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EDITORIAL

OBSTETRICS & MIDWIFERY

SHORT COMMUNICATION

REVIEW ARTICLE

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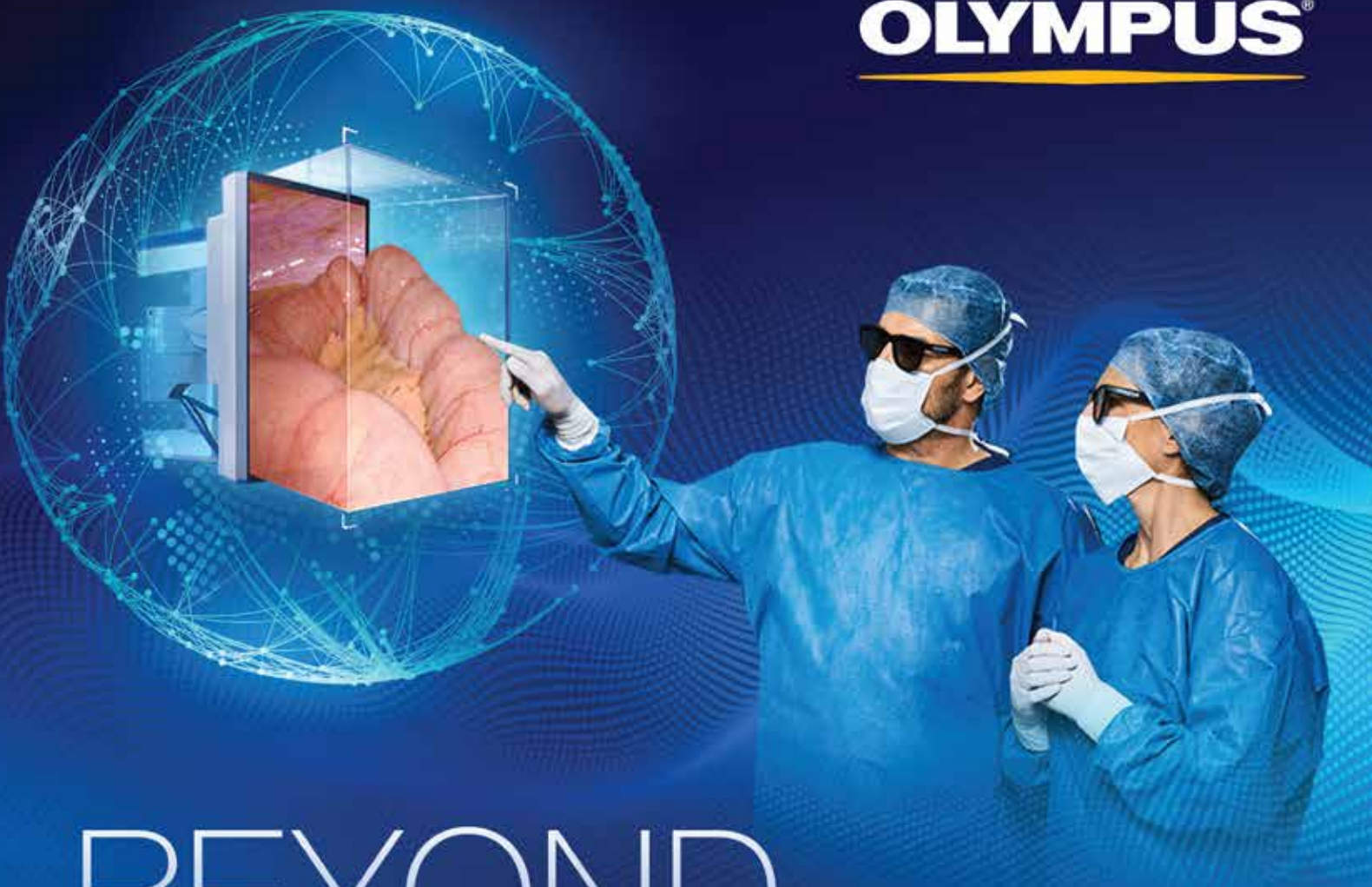

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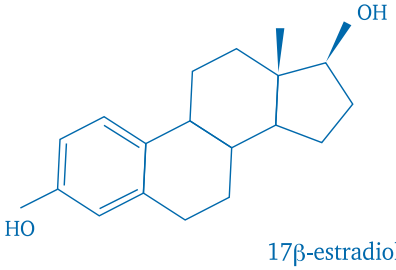

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What Estrofem® is and what it is used for

Estrofem® is a Hormone Replacement Therapy (HRT). It contains the female hormone estradiol.Estrofem® is used in postmenopausal women, particularly in women who have had their womb removed (have had a hysterectomy) and therefore do not require combined oestrogen/progestagen therapy. Estrofem® is used for:

- **Relief of symptoms occurring after menopause**

During the menopause, the amount of oestrogen produced by a woman's body drops. This can cause symptoms such as hot face, neck and chest ('hot flushes'). Estrofem® alleviates these symptoms after menopause. You should only be prescribed Estrofem® if patient symptoms seriously hinder daily life.

- **Prevention of osteoporosis** (thinning of the bones). There is only limited experience of treating women older than 65 years. The use of HRT carries risks which need to be considered when deciding whether to start taking it, or whether to carry on taking it.The experience in treating women with a premature menopause (due to ovarian failure or surgery) is limited

Do not take Estrofem®

- If patients have or have ever had **breast cancer,** or if you are suspected of having it.
- If patients have or have had **cancer which is sensitive to oestrogens,** such as cancer of the womb lining (endometrium), or if you are suspected of having it.
- If patients have any **unexplained vaginal bleeding**.
- If patients have **excessive thickening of the womb lining** (endometrial hyperplasia) that is not being treated.
- If patients have or have ever had **a blood clot in a vein** (thrombosis), such as in the legs (deep venous thrombosis) or the lungs (pulmonary embolism).
- If patients have a **blood clotting disorder** (such as protein C, protein S or antithrombin deficiency).
- If patients have or recently have had a disease caused by blood clots in the arteries, such as a **heart attack, stroke** or **angina.**
- If patients have or have ever had a **liver disease** and your liver function tests have not returned to normal.
- If patients have a **rare blood problem called 'porphyria'**, which is passed down in families (inherited).
- If patients are **allergic** (hypersensitive) to **estradiol** or any of the other ingredients of Estrofem® (listed in section 6, Further information).

If any of the above conditions appear for the first time while taking Estrofem®, stop taking it at once and consult your doctor immediately.

Take one tablet every day, at about the same time each day.

Once you have finished all the 28 tablets in the pack, start a new pack continuing the treatment without interruption.

For instructions on the use of the calendar pack, see *USER INSTRUCTIONS* at the end of the package leaflet.

Possible side effects

The following diseases are reported more often in women using HRT compared to women not using HRT:

- breast cancer
- abnormal growth or cancer of the lining of the womb (endometrial hyperplasia or cancer)
- ovarian cancer
- blood clots in the veins of the legs or lungs (venous thromboembolism)
- heart disease
- stroke
- probable memory loss if HRT is started over the age of 65.

For more information about these side effects, see full product insert.

How to store Estrofem®

Keep out of the reach and sight of children.

Do not use Estrofem® after the expiry date, which is stated on the label and carton. The expiry date refers to the last day of that month.

Store below 30°C. Do not refrigerate.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment

What Estrofem® contains

The active substance is estradiol 1 mg (as estradiol hemihydrate).Other ingredients are: lactose monohydrate, maize starch, hydroxypropylcellulose, talc and magnesium stearate.The film-coating contains: hypromellose, talc, titanium dioxide (E171), propylene glycol and red iron oxide (E172).

What Estrofem® looks like and contents of the pack

The film-coated tablets are red, round with a diameter of 6 mm. The tablets are imprinted NOVO 282 on one side.

Pack sizes available:

- 1×28 film-coated tablets

Not all pack sizes may be marketed.

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- Include full name(s), degree(s) and affiliations(s) of author(s): list under file
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Abstract

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- 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)

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- 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)

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- Tables should be numbered consecutively in their order of appearance in the text
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dTap = Tetanus toxoid, reduced diphtheria toxoid & acellular pertussis

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Boostrix should be administered in accordance with local official recommendations.[1]

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The use of ***Boostrix*** may be considered during the third trimester of pregnancy. Human data from prospective clinical studies on the use of ***Boostrix*** during the first and second trimester of pregnancy are not available. However, as with other inactivated vaccines, it is not expected that vaccination with ***Boostrix*** harms the foetus at any trimester of pregnancy. The benefits versus the risks of administering ***Boostrix*** during pregnancy should be carefully evaluated.

* In Hong Kong Market as of Dec 2019

Reference:

1.Boostrix Hong Kong Full Prescribing Information. Version GDS10. 2. Sanofi dTap Hong Kong Full Prescribing Information 2017. 3. CDC. Pertussis (Whooping Cough): Complications. Available at: https://www.cdc.gov/pertussis/about/complications.html. Accessed Feb 2020. 4. Hong JY. Update on pertussis and pertussis immunization. Korean J Pediatr. 2010;53:629–633. 5. Centre of Health Protection. Scientific Committee on Vaccine Preventable Diseases Consensus Recommendations on Pertussis Vaccination for Pregnant Women in Hong Kong. Feb 2019.

Abbreviated Prescribing Information

Name of the Medicinal Product: *Boostrix*. **Qualitative and Quantitative Composition:** 1 dose (0.5 ml) contains not less than 2 IU diphtheria toxoid, not less than 20 IU of tetanus toxoid, 8 mcg of pertussis toxoid, 8 mcg of filamentous haemagglutinin, 2.5 mcg of pertactin, adsorbed on aluminium hydroxide, hydrated and aluminium phosphate. **Indications:** Indicated for booster vaccination against diphtheria, tetanus and pertussis of individuals from the age of four years onwards. **Posology and Administration:** A single 0.5 ml dose of the vaccine is recommended. The use of *Boostrix* may be considered during the third trimester of pregnancy. **Method of administration:** *Boostrix* is for deep intramuscular injection, preferably in the deltoid region. **Contraindications:** Subjects with known hypersensitivity to any component of the vaccine or to subjects having shown signs of hypersensitivity after previous administration of diphtheria, tetanus or pertussis vaccines; Subject has experienced an encephalopathy of unknown aetiology, occurring within 7 days following previous vaccination with pertussis-containing vaccine. Administration should be postponed in subjects suffering from acute severe febrile illness As with other vaccines, administration of *Boostrix* should be postponed in subjects suffering from acute severe febrile illness **Special Warnings and Precautions for Use:** If any of the following events are known to have occurred in temporal relation to receipt of pertussis-containing vaccine, the decision to give doses of pertussis-containing vaccines should be carefully considered: temperature of ≥ 40.0°C within 48 hours of vaccination, not due to another identifiable cause; collapse or shock-like state (hypotonic-hyporesponsiveness episode) within 48 hours of vaccination; persistent, inconsolable crying lasting ≥ 3 hours, occurring within 48 hours of vaccination; convulsions with or without fever, occurring within 3 days of vaccination. *Boostrix* should under no circumstances be administered intravenously. Syncope (fainting) can occur following, or even before, any vaccination especially in adolescents as a psychogenic response to the needle injection. It is important that procedures are in place to avoid injury from faints. As with any vaccine, a protective immune response may not be elicited in all vaccinees. **Interactions:** If *Boostrix* is to be given at the same time as another injectable vaccine or immunoglobulin, the products should always be administered at different sites **Fertility, pregnancy and Lactation:** ***Pregnancy:*** The use of *Boostrix* may be considered during the third trimester of pregnancy. Limited data indicate that maternal antibodies may reduce the magnitude of the immune response to some vaccines in infants born from mothers vaccinated with *Boostrix* during pregnancy. The clinical relevance of this observation is unknown. **Breastfeeding:** The effect of administration of *Boostrix* during lactation has not been assessed. Nevertheless, as *Boostrix* contains toxoids or inactivated antigens, no risk to the breastfed infant should be expected. The benefits versus the risk of administering *Boostrix* to breastfeeding women should carefully be evaluated by the health-care providers. **Adverse Reactions: Clinical Trial Data:** *Children from 4 to 9 years of age* upper respiratory tract infection; anorexia; irritability; somnolence, headache and disturbances in attention; conjunctivitis; diarrhoea, vomiting, gastrointestinal disorders; rash; injection site reactions (including pain, redness and swelling), fatigue, fever ≥ 37.5 °C (including fever > 39 °C), other injection site reactions (such as induration) and pain. *Adults, adolescents and children from the age of 10 years onwards:* upper respiratory tract infection, pharyngitis; lymphadenopathy; headache, dizziness, syncope; cough; nausea, gastrointestinal disorders, diarrhoea, vomiting; hyperhidrosis, pruritus, rash; arthralgia, myalgia, joint stiffness, musculoskeletal stiffness; injection site reactions (including pain, redness and swelling), fatigue, malaise, fever ≥ 37.5°C, injection site reactions (such as injection site mass and injection site abscess sterile), fever > 39 °C, influenza like illness and pain. Data on 146 subjects suggests a small increase in local reactogenicity (pain, redness, swelling) with repeated vaccination according to a 0, 1, 6 months schedules in adults (>40 years of age). ***Post Marketing Data:*** Angioedema, allergic reactions, including anaphylactic and anaphylactoid reactions, convulsions (with or without fever), urticaria, extensive swelling of the vaccinated limb, asthenia. **Please read the full prescribing information prior to administration. Full prescribing information is available on request from GlaxoSmithKline Ltd, 23/F, Tower 6, The Gateway, 9 Canton Road, Tsimshatsui, Kowloon, Hong Kong.** Abbreviated Prescribing Information prepared in 11 Feb 2020 based on version HK022019 (GDS10/IPI11/MHRA20181214). For adverse event reporting, please call GlaxoSmithKline Limited at (852) 3189 8989 (Hong Kong) or (853) 2871 5569 (Macau), or send an email to us at HKAdverseEvent@gsk.com.

PM-HK-BOO-ADVT-190001 (01/2022) Date of preparation: 01/02/2020

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Ferinject® Abbreviated Product Information

Note: Before prescribing, please read the Summary of Product Characteristics.

Pharmaceutical form: Ferric carboxymaltose as solution for injection/infusion. **Indications:** Ferinject® is indicated for treatment of Iron Deficiency when oral iron preparations are ineffective or cannot be used. The diagnosis must be based on laboratory tests. **Administration:** The cumulative dose for repletion of iron using Ferinject® is determined based on the patient's body weight and haemoglobin level and must not be exceeded. The table in the Summary of Product Characteristics should be used to determine the cumulative iron dose. A single dose of Ferinject® should not exceed 1000 mg of iron per day. A maximum of 1000 mg of iron once a week can be administered. **Contraindications, Warnings, Overdose:** The use is contraindicated in cases of known hypersensitivity to Ferinject® or any of its excipients, anaemia not attributed to Iron Deficiency and evidence of iron overload or disturbances in utilization of iron. Do not administer by SC or IM route. Closely monitor patients for signs and symptoms of hypersensitivity during and for at least 30 minutes following each administration. Stop treatment if allergic or signs of intolerance occur. Therefore, facilities for cardio-pulmonary resuscitation must be available. In patients with liver dysfunction, parenteral iron should only be administered after careful risk/benefit assessment. Parenteral iron must be used with caution in case of acute of chronic infection, history of asthma, eczema or atopic allergies. Discontinue use in patients with ongoing bacteraemia. Stop immediately in case of paravenous leakage. A careful risk/benefit evaluation is required before use in pregnancy. Not recommended in children < 14 yr. Monitoring of iron parameters such as serum ferritin and transferrin saturation may assist in recognizing iron accumulation. **Undesirable effects:** Common (1% to <10%): Hypophosphataemia, headache, dizziness, flushing, hypertension, nausea, injection/infusion site reactions. **Interactions:** Oral iron therapy should not be started for at least 5 days after the last injection of Ferinject®. **Legal category:** Prescription Only Medicine (POM). **Date of preparation:** 30th Oct 2017. Full prescribing information provided upon request.

*For more information, please consult with the local representative.

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Editorial
How has COVID-19 impacted obstetrics?

Introduction

As of 2 December 2020, Hong Kong has experienced four waves of coronavirus disease 2019 (COVID-19), which is caused by severe acute respiratory syndrome–related coronavirus 2 (SARS-CoV-2), with 6500 confirmed or probable cases and 110 deaths[1]. At least 20 of these cases involved pregnant women. The pandemic has exerted significant strain on the healthcare system and workers worldwide. To contain and mitigate the spread of the disease, obstetricians have implemented a series of infection control protocols such as banning of birthing partners and wearing masks during labour and delivery. However, the inconvenience and challenges these protocols have brought cannot be overlooked.

