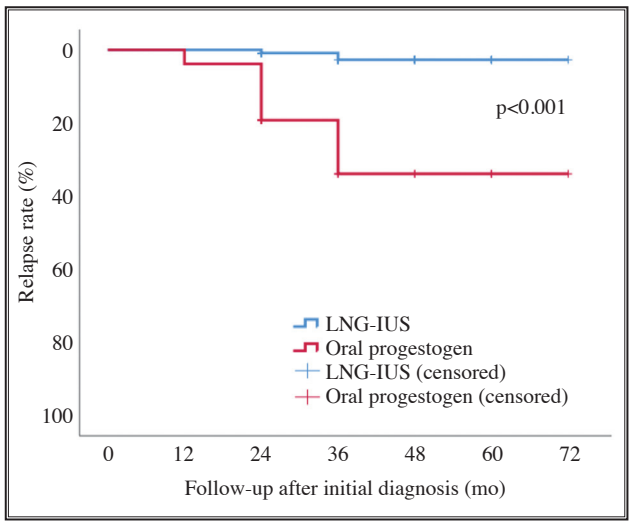


Figure 3. Kaplan–Meier survival curves for endometrial hyperplasia relapse over the course of 72 months in women with regression after treatment with a levonorgestrel-releasing intrauterine system (LNG-IUS) or oral progestogens.

identified in the literature.

The continuous slow release of progestogens onto the endometrium by the LNG-IUS is suggested to contribute to its higher efficacy than oral progestogens[7,15]. In addition, the relatively favourable adverse effect profile of the LNG-IUS might improve women's tolerance and compliance with treatment, compared with oral progestogens. Nevertheless, 73 (25.6%) of 285 women preferred oral progestogens; these women were more likely to be nulliparous or have uterine fibroids or adenomyosis. Five women with repeated dislodgements and two women with pelvic infections requested a change to oral progestogens treatment. Thus, it is important to emphasise the higher efficacy of LNG-IUS in achieving disease regression to these women. Some nulliparous women might be reluctant to opt for LNG-IUS because of fertility concerns; they should be reassured that there is no delay in fertility after LNG-IUS removal[16-18].

Table 2. Univariate and multivariate analyses for disease regression after 12 months of treatment

Variable	Univariate analysis			Multivariate analysis	
	Women with regression (n=251)*	Women with non-regression (n=34)*	p Value	Adjusted odds ratio (95% confidence interval)	p Value
Age at diagnosis, y	46.0 (10)	45.5 (10)	0.347	1.014 (0.951-1.081)	0.681
Menopausal status			0.008	5.796 (1.283-26.180)	0.022
Premenopausal (n=273)	244 (89.4)	29 (10.6)			
Postmenopausal (n=12)	7 (58.3)	5 (41.7)			
Parity			0.451	1.555 (0.580-4.168)	0.380
Nulliparous (n=109)	98 (89.9)	11 (10.1)			
Multiparous (n=176)	153 (86.9)	23 (13.1)			
Body mass index, kg/m^2			0.393	0.811 (0.321-2.051)	0.659
<30 (n=200)	174 (87.0)	26 (13.0)			
≥30 (n=85)	77 (90.6)	8 (9.4)			
Diabetes mellitus			0.305	1.704 (0.624-4.654)	0.299
Yes (n=42)	35 (83.3)	7 (16.7)			
No (n=243)	216 (88.9)	27 (11.1)			
Endometrial cavity length			0.151	1.675 (0.480-5.847)	0.419
≤10 cm (n=264)	235 (89.0)	29 (11.0)			
>10 cm (n=21)	16 (76.2)	5 (23.8)			
Polycystic ovary syndrome			>0.99	0.915 (0.207-4.052)	0.907
Yes (n=30)	27 (90.0)	3 (10.0)			
No (n=255)	224 (87.8)	31 (12.2)			
Progestogen treatment			<0.001	7.509 (3.277-17.203)	<0.001
Levonorgestrel-releasing intrauterine system (n=212)	199 (93.9)	13 (6.1)			
Oral progestogens (n=73)	52 (71.2)	21 (28.8)			

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

In addition, they should be encouraged to conceive after disease regression in at least one endometrial sample. Women with fibroids or adenomyosis also preferred oral progestogens. Although women's wishes should be respected, we would recommend LNG-IUS as the first-line treatment for all women, except for those with distorted anatomy of the uterine cavity or a significantly increased cavity length.