Impact on patients

Some pregnant women may delay seeking medical advice because of concerns of contracting the virus in hospitals or clinics, missing the optimal time for treatments. They may miss fetal growth assessments, and thus fetal growth parameters and liquor volume may not be adequately monitored, resulting in late diagnosis of fetal growth problems and complications in monochorionic twin pregnancies. Some may miss antenatal visits and even avoid seeking medical attention for non-specific symptoms in pregnancy such as mild abdominal discomfort, mild leaking sensation, and altered fetal movement, thus delaying the diagnosis of pregnancy complications. Nonetheless, the pandemic has led to the promotion of telemedicine. On some occasions, women are triaged by telephone before deciding if they require admissions for further in-person assessments. We should take this opportunity to train healthcare workers to use telemedicine safely without jeopardising patient safety and to develop the infrastructure to support its use.

Clinical care during labour and delivery has also been affected by the pandemic. Under the strict infection control measures of the Hospital Authority, public hospital visitation has been suspended, with exceptions given on compassionate grounds with clinical consideration. As a result, labour companionship has been suspended in public hospitals. The ban was only relaxed intermittently when the incidence of COVID-19 dropped. Labour companionship, either with the husband or other important family members, is a component of quality of care during labour. The ban is likely to lead to less satisfactory labour and delivery experience, with suboptimal emotional and physical support. Some women opt to deliver in private hospitals instead.

The use of nitrous oxide (Entonox) as pain relief during labour has also been affected. There is evidence that SARS-CoV-2 can be spread through aerosol-generating procedures, including tracheal intubation and extubation, non-invasive ventilation, and respiratory tract suctioning[2]. The use of Entonox may increase aerosolisation and the spread of the virus. However, a review suggests that using Entonox will not contribute to the transmission of the virus during labour[3]. A standard single-patient <0.05-μm pore size hydrophobic filter is suggested to be put on the Entonox mouthpiece to prevent contamination of the delivery system during use. Women in labour are required to wear a surgical mask when not using the mouthpiece throughout the labour process, thus the use of Entonox becomes less readily available and less popular. Although there is inconsistent evidence on whether wearing a surgical mask has a detrimental effect on exercise capacity or performance[4-6], it is associated with a higher level of subjective discomfort and increased perception of exertion[6]. The labour process is, therefore, potentially more exhausting with a surgical mask on, further affecting the labour experience.

The postnatal care of women has been affected, especially to those positive for or with suspected SARS-CoV-2 infection. The Hospital Authority imposes separation between neonates and COVID-19-positive mothers, aiming to protect newborns from the potential harm of horizontal infection, but the justification is questionable. A retrospective cohort study in New York suggests that mother-baby separation and avoiding direct breastfeeding may not be warranted to prevent SARS-CoV-2 transmission[7]. The Royal College of Obstetricians and Gynaecologists (RCOG) recommends skin-to-skin care if the neonate is well and not requiring further medical management, while a precautionary approach should be taken in babies who need to be admitted to the neonatal unit[3]. The World Health Organization also advises against the separation of newborns from their infected mothers because the risk of contracting the virus by newborns is relatively low and the infection is typically mild or

asymptomatic[8]. Although the separation policies may be justifiable at present, they may fail to fully account for the short- and long-term impact of mother-baby separation, given the low infant risk of contracting COVID-19 and the importance of proximity and breastfeeding for infants' and women's health[9]. For mothers with negative COVID-19 status, the suspension of hospital visitation could make them more susceptible to postnatal depression when they should be sharing the joy and happiness with their families.

Impact on the workforce

The mental stress of working with an increased risk of contracting SARS-CoV-2 and the concern of transmitting the virus to family and friends should not be underestimated. In a cross-sectional study in the United Kingdom, obstetricians and gynaecologists are associated with a higher rate of both major depressive disorder and generalised anxiety disorder, compared with the UK-wide estimates[10]. The most significant factor for work-related changes to mental health was the need to keep abreast with the frequently changing guidelines and protocols related to COVID-19. For instance, earlier the RCOG guidance suggested that the use of Entonox might facilitate the transmission of the virus, but the latest guidelines published in July 2020[3] stated that there is no reason to avoid its use during labour. The second most significant factor was the concern about being able to provide competent medical care if deployed to a new area. These concerns are not exclusive to the women's healthcare community. It is essential that local departments and the specialty as a whole raise awareness of the high prevalence of mental health conditions and create a supportive environment to facilitate healthcare workers seeking help.

In addition, the pandemic has disrupted training for trainees. At the peak of the pandemic, in order to redistribute resources (personal protective equipment, hospital beds, and staff) to look after COVID-19 cases, the number of elective procedures and outpatient appointments were reduced, as were training opportunities for trainees. Membership examinations of RCOG in the summer were cancelled or postponed worldwide, thus trainees' career progression was affected. In a cross-sectional survey on obstetrics and gynaecology residency training programme in Italy, 60% of the residents perceived that their training was irreversibly compromised[11]. Nevertheless, the pandemic has brought forward the transition from the traditional paper formats of examination and assessment to computer-based testing. It has also strengthened the public-private partnership in facilitating elective operations.

Medical, nursing, and midwifery students' training has all been disrupted immensely. To limit the potential spread of COVID-19 inside hospitals, clinical attachments for medical students have been halted for at least 4 months in Hong Kong. Although this enables the use of multimedia to facilitate student education, the implications of reduced clinical exposure and experience are long-lasting. There is uncertainty regarding how long the situation persists. It is important to recognise the limitation of online teaching and virtual activities and to facilitate face-to-face clinical activities whenever possible.

Impact on research

As of 1 December 2020, there are 51 vaccines in clinical trials and 163 candidate vaccines in preclinical trials[12]. Although the United Kingdom is the first country to approve the COVID-19 vaccine developed by Pfizer and BioNTech, the Medicines and Healthcare products Regulatory Agency states that there are no or limited data relating to pregnant or breastfeeding women and has advised against its use in this group of people at present[13]. Continuous research is crucial to determine the effectiveness and safety of the vaccine during fertility treatments, pregnancy, and lactation. We observe a decline in birth rate contributed by families delaying pregnancy for fear of the unknown associated with COVID-19. This highlights the urgent need to include pregnant women in vaccine trials. We urge regulatory agencies to revisit their policies for the inclusion of pregnant women.

Current evidence suggests that being pregnant is not associated with an increased risk of contracting the virus[14], but those with obesity or other chronic comorbidities are[15]. There is insufficient evidence to indicate that contracting the virus will increase the risk of having a miscarriage or spontaneous preterm birth[16]. However, transplacental or vertical transmission remains a possibility. A case study demonstrated transplacental transmission of SARS-CoV-2 during the last weeks of pregnancy by immunohistochemistry and a much higher viral load in placental tissues than in amniotic fluid and maternal or neonatal blood[17]. It remains unclear what exactly increases the risk of vertical transmission. Research requires funding (public or private), which is finite. Allocating more resources to one area means other research topics may be neglected. We have the responsibility to remain committed to adequate, fair, and sustained research and development funding in all areas.

Conclusion

The impact of the COVID-19 pandemic on

women's healthcare has been profound, affecting patients, front-line workers, and researchers. It is almost certain that there will be more waves of the disease before a vaccine or an effective therapeutic drug becomes widely available. It is vital for the community to work together in this challenging time and take it as an opportunity to improve practice and training, which may be useful in the post-COVID-19 era.

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Single, double, and triple modalities of uterine-sparing treatment for primary postpartum haemorrhage: a 14-year retrospective cohort study

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Introduction: To evaluate the success rate and short-term complications of single, double, and triple modalities of uterine-sparing treatment (UST) for primary postpartum haemorrhage (PPH).
Methods: We retrospectively reviewed records of women who underwent UST for PPH between 2006 and 2019 in Tuen Mun Hospital. The success rates of single, double, and triple modalities of UST (derived from the number of haemostatic hysterectomies prevented) were compared, as were short-term complications between single and double modality groups.
Results: Of 221 women who underwent UST for primary PPH, 174 (78.7%) received single, 44 (19.9%) received double, and 3 (1.4%) received triple modalities of UST. The three groups were comparable, except that there were more nulliparous women in the double than single modality group, more women having caesarean sections in the single than double or triple modality group, and more uterine atony in the double or triple than single modality group. The success rate of haemostasis decreased from 94.3% after single modality to 90.9% after double modalities to 0% after triple modalities ($p<0.001$). All three women with triple modalities of UST eventually underwent haemostatic hysterectomy. The single and double modality groups were comparable in terms of short-term complications.
Conclusion: Single and double modalities of UST were effective and safe in treating primary PPH. Early resort to hysterectomy should be considered if double modalities of UST failed to achieve haemostasis.

Keywords: Hemostasis; Hysterectomy; Postpartum hemorrhage; Uterine haemorrhage

Introduction

Postpartum haemorrhage (PPH) is an important cause of maternal morbidity and mortality. It occurs in 5% of the deliveries and is classified as severe in 1% of cases[1,2]. Primary PPH is defined as genital tract bleeding of ≥500 mL within 24 hours of birth. When uterotonic drugs fail to stop haemorrhage, uterine-sparing treatments (UST) such as intrauterine balloon tamponade, uterine compression suture, pelvic artery ligation, and pelvic artery embolisation are indicated. None of the modalities is superior to the others[3]. There are no adverse effects of UST on menstruation and fertility outcomes[4]. When haemostasis is not achieved after a single modality of UST, use of the second modality is suggested[5]. Nevertheless, there is no evidence regarding the efficacy and potential complications of multiple UST. Devascularisation of the uterus can result in ischaemic events to the endometrium-myometrium interface. Uterine necrosis has been reported after uterine compression suture[6-8], pelvic artery embolisation[9], or a combination of compression suture and vascular ligation[10], with fever and abdominal pain on the third day postpartum. Computed tomography shows the presence of gas bubbles in the myometrium. The present study aimed to determine the success rate of single, double, and triple modalities of UST in achieving haemostasis, and to compare the incidence of short-term complications between single and double modalities.

Methods

This retrospective study was approved by the New Territories West Cluster Ethics Committee (reference: NTWC/CREC/15039). Women who underwent UST in Tuen Mun Hospital from April 2006 to February 2019 were followed up at 6 weeks postpartum. Demographic, antenatal, and intrapartum data were retrieved. The success rate of single and multiple modalities of UST was derived from the number of hysterectomies prevented.

The surgical techniques and suture materials were standardised. Uterine compression suture (including B-Lynch suture and Hayman suture) were performed with No. 1 Monocryl. Cho suture and uterine artery

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ligation (UAL) were performed with No. 1 Vicryl. Uterine artery embolisation was performed by radiologists in operating rooms or radiology suites. Bakri balloons (Bakri Postpartum Balloon, Cook Medical) were the preferred UST in women with uterine atony after vaginal deliveries. Sequence of UST was decided by the treating physician case by case. Failure of a modality was defined clinically by ongoing bleeding after 15 minutes. To minimise the risk of maternal sepsis, one week of empirical antibiotics (750 mg intravenous cefuroxime and 500 mg intravenous metronidazole) was prescribed.

Short-term complications of UST (within 6 weeks postpartum) were recorded, including secondary PPH (abnormal genital tract bleeding between 24 hours and up to 12 weeks postnatally[11]), endometritis, puerperal sepsis (infection plus systemic manifestations developing after birth until 6 weeks postnatally[12]), pyometra, haematometra, uterine necrosis, and vessel complications (thrombosis, dissection, aneurysm, and pseudoaneurysm).

The amount of lochia, presence of abdominal pain, abnormal vaginal discharge or fever were recorded at postnatal 6 weeks. A routine gynaecological examination was performed. Genital swabs and blood tests were taken if infection was suspected. Ultrasonography of the pelvis was performed if there was abnormal vaginal bleeding. Women who lost to follow-up were contacted by phone, and appointments were offered for symptomatic cases.

Statistical analysis was performed using SPSS (Windows version 21; IBM Corp, Armonk [NY], US). Women in the three groups of modalities of UST were compared using the one-way ANOVA, Fisher's exact test, or Chi-squared test. Short-term complications between single and double modalities of UST were compared using the Chi-squared test or Fisher's exact test. A p value of <0.05 was considered statistically significant.

Results

Of 72 596 deliveries in our unit in the past 14 years, 221 (0.3%) women underwent UST for primary PPH. Among them, 174 (78.7%) received single, 44 (19.9%) received double, and 3 (1.4%) received triple modalities of UST. Eight (3.6%) women had a history of PPH. The amount of blood loss ranged from 500 mL to 12 000 mL (median, 2400 mL). The commonest cause of PPH was uterine atony (42.5%). Regarding the mode of delivery, 198 (89.6%) women had caesarean sections, 20 (9.0%) had normal vaginal deliveries, and 3 (1.4%) had vacuum extractions. Women who underwent UST were comparable in terms of maternal, antepartum, and intrapartum characteristics, except that there were more nulliparous women in the double than single modality group, more women having caesarean sections in the single than double or triple modality group, and more uterine atony in the double or triple than single modality group (Table 1). The median blood loss increased from 2000 mL after single modality to 4800 mL after triple modalities, whereas the use of recombinant factor VIIa and blood products transfusion increased with the number of modalities performed (Table 1).

Of 174 women with single modality of UST, 162 (93.1%) delivered by caesarean sections, 9 (5.2%) vaginally, and 3 (1.7%) by vacuum extractions. UAL was most commonly performed (n=110, 63.2%), followed by compression suture (n=38, 21.8%) [Table 2]. Single modality of UST successfully achieved haemostasis in 164 (94.3%) women. The remaining 10 (5.8%) women failed to achieve haemostasis and necessitated hysterectomy despite having had UAL (n=5), uterine artery embolisation (n=3), or compression suture (n=2); the causes of PPH were uterine atony (n=6), morbid adherence of the placenta (n=2), placenta praevia (n=1), and vaginal haematoma extending into the broad ligament (n=1).

Of 44 women with double modality of UST, 34 (77.3%) delivered by caesarean sections and 10 (22.7%) vaginally. A combination of UAL and compression suture was most commonly performed (n=30, 68.2%) [Table 2]. Double modality of UST successfully achieved haemostasis in 40 (90.0%) women. The remaining 4 (9.1%) women failed to achieve haemostasis and necessitated hysterectomy despite having had UAL plus compression suture (n=3) or compression suture plus uterine artery embolisation (n=1); the causes of PPH were uterine atony (n=3) and placenta praevia (n=1).

In the three women with triple modality of UST for uterine atony, one underwent Bakri ballooning and then laparotomy for UAL and then compression suture, and two underwent Hayman's suture and then UAL and then traditional B-Lynch suture (Table 2). However, all these women failed to achieve haemostasis and necessitated hysterectomy.

The success rate of haemostasis decreased from 94.3% after single modality to 90.9% after double modalities to 0% after triple modalities ($p<0.001$, Table 2). The single and double modality groups were comparable in terms of short-term complications such as secondary PPH (4.0% vs

Table 1. Maternal, antepartum, and intrapartum characteristics of women who underwent single, double, or triple modalities of uterine-sparing treatment

Characteristic	Single modality (n=174)*	Double modalities (n=44)*	Triple modalities (n=3)*	p Value
Age, y	34 (31.0-37.0)	32.5 (28.3-35.0)	31	0.08
Chinese	169 (97.1)	43 (97.7)	3 (100)	>0.99
Body mass index, kg/m^2	22.1 (20.6-24.7)	21.8 (20.4-24.8)	27.3	0.090
Nulliparity	71 (40.8)	28 (63.6)	1 (33.3)	0.014
Natural conception	144 (82.8)	34 (77.3)	3 (100)	0.666
Multiple pregnancy	23 (13.2)	6 (13.6)	0 (0)	>0.99
Previous caesarean section	48 (27.6)	8 (18.2)	2 (66.7)	0.124
History of postpartum haemorrhage	7 (4)	1 (2.3)	0 (0)	>0.99
Polyhydramnios	3 (1.7)	3 (6.8)	0 (0)	0.170
Fibroid ≥3 cm	9 (5.2)	3 (6.8)	0 (0)	0.756
History of antepartum haemorrhage	56 (32.2)	7 (15.9)	0 (0)	0.058
Gestation at delivery, weeks	39 (1)	38.5 (3)	38	0.10
Mode of delivery				0.004
Vaginal/instrumental delivery	12 (6.9)	10 (22.7)	1 (33.3)	
Caesarean section	162 (93.1)	34 (77.3)	2 (66.7)	
Intrapartum fever (≥38.5°C)	4 (2.3)	0 (0)	0 (0)	0.607
Induction of labour	26 (14.9)	13 (29.5)	0 (0)	0.066
Use of tranexamic acid	53 (30.5)	21 (47.7)	1 (33.3)	0.085
Use of recombinant factor VIIa	4 (2.3)	7 (15.9)	1 (33.3)	0.001
Blood products transfused, units				
No. of red blood cell	2 (3)	8 (6)	8	<0.001
No. of platelet	0 (18)	8 (5)	8	<0.001
No. of fresh frozen plasma	0 (4)	8 (7)	8	<0.001
Blood loss, mL	2000 (1300-3000)	3550 (2500-4875)	4800	<0.001
Birthweight, kg	2.92 (2.49-3.22)	2.85 (2.44-3.55)	3.30	0.630
Primary cause of postpartum haemorrhage				0.008
Uterine atony	76 (43.7)	30 (68.2)	3 (100)	
Placenta praevia/ morbidly adherent placenta	92 (52.9)	11 (25)	0 (0)	
Genital tract trauma	5 (2.9)	1 (2.3)	0 (0)	
Coagulopathy	1 (0.5)	2 (4.5)	0 (0)	

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

9.1%), endometritis (1.7% vs 6.0%), haematometra (0% vs 2.3%), and vessel complications namely iliac artery dissection (0% vs 2.3%) [Table 3]. No patients developed pyometra, uterine necrosis, or ureteric injury.