One (1.1%) of 95 women in the LNG-IUS group and four (21.1%) of 19 women in the oral progestogens group had a EH relapse at 24 months despite disease regression. This finding differs from that in a multicentre randomised trial in which the relapse rate after 6 months of treatment with LNG-IUS was 41% and was similar between the two treatment arms at 24-month post-treatment[19]. This discrepancy may be due to differences in the duration of the treatment with LNG-IUS, which was kept in place for 5 years if tolerated by our patients. Among those diagnosed with EH, the incidence of EC was higher (but not significantly) in the oral progestogens group than the LNG-IUS group (4.1% vs 2.8%). The non-significance may be due to the small sample size in women with endometrial biopsies after the initial 12 months' treatment. Owing to a higher risk of disease relapse and hysterectomy rate due to treatment failure, we recommend regular annual surveillance in women after oral progestogens treatment. Further long-term surveillance should be considered in those with significant risk factors. Because oral progestogen is a one-off 6-month treatment, LNG-IUS is recommended for long-term endometrial protection after completion of initial oral treatment, especially for those with additional risk factors.

Postmenopausal status was identified as a risk factor for EH non-regression at 12 months, after adjusting for age and BMI. This finding is consistent with that in a previous study[19]. Disease regression was not associated with age, obesity, nulliparity, diabetes, hypertension, and size of endometrial cavity. This finding is consistent with that in other studies[20-23]. Increased incidence of progression to EC in postmenopausal women is possibly because obese older women have increased susceptibility to unopposed oestrogen[24]. We believe that the pathophysiology of EH in postmenopausal women is likely more complex than it is currently understood[25-28].

Apart from standard progestogen treatment, surgical treatment (hysterectomy with bilateral salpingo-oophorectomy) should be considered as the definitive management for postmenopausal women with EH. Yet, women should consider the surgical risks and the risk factors for EH when making decision to undergo a hysterectomy. Women who are reluctant to undergo a hysterectomy should receive annual endometrial biopsies after disease regression to monitor disease relapse or progression.

There are several limitations to this study. There may be recall bias in this retrospective study. The lack of a central pathology review to identify women with non-atypical EH might affect the overall outcome of the study. Not all women had long-term endometrial biopsies because some were diagnosed and treated recently. According to our centre's practice, regular endometrial surveillance after 12 months is offered to those with symptom recurrence or at a higher risk of relapse. Hence, we may unintentionally omit those with EH relapse or EC or mild symptoms such that the relapse went undetected. Similarly, we could not provide the median duration of the LNG-IUS treatment in asymptomatic women with disease regression who were discharged from monitoring at 12 months. Although no women had EH relapse after 36 months, the sample size after censor was small. Owing to the small number of women with EH relapse, our study lacks the power to identify other predictors for EH relapse.

Conclusions

In women with non-atypical EH, treatment with LNG-IUS leads to a higher regression rate at 12 months, a lower relapse rate within 36 months, and a lower rate of hysterectomy due to treatment failure, compared with treatment with oral progestogens. Postmenopausal status and treatment with oral progestogens are risk factors for treatment failure. Regular endometrial surveillance should be provided to women at risk. Hysterectomy is recommended for postmenopausal women.

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 disclosed no conflicts of interest.

Funding/support

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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 New Territories West Cluster Research Ethics Committee (reference: CIRB-2022-062-1). The patients were treated in accordance with the tenets of the Declaration of Helsinki.

Acknowledgement

We thank Ms Nicole Chan for her administrative support.

References

1. Kurman RJ, Kaminski PF, Norris HJ. The behavior of endometrial hyperplasia. A long-term study of "untreated" hyperplasia in 170 women. Cancer 1985;56:403-12. Crossref
2. Reed SD, Newton KM, Clinton WL, et al. Incidence of endometrial hyperplasia. Am J Obstet Gynecol 2009;200:678.e1-6. Crossref
3. Anastasiadis PG, Skaphida PG, Koutlaki NG, Galazios GC, Tsikouras PN, Liberis VA. Descriptive epidemiology of endometrial hyperplasia in patients with abnormal uterine bleeding. Eur J Gynaecol Oncol 2000;21:131-4.
4. Lacey JV Jr, Sherman ME, Rush BB, et al. Absolute risk of endometrial carcinoma during 20-year follow-up among women with endometrial hyperplasia. J Clin Oncol 2010;28:788-92. Crossref
5. Terakawa N, Kigawa J, Taketani Y, et al. The behavior of endometrial hyperplasia: a prospective study. Endometrial Hyperplasia Study Group. J Obstet Gynaecol Res 1997;23:223-30. Crossref
6. Gallos ID, Shehmar M, Thangaratinam S, Papapostolou TK, Coomarasamy A, Gupta JK. Oral progestogens vs levonorgestrel-releasing intrauterine system for endometrial hyperplasia: a systematic review and meta-analysis. Am J Obstet Gynecol 2010;203:547.e1-10. Crossref
7. Gallos ID, Krishan P, Shehmar M, Ganesan R, Gupta JK. LNG-IUS versus oral progestogen treatment for endometrial hyperplasia: a long-term comparative cohort study. Hum Reprod 2013;28:2966-71. Crossref
8. Management of Endometrial Hyperplasia (Green-top Guideline No. 67). Royal College of Obstetricians and Gynaecologists (RCOG) and the British Society for Gynaecological Endoscopy (BSGE) Joint Guideline, February 2016.
9. Committee on Gynecologic Practice Society of Gynecologic Oncology. Committee Opinion No. 631 – Endometrial Intraepithelial Neoplasia. Obstet Gynecol 2015;125:1272-78. Crossref
10. Ring KL, Mills AM, Modesitt SC. Endometrial hyperplasia. Obstet Gynecol 2022;140:1061-75. Crossref
11. Auclair MH, Yong PJ, Salvador S, Thurston J, Colgan TTJ, Sebastianelli A. Guideline No. 390 -Classification and Management of Endometrial Hyperplasia. J Obstet Gynaecol Can 2019;41:1789-800. Crossref
12. The Hong Kong College of Obstetricians and Gynaecologists. Guidelines on Clinical Management of Endometrial Hyperplasia. Available at: https://www.hkcog.org.hk/hkcog/Download/Guidelines_on_Clinical_Management_of_Endometrial_Hyperplasia.pdf.
13. Ørbo A, Arnes M, Hancke C, Vereide AB, Pettersen I, Larsen K. Treatment results of endometrial hyperplasia after prospective D-score classification: a follow-up study comparing effect of LNG-IUD and oral progestins versus observation only. Gynecol Oncol 2008;111:68-73. Crossref
14. Varma R, Soneja H, Bhatia K, et al. The effectiveness of a levonorgestrel-releasing intrauterine system (LNG-IUS) in the treatment of endometrial hyperplasia—a long-term follow-up study. Eur J Obstet Gynecol Reprod Biol 2008;139:169-75. Crossref
15. Nilsson CG, Haukkamaa M, Vierola H, Luukkainen T. Tissue concentrations of levonorgestrel in women using a levonorgestrel-releasing IUD. Clin Endocrinol (Oxf) 1982;17:529-36. Crossref
16. FSRH Clinical Guideline: Intrauterine Contraception. Available at: https://www.fsrh.org/documents/ceuguidanceintrauterinecontraception/.
17. National Institute for Clinical Excellence. Long-acting reversible contraception: the effective and appropriate use of long-acting reversible contraception. Available at: https://www.nice.org.uk/guidance/cg30/documents/longacting-reversible-contraception-clinical-guideline-first-consultation-nice-guideline2.
18. Mansour D, Gemzell-Danielsson K, Inki P, Jensen JT. Fertility after discontinuation of contraception: a comprehensive review of the literature. Contraception 2011;84:465-77. Crossref
19. Ørbo A, Arnes M, Vereide AB, Straume B. Relapse risk of endometrial hyperplasia after treatment with the levonorgestrel-impregnated intrauterine system or oral progestogens. BJOG 2016;123:1512-9. Crossref
20. Yin J, Ma S, Shan Y, et al. Risk factors for recurrence in patients with atypical endometrial hyperplasia and endometrioid adenocarcinoma after fertility-sparing treatments. Cancer Prev Res (Phila) 2020;13:403-10. Crossref
21. Pal N, Broaddus RR, Urbauer DL, et al. Treatment of low-risk endometrial cancer and complex atypical hyperplasia with the levonorgestrel-releasing intrauterine device. Obstet Gynecol 2018;131:109-16. Crossref

22. Zhou S, Xu Z, Yang B, et al. Characteristics of progestin-insensitive early stage endometrial cancer and atypical hyperplasia women receiving second-line fertility-sparing treatment. J Gynecol Oncol 2021;32:e57. Crossref
23. Yang X, Wang J. The role of metabolic syndrome in endometrial cancer: a review. Front Oncol 2019;9:744. Crossref
24. Rotenberg O, Fridman D, Doulaveris G, et al. Long-term outcome of postmenopausal women with non-atypical endometrial hyperplasia on endometrial sampling. Ultrasound Obstet Gynecol 2020;55:546-51. Crossref
25. Hedrick Ellenson L, Ronnett BM, Kurman RJ. Precursor Lesions of Endometrial Carcinoma. In: Kurman RJ, Hedrick Ellenson L, Ronnett BM, editors. Blaustein's Pathology of the Female Genital Tract, 6th ed. New York: Springer; 2010;360-1. Crossref
26. Scully RE, Bonfiglio TA, Kurman RJ, Silverberg SG, Wilkinson EJ. Uterine Corpus. In: Histological Typing of Female Genital Tract Tumours, 2nd ed. New York: Springer-Verlag; 1994:13. Crossref
27. Silverberg SG, Mutter GL, Kurman RJ, Kubik-Huch RA, Nogales F, Tavassoli FA. Tumors of the Uterine Corpus: Epithelial Tumors and Related Lesions. In: Tavassoli FA, Stratton MR, editors. WHO Classification of Tumours: Pathology and Genetics of Tumours of the Breast and Female Genital Organs Lyon: IARC Press; 2003:221-32.
28. Emons G, Beckmann MW, Schmidt D, Mallmann P; Uterus commission of the Gynecological Oncology Working Group (AGO). New WHO Classification of Endometrial Hyperplasias. Geburtshilfe Frauenheilkd 2015;75:135-6. Crossref