Discussion

Uterine atony is the commonest cause of PPH[13]. In the present study, most women who underwent two modalities of UST were nulliparous, as obstetricians tried to preserve the uterus in these women. The success rate of haemostasis by single and double modalities of UST was 94.3% and 90.0%, respectively, which are higher than the 84% to 91.7% after single modality of UST reported in a systematic review[3]. The combined use of B-Lynch suture and stepwise pelvic artery devascularisation prevented 80% of haemostatic hysterectomy[14]. However, the success rate dropped to 0% after triple modalities. UAL was the first UST performed in our centre and has been preferred

Table 2. Types of uterine-sparing treatment in the single, double, and triple modality groups

Modality	No. (%) of women	No. (%) of women avoided hysterectomy
Single modality	174 (78.7)	164 (94.3)
Uterine artery ligation	110 (63.2)	105
Compression suture	38 (21.8)	36
B-Lynch suture	14 (8.0)	-
Hayman's suture	24 (13.8)	-
Balloon tamponade	12 (6.9)	12
Uterine artery embolisation	14 (8.0)	11
Double modalities	44 (19.9)	40 (90.9)
Uterine artery ligation + compression suture	30 (68.2)	27
Uterine artery ligation + Cho's suture	2 (4.5)	-
Uterine artery ligation + B-Lynch suture	10 (22.7)	-
Uterine artery ligation + Hayman's suture	18 (40.9)	-
Balloon tamponade + uterine artery embolisation	10 (22.7)	10
Uterine artery ligation + uterine artery embolisation	2 (4.5)	2
B-Lynch suture + uterine artery embolisation	1 (2.3)	0
Hayman's + B-Lynch suture	1 (2.3)	1
Triple modalities	3 (1.4)	0 (0)
Uterine artery ligation + Hayman's suture + B-lynch suture	2 (66.7)	0
Balloon tamponade + uterine artery ligation + Hayman's suture	1 (33.3)	0

Table 3. Short-term complications in single and double modality groups

Complication	Single modality (n=174)*	Double modalities (n=44)*	p Value
Secondary postpartum haemorrhage	7 (4.0)	4 (9.1)	0.236
Endometritis	3 (1.7)	3 (6.8)	0.098
Puerperal sepsis	13 (7.5)	2 (4.5)	0.741
Pyometra	0 (0)	0 (0)	>0.99
Haematometra	0 (0)	1 (2.3)	0.202
Uterine necrosis	0 (0)	0 (0)	>0.99
Vessel complications	0 (0)	1 (2.3)	0.202

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

by our obstetricians since 2007. Two women with triple modalities underwent B-Lynch suture after Hayman's suture failed, with the old suture completely removed.

There is no consensus on the sequence of modalities of UST to achieve haemostasis. The use of double modalities is supported because the success rate is comparable to that with single modality, with no increase in complication rates. One study reported that 14 (93.3%) of 15 women had uneventful recovery after double modalities of UST, and the remaining woman had pyometra[14]. In addition, safety, fertility, and obstetric outcomes are reassuring following the combined use of embolisation and B-Lynch suture[15]. However, the use of triple modalities is a factor of poor prognosis; other factors include a delay in deciding on UST, a lack of decisional clinical algorithm, hypovolaemic shock, and the irregular supply of blood products[16]. We recommend that haemostatic hysterectomy should be

resorted to after failing two modalities to avoid further blood loss and delay of performing hysterectomy resulting in disseminated intravascular coagulopathy, which makes haemostasis more difficult.

Our study is limited by the differences in the number of women who underwent different modalities of UST. Furthermore, other factors affecting the success rate of UST were not assessed, including the time interval from the diagnosis of PPH to the initiation of UST, the availability of skilled surgeons, and the rate of correction of disseminated intravascular coagulopathy. The optimal treatment option could not be inferred. Uterine curettage was reported to successfully drain the haematometra after the use of UAL, B-lynch suture, or square suture at 4 months postpartum without recurrences[17]. In the only patient with haematometra who presented with persistent spotting and pelvic pain at 6 weeks postpartum, the haematometra was completely drained under antibiotics cover by the uterine aspirator without anaesthesia. The long-term menstrual and fertility outcomes warrant further studies.

Conclusion

Single and double modalities of UST were effective and safe in treating primary PPH. Early resort to hysterectomy should be considered if double modalities of UST failed to achieve haemostasis.

Conflicts of interest

The authors have no conflicts of interest to disclose.

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Supermorbid obesity in pregnancy

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Objective: We aimed to carry out an audit and service evaluation for women with supermorbid obesity to ensure that adequate planning is in place for intrapartum and post-delivery care, and to review delivery outcomes and complications.
Methods: Records of pregnant women with supermorbid obesity (body mass index ≥50) who delivered in Rotherham General Hospital, United Kingdom, between January 2018 and December 2019 were retrospectively reviewed. Body mass index was recorded at booking and repeated at 36 weeks. Glucose tolerance test was performed between 26 and 28 weeks of gestation. Antenatal anaesthetic review was carried out at around 36 weeks in the dedicated clinic, along with risk assessment for manual handling. Appropriate antenatal and postnatal thromboprophylaxis was given. Postnatal skin care assessment was performed. Intravenous antibiotics were given before caesarean section, and oral antibiotics were given for 5 days after caesarean section. The time of artificial rupture of membranes (ARM) in relation to the time of delivery was recorded, as were perinatal and neonatal outcome of delivery and complications.
Results: Of 4962 deliveries, 30 (0.6%) were by supermorbid obese women aged 20 to 34 years (n=24) or ≥35 years (n=6) who were primigravidas (n=15) or parity ≥1 (n=15). One woman had gestational diabetes mellitus; none had major antenatal complications or medical disorders. Of the 30 women, nine laboured spontaneously (8 vaginal delivery, 1 emergency caesarean section), 13 underwent induction of labour (6 vaginal delivery, 4 instrumental delivery, 3 emergency caesarean section), and eight had an elective caesarean section. The proportion of women delivering out of hours (20:30-08:30) was 33% if ARM was during 06:00-12:00 and 80% if ARM was during 12:00-18:00. Consultant was present in all caesarean sections, except for one performed by a senior trainee. All women received preoperative antibiotics before caesarean section. Oral antibiotics were given for 5 days postoperatively in all but one patient with caesarean section, with four receiving intravenous antibiotics for 24 hours. Nine (30%) women had minor PPH and one (3.3%) had major PPH related to uterine atony following an elective caesarean section. One (3%) baby was large for gestation (>90th centile) and three (10%) were small for gestation (<5th centile). There was no immediate admission to neonatal unit. Initial breastfeeding rate was 56%. All women with vaginal or instrumental delivery were discharged home by day 2, those with elective caesarean section by day 3, and those with emergency caesarean section by day 5.
Conclusion: We adhered to most auditable criteria. There is room for improvement in terms of review by anaesthetists in the clinic or on first admission in labour. We have developed a pathway to start the induction process towards the beginning of the week and earlier during the day. Healthcare professional should discuss potential risks and management options with women with obesity presenting for the first time during pregnancy. A brief intervention on weight management should be delivered in an effective and sensitive manner to help reduce the long-term burden of morbidity associated with supermorbid obesity.

Keywords: Labor, induced; Obesity, morbid; Pregnancy complications

Introduction

In the United Kingdom (UK), 21.3% of antenatal women are obese and only 47.3% have normal body mass index (BMI)[1]. The prevalence of obesity in pregnancy in the UK has increased from 9% to 10% in the early 1990s to 16% to 19% in the 2000s[1].

The MBRRACE-UK reported that 34% of the women who died in 2015 to 2017 were obese and a further 24% were overweight[2]. Obesity is independently associated with higher odds of dying from pregnancy complications. Obesity in pregnancy contributes to increased morbidity and mortality for mothers and babies.

In 2010, the Centre for Maternal and Child Enquiries (CMACE) conducted the first nationwide survey of maternity services for women with obesity[3]. These women in pregnancy are burdened by comorbidities, complications, and poor outcomes.

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The UK-wide obstetric surveillance system reported that one in 1000 pregnant women in the UK had a BMI of ≥50[4]. According to the National Health Services Digital, in 2018 the highest levels of obesity were found in Yorkshire and Humber and West Midlands[5]. Rotherham is a town in South Yorkshire County. According to the Daily Telegraph, 75% of the population of Rotherham is overweight or obese, the highest of any city in the UK[6].

Rotherham General Hospital has an annual delivery rate of nearly 2600. The challenges in the obstetric and anaesthetic care of supermorbid obese women prompted us to carry out an audit and service evaluation in this cohort of women to ensure that care is provided as per the standards based on the Royal College of Obstetricians and Gynaecologists (RCOG) guidance[1] (Table 1). We aimed to review our services to ensure adequate planning is in place for intrapartum and post-delivery care, and to review delivery outcomes and complications.

Methods

Records of pregnant women with supermorbid obesity (BMI of ≥50) who delivered in Rotherham General Hospital between January 2018 and December 2019 were retrospectively reviewed. BMI was recorded at booking and repeated at 36 weeks. Glucose tolerance test was performed between 26 and 28 weeks of gestation. Antenatal anaesthetic review was carried out at around 36 weeks in the dedicated clinic, along with risk assessment for manual handling. Appropriate antenatal and postnatal thromboprophylaxis was given. Postnatal skin care assessment was performed. Intravenous antibiotics were given before caesarean section, and oral antibiotics were given for 5 days after caesarean section.

The time of artificial rupture of membranes (ARM) was recorded. It was divided into four slots: 06:00-12:00, 12:00-18:00, 18:00-00:00, and 00:00-06:00. The time of delivery, in particular, the number of women delivering out of hours (20:30-08:30), in relation to the time of ARM was investigated. It is our routine practice to use one cycle of Propess (10 mg Dinoprostone vaginal delivery system) or Rusch balloon for 24 hours in cases with unfavourable Bishop scores. In cases where ARM cannot be performed, a repeat 24-hour cycle of either method is used alternatively.

Rates of spontaneous vaginal deliveries, instrumental deliveries, and caesarean sections were compared against Confidential Enquiry into Maternal and Child Health (CEMACE) national data. Neonatal data (the number of large for gestation or growth-restricted babies, admission to special care unit, and initial breastfeeding) were collected, as were overall delivery outcome and any major intrapartum or postpartum complications.

Results

Of 4962 deliveries between January 2018 and December 2019, 30 (0.6%) were by supermorbid obese women aged 20 to 34 years (n=24) or ≥35 years (n=6) who were primigravidas (n=15) or parity 1 and above (n=15). Only one woman had gestational diabetes mellitus; none had major antenatal complications or medical disorders.

Table 1. Auditable criteria and percentage of women achieved

Audit criteria	Standard %	% (No.) of women achieved
Antenatal		
Record of body mass index at booking and at 36 weeks in handheld notes and electronic system prior to delivery	>90	100 (30/30)
Glucose tolerance test in pregnancy	>90	100 (30/30)
Antenatal anaesthetic review	>90	80 (24/30)
Risk assessment for manual handling in the third trimester	>90	80 (24/30)
Assessment for thromboprophylaxis and received of correct dose	>90	100 (30/30)
Postnatal		
Appropriate antibiotic prophylaxis		
Pre-caesarean section	>90	100 (12/12)
Post-caesarean section	>90	91 (11/12)
Postnatal thromoboprophylaxis at correct dose	>90	100 (30/30)
Skin care assessment	>90	87 (26/30)

Table 2. Delivery outcomes and complications

Outcome	No. (%) of pregnant women with body mass index of ≥50 (n=30)	% in Confidential Enquiry into Maternal and Child Health
Induction of labour	13 (43)	36
Normal vaginal delivery	14 (47)	47
Instrumental delivery	4 (13)	5.8
Overall caesarean section	12 (40)	45
Emergency caesarean section	4 (13)	25.4
Elective caesarean section	8 (27)	19.6
Shoulder dystocia	2/18 (1.2)	-
Difficult access at caesarean section following failed trial	1/12 (8.3)	-
Readmission with wound infection following caesarean section	1/12 (8.3)	-
Return to theatre for atony	1/30 (3.3)	-

Table 3. Time of artificial rupture of membranes in relation to the delivery time

Time of artificial rupture of membranes	Delivery time
12:00-18:00	
13:45	02:29
14:15	07:30
14:15	19:56
17:00	05:00
15:46	20:54
06:00-12:00	
09:20	03:20
10:00	16:07
10:40	19:42
00:00-06:00	
04:50	08:51

Of the 30 women, nine laboured spontaneously, 13 had induction of labour, and eight had an elective caesarean section (Table 2). All women with spontaneous labour presented between 37 and 40 weeks; eight had vaginal delivery and one had emergency caesarean section for failure to progress. Of the 13 women who had induction of labour, six had vaginal delivery, four had instrumental delivery, and three had emergency caesarean section. Propess was used initially in three women and Rusch balloon in five. Nine underwent ARM between 06.00 and 18.00, except for one. The proportion of women delivering out of hours (20:30-08:30) was 33% if ARM was during 06:00-12:00 and 80% if ARM was during 12:00-18:00 (Table 3). The indications for the eight elective caesarean sections included previous one or two caesarean sections and malpresentation.

A consultant was present in all caesarean sections, except for one, which was performed by a senior trainee. All women received preoperative antibiotics prior to caesarean section. Oral antibiotics were given for 5 days postoperatively in all but one patient with caesarean section, with four receiving intravenous antibiotics for 24 hours. It is our routine practise to use negative pressure dressings in women with BMI of ≥45; 10 of 12 women with caesarean sections received negative pressure dressings. Continuous subcuticular sutures were used in 10 caesarean sections (Monocryl, n=7; Prolene, n=3) and interrupted sutures with Prolene were used in two cases.

20 (66%) women delivered without primary postpartum haemorrhage (PPH) [blood loss of ≥500 ml], whereas nine (30%) had minor PPH (blood loss of 500-1000 ml) and one (3.3%) had major PPH (blood loss of >1000 ml) related to uterine atony following an elective caesarean section and had to be returned to theatre for intrauterine balloon tamponade.

26 (86%) babies were between 10th to 89th centile, whereas one (3%) were large for gestation (>90th centile) and three (10%) were small for gestation (<5th centile). There was no immediate admission to neonatal unit. Initial breastfeeding rate was 56%. All women with vaginal or

instrumental delivery were discharged by day 2, those with elective caesarean section by day 3, and those with emergency caesarean sections by day 5.

Discussion

Obesity is a trend described as 'global epidemic' by the World Health Organization[7]. Obesity is associated with increased number of pregnancy-related complications and serious adverse outcomes including miscarriage, fetal congenital anomaly, thromboembolism, gestational diabetes, preeclampsia, dysfunctional labour, PPH, wound infections, stillbirths, and neonatal deaths. It is also associated with higher rates of induction of labour and caesarean section and lower breastfeeding rate, compared with women with normal BMI[3]. Maternal obesity, in particular supermorbid obesity, poses management problems (relating to the increased risks of complications in pregnancy) and medical, surgical, and technical challenges in providing safe maternity care.

There has been an increased prevalence of supermorbid pregnant women at our hospital, with nearly 6/1000 women having a BMI of ≥50. Healthy lifestyle advice is given and dietician referral is offered along with a patient information leaflet at initial visit. Glucose tolerance test is booked between 26 and 28 weeks. Growth scans are carried out from 28 weeks every 3 weekly until delivery. At 36 weeks, an appointment in the anaesthetic clinic is booked along with risk assessment for manual handling.