Hong Kong J Gynaecol Obstet Midwifery 2023;23(2):135-9 | https://doi.org/10.12809/hkjgom.23.2.348

Tsan Yuk Hospital: a century of dedicated obstetrical service

Barry Ming-Chak LAW
Pui-Wah HUI
Department of Obstetrics and Gynaecology, Queen Mary Hospital, Hong Kong SAR, China

For over a century, Tsan Yuk Hospital (TYH) has embodied excellence in clinical service, training, and research. It is synonymous with maternity care for many in Hong Kong. Its mission is best summarised by its Chinese name 贊育醫院, meaning to support and nurture newborns, and its slogan 好生之謂德 保赤以為懷 (outside the old TYH), which refers to safeguarding precious new lives.

Foundation

Prior to the establishment of TYH in 1922, many local women gave birth at home, with minimal support from untrained grannies. Safety and hygiene were great concerns. Pregnancies and deliveries were associated with significant morbidities and mortalities.

With the foresight of Dr Alice Hickling (Hong Kong's first female doctor) and generous support from Dr Seen-Wan Tso (chairman of the Chinese Public Dispensary), the government, and various charitable organisations, TYH opened on 17 October 1922 (Figure 1). It aimed to provide much-needed maternity services and train local girls to be midwives[1-7].

The original TYH was situated at the junction of Western Street and Third Street, on the slope between Queen's Road West and Bonham Road (Figures 2-4). The building consisted of four storeys and a basement, with 30 beds donated by Tung Wah Hospital. In its first year of operation, there were 436 admissions.

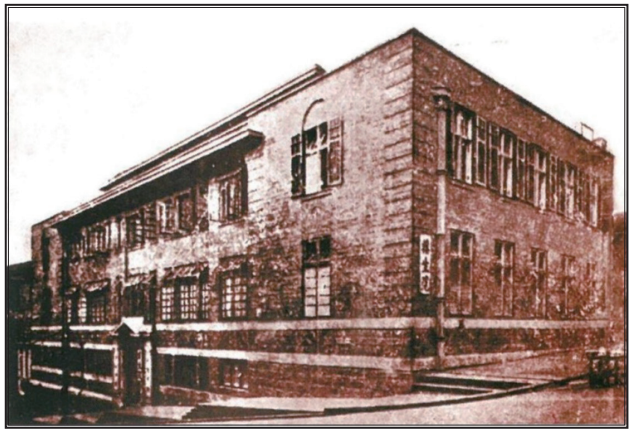


Figure 1. The old Tsan Yuk Hospital when it was established in 1922.

Figure 2. The slogan 好生之謂德 保赤以為懷 at the entrance of the old Tsan Yuk Hospital.

Figure 3. The main entrance of the old Tsan Yuk Hospital.

Correspondence to: Dr Pui-Wah HUI
Email: apwhui@hku.hk

Figure 4. Pregnant women gathering at the entrance of the old Tsan Yuk Hospital.

Development

Following his appointment as The University of Hong Kong's first professor of obstetrics, Prof Richard Edwin Tottenham performed the first-ever Caesarean section in Hong Kong in June 1925. He recognised TYH's potential as a teaching hospital and subsequently transferred the teaching of both obstetrics and gynaecology there.

According to Prof Daphne Wai-Chan Chun's article published in 1972 to celebrate the hospital's golden jubilee[1], TYH changed from a charitable institution to a government hospital in 1934 and doubled its number of beds to 60. With the addition of neonatologists and anaesthetists, TYH could provide care for both pregnant women and newborns. This progress could not have been accomplished without leadership of the many visionaries.

Dr Doraisamy Kumara Samy and then Prof William Charles Wallace Nixon succeeded Prof Tottenham as Heads of Obstetrics and Gynaecology at The University of Hong Kong. In 1938, Prof Gordon King took up the headship and led the Department for the next 18 years, during which the demand for maternity services and training facilities grew exponentially, driven by an influx of refugees from mainland China. Unfortunately, TYH closed in September 1944 during the Japanese occupation, and many of its records were lost. After the war ended in September 1945, the hospital resumed its services.

TYH always experienced bed shortages, as the number of admissions grew to 1000 within 5 years. Even after gynaecological services were moved to Queen Mary Hospital in 1937 and TYH was entirely devoted to obstetric patients, the number of annual admissions soared after the war, peaking at 7000. With a pressing need for more beds and more trainings for midwives and obstetricians, a new TYH building was commissioned at 30 Hospital Road and opened on 13 June 1955 (Figure 5), thanks to Prof King's efforts and the Hong Kong Jockey Club's generosity.

The seven-storey building housed 200 beds. It had accommodations for medical officers, midwives, and medical students. The antenatal clinic was on the ground floor, where it remains to this day. Obstetric wards, for both antenatal and postnatal patients, were located over four floors, each with its own delivery suite. The wards were named after famous obstetricians such as the Barnes ward (for first-stage labour) on the first floor and the Smellie ward in the west wing of the first floor (Figures 6 and 7).

The number of annual admissions continued to increase and reached 10 865 in 1957. Therefore, in 1958, admissions were strictly limited to higher-risk patients including primigravidae, grand multiparae, and patients

Figure 5. The new Tsan Yuk Hospital opened in June 1955.

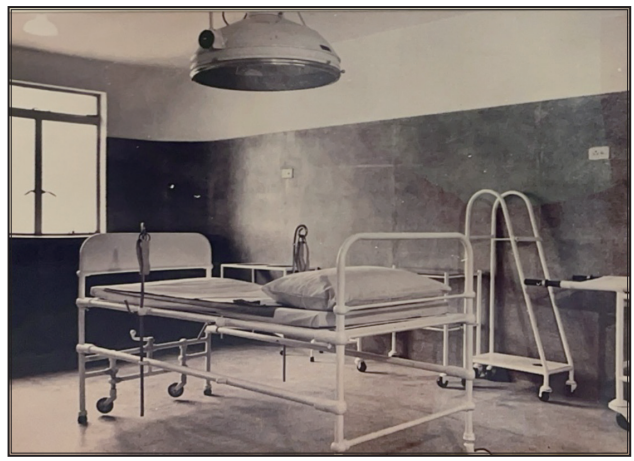


Figure 6. The setting of a labour ward.

with medical or obstetrical complications. The labour ward was centralised over six rooms on the first floor, and the adjacent ward was converted to a first-stage labour ward. The second floor was renovated into three postnatal wards, and the third floor was used to prepare for Caesarean sections (Figure 8). The fourth floor was converted into a nursery for low-birthweight babies and a neonatal intensive care unit (Figure 9).

In 1957, Prof Daphne Wai-Chan Chun was appointed Head of the Department of Obstetrics and Gynaecology. She pioneered a system of obstetric audit at TYH. Under her leadership, despite the soaring number of deliveries, the low maternal and perinatal mortality rates gained international recognition[8-10]. Additionally, the number of midwives trained increased substantially; graduated midwives could safely handle births at homes and in private maternity centres in Hong Kong. In 1956, the postgraduate training at TYH was formally accredited by the Royal College of Obstetricians and Gynaecologists.

Figure 7. The Smellie ward, named after Scottish obstetrician Dr William Smellie.

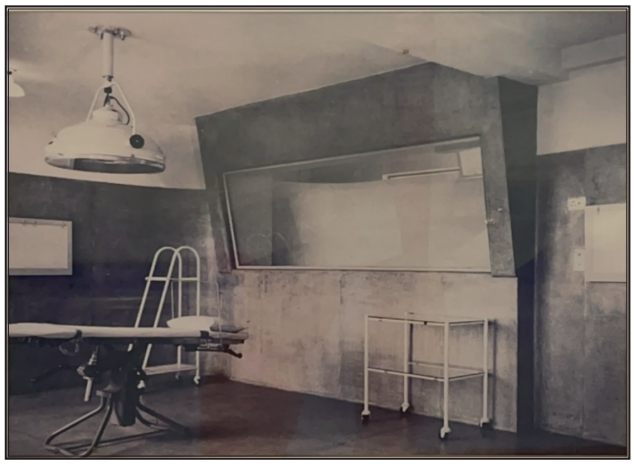


Figure 8. The setting of an operating theatre.