The rate of gestational diabetes is three-fold higher in obese women compared with those with normal BMI[8-11]. In our cohort, the rate was quite low (3.3%, n=1) probably because most women were of younger age-group (20-34 years). Obesity and gestational diabetes in combination are associated with adverse pregnancy outcomes[12]. Age ≥35 years is an independent risk factor for type-2 diabetes, gestational diabetes, and pregnancy-induced hypertension. In our cohort, the rate of pregnancy-related hypertensive disorders (pregnancy-induced hypertension, preeclampsia, essential hypertension) was 20%, which is much higher than the 1.9% in the general population. In our hospital, all women with BMI of ≥35 are assessed for the risk of developing preeclampsia based on the NICE criteria[13] and receive 150 mg aspirin from 12 weeks gestation.

Obesity is a risk factor for thromboembolism, and risk assessment should be carried out at first antenatal visit, during pregnancy (if admitted or develop intercurrent problems), intrapartum, and postpartum[1], based on the RCOG guidance on thromboembolism.[14]

Risk assessment for manual handling is performed in the third trimester to determine any specific requirements for labour and birth in terms of patient factors, equipment, communication, building space, and organisational and staff issues[15]. Our hospital has a list of equipment with weight limits, which is a minimum requirement for maternity services within National Health Service Litigation Authority's Clinical Negligence Scheme for Trusts maternity risk management standards[1]. Postnatal skin care assessment is performed to identify early signs of pressure sores that can be worsened by immobility[16].

Pregnant women with a BMI of ≥40 should have an antenatal consultation with an obstetric anaesthetist, so that potential difficulties with venous access, regional or general anaesthesia can be identified. An anaesthetic management plan for labour and delivery should be discussed and documented in the medical records. UK-wide obstetric surveillance system data showed that 25% of maternal cardiac arrests are related to anaesthesia and 75% of these women are obese[17]. On admission for delivery, venous access should be established early on in labour. An early epidural is advocated by Royal College of anaesthetists. An epidural top-up in a well-established epidural is the quickest way anaesthesia can be gained in a prompt and safe way for an emergency delivery. The epidural re-site rate increases with increasing BMI (17%), compared with the 3% in the control group[18]. The increased difficulties associated with provision of general and regional anaesthesia can lead to increased decision-to-delivery time, particularly when a category I or II caesarean section is required[1]. In our cohort, general anaesthesia was not needed. Nonetheless, it is a challenge, with difficulties in airways management including difficult bag mask ventilation and failed intubation with higher risk of desaturation[19] and postoperative atelectasis.

In our cohort, 30% of women laboured spontaneously, which is much lower than the 69% in the general population. The rate of induction of labour was 43%, which is double the rate in the general population of 20%. Caesarean sections accounted for 40% of all singleton deliveries, which is comparable with the 45% reported in the CMACE study group but is substantially higher than the 25% among the general maternity population in England. In the CEMACE study, each unit increase in BMI >35 is associated with an increased risk of induction of labour and caesarean sections. Delay in ARMs leads to out-of-hours delivery, which is a challenge when emergency caesarean section is needed. It is advisable to have a consultant presence unless the registrar has competency. Obesity is a

risk factor for PPH6, and active management of labour is advisable[1].

In the CEMACE study group, women with a BMI ≥35 are more likely to stay in hospital for ≥7 days after childbirth, even after adjusting for the mode of delivery. However, our women were discharged at a maximum of 5 days after delivery.

Babies born to mothers with obesity are up to 1.5 times more likely to be admitted to a neonatal intensive care unit and twice as likely to be stillborn, compared with women with healthy BMI[3]. In our cohort, there was no stillbirth or immediate admission to neonatal unit. Women with obesity are less likely to breastfeed, possibly owing to social factors, difficulty in latching on, or endocrine disturbance. More than half of our women were able to initiate breastfeeding.

The risk of wound infection is higher in obese women than in healthy women, with an adjusted odds ratio of 2.24 (95% confidence interval, 1.91-2.64)[10]. A systematic review of randomised trials showed a significantly lower incidence of wound infections with antibiotic prophylaxis in the general maternity population[20]. Although negative pressure dressings result in a reduced rate of surgical site infections in non-obstetric populations[21], evidence for their use in obese obstetric populations is insufficient[22,23]. In obese pregnant women, the risk of surgical site infection reduces with interrupted suturing compared with subcuticular suturing, although the latter shows better short-term cosmetic results and less skin closure time[24,25].

Conclusion

Our hospital adhered to most of the auditable criteria. There is room for improvement in terms of review by anaesthetists in the clinic or on first admission in labour. We have developed a pathway to start induction process towards the beginning of the week and earlier during the day, with the aim of carrying out ARMs early in the morning to increase the chance of delivering during weekdays and within working hours. Healthcare professional should discuss potential risks and management options with women with obesity presenting for the first time during pregnancy. A brief intervention on weight management should be delivered in an effective and sensitive manner to help reduce the long-term burden of morbidity associated with supermorbid obesity.

Declaration

The authors have no conflict of interest to disclose.

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Views of Chinese women with perinatal loss on seeing and holding the baby

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Objective: To explore the views of Hong Kong Chinese women who experienced perinatal loss on seeing and holding the baby and on commemoration.
Methods: Chinese women who had experienced second-trimester miscarriage, termination of pregnancy for fetal anomaly (TOPFA), stillbirth, or neonatal death within 5 years and had been under the care of the Grief Counselling and Support Team in a regional hospital in Hong Kong were recruited to complete a questionnaire through telephone interview or self-administration between May and December 2019.
Results: Of 56 women recruited, 51 (91%) with a mean age of 35 years completed the questionnaire through self administration (n=26) or telephone interview (n=25). The cause of perinatal loss included second trimester miscarriage (n=14), TOPFA (n=23), stillbirth (n=7), and neonatal death (n=7). The mean gestation was 22 (range, 14-38) weeks. The mean time from perinatal loss to survey was about 30 (range, 1-47) weeks. 52.9% of the participants were primiparous, and 45.1% had a living child. 33.3% of participants had a history of perinatal loss. 36 (70.6%) participants reported to have seen and 30 (58.8%) reported to have held, touched, or kissed the baby. Six themes were identified from the experience of seeing and holding the baby: natural experience: inborn parenthood, positive feeling in the traumatic life event, negative emotions, sense of relief, avoiding regret, and psychological preparation matters. All participants who had seen and held her baby did not regret their choice. However, among the 21 participants who did not see and/or hold the baby, five (23.8%) regretted. 44 (86.3%) participants had commemorated the baby; 54.5% of them were guided by midwives/nurses.
Conclusion: The current study helps healthcare providers to better understand Hong Kong Chinese women's views and experience on seeing and holding the baby, and to guide them to provide better bereavement care in a more culturally sensitive manner.

Keywords: Bereavement; Fetal death; Stillbirth

Introduction

Perinatal death represents multiple losses to parents, including the loss of a significant person, some aspects of the self, and a dream[1]. Parents with perinatal loss have seven times higher risk of developing post-traumatic stress disorder symptoms and four times higher risk of developing depressive symptoms[2].

Bereaved parents often have difficulty in articulating their preference on whether to see and hold the baby and to keep any mementoes of the baby. Thus, guidance and support by healthcare providers are important. However, healthcare professionals may not be able to provide effective bereavement care owing to emotional, knowledge, and system-based barrier[3]. There is controversy on the management of seeing and holding the baby.

Some bereaved parents considered that contact with their stillborn baby validated the birth and life[4]. Seeing and holding the baby is associated with less depressive and anxiety symptoms, better sleep, more satisfaction with hospital care, and less regret[5-8]. Parents may express regret for the missed opportunity to see the baby and make tangible memories[9]. In contrast, some bereaved women who have seen and held the stillborn baby have more anxiety and post-traumatic stress disorder symptoms[10]. Thus, healthcare providers used to not routinely encourage mothers to see and hold the baby. This raises concerns in many bereaved parents, midwives/nurses, and bereaved parent support groups, leading to public campaigns and proliferation in research[8,11], and then the National Institute for Health and Care Excellence (NICE) guideline[12] recommends that experienced healthcare professionals are encouraged to discuss with women and her family about the option of seeing or holding the baby, having mementoes, or seeing photographs of the baby.

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Since 1995, the Grief Counselling and Support Team (the Bereavement Team) has been established in the Department of Obstetrics and Gynaecology, Pamela Youde Nethersole Eastern Hospital in Hong Kong. The Bereavement Team comprises midwives, nurses, obstetricians, gynaecologists, social worker, clinical psychologist, and peer support volunteers. Women who experienced perinatal loss after the second trimester or beyond caused by miscarriage, termination of pregnancy due to fetal anomaly (TOPFA), stillbirth, or neonatal death (NND) are referred to the Bereavement Team. A dedicated midwife or nurse provides bereavement care for the grieving mother and accompanies the bereaved parents to see and hold the baby if the parents choose to do so. The practice may vary owing to various reasons such as personal belief and experience.

Talking about death is a taboo in Chinese culture, especially when the death is at a young age. However, in recent years, bereaved Chinese parents in Hong Kong are more willing to share their views and recognise the perinatal loss, especially for those under 24 gestational weeks[13,14]. This study aimed to explore the views of Hong Kong Chinese women who experienced perinatal loss on seeing and holding the baby and on commemorating the baby.

Methods

The study was approved by the Hong Kong East Cluster Research Ethics Committee (reference: HKECREC-2019-022). Written informed consent was obtained from each participant. Confidentiality and anonymity were affirmed. Chinese women who experienced the loss of a baby or fetus (caused by miscarriage, TOPFA, stillbirth, or NND) perinatally (from second trimester [12 gestational weeks] to 28 days of life after birth) within 5 years and had been under the care of the Bereavement Team were purposively recruited. A cross-sectional and qualitative phenomenological research design was used. Qualitative phenomenological design aids investigation of the in-depth meaning of participants' lived experience[15], facilitating exploration on grieving mothers' view.

Participants were asked to complete a questionnaire in Chinese through telephone interview or self-administration between May and December 2019. The questionnaire comprises four structured open-ended questions about the experience of seeing and holding the baby and commemoration activities for the baby. Probing questions and examples were given to aid reflection and expression following the main questions (Table 1). During telephone interview (lasting about 15 to 20 minutes), attentive listening was used. The participants' exact words were recorded, together with non-verbal expressions (pause and emotional change such as weeping), and the telephone interview was transcribed in Chinese and then translated to English for analysis. To increase study credibility and confirmability, participants were asked to verify whether the transcript truly and completely reflected their views and experience. The interview notes and field notes were completed right after each telephone interview to ensure accuracy and minimise memory loss. Personal belief and bias were avoided through continuous application of reflexivity and bracketing to maintain openness and non-judgment to participants' views and experience. The Bereavement Team is good at establishing a trusting relationship with participants to enable participants to express their views and experiences in comfort, and is sensitive to participants' verbal and non-verbal expression.

Data were categorised and coded, and themes were identified. To increase study confirmability and dependability, thematic analysis was performed by two authors independently. Differences and similarities in the codes and themes were compared and discussed, and a consensus was reached. Recruitment of participants was

Table 1. Structured open-ended questions with follow-up probing questions and examples

Q1	Did you see your baby? Why or why not? What happened? (eg, initiated by you? Under nurse's encouragement? Saw the baby naturally? Who accompanied you to see?) Did the nurse give you psychological preparation beforehand? (eg, described what the baby looks like first) How did you feel? (eg, fear, touched, natural, sad, annoyed, relieved, positive, negative, painful but tolerable)
Q2	Did you hold/touch your baby? Why or why not? How did you feel?
Q3	Did you regret your choice? Why? If you could choose again, what would you choose?
Q4	Did you commemorate your baby? If yes, what did you do? How did you feel? (eg, treasured baby-related mementoes such as footprints, ultrasound photos; cleansed baby's face; sent towel as gift to baby; wrote letter to baby; made commemoration booklet; named the baby; arranged rituals or religious ceremony; did good deeds under the name of the baby?) Did the healthcare providers offer any help? (eg, give advice, encouragement)

stopped when data saturation reached (when no new codes emerged and sufficient data collected in terms of thick and rich description). Psychological support and counselling would be provided by the Bereavement Nurse after the interview if needed.

Results

Of 56 women recruited, 51 (91%) with a mean age of 35 years completed the questionnaire through self administration (n=26) or telephone interview (n=25) [Table 2]. The cause of perinatal loss included second-trimester miscarriage (n=14), TOPFA (n=23), stillbirth (n=7), and NND (n=7). The mean gestation was 22 (range, 14-38) weeks. The mean time from perinatal loss to survey was about 30 (range, 1-47) weeks. 52.9% of participants were primiparous, and 45.1% had a living child. 33.3% of participants had a history of perinatal loss.

36 (70.6%) participants reported to have seen and 30 (58.8%) reported to have held, touched, or kissed the baby. Of the 36 who saw the baby, 13 (36.1%) initiated the request, 14 (38.9%) were asked or encouraged by midwives/nurses, five (13.9%) initially declined but later changed their mind, and four did not mention or just saw the baby naturally. Six themes were identified from the experience of seeing and holding the baby.

Theme 1 was 'natural experience: inborn parenthood'. Many participants affirmed the mother-and-child relationship and had a strong natural desire to see and touch/hold the baby. *"She is my daughter, my precious treasure. I want to see her very much! I will remember her face well with effort."* (case 5, Stillbirth, 27 gestational weeks) *"It happened naturally."* (case 18, TOPFA, 23 gestational weeks) *"[Seeing baby] as a remembrance. After seeing the baby, [I] touched and held the baby naturally."* (case 26, miscarriage, 15 gestational weeks)

Theme 2 was 'positive feeling in the traumatic life event'. Despite experiencing a traumatic life event, many participants reported positive feelings in the process of seeing and holding the baby. Participants treasured this moment to have intimate contact with the baby. Some identified family traits from baby's appearance, whereas others remarked her baby as beautiful, adorable, and peaceful. This helped create a fond memory. *"We were emotionally calm. [We] also talked with the baby in a gentle voice."* (case 47, TOPFA, 21 gestational weeks) *"I had held [and] touched the baby's hands and feet. Looking at her hands and feet… as [this was] the second pregnancy, [I] would compare [the baby] with [my] elder daughter. [She] had long hands and legs like her elder sister…"* (case 51, TOPFA, 23 gestational weeks) *"I had held my baby. A nurse helped to place my baby into my arms. [I] felt she was very comfortable, without any pain. Also, [she was] warm and of considerable weight. [Her] lips were red. I thought the nurse had put some lipstick on her, but it was my baby's own colour."* (case 52, stillbirth, 34 gestational weeks)

Table 2. Demographic characteristics of participants (n=51)

Characteristic	Value
Age, y	35.4±4.8 (23-46)
Cause of perinatal loss	
Miscarriage	14 (27.5)
Termination of pregnancy due to fetal anomaly	23 (45.1)
Stillbirth	7 (13.7)
Neonatal death	7 (13.7)
Gestation, weeks	21.7±5.5 (14-38)
Type of pregnancy	
Spontaneous	47 (92.2)
In vitro fertilisation / intrauterine insemination	4 (7.8)
No. of living children	
0	27 (52.9)
1	23 (45.1)
2	1 (2.0)
Education level	
Primary	1 (2.0)
Secondary	26 (51.0)
Tertiary	24 (47.1)
History of perinatal loss	
No	34 (66.7)
Yes	17 (33.3)
Time from perinatal loss to interview, weeks	30.3±11 (1-47)

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

Theme 3 was 'negative emotions'. Some participants expressed sorrow, grief, and even guilty feeling in the process of seeing and holding the baby. *"…I felt miserable. Other [babies] were born with beating heart, but my [baby] was not. [I am] very depressed."* (case 31, miscarriage, 14 gestational weeks) *"… being his parents, [we] want to see him. [I] felt miserable. [I] couldn't protect him. [I] felt guilty for him. (crying)…"* (case 33, miscarriage, 18 gestational weeks)

Theme 4 was 'sense of relief'. Some participants reported that the negative emotions were bearable or even resolved during the process of seeing and holding the baby. Some even expressed a sense of relief. *"[I] feel good [as I] can see the baby for the last time. Baby is being cleaned properly and [she is] even being tied with ribbon nicely. Baby is very peaceful. I feel good. [I can] see the baby is very comfortable."* (case 22, miscarriage, 14 gestational weeks) *"[I] had held [my] baby. [I] felt heartbroken and sorrowful, but these feelings were resolved."* (case 39, miscarriage, 19 gestational weeks) *"… When I saw my daughter, it was very touching and sorrowful. Seeing my daughter made me feel no regret. It was bearable."* (case 51, TOPFA, 23 gestational weeks)

Theme 5 was 'avoiding regret'. Some participants worried that they might not have another chance to see the baby again, and this might induce regret. *"Because she is also my daughter, although she is only 22 gestational weeks' old, she is still a treasure in my heart. If I had not seen my daughter for the last time, I believe I must regret."* (case 54, TOPFA, 21 gestational weeks)

Theme 6 was 'psychological preparation matters'. Some participants recalled positive feelings if they were psychologically prepared by midwives/nurses' explanation before seeing and holding the baby. In contrast, some participants were fearful if they were not psychologically prepared beforehand. *"The nurse had told me that as the baby was very premature, she did not look like [a] full-term [baby]. But [whose skin colour was] somewhat redder. This made me psychologically prepared…. [I] thought the baby was beautiful like an angel…"* (case 42, TOPFA, 23 gestational weeks) *"[I was] scared. She [the baby] was very red, unlike usual baby [whose skin colour] is very white. The nurse had not mentioned that before. It would be better if [the nurse] had told [me] and [I] was psychologically prepared."* (case 38, TOPFA, 18 gestational weeks)

15 (29.4%) participants did not see the baby and 20 (39.2%) participants did not hold/touch the baby, mostly owing to fear (non-specific fear, fear to be too mournful, lose emotional control, and fearful to have a stronger emotional attachment to the baby). Four participants did not know they could hold/ touch her baby.