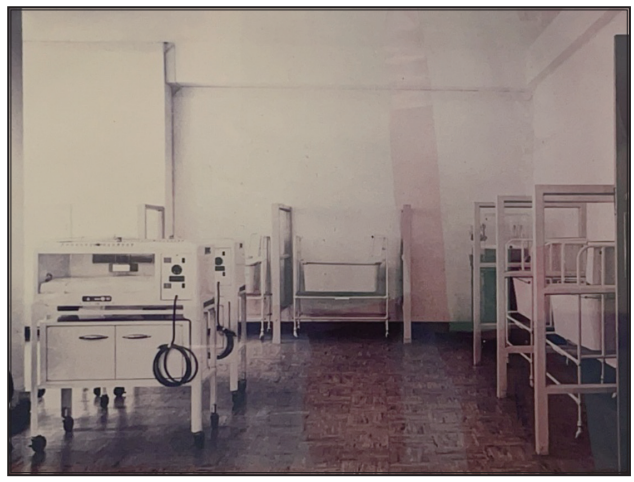


Figure 9. The setting of a nursery unit with incubators.

Throughout the 1960s, TYH served as a backup for a number of maternity homes in both the public and private sectors. Its 'Flying Squad' (comprising medical doctors, housemen, and medical students) was dispatched to maternity centres to help labouring women with complications. In addition, Dr Kin-Hung Lee pioneered intrapartum foetal monitoring, which was a cutting-edge procedure in those days.

Transformation

In 1972, Prof Ho-Kei Ma took the headship of the Department of Obstetrics and Gynaecology. She identified the need to improve the diagnosis of congenital anomalies and genetic counselling for fetal chromosomal and structural anomalies. To this end, Prof Ma supported Dr Vivian Wong in training in ultrasonography with Prof John Hobbins at Yale University, and supported Dr Joseph Woo in training in obstetric ultrasound and cytogenetics in Glasgow. With a donation from Mrs Wu Chung, the prenatal diagnostic laboratory commenced service in March 1981 (Figure 10). It was the first public laboratory in Hong Kong to perform prenatal cytogenetic analysis.

In collaboration with Prof Vivian Chan from The University of Hong Kong's Department of Medicine and

Figure 10. Opening ceremony of the Mrs Wu Chung Prenatal Diagnostic Laboratory in 1981.

Prof Yuet-Wai Kan from the University of California, San Francisco, TYH (led by Dr Arabinda Ghosh) steered the genetic diagnosis of thalassemia, haemophilia, muscular dystrophies, and spinal muscular atrophy. TYH became a pioneer in obstetric research and prenatal diagnosis services and provided a strong foundation for training subspecialists in maternal-fetal medicine in Hong Kong.

TYH was reorganised for more efficient utilisation. In the years when TYH was still offering a full maternity service, the ground floor housed the outpatient clinic and university departmental office. The first floor housed the first-stage labour ward (Barnes Ward), the labour ward, and an operating theatre. The prenatal diagnosis laboratory and clinic were on the second floor and in the north wing of the fourth floor, whereas the antenatal ward (Ballantyne Ward) and postnatal ward (Simpson Ward) were on the third floor. The neonatal unit and a semi-private ward were located on the fourth floor.

The present day

TYH has adapted to the ever-changing needs of our society. It has transformed into a comprehensive ambulatory centre, incorporating services in family medicine, psychiatry, and physiotherapy, in addition to offering state-of-the-art prenatal and genetic diagnosis research and services.

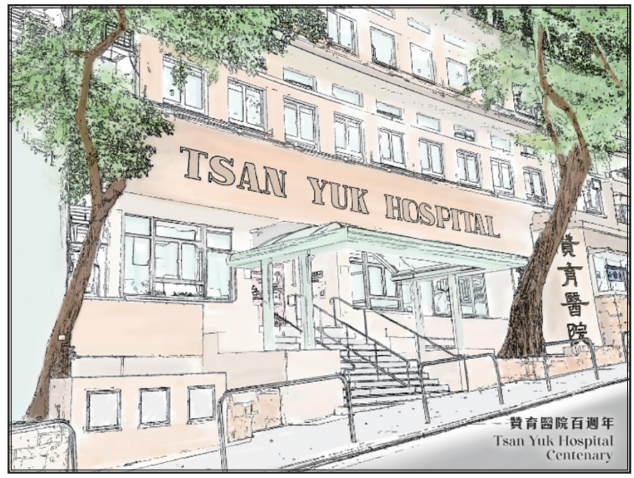


Figure 11. Drawing to commemorate Tsan Yuk Hospital's centenary.

The last delivery on 3 November 2001 marked the end of TYH as a standalone maternity hospital. Since then, the obstetric and newborn inpatient services have moved to Queen Mary Hospital. However, the antenatal booking clinic and the prenatal diagnostic clinic remain. The prenatal diagnostic laboratory has expanded the genetic and genomic development into chromosome microarray, whole exome sequencing, and whole genome sequencing. As a subspeciality training centre accredited by the Royal College of Obstetricians and Gynaecologists since 2000 and the Hong Kong College of Obstetricians and Gynaecologists since 2008, TYH has nurtured many renowned obstetricians and maternal-fetal medicine subspecialists for Hong Kong.