All participants who saw and held the baby did not regret their choice. However, among the 21 participants who did not see and/or hold the baby, five (23.8%) regretted. One became ambivalent about the previous choice of not seeing and holding her baby. One who saw but did not hold her baby reflected, *"[I am] regretted. If [I] could choose once again, I would like to see and hold [my baby]."* (case 13, miscarriage, 15 gestational weeks) One who did not see or hold her baby exclaimed, *"[I am] regretted because it was the single last [chance]."* (case 15, NND, 24 gestational weeks)

44 (86.3%) participants reported that they did something to commemorate her baby; 24 (54.5%) of them were under midwives/nurses' guidance. 26 (59.1%) participants treasured tangible tokens for remembrance, including antenatal ultrasound photos, baby photos and footprints, and commemoration booklet given by the Bereavement Team. 18 (40.9%) participants wrote letters or cards to her baby. Some regarded this as a way to talk to her baby. Some felt relieved while writing a letter to her baby. 15 (34.1%) participants gave presents to her baby, including clothes, towels, toys, and sibling's painting. 19 (43.2%) participants arranged rituals or religious ceremony for her baby. 11 (25%) participants named their babies. Three (6.8%) participants showed benevolence to others under the name of her baby such as sewing baby hats for other prematurely born babies. Some commented that without midwives/nurses' suggestion, they did not know they could do such commemoration for her baby.

Discussion

This is the first qualitative study to date about the experience of Chinese women with perinatal loss in Hong Kong on seeing and holding the baby. Many participants affirmed the mother-and-child relationship and had a natural strong desire to see her baby. Mother-infant attachment started long before baby's birth[16]. Maternal love has attached firmly to the growing infant since the earliest stages of pregnancy[16].

For some participants, it might also be the last chance to see their beloved babies. Similar to a study on mothers' experience about their contact with the stillborn baby[17], our participants also expressed that it was a highly emotional and grief experience. However, many participants also reported positive feelings when they saw and held their baby. They treasured the precious moment to have intimate contact with their baby. They enjoyed the moment when they found family traits in their baby. The process of seeing and holding the baby directed the feeling of heartbreaking and intense sadness to fond memory and happiness[17]. Furthermore, many participants gained a sense of relief after seeing the baby who was peaceful and beautiful. A systematic review also reported that parents who had seen or held their baby had positive outcomes[8].

Consistent with a study in Taiwan[18], some participants chose to see and hold the baby to avoid regret. Our study showed that all participants who had seen and held the baby did not regret their choice. In contrast, among those who did not see and/or hold the baby, 23.8% regretted. Furthermore, five (13.9%) who initially did not want to see the baby changed their mind later and decided to see the baby. Bereaved parents felt psychologically incapacitated in absorbing information, making a decision, or expressing their preference. The bereaved parents value healthcare professionals' guidance and encouragement[4,9,19]. A meta-synthesis reported that parents regretted if they missed the opportunity or had insufficient time to spend with their baby and they were left with a lack of memories[9]. Healthcare professionals should discuss actively with parents about their options and preference on seeing and holding the baby, and to provide these opportunities repeatedly in a sensitive way[9].

Our study showed that psychological preparation before seeing and holding the baby was very important, especially when the baby was very premature. Participants reported positive feeling when they were psychologically prepared by midwives/nurses about the appearance of the baby. In contrast, they were fearful during the contact if they had not been psychologically prepared. This emphasised the crucial role of the healthcare providers, mainly midwives or nurses in clinical practice, in guiding and influencing the bereaved mothers to have a positive or negative experience of contact with the baby.

86.3% of our participants commemorated their babies and 54.5% of them did the commemoration under midwives/nurses' guidance. This indicated that commemorating the baby is well accepted in our participants and the importance of midwives/nurses' role in the process. Perceived professional support and opportunities to share the memory of the baby were associated with fewer post-traumatic stress disorder symptoms[20]. Parents used tokens or performed rituals of remembrance to connect with the baby. These brought a sense of closure to mothers and social acknowledgement to the baby. This is a kind of adaptive coping strategies to help mothers to cope with the grief and other related responses after baby loss[21,22].

Some participants reported negative emotions such as sorrow, grief, and guilty when they saw and held their baby. These could be normal grief reactions after perinatal loss. It is also possible that seeing and holding the baby may not be good for some mothers. A meta-synthesis of qualitative studies reported that parents had different preferences and needed different levels of guidance from healthcare providers for deciding on seeing and holding the baby, and so the support should be tailored[4]. It is important to discuss with bereaved parents sensitively about the option of seeing and holding the baby, and to allow time for them to decide. This shall include detailed explanations of possible emotional reactions elicited, including positive and negative ones, sense of regret, psychological preparation before seeing and holding the baby in a sensitive manner. Every bereaved parent may grief differently due to personal, cultural, and religious needs. Thus, healthcare providers shall provide tailored and individualised bereavement care, including memory making, seeing and holding the baby[23].

There are limitations to this study. All participants received hospital-based bereavement service, and such service may vary in different hospitals. Nonetheless, to increase the representativeness, purposive sampling was used to include participants with different types of perinatal loss. In addition, telephone interviews were not audiotaped owing to limitations of resources and technical issues. Telephone interviews were recorded by taking detailed interview notes with field notes. The interview notes might be incomplete owing to distraction or might be biased by the interviewer's memory. Thus, authors were reflexive throughout the study and adopted strategies to minimise biases. Future research may consider investigating the views and experience of bereaved fathers on seeing and holding the baby and compare those with the bereaved mothers', as well as investigating the bereaved parents' views and experience on other bereavement management such as discussion of postmortem.

Conclusion

Perinatal loss is a traumatic life event for women and their family. The current study helps the healthcare providers to understand more about Hong Kong Chinese women's views and experience about seeing and holding the baby and their preference in commemorating their baby. This guides healthcare providers to provide better bereavement care.

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Declaration

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Pregnant women's opinions on universal screening for COVID-19 during hospital admission: a cross-sectional survey

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Introduction: The present study aimed to evaluate pregnant women's opinions on universal screening for COVID-19 during hospital admission.
Methods: Between 1 September 2020 and 24 November 2020 in the antenatal ward and labour ward of United Christian Hospital, a self-administrated questionnaire (in Chinese and English) on universal screening was distributed to all obstetric patients upon admission (or after delivery).
Results: Of 600 questionnaires distributed, 520 (86.7%) were returned. Of these, 11 were excluded owing to missing answers and 509 were included in analysis. All respondents had negative results of COVID-19. 98.4% of the women agreed with universal screening for all obstetric patients on admission. 69.0%, 73.9%, and 72.1% of women considered that a negative COVID-19 result would have a positive effect on their own care, their baby's care, and their family, respectively, with 82.1% feeling more ready to breastfeed and 84.9% feeling more at ease to look after their babies after delivery. 97.2% thought that all staff in the obstetric ward should have COVID-19 screening. A logistic regression model showed that women with tertiary education or above (odds ratio [OR]=2.361, p<0.001) and with emergency admission (rather than elective admission) [OR=1.686, p=0.018] were more likely to believe that a negative screening result would have positive effects on her care, whereas women with tertiary education or above (OR=3.615, p<0.001) were more likely to believe that a negative result would have a positive impact on their baby's care.
Conclusion: Universal screening for COVID-19 on admission is well supported by obstetric patients.

Introduction

As of the end of November 2020, the COVID-19 pandemic has affected >6.2 million people worldwide[1]. On 23 January 2020, Hong Kong confirmed the first cases of COVID-19 infection, which were identified in individuals who travelled from Wuhan to Hong Kong by high-speed rail and by air[2]. As of 6 December 2020, Hong Kong had 6898 confirmed cases[3]. The Hong Kong government has tightened measures in social distancing, extended testing services in community centres, outpatient clinics, and private sectors, and adopted mandatory screening for 'high risk' groups[3].

Pregnant women in Hong Kong lack a comprehensive understanding of COVID-19, particularly on its effect on pregnancy[4]. Many expressed high levels of concerns on its contraction during pregnancy and showed high degrees of acceptance of universal screening at certain time points of their pregnancy, although the optimal timing suggested varied[4].

The latest guideline by the Royal College of Obstetricians and Gynecologists recommends that SARS-CoV-2 testing should be offered to all pregnant women admitted to hospitals in England regardless of symptoms and that their intended birth partner should also be screened[5]. The prevalence of COVID-19 in the United Kingdom far exceeded that of Hong Kong. It remains controversial whether Hong Kong should adopt a similar policy and whether our obstetric patients support such mandatory screening. Since 17 August 2020 in United Christian Hospital, screening for COVID-19 has extended to all asymptomatic in-patient admissions (both elective and emergency). For elective admissions, deep throat saliva is collected for testing 1 day before the scheduled admission. For emergency admissions, deep throat saliva is collected after 2 hours of fasting. For those already in active labour on admission, nasopharyngeal swabs are taken by healthcare workers. Results are usually available within 6 hours. For urgent cases, results are available within

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2 hours, using the GeneXpert, a cartridge-based nucleic acid amplification test. This study aimed to explore pregnant women's view on universal screening of COVID-19 during hospital admission.

Methods

This survey study was approved by the Kowloon Central / Kowloon East Cluster Research Ethics Committee (reference: KCC/KEC-2020-0300). Participants were informed the details of the study; anonymity was ensured. Women who were aged <18 years, cognitively impaired, or not able to understand Chinese/English were excluded. Between 1 September 2020 and 24 November 2020 in the antenatal ward and labour ward of United Christian Hospital, a self-administrated questionnaire (in Chinese and English) on universal screening was distributed to all obstetric patients upon admission (or after delivery). The questionnaire comprised seven questions on patient demographics and 15 questions on universal screening for COVID-19 during hospital admission.

The sample size was estimated to be 390 assuming that 50% of them would accept universal screening and a random error of up to 5% with 95% confidence level. Assuming the response rate to be 80%, distribution of 500 questionnaires was sufficient. Comparisons were made using the Chi-squared test or Fisher's exact test. A multivariable logistic regression analysis model was constructed to identify clinical covariates associated with pregnant women's acceptance of mandatory universal screening of COVID-19. A p value of <0.05 was considered statistically significant.

Table 1. Characteristic of respondents

	No (%) of respondents	No. (%) of respondents agreeing that universal screening has positive effects on their care		p Value	No. (%) of respondents agreeing that universal screening has positive effects on their baby's care		p Value
Maternal age, y				0.705			0.678
<35	368 (72.3)	252 (71.8)			270 (71.8)		
≥35	141 (27.7)	99 (28.2)			106 (28.2)		
Parity				0.142			0.214
0	234 (46.0)	169 (48.1)			179 (47.6)		
≥1	275 (54.0)	182 (51.9)			197 (52.4)		
Ethnicity				0.959			0.460
Chinese	474 (93.1)	327 (93.2)			352 (93.6)		
Non-Chinese	35 (6.9)	24 (6.8)			24 (6.4)		
Education level				<0.001			<0.001
Non-tertiary	294 (57.8)	181 (51.6)			189 (50.3)		
Tertiary or above	215 (42.2)	170 (48.4)			187 (49.7)		
Family monthly income				0.220			0.027
<$20 000	192 (37.7)						
$20 001 to $40 000	210 (41.3)	<$40 000	272 (77.5)		<$40 000	288 (76.6)	
$40 001 to $60 000	72 (14.1)	≥$40 000	79 (22.5)		≥$40 000	88 (23.4)	
>$60 000	35 (6.9)						
Gestation, weeks				0.471			0.373
24-27	64 (12.6)						
28-31	42 (8.3)						
32-36	63 (12.4)	<37	113 (32.2)		<37	129 (34.3)	
≥37	340 (66.8)	≥37	238 (67.8)		≥37	247 (65.7)	
Admission type				0.015			0.500
Emergency	386 (75.8)	277 (78.9)			288 (76.6)		
Elective	123 (24.2)	74 (21.1)			88 (23.4)		

Results

Of 600 questionnaires distributed, 520 (86.7%) were returned. Of these, 11 were excluded owing to missing answers and 509 were included in analysis. All respondents had negative results of COVID-19. 27.7% were of advanced maternal age (≥35 years) and 46.0% were nulliparous. 42.2% had education level of tertiary or above. 21% had family income of ≥$40 000 per month. 66.8% were at term gestations (≥37 weeks) and 75.8% were emergency admissions (Table 1).

Of 509 women, 501 (98.4%) submitted deep throat saliva specimens and eight (1.6%) submitted nasopharyngeal swab specimens. More women felt that nasopharyngeal swab was uncomfortable (4.4% vs 37.5%, p=0.005) but considered that both sampling methods were convenient and acceptable (Table 2).

98.4% of the women agreed with universal screening for all obstetric patients on admission. 85.9% felt relieved if all patients in the ward had been screened for COVID-19. 85.1% considered that the test should not be allowed to opt out. 69.0%, 73.9%, and 72.1% of women considered that a negative COVID-19 result would have a positive effect on their own care, their baby's care, and their family, respectively, with 82.1% feeling more ready to breastfeed and 84.9% feeling more at ease to look after their babies after delivery. 97.2% thought that all staff in the obstetric ward should have COVID-19 screening (Table 3).

More women who considered that a negative COVID-19 test would have positive effects on their own care had tertiary education or above (79.1% vs 61.6%, p<0.001) and emergency admission (71.8% vs 60.2%, p=0.015) [Table 1]. More women who considered that a negative COVID-19 test would have positive effects on their baby's care had tertiary education or above (87.0% vs 64.3%, p<0.001) and family monthly income of ≥$40 000 (82.2% vs 71.6%, p=0.027) [Table 1]. In a binary logistic regression analysis, education level and the type of admission remained significant factors (Table 4).

Discussion

To control the outbreak, public compliance in precautionary behaviours is equally important to rapid and accurate diagnostic testing for COVID-19[6]. The preferred initial diagnostic test for COVID-19 is to detect SARS-CoV-2 RNA using the reverse-transcriptase polymerase chain reaction assay, from upper respiratory tract specimens[7], which include nasopharyngeal or oropharyngeal specimens, nasal swab specimens from both anterior nares, nasal mid-turbinate swab, nasopharyngeal wash / aspirate specimen, and saliva specimen. These specimens are usually collected by trained healthcare professionals, except for saliva specimens, which can be collected by the person at home or being supervised at the testing site[7].

In early September 2020, the Hong Kong government conducted a voluntary community screening programme and obtained nearly 1.8 million specimens. The programme identified 32 new confirmed cases, among which 13 were asymptomatic and 20 were local cases with unknown source of infection[8]. Since August 2020, the Hospital Authority has extended screening for COVID-19 to all asymptomatic in-patients and patients attending day services. The use of deep throat saliva specimens waives the need for healthcare workers to collect the specimen and thus reduces the use of personal protective equipment. Most respondents considered this method more acceptable and convenient than nasal and pharyngeal swabs. Saliva samples have a greater sensitivity for detecting early infection or screening asymptomatic patients, and results are more consistent throughout the course of infection[9]. Moreover, collection of nasopharyngeal swabs may cause discomfort to patients and increase exposure risks for healthcare workers[9].