Celebration

Year 2022 marked TYH's centenary (Figure 11), an occasion commemorated by Hong Kong's obstetric and gynaecological community, with the slogan 贊譽百載 育護未來. A centennial album and song entitled 愛、生命、同行 Love, Life, Keep Going was produced by staff members of the obstetric team[11]. It represents how TYH safeguards the wellbeing mothers and babies through the 40-week journey from conception to birth, as it has for the past 100 years. TYH will continue to cherish new lives and be a beacon of excellence in the development of obstetrics and gynaecology in Hong Kong and worldwide.

Happy 100 years young to TYH!

References

1. 《贊育醫院金禧特刊(一九二二年至一九七二年)》，香港:贊育醫院，1972年
2. 《贊育醫院七十五周年紀念》，香港:醫院管理局，1997年
3. 《贊育醫院百周年紀念特刊》，香港:醫院管理局，2022年
4. Lee KH. Stories of obstetrics and gynaecology in the 1960s. Hong Kong J Gynaecol Obstet Midwifery 2006;6:49-56.
5. [RTHK 香港電台]. 8 November 2022. 醫生與你：【醫學．人】三代婦產科專科醫生 – 黃譚智媛醫生、李之朋醫生、許佩華醫生（上）. Available at: https://www.youtube.com/watch?v=xSTtpUwRqdk&ab_channel=RTHK%E9%A6%99%E6%B8%AF%E9%9B%BB%E5%8F%B0.
6. [RTHK 香港電台]. 15 November 2022. 醫生與你：【醫學．人】三代婦產科專科醫生 – 黃譚智媛醫生、李之朋醫生、許佩華醫生（中）. Available at: https://www.youtube.com/watch?v=9n66w34gSnU&ab_channel=RTHK%E9%A6%99%E6%B8%AF%E9%9B%BB%E5%8F%B0.
7. [RTHK 香港電台]. 22 November 2022. 醫生與你：【醫學．人】三代婦產科專科醫生 – 黃譚智媛醫生、李之朋醫生、許佩華醫生（下）. Available at: https://www.youtube.com/watch?v=cr5DAGhboOY&ab_channel=RTHK%E9%A6%99%E6%B8%AF%E9%9B%BB%E5%8F%B0.
8. Woo JS, Chan PH, Wong VC, Ma HK. Trends in perinatal mortality at a Hong Kong hospital. Int J Gynaecol Obstet 1983;21:227-32. Crossref
9. Duthie SJ, Ghosh A, Ma HK. Maternal mortality in Hong Kong 1961-1985. Br J Obstet Gynaecol 1989;96:4-8. Crossref
10. Duthie SJ, Lee CP, Ma HK. Maternal mortality in Hong Kong 1986-1990. Br J Obstet Gynaecol 1994;101:906-7. Crossref
11. 贊育醫院百周年紀念歌曲：《愛、生命、同行》. Tsan Yuk Hospital Centennial Song: Love, Life, Keep Going. Available at: https://www.youtube.com/watch?v=Rg__mGB0SBw.

Hong Kong J Gynaecol Obstet Midwifery 2023;23(2):140 | https://doi.org/10.12809/hkjgom.23.2.349

Obituary
In memory of Prof LEE Kin Hung

Prof LEE Kin Hung, MBBS, MD, FRCOG, FHKAM (O&G)

With profound sadness, we mourn the passing of Prof LEE Kin Hung, an eminent figure in obstetrics and gynaecology in Hong Kong.

Prof Lee was graduated from The University of Hong Kong in 1958. He embarked on his career in the university's Department of Obstetrics and Gynaecology in the following year. He was promoted to Senior Lecturer in 1969. He became a member of the Royal College of Obstetricians and Gynaecologists in 1965 and a fellow in 1984. In 1971, The University of Hong Kong awarded him the degree of Doctor of Medicine, the first person outside the Department of Medicine to be so honoured. In 1993 when the Hong Kong Academy of Medicine was set up, he was one of the foundation Fellows.

Prof Lee's research concentrated on obstetrics. His MD thesis—The use of amnioscopy and fetal blood sampling in the diagnosis of fetal distress—was at the cutting edge of research for its time. He co-edited the bilingual textbook *Practical Obstetrics*, the first local obstetrics textbook. He has also served as Medical Superintendent of Tsan Yuk Hospital. In 1975, he established his own private practice.

Outside of his academic work, Prof Lee contributed greatly to Hong Kong. He served on the Council of the Obstetrical and Gynaecological Society of Hong Kong as Honorary Secretary from 1967 to 1973 and President from 1973 to 1975. In addition, he gave years of service to the Medical Council of Hong Kong, culminating in chairing the Council from 2000 to 2003. Between 1970 and 2000, he held several posts in the Hong Kong Medical Association, ultimately becoming its President from 1994 to 1998. He was a Hong Kong Affairs Advisor from 1995 to 1997, specifically a Selection Committee member and an Election Committee member of the medical subsector. He also served in many other capacities, including a member of the Health and Medical Advisory Committee from 1992 to 2002.