Although there is no evidence that pregnant women are more susceptible of contracting COVID-19 than the general population, as in the SARS epidemic in 2003[10], there is increased anxiety among pregnant women about their own health, their partner's health, and their child's health, as well as pregnancy outcomes[11]. There is no concrete

Table 2. Opinions on sampling methods for COVID-19 screening

Question	Patients submitting deep throat saliva (n=501)	Patients submitting nasopharyngeal swab (n=8)	p Value
The screening method is convenient	484 (96.6)	8 (100.0)	1.000
The screening method is uncomfortable	22 (4.4)	3 (37.5)	0.005
The screening method is acceptable	496 (99.0)	7 (87.5)	0.091
Want to choose alternative screening method	85 (17.0)	3 (37.5)	0.145

Table 3. Opinions on universal screening during hospital admission

Question	No. (%) of respondents
Agree with universal screening	
Yes	501 (98.4)
No	8 (1.6)
Felt relieved if all the patients in the ward have been screened for COVID-19	
Yes	437 (85.9)
No	38 (7.5)
No difference	34 (6.7)
Agree that patients should be allowed to opt out the COVID-19 screening	
Yes	76 (14.9)
No	433 (85.1)
Think that a negative COVID-19 result has a positive effect on her care	
Yes	351 (69.0)
No	83 (16.3)
No difference	75 (14.7)
Think that a negative COVID-19 result will have a positive effect on her baby's care	
Yes	376 (73.9)
No	76 (14.9)
No difference	57 (11.2)
Think that a negative COVID-19 result has a positive effect on her family	
Yes	367 (72.1)
No	77 (15.1)
No difference	65 (12.8)
Think that a negative COVID-19 result will make her more ready to breastfeed after delivery	
Yes	418 (82.1)
No	33 (6.5)
No difference	58 (11.4)
Think that a negative COVID-19 result will make her more at ease to look after the baby after delivery	
Yes	432 (84.9)
No	26 (5.1)
No difference	51 (10.0)
Think that all the hospital staff in obstetric ward should have covid-19 screening	
Yes	495 (97.2)
No	14 (2.8)
When should the COVID-19 screening for obstetric patients on admission be discontinued	
When there are no more new cases worldwide	195 (38.3)
When there are no more new cases in Hong Kong	135 (26.5)
When the number of new cases in Hong Kong are fewer than a certain number per day such as 50	29 (5.7)
When vaccines for COVID-19 are available	150 (29.5)

evidence of vertical transmission of COVID-19 through breastfeeding[12]. Breastfeeding and skin-to-skin contact should continue during the COVID-19 pandemic after weighing potential benefits of breastfeeding and potential risks of pathogen transmission during breastfeeding[12-14]. Among Hong Kong pregnant women, up to 11.6% opted not to breastfeed because they believed that breastmilk could be a vehicle for COVID-19 transmission even if they were asymptomatic[4]. In our cohort, over 80% of women felt more reassured in breastfeeding and taking care of the baby when the screening test result was negative. Therefore, universal screening may help to relieve psychological stress of women and may be a useful tool in promoting breastfeeding during the pandemic.

In our study, education level was a significant factor affecting women's views on universal screening. A higher proportion of women with tertiary education believed that a negative screening result would have positive effects on their own and their baby's care. In contrast, our earlier study showed that pregnant women who opted out of universal screening during the antenatal course tended to have higher family monthly income (≥$40 000) or higher intention to deliver in private hospitals[4]. Therefore, the acceptance of universal screening was significantly higher in the present cohort. With repeated waves of COVID-19, the acceptance of universal screening is expected to increase.

Nearly all respondents agreed that hospital staff should be screened, which so far was not yet a policy adopted in the Hospital Authority hospitals. In a systemic review and meta-analysis of the prevalence of SARS-CoV-2 infection among healthcare workers globally, 11% healthcare workers were tested positive, with 7% being positive for the presence of antibodies and as high as 40% were asymptomatic at time of diagnosis, with nurses (48%) followed by physicians (25%) being the most frequently affected[14]. Because a significant portion of healthcare workers who test positive are asymptomatic, policymakers and hospital administrators should formulate plans to screen healthcare workers regularly, in order to minimise transmission risks and to meet the expectations of patients.

In our survey, 38% and 26% of respondents chose to stop screening when no new case is confirmed worldwide and in Hong Kong, respectively. Nearly 30% believed screening can be stopped when vaccines for COVID-19 are available, and 5.7% believed screening can be discontinued when the number of confirmed cases in Hong Kong drops to a certain number. Nonetheless, there is still a need to continue universal screening for all patients. The policy

Table 4. Factors affecting opinions on universal screening

Factors	B	SE	Wald	p Value	Odds ratio (95% confidence interval)
Believed that a negative COVID-19 result has positive effects on her care					
Tertiary education	0.859	0.207	17.181	<0.001	2.361 (1.573-3.544)
Emergency admission	0.522	0.220	5.671	0.018	1.686 (1.095-2.597)
Believed that a negative COVID-19 result has positive effects on her baby's care					
Tertiary education	1.285	0.250	26.517	<0.001	3.615 (2.217-5.897)
Family monthly income ≥$40000	0.095	0.300	0.099	0.752	1.099 (0.610-1.981)

should be regularly reviewed with respect to the incidence of COVID-19 infections and the cost-effectiveness of screening.

There are limitations to this study. The questionnaires were collected between the third and fourth wave of COVID-19 outbreak in Hong Kong. Results drawn from this survey reflect only the women's views at a certain point of time and may not be generalised to other populations or other time periods.

Conclusions

Universal screening for COVID-19 on admission to hospital is supported by obstetric patients, with deep throat saliva being the preferred method. Patients with higher education levels are more likely to believe that a negative screening result will have positive effects on their care and their babies' care, and are more relieved and reassured to breastfeed and to take care of their babies. Efforts should be made to promote COVID-19 screening for all women during antenatal care before admission and delivery.

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Ethics approval

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Author contributions

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.
Concept or design of the study: Chow CY, Kong CW
Acquisition of data: Chow CY, Lok WY, Kong CW
Analysis or interpretation of data: All authors
Drafting of the manuscript: Chow CY, Kong CW, To WWK
Critical revision for important intellectual content: All authors

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Appendix

We would appreciate it if you could spend 10 minutes completing the following questionnaire.
Please fill in the questionnaire and tick in the box where appropriate.
Choose only one option unless otherwise specified.
Please return the completed questionnaire to us before you are discharged from hospital.

Section 1: Background

1) What is your age? _____
2) How many babies have you delivered before?
   ❑ 0 ❑ 1 ❑ 2 ❑ 3 or above
3) What is your ethnicity?
   ❑ Chinese/ Hong Kong/ Taiwanese
   ❑ Filipino
   ❑ Pakistani
   ❑ Indian
   ❑ Caucasian
   ❑ Others: please specify _____
4) What is your education level?
   ❑ Primary school or below ❑ Secondary school ❑ Tertiary or above
5) What is your family income per month?
   ❑ <$20 000
   ❑ $20 000-$40 000
   ❑ $40 000-$60 000
   ❑ ≥$60 000
6) What is your current gestation?
   ❑ 24-27 weeks
   ❑ 28-31 weeks
   ❑ 32-36 weeks
   ❑ ≥37 weeks
7) What is your reason for the current admission?
   ❑ In labour/ show/ leaking/ uterine contractions
   ❑ Per vaginal bleeding
   ❑ Decrease fetal movement
   ❑ Induction of labour
   ❑ Planned caesarean section
   ❑ Clinically admitted for further work up such as diabetes for sugar profile
   ❑ Other reason: please specify_____

Appendix (cont'd)

Section 2: Opinions on universal screening for COVID-19 on hospital admission

1) What is the route of COVID-19 screening that you have performed?
   ❑ deep throat saliva ❑ nasopharyngeal swab
2) Do you think that the route of screening that you have undergone is convenient?
   ❑ Yes ❑ No
3) Have you felt uncomfortable with this route of screening?
   ❑ Yes ❑ No
4) Do you think that the route of screening that you have undergone is acceptable?
   ❑ Yes ❑ No
5) Will you prefer to choose another route of sampling if you have the choice?
   ❑ Yes ❑ No
6) Do you agree that the hospital should provide this COVID-19 screening for all obstetric patients upon admission?
   ❑ Agree
   ❑ Disagree
   If you disagree, the reason is:
   ❑ No need to do this screening at all
   ❑ No need to screen all the patients unless they have symptoms or travel or contact history
   ❑ Only need to screen those patients that are in labour or going to be delivered
   ❑ Other reasons, please specify: _____
7) Do you feel more relieved if all the patients in the ward had been screened for COVID-19?
   ❑ Yes ❑ No ❑ No difference
8) Do you think that patients should be allowed to opt out the screening if they don't want to have the test?
   ❑ Yes ❑ No
9) Do you think that a negative COVID-19 result will have a positive effect to your care?
   ❑ Yes ❑ No ❑ No difference
10) Do you think that a negative COVID-19 result will have a positive effect to your baby's care?
    ❑ Yes ❑ No ❑ No difference
11) Do you think that a negative COVID-19 result will have a positive effect to your family?
    ❑ Yes ❑ No ❑ No difference
12) Do you think that a negative COVID-19 test result will make you more ready to breastfeed after your delivery?
    ❑ Yes ❑ No ❑ No difference
13) Do you think that a negative COVID-19 test result will make you more at ease to look after your baby after your delivery?
    ❑ Yes ❑ No ❑ No difference
14) Do you think that all the staff in the obstetric ward should also be screened for COVID-19 infection regularly to make sure they are not infected?
    ❑ Yes ❑ No
15) Do you think that screening for COVID-19 for obstetric patients on admission should continue under which of the following situation?
    ❑ When there are no more new cases worldwide
    ❑ When there are no more new cases in Hong Kong
    ❑ When new case numbers in Hong Kong are fewer than a certain number per day, eg 50
    ❑ When vaccines for COVID-10 are available

~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~ End~~~~~~~~~~~~~~~~~~~~~~~~~~~~

This is the end of the questionnaire. Thank you very much for completing this questionnaire!
Please return the completed questionnaire us before you are discharged from hospital.
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Spontaneous septostomy of monochorionic dichorionic twin pregnancy: a case series

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We present four cases of confirmed spontaneous septostomy in monochorionic diamniotic twin pregnancy and one false positive case in a regional hospital in Hong Kong between 2011 and 2017. Three of the cases of spontaneous septostomy were detected antenatally.

Keywords: Amnion; Chorion; Pregnancy, twin; Umbilical cord

Introduction

Multiple pregnancy is high risk. With the increasing use of artificial reproductive techniques, the number of twin pregnancies is increasing. Ultrasound assessment of chorionicity and amnionicity starting at first trimester is important because different types of twin pregnancies have different risk management. We present five cases of spontaneous septostomy in women with monochorionic diamniotic (MCDA) twin pregnancy. Early detection is important in reducing morbidity and mortality of both twins.

Case presentation

Case 1

In 2011, a 28-year-old, parity 0 woman with spontaneous MCDA twin pregnancy was followed up in our unit. She had impaired glucose tolerance and developed pre-eclampsia since 30 weeks of gestations. She was admitted to our hospital for close monitoring of the blood pressure and for fetal monitoring using ultrasonography and cardiotocography. At 31 weeks of gestation, ultrasonography showed intrauterine growth retardation of the left twin, while the right twin (leading twin) had normal growth. At 32 weeks of gestation, there was swabbing of the twin positions and disappearance of a part of the inter-twin membrane. Steroid prophylaxis was given to prevent preterm delivery. At 33 week of gestation, lower segment caesarean section was performed in view of pre-eclampsia, selective intrauterine growth retardation, and possible spontaneous septostomy. Intra-operatively, twin 2 was delivered after twin 1 without the need of membrane rupture (Figure 1). Twin 1 had a birth weight of 1.89 kg and an Apgar score of 8(1)10(5), whereas twin 2 had a birth weight of 1.31 kg and an Apgar score of 9(1)10(5).

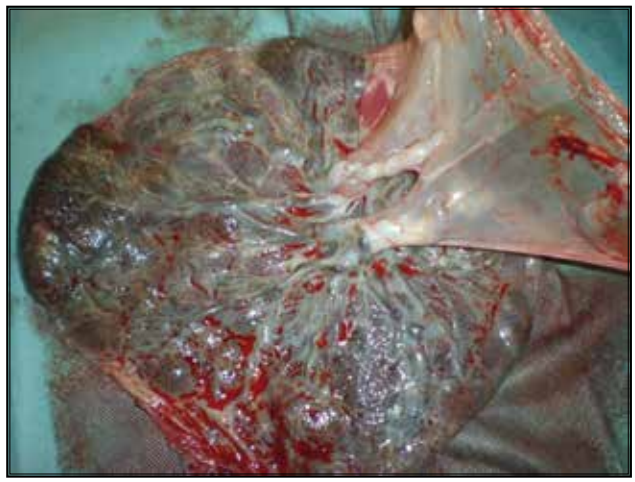

Figure 1. Case 1: intertwin membrane is absent

Case 2

In 2014, a 28-year-old, parity 0 woman with spontaneous MCDA twin pregnancy was followed up in our unit. Ultrasonography showed the right twin having an umbilical cord with one artery (rather than two) and one vein, while the left twin was normal. The intertwin membrane was observed. Regular ultrasonography showed intrauterine growth restriction of the right twin since 34 weeks of gestation, but the patient refused early delivery. At 36 weeks of gestation, elective lower segment caesarean section was performed on request. Intra-operatively, twin 2 was delivered spontaneously without any membrane ruptured after twin 1 was delivered. On gross examination of the placenta, the intertwin membrane was not seen, and both umbilical cords were close at their insertion sites. Twin 1 was a boy with a birth weight of 2.52 kg and an

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Apgar score of 9(1)10(5), whereas twin 2 was a boy with a birth weight of 2.24 kg and an Apgar score of 9(1)10(5). Spontaneous septostomy was diagnosed after delivery.

Case 3

In July 2016, a 31-year-old, parity 0 woman with spontaneous MCDA twin pregnancy (confirmed at 13 weeks of gestation) was followed up in our unit. At 28 weeks of gestation, spontaneous septostomy was suspected, as no definite inter-twin septum was seen and the only remnant of membrane was seen at the right upper quadrant (Figure 2) and left upper quadrant. There was 'cross-over' of the cord at the centre (Figure 2) but no evidence of cord entanglement. The pregnancy was managed as monochorionic monoamniotic twin with regular ultrasonographic monitoring. In view of the risk of preterm delivery, steroid prophylaxis was given, with an aim of early delivery. At 33 weeks of gestation, elective lower segment caesarean section was performed. Twin 1 (left twin) weighed 1.332 kg and twin 2 (right twin) weighed 1.71 kg. The placenta showed twisting of the cords for two rounds.

Case 4

In December 2016, a 32-year-old, parity 0 woman with spontaneous MCDA twin pregnancy (confirmed at 12 weeks of gestation) were followed up at our unit. At 18 weeks of gestation, ultrasonography showed a single umbilical artery for the right twin and normal two umbilical arteries for the left twin. At 32 weeks of gestation, no membrane was observed between two cord insertions, but the intertwin membrane was seen in other parts. There was a switch of position of the twins, with the fetus having a single umbilical artery at the upper left part. Growth of both fetuses was satisfactory with normal liquor and dopplers. There was no evidence of cord entanglement. In view of suspected spontaneous septostomy, prophylactic steroid was given. At 33 weeks and 6 days of gestation, lower segment caesarean section under spinal anaesthesia was performed. Twin 1 (right twin) was a girl with a birth weight of 1.740 kg and twin 2 (left twin) was a girl with a birth weight of 1.825 kg with a good Apgar score. A defect over the intertwin membrane was noted. Both twins were admitted to the special care baby unit for close monitoring. The left twin underwent ultrasonographic assessment of the kidneys for the single umbilical artery.