In recognition of his outstanding contribution to medical education for the public, Prof Lee was appointed Member of the Order of the British Empire in 1996. We still fondly remember his enthusiastic participation in public health education activities, including the television series *Doctor and You*.

In 2004, Prof Lee was appointed Honorary Professor at the Faculty of Medicine, The University of Hong Kong. In the same year, he was elected to be a member of the Standing Committee of the Convocation and a member of the Court of The University of Hong Kong. He was also an active member of The University of Hong Kong Medical Alumni Association, serving as its President from 2004 to 2008.

Prof Lee was a true leader in our field. He will be remembered for his expertise, contributions, humour, and friendly smile. His dedication to advancing our field is an inspiration to us all. He is survived by his wife—Dr HP Lau—and his daughter. We extend our thoughts and deepest condolences to Prof Lee's family. He will be greatly missed by all who knew him.

Karen KL Chan
Chairperson, Department of Obstetrics and Gynaecology, School of Clinical Medicine, The University of Hong Kong
President, Hong Kong College of Obstetricians and Gynaecologists

KK Tang
President, Obstetrical and Gynaecological Society of Hong Kong

AQUACEL® Ag Surgical

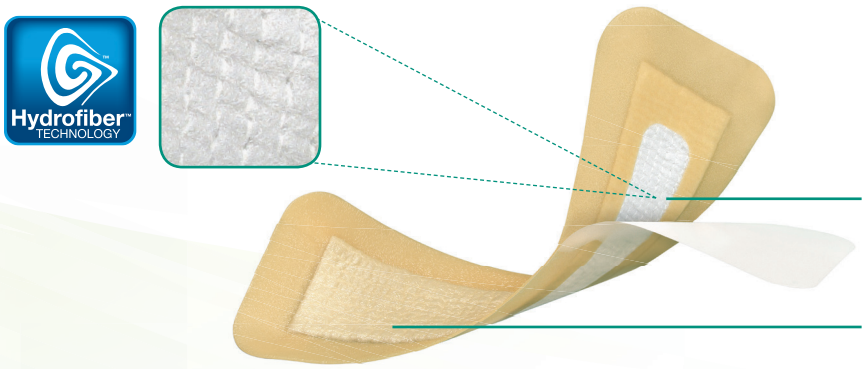
Post-operative protection for surgical wounds*

CESAREAN INCISION

Because you have **more important things** to think about.

Your guide to **AQUACEL® Ag** Surgical dressing.

An innovative design to handle post-operative challenges after a **Cesarean Incision**



Unique dressing *designed to flex with the skin during body movement - can be left in place for up to seven days**

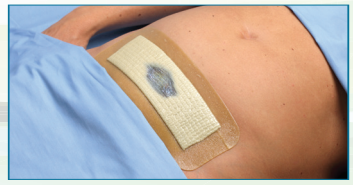
7 DAYS

Hydrofiber® Technology, *absorbs and locks in fluid, including harmful bacteria[1] †, and can help reduce the risk of wound infection**

Waterproof, viral, and bacterial barrier *(when intact and with no leakage)† – can be worn in the shower*

PLEASE CALL YOUR HEALTH CARE PROFESSIONAL IF:

- Your dressing does not stay in place
- A large amount of fluid comes out of your incision and reaches any side of the dressing
  Note: It is normal to have a small amount of spotting
- You experience any of the following[2]:
  - Fever higher than 100.4° F (38° C)
  - Unusual pain, redness, swelling or odor around the dressing
  - Heat or warmth around your incision
  - A full and hard feeling in your belly



Acceptable amount of fluid

Dressing needs to be changed

* Refer to package insert for full instructions for use.
† As demonstrated *in vitro.*

REFERENCES: 1. Walker M, Hobot JA, Newman GR, Bowler PG. Scanning electron microscopic examination of bacterial immobilization in a carboxymethylcellulose (Aquacel) and alginate dressings. Biomaterials.2003; 24:883-890.8.
2. American Pregnancy Association. Care After a C Section: Physical and Emotional. Available at: http://americanpregnancy.org/labor-and-birth/cesarean-aftercare/. Accessed May 24, 2018.

convatec
— forever caring —

For more information
Please call +852 2516 9182 / cshk@convatec.com or visit **www.convatec.com.hk**
Address: Unit 1901, 19/F, Yue Xiu Building,160-174 Lockhart Road, Wan Chai, Hong Kong