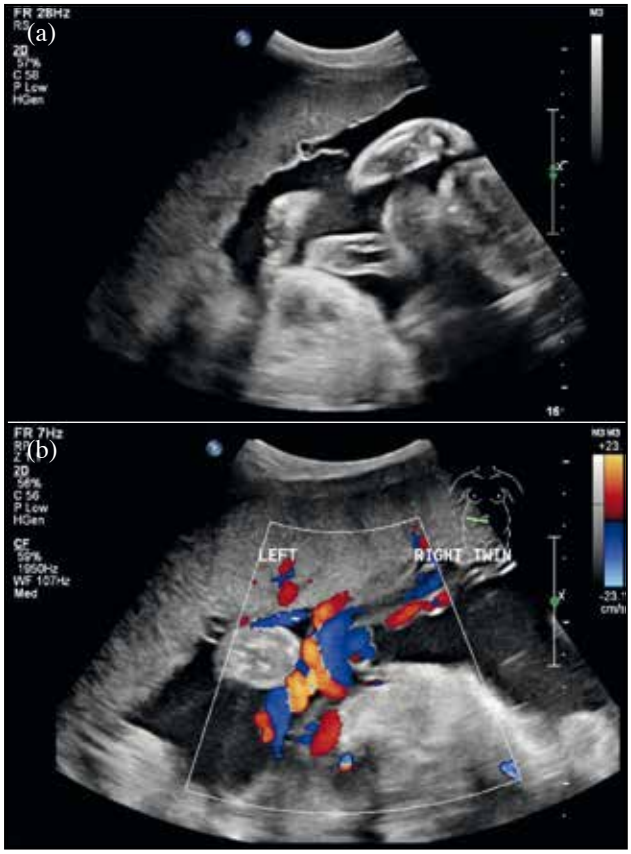

Figure 2. Case 3: ultrasonographs showing (a) remnant of the intertwin membrane and (b) 'cross-over' of the two cords

Case 5

In 2017, a 29-year-old, parity 1 woman with spontaneous MCDA twin pregnancy (confirmed at 13 weeks of gestation) was followed up at our unit. There was discordance of the thickness of nuchal translucency. The patient declined invasive test and opted for non-invasive prenatal testing in a private hospital, with negative results. Ultrasonography showed polyhydramnios in the left twin but no other evidence of twin-twin transfusion syndrome. At 34 weeks of gestation, the only remnant of the intertwin membrane was seen at the upper cavity, with 'normalisation' of the liquor. At 35 weeks of gestation, elective lower segment caesarean section was performed uneventfully. Twin 1 was a boy weighing 2.09 kg and twin 2 was a boy weighing 2.08 kg. As the inter-twin septum was present upon delivery, this case was a false positive.

Discussion

Spontaneous septostomy, or pseudo-amniotic twin in monochorionic diamniotic twin pregnancy has been described, but only one case report of spontaneous septostomy in dichorionic twin was reported[1]. The actual incidence is unknown as reported cases are limited. Within 7 years in our hospital, 613 pairs of twin pregnancy were delivered, and 141 (23%) were estimated to be MCDA according to our previous cohort study[2]. Therefore, the incidence of spontaneous septostomy in MCDA twin is estimated to be 4/141=2.8%.

Monochorionic twin pregnancies are associated

with higher perinatal risks, compared with dichorionic twins. The vascular anastomosis in monochorionic twins increased the perinatal risks of preterm deliveries, twin-twin transfusion syndrome, selective growth discordancy, and intrauterine death[3]. The chorionicity should thus best be determined before 14 weeks of gestation[4]. Our patients received ultrasonographic examination at 12 to 13 weeks of gestation. A thin intertwin membrane without lambda sign is indicative of monochorionic diamniotic twin.

According to the Royal College of Obstetricians and Gynaecologists guideline[4], 'mapping' of fetuses, fetal parameters, and liquor volume by measuring single deepest pocket, umbilical dopplers, and middle cerebral artery dopplers should be documented in every scan. In case 4, one of the fetuses had a single umbilical artery, which allowed us to identify the swapping of the position and hence identifying the spontaneous septostomy. In case 2, we missed the clue of a single umbilical artery in one fetus, which is associated with selective intrauterine growth restriction. These cases highlight the importance of detailed mapping of the fetuses in detection of spontaneous septostomy.

Spontaneous septostomy leads to the change of two separated compartments into one single compartment that resembles monochorionic monoamniotic twins[5]. Its main risk is cord entanglement, which occurs in about 60% of spontaneous septostomy and in almost all monochorionic monoamniotic twins[6]. Cord entanglement can lead to fetal demise of both twins[7]. Other risk associated with septostomy is preterm delivery and amniotic band syndrome[8]. However, there are also cases of septostomy without any complications[1].

Identification of the septostomy depends on clinical suspicious. Features suggestive of spontaneous septostomy include free-floating or folded sheets of amnion[9] in the gestational sac and body, limbs, or umbilical cord of one twin prolapsed through two chorions into the other sac[1]. Careful inspection of the intertwin membrane is recommended through visualising the whole course of the membrane as much as possible at every follow-up examination[5]. The distance between the cord should be documented, as it may be associated with cord entanglement[9]. In our patients, defect of the intertwin membrane was identified when the position of the fetuses switched or when the only remnant of the membrane was seen or when the cords crossed. Nonetheless, case 5 highlighted the pitfall of a false alarm by the absence of part of the inter-twin septum, sudden equalisation of the liquor volume, and suspected cord entanglement. In our series, both the prenatal detection rate and the positive predictive value was 75% (3/4).

Conclusion

Spontaneous septostomy is uncommon but can complicate monochorionic diamniotic twin pregnancy with adverse perinatal outcomes. Prenatal detection with high clinical suspicions and detailed mapping is important during serial antenatal scans. Early detection and management improve outcome.

Declaration

The authors have no conflict of interest to disclose.

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Prevalence and outcomes of hepatic flare in hepatitis B carriers during pregnancy

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Introduction: The aim of this study was to examine the prevalence and severity of hepatic flare among pregnant women with chronic hepatitis B (CHB) and to assess pregnancy and neonatal outcomes.
Methods: Records of all hepatitis B surface antigen-positive pregnant women who had their first antenatal visit between January 2017 and December 2018 and had a live birth in the Department of Obstetrics and Gynaecology, Queen Elizabeth Hospital, Hong Kong were retrospectively reviewed. Hepatic flare was defined as an alanine aminotransferase (ALT) ≥2 times the upper limit of normal, which is 19 U/L for females. Pregnancy and neonatal outcomes between those with and without hepatic flare were compared.
Results: 6.3% of pregnant women with CHB had hepatic flare, with ALT level ranging from 39 to 179 IU/L. None of the women had hyperbilirubinemia or liver failure. In those with hepatic flare, the median hepatitis B virus DNA level was 5.77 $\log^{10}$ IU/mL. The rate of postpartum haemorrhage was higher in those with hepatic flare (19.4% vs 10.8%, p=0.024).
Conclusion: 6.3% of pregnant women with CHB had hepatic flare. The rate of postpartum haemorrhage was higher in those with hepatic flare. Monitoring of liver function is recommended in pregnant women with CHB and hepatic flare.

Keywords: Hepatitis B; Pregnancy

Introduction

Worldwide, 257 million people are estimated to be chronically infected with hepatitis B virus (HBV)[1], which can lead to cirrhosis and liver cancer. In Hong Kong, the seroprevalence of HBV is 7.8% in the general population[2] and 4.5% among antenatal women[3]. Although most pregnant women with chronic hepatitis B infection (CHB) are generally well, cases of hepatic flares[4-9] or acute liver failure[4,7,8] have been reported. Current opinions on the impact of HBV on pregnancy and perinatal outcomes are conflicting[10-15]. CHB is associated with gestational diabetes mellitus, antepartum haemorrhage, preterm labour, preterm premature rupture of membrane, lower Apgar score, and postpartum haemorrhage (PPH)[12-15]. Pregnant women with severely abnormal liver function are more likely to have postpartum haemorrhage, puerperal infection, premature birth, and fetal death[7,14].

In Hong Kong, all pregnant women are screened for hepatitis B surface antigen (HBsAg). Since October 2016, liver function test (LFT) has been routinely carried out for pregnant women positive for HBsAg in the Queen Elizabeth Hospital, Hong Kong. Those with hepatic flares are referred to hepatologists for assessment and monitoring of liver function. HBV DNA levels are checked, and antivirals may be prescribed. Nonetheless, the rate and consequence of hepatic flare in Hong Kong pregnant women remain unknown. These data can guide monitoring and management during pregnancy and counselling for pregnant women with CHB. Thus, the present study aimed to determine the prevalence and severity of hepatic flare in pregnant women with CHB and to assess the maternal and perinatal outcomes.

Methods

This study was approved by the Kowloon Central/ Kowloon East Cluster Research Ethics Committee (reference: REC (KC/KE)-20-0109/ER-2). Records of all HBsAg-positive pregnant women who had their first antenatal visit between January 2017 and December 2018 and had a live birth in the Department of Obstetrics and Gynaecology, Queen Elizabeth Hospital, Hong Kong were identified using the ICD codes. Data collected included demographics, laboratory results, medical history, and antenatal, intrapartum, and postpartum records. Those with multiple comorbidities, multiple pregnancies, or incomplete data (eg, LFT not performed or delivered elsewhere) were excluded, as were those with hepatic flare secondary to known alcoholic liver disease, other viral hepatitis, drug-induced hepatic injury, or other liver diseases.

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Hepatic flare was defined as an alanine aminotransferase (ALT) level ≥2 times the upper limit of normal[16], which is 19 U/L for females[17]. Its severity was determined based on the ALT level, any episode of liver decompensation (including ascites, variceal bleeding, or hepatic encephalopathy), and bilirubin and HBV DNA levels.

Pregnancy outcomes between those with and without hepatic flare were compared, including rates of antepartum complications (antepartum haemorrhage, pre-eclampsia, gestational diabetes mellitus, intrauterine growth restriction, and preterm premature rupture of membrane), delivery gestational age, rate of preterm delivery, intrapartum and postpartum outcomes (rate of induction of labour, mode of delivery, blood loss, and PPH [blood loss of >500 mL[18]]), and neonatal outcomes (rate of fetal distress, birth weight, Apgar score at 5 minutes, and neonatal intensive care unit admission).

Statistical analysis was performed using SPSS (Mac version 26; IBM Corp, Armonk [NY], US). Continuous variables were analysed using the t-test and categorical variables using the Chi-squared test or Fisher's exact test. A p value of <0.05 was considered statistically significant.

Results

Of 661 (5.8% of the total) pregnant women with CHB, 169 were excluded owing to no LFT performed (n=8), miscarriages or termination of pregnancy (n=30), lost to follow-up or delivery in other hospitals (n=117), or twin pregnancies (n=14). None of these cases had other known underlying liver disease or multiple comorbidities. The remaining 492 women were included for analysis (Figure). The median gestational age when the LFT was taken was 21 weeks. There were more nulliparous women in the hepatic flare group (61.3% vs 42.2%, p=0.042, Table 1).

31 (6.31%) pregnant women with CHB had hepatic flare at booking, with an ALT level ranging from 39 to 179 (median, 50) IU/L. Of them, 27 (87%) had ALT ≥2 times the upper limit of normal and four (12.9%) had ALT ≥5 times the upper limit of normal. All women had normal bilirubin levels (5.23±2.54 μmol/L), and none had liver failure during pregnancy.

Of the 31 women with hepatic flare, 23 (74.2%) had HBV DNA checked, with levels ranging from 17.7 IU/mL to >9 $\log_{10}$ IU/mL (median, 5.77 $\log_{10}$ IU/mL). The level was ≥5.3 $\log_{10}$ IU/mL in 15 (65%) women and ≥7 $\log_{10}$ IU/mL in nine (39%) women. There was no correlation between ALT and HBV DNA levels (r=0.005, p=0.982). Antiviral drugs were initiated in 21 (4.2%) women to prevent maternal-to-child transmission. Of them, 13 had hepatic flare and eight had HBV DNA levels >5.3 $\log_{10}$ IU/mL.

Women with hepatic flare had a higher rate of PPH (19.4% vs 10.8%, p=0.024) but a similar volume of blood loss during delivery (342 mL vs 307 mL, p=0.402), and had a higher Apgar score at 5 minutes (8.61 vs 8.31, p=0.017) but a similar rate of having an Apgar score <7 at 5 minutes (0% vs 1.1%, p=0.721) [Table 2].

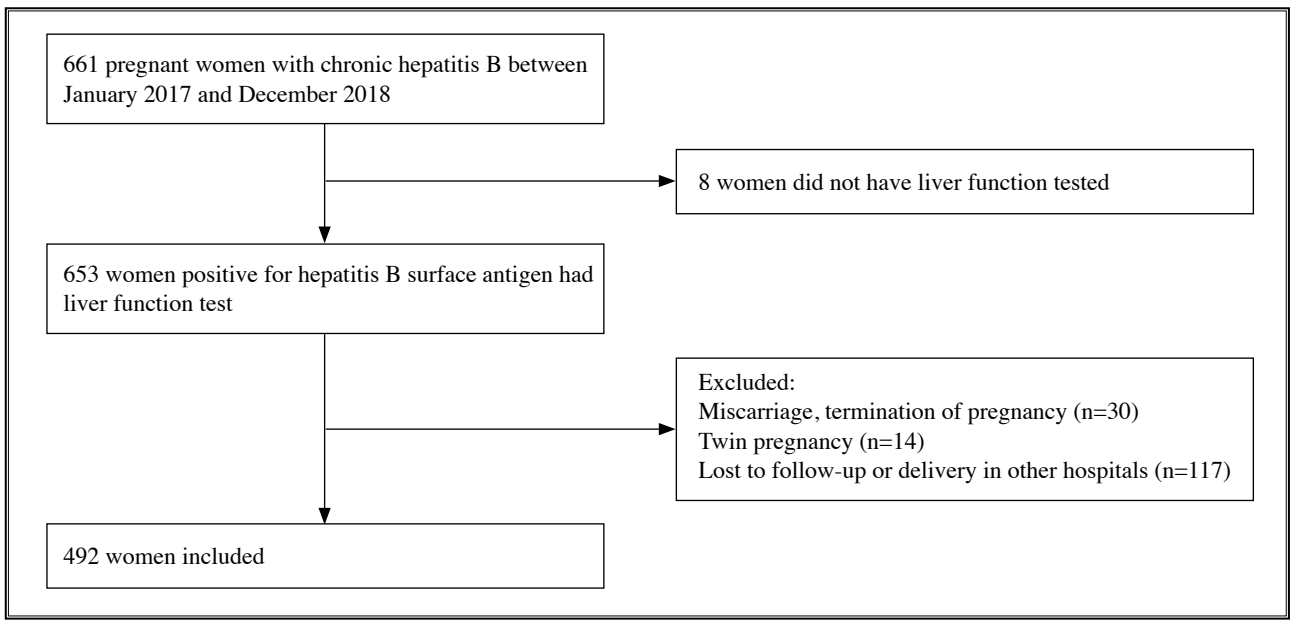

Figure. Flowchart of inclusion of pregnant women with chronic hepatitis B and hepatic flare

Table 1. Pregnant women with chronic hepatitis B stratified by the presence of hepatic flare

Demographic	Without hepatic flare (n=461)	With hepatic flare (n=31)	p Value
Maternal age, y	33.52±4.05	33.29±4.18	0.756
Advanced maternal age	182 (39.5)	9 (29)	0.262
Body mass index, kg/m^2	21.63±3.32	22.68±3.88	0.092
Nulliparous	195 (42.3)	19 (61.3)	0.042
Smoking	18 (3.9)	1 (3.2)	0.849
Drinking	1 (0.2)	0 (0)	0.937
Substance abuse	3 (0.7)	0 (0)	0.822
Education level			0.900
Primary	10 (2.2)	1 (3.2)	
Secondary	245 (53.1)	17 (54.8)	
Tertiary	206 (44.8)	13 (41.9)	

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

Table 2. Pregnancy and neonatal outcomes of pregnant women with chronic hepatitis B stratified by the presence of hepatic flare

Pregnancy and neonatal outcome	Liver function test		p Value
	Normal (n=461)	Abnormal (n=31)	
Antepartum haemorrhage	24 (5.2)	1 (3.2)	0.522
Pre-eclampsia	8 (1.7)	1 (3.2)	0.446
Gestational diabetes	70 (15.2)	7 (22.6)	0.304
Intrauterine growth restriction	14 (3.0)	1 (3.2)	0.629
Preterm premature rupture of membrane	8 (1.7)	0 (0)	0.592
Preterm delivery	30 (6.5)	1 (3.2)	0.711
Gestational age, weeks	38.45±1.69	38.32±1.45	0.679
Induction of labour	196 (42.5)	18 (58.1)	0.091
Mode of delivery			
Vaginal	284 (61.6)	15 (48.4)	0.133
Instrumental	33 (7.2)	5 (16.1)	
Caesarean section	144 (31.2)	11 (35.5)	
Blood loss	307.26±10.41	341.94±38.17	0.402
Postpartum haemorrhage	50 (10.8)	6 (19.4)	0.024
Birth weight, g	3155.32	3085.48	0.405
Fetal distress	12 (2.6)	1 (3.2)	0.603
Apgar score at 5 min	8.31	8.61	0.017
Apgar score <7 at 5 min	5 (1.1)	0 (0)	0.721
Neonatal intensive care unit admission	65 (14.1)	4 (12.9)	0.553

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

Discussion

In the present study, the incidence of hepatic flare was 6.3%, which is lower than the 9% to 14% reported from other studies[4-6]. The timing of LFT, which was usually in the second trimester, may account for the lower incidence, as the risk of hepatic flare is highest in the first trimester and then gradually decline during pregnancy[5,19]. The LFT was performed only once at booking and was not repeated if it was normal; flare up in later gestations could have been missed.

In the second and third decades of life, transition from the immune tolerance phase to the immune-active phase of perinatally acquired HBV is common. Spontaneous HBeAg seroconversion is frequently accompanied by an increase in the ALT level[20]. In addition, pregnancy increases spontaneous HBeAg seroconversion[21,22]. Routine LFT for pregnant women may identify those in the immune-active phase of CHB. Immune modulation occurs during pregnancy in order to tolerate paternal semi-allogeneic tissues and prevent fetus rejection[23]. As HBV infection is predominantly an immune-mediated disease[24], immune and hormonal changes during pregnancy facilitate viral activity and is responsible for hepatic flare during pregnancy[5,7]. This may explain why more nulliparous women, who are more likely to have immune maladaptation[25], have hepatic flare.

Pregnant women with high viral load are more likely to have hepatic flare[5]. Viraemic mothers have significantly higher ALT level[26]. However, there was no correlation between ALT and HBV DNA levels (r=0.005, p=0.982), although half of pregnant women with hepatic flare had HBV DNA level >5.3 $\log^{10}$ IU/mL. This may be due to the small sample size with HBV DNA level tested, as HBV DNA levels were not checked in most pregnant women with normal ALT level. However, eight women without hepatic flare were found to have high viral loads and were prescribed with antivirals for prevention of maternal-to-child transmission. Checking HBV DNA level routinely in all pregnant women with CHB can identify those with high viral load, even if they do not have flare, so that antenatal antivirals can be prescribed. Since August 2020, HBV DNA level has been assessed for all pregnant women with CHB in our hospital.

The risk of PPH increases in pregnant women with CHB[15]. During hepatic flare, hepatic cells are damaged, affecting the synthesis of the coagulation factor. In women with hepatic flare, the rates of induction of labour and instrumental delivery were higher, which may account for the higher incidence of PPH.

Obstetric causes of hepatic flare such as pre-eclampsia and acute fatty liver of pregnancy are difficult to be differentiated from HBV flare during antenatal period[27]. These obstetric causes may also result in increased use of induction of labour or instrumental delivery. However, there was no difference in neonatal outcomes, including the rate of prematurity, birth weight, rate of fetal distress, and neonatal intensive care unit admission.

The treatment goals for CHB in pregnancy are to monitor for any maternal flare and prevent maternal-to-child transmission[21,28]. Checking ALT level in HBV-infected pregnant women at booking visits is recommended to screen for possible flare and determine severity and guide management. For many women, the initial diagnosis of HBV infection is made during pregnancy. LFT at booking can determine the severity of liver condition and exclude any unrecognised severe conditions such as liver cirrhosis. Monitoring of liver function in pregnancy can identify pregnant women with hepatic flare who may need antivirals.

The findings of the present study can be used to guide counselling of pregnant women with CHB. Severe hepatic flare with complications can be fatal. Monitoring is advised, and use of antivirals may be indicated. The risk of PPH in those with hepatic flare should be aware. Blood tests for platelet count and coagulation should be performed; any coagulopathy should be reversed.

There are limitations to our study. First, LFT was performed once only during the first antenatal visit. Changes in the later gestation could have been missed, and the effect of pregnancy on liver disease progress cannot be assessed. Second, other causes of deranged live function were not ruled out such as fatty liver or other viral infections. Third, the effect of antiviral treatment to pregnancy outcome was not evaluated. Fourth, the HBeAg status was not checked, so the phase of HBV disease and the effect of HBeAg could not be assessed.

Conclusion

About 6.3% of pregnant women with CHB had hepatic flare; 12.9% of them had ALT level ≥5 times the upper limit of normal. None had liver decompensation. The rate of PPH was higher in pregnant women with hepatic flare. Monitoring of liver function is recommended in pregnant women with CHB and hepatic flare.

Declaration

The authors have no conflict of interest to disclose.

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Ultrasonographic tracking of the proximal humerus during second stage of labour for detection of shoulder dystocia

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We conducted a pilot study of ultrasonographic tracking of anterior shoulder engagement at the second stage of labour to look for any warning sign for shoulder dystocia in 12 women.

Keywords: Shoulder dystocia; Ultrasonography

Introduction

Traditionally, shoulder dystocia can only be observed through the 'turtle sign' after delivery of fetal head. The International Society of Ultrasound in Obstetrics and Gynaecology recommends that ultrasonography be used to ascertain fetal head position and station before considering instrumental vaginal delivery[1]. Ultrasonographic examination of the scapular orientation to determine shoulder engagement has been reported[2], as has continuous tracking of the proximal humerus (anterior shoulder) as direct visualisation of the shoulder engagement[3]. We carried out a pilot study to look for any warning sign of shoulder dystocia at the second stage of labour by continuous tracking of the proximal humerus.

Methods

This study was approved by Kowloon Central / Kowloon East Cluster Research Ethics Committee (reference: KC/KE-19-0160/ER-4). From January 2016 to August 2018, 12 non-consecutive women with full-term singleton pregnancy at risk of shoulder dystocia were recruited. The risk factors included short stature, macrosomia, previous shoulder dystocia, oxytocin augmentation, prolonged second stage, and vacuum extraction (Table 1). The ultrasonographic probe was

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Table 1. Demographics of the 12 women

Case	Age, y	Parity	Gestation, weeks	Risk factors for shoulder dystocia	Onset of labour
1	31	1	39	Short stature, polyhydramnios, prolonged second stage	Induction of labour
2	26	0	40	Nil	Augmentation
3	40	3	38	Previous macrosomia, gestational diabetes mellitus / large for gestational age	Induction of labour
4	40	1	39	Previous shoulder dystocia, gestational diabetes mellitus	Induction of labour
5	40	0	38	Prolonged second stage	Induction of labour
6	32	0	38	Polyhydramnios, prolonged second stage	Induction of labour
7	34	0	39	Maternal fever, prolonged second stage	Induction of labour
8	22	0	38	Nil	Induction of labour
9	31	0	39	Hypertension	Induction of labour
10	27	1	39	Large for gestational age, prolonged second stage	Induction of labour
11	40	0	39	Gestational diabetes mellitus, large for gestational age	Induction of labour
12	26	0	39	Pre-eclampsia, prolonged second stage	Induction of labour

placed sagittally and perpendicular to the suprapubic region of the maternal abdomen. The proximal humerus was traced continuously from the expulsive phase before crowning of the fetal head until the delivery of the baby.

Results

Two phases of anterior shoulder engagement were observed. For the nine women without shoulder dystocia, the proximal humerus of the baby moved downwards simultaneously with the descent of the baby head at the initial phase, followed by the disappearance of the proximal humerus just before delivery of the baby head (Figure 1). For the three women complicated by shoulder dystocia, the proximal humerus of the baby descended horizontally at the initial phase, and the proximal humerus was persistently visualised above the pubic symphysis even after delivery of the baby head (Figure 2). All babies were delivered by external or internal manoeuvres within 2 minutes of delivery of the baby head. There were no adverse birth outcomes (Table 2).

Discussion

To the best of my knowledge, we are the first to study the shoulder engagement of the baby by ultrasonographic tracking of the proximal anterior humerus during delivery. Although the time interval between the ultrasonographic findings and occurrence of shoulder dystocia is short, this finding may be a potential warning sign for shoulder dystocia. Further research with a larger sample size is needed to verify these ultrasonographic observations, which can be classified into normal delivery and complicated by shoulder dystocia. On speculation, those with clavicular fracture may represent an intermediate group.

Conclusion

Engagement of the anterior shoulder during the

Figure 1. Normal engagement of the anterior shoulder by transabdominal ultrasonography (sagittal plane over suprapubic region).

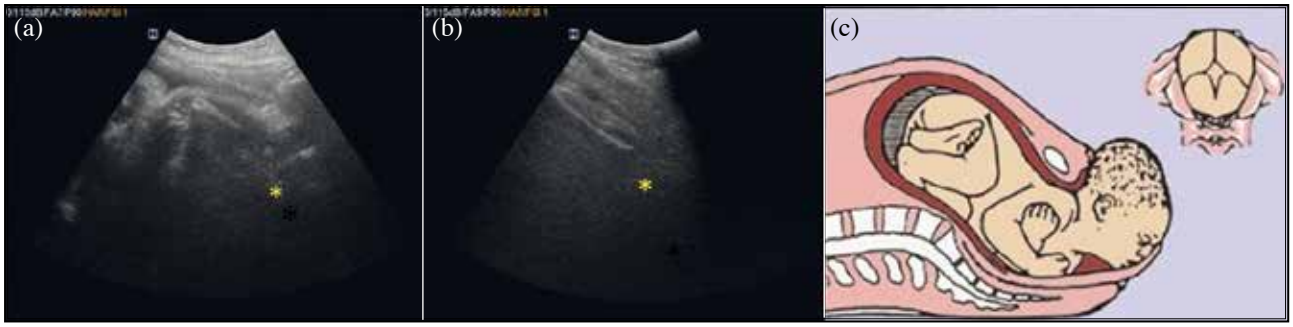

Figure 2. Second phase of shoulder engagement upon crowning/delivery of the baby head: (a) normal engagement of anterior shoulder with disappearance of the proximal humerus (asterisk), (b) persistence visualisation of the proximal humerus in a case of shoulder dystocia (asterisk), and (c) schematic representation.

Table 2. Transabdominal ultrasonographic findings and pregnancy outcome

Case	Fetal head position	Direction during descent	Proximal anterior humerus seen above pubis		Mode of delivery	Birth weight, kg	Apgar score	Shoulder dystocia	Remarks
			At crowning	At head out					
1	Direct occiput anterior	Downward	Yes	No	Normal spontaneous	3.82	8, 9	No	-
2	Left occiput anterior	Downward	Yes	No	Normal spontaneous	3.18	8, 9	No	-
3	Direct occiput anterior	Downward	Yes	No	Normal spontaneous	4.3	10, 10	No	-
4	Right occiput anterior	Downward	No	No	Normal spontaneous	3.78	9, 10	No	-
5	Right occiput anterior	Downward	No	No	Vacuum extraction	3.01	8, 9	No	-
6	Right occiput posterior	Downward	Yes	No	Vacuum extraction	3.21	8, 9	No	-
7	Right occiput anterior	Horizontal	Yes	Yes	Vacuum extraction	3.58	8, 10	Yes	Head to delivery interval=1 min 40 sec, delivered by posterior arm
8	Right occiput posterior	Horizontal then Downward	Yes	No	Vacuum extraction (non-reassuring fetal status)	2.81	9, 10	No	Fracture left clavicle
9	Right occiput transverse	Horizontal then Downward	Yes	Yes	Vacuum extraction (non-reassuring fetal status)	2.56	8, 9	Yes	Head to delivery interval=1 min, delivered by posterior arm
10	Right occiput anterior	Horizontal then downward	Yes	Yes (bounced back after transient engage-ment)	Vacuum extraction	3.85	9, 10	Yes	Head to delivery interval=30 sec, delivered by McRobert & suprapubic pressure
11	Right occiput posterior	Downward	No	No	Vacuum extraction (non-reassuring fetal status)	3.74	9, 10	No	-
12	Right occiput posterior	Downward	No	No	Vacuum extraction (4 pulls)	3.01	8, 9	No	-

second stage of labour can be observed by transabdominal ultrasonography. Difference between those with and without shoulder dystocia are observed.

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Declaration

The authors have no conflicts of interest to disclose. An abstract of a study of our first nine cases has been published in: WL Lau, V Ng, L Lai, et al. OC16.05: Sonographic assessment of shoulder engagement and a novel sign in early recognition of shoulder dystocia. Ultrasound Obstet Gynecol 2018;52(Suppl 1):1-65.

Author contributions

WLL was responsible for literature review, data collection, result interpretation, and manuscript writing. VC and VN contributed to manuscript review. All authors approved the final version to be published and agreed to be accountable for the accuracy and integrity of the work.

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Prevention of maternal-to-child transmission of hepatitis B: a narrative review

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Chronic hepatitis B virus (HBV) infection can result in cirrhosis and hepatocellular carcinoma. Most chronic HBV infections are caused by mother-to-child transmission during the perinatal period. The World Health Organization aims to eradicate HBV globally by 2030. Hong Kong has implemented a wide range of preventive strategies to decrease maternal-to-child transmission. This review summarises the experience in Hong Kong and the current recommendations to prevent HBV vertical transmission.

Keywords: Antiviral agents; Hepatitis B virus; Infectious disease transmission, vertical; Pregnancy; Vaccination

Introduction

Around 257 million people have chronic hepatitis B virus (HBV) infection, and around 887 000 people have died from HBV-related complications. Only 10.5% of chronic carriers (27 million people) are aware of their infection[1], and most carriers are unrecognised, with no monitoring or treatment. In Hong Kong, the prevalence of HBV has decreased steadily from 1990 to 2018[2] but remains high (7.8%) according to the territory-wide prevalence study in 2015-2016[3]. HBV infection can be acquired through vertical or horizontal transmission, but the former has a higher chance of progressing to chronic infection. This review focuses on maternal-to-child transmission (MTCT) of HBV and its prevention in Hong Kong.

Preventive strategies

Hong Kong was once an area of high HBV endemicity. Different preventive strategies have been implemented to bring down its prevalence. Antenatal screening of hepatitis B surface antigen (HBsAg) is performed in all pregnant women, aiming to identify unrecognised chronic carriers. HBV vaccination and hepatitis B immunoglobulin (HBIg) injection to newborns of carrier mothers have been implemented since 1984, and universal neonatal HBV vaccination has been implemented since 1988[4]. The HBV carriage rate has decreased steadily between 1990 and 2018 from 11.3% to 4.5% in the antenatal population and from 9.6% to 4.9% in the premarital check-up population[2].

Aiming to eradicate HBV vertical transmission, triage of women with a high viral load to receive tenofovir disoproxil fumarate (TDF) has introduced in Queen Mary Hospital and Prince of Wales Hospital since January 2020 and has expanded to other units since August 2020. This is in line with the World Health Organization target to decrease the prevalence of HBV infection in children to 0.1% (ie, 90% reduction in the incidence of new HBV infections) by 2030[5-7].

Knowledge and healthcare pattern

Only around 14% of the adult population in Hong Kong have a good knowledge of HBV infection[8]. Pregnant women in Hong Kong have insufficient knowledge on the modes of transmission, prevention, and possible sequelae of HBV infection[9]. Most pregnant HBV carriers in Hong Kong are not evaluated by a hepatologist during and after delivery (86.4% and 52.6%, respectively), although 91% of them are aware of their HBV carrier status before pregnancy[10]. Pregnancy initiates basic biochemical and virological investigations as well as multidisciplinary care (with hepatologists) for these HBV carriers. Long-term care of these women decreases MTCT by starting antiviral treatment in the third trimester in women with high HBV DNA.

MTCT and immunoprophylaxis failure

When HBIg or vaccination is not given to the newborns of HBV carriers, the rate of MTCT can be as high as 73%. A completed course of HBV vaccination reduces the MTCT rate to ~21% and further to 2.9% to 6.8% with the addition of birth dose HBIg[11]. Timely administration of HBIg and birth dose HBV vaccine within 1 to 2 hours can reduce the MTCT rate to as low as 0.9% to 2%[12,13].

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Immunoprophylaxis failure (IF) refers to persistent MTCT despite neonatal HBIg and HBV vaccination and is defined by seropositive HBsAg or HBV DNA level at 2 to 3 months after completion of vaccination[14]. The mechanisms of IF include germline infection at conception, maternal blood contamination at the time of prenatal invasive procedures, and contact with maternal secretion during labour. The risk of IF increases with a positive hepatitis B e antigen status and high HBV DNA viral load[15]. The IF rate depends on the provision and the coverage of HBIg and HBV vaccination. Among Hong Kong children aged 2 to 5 years, the coverage of the three doses of HBV vaccination is almost 100%, but the IF rate remains at 1.1%, according to a multicentre study in 2014-2016[2]. Positive hepatitis B e antigen and high HBV DNA viral load of ≥8 $\log_{10}$ copies/mL (≥7.23 $\log_{10}$ IU/mL) at 28 to 30 weeks are predictors of IF[16].

Maternal antiviral treatment

A high viral load is a predictor of IF. Viral load suppression through antiviral treatment during pregnancy can prevent IF in highly viraemic pregnant women. Lamivudine, telbivudine, and TDF are nucleoside and nucleotide analogues that can be used safely during pregnancy for the prevention of MTCT[17]. TDF is the preferred treatment as it has a high potency and a strong barrier to resistance[18,19]. In a study in China involving 200 HBV carrier mothers with HBV DNA >200 000 IU/mL, daily 300 mg oral TDF from 30 to 32 weeks of gestation significantly lowered maternal HBV DNA at delivery and neonatal infection (intention to treat analysis: 5% vs 18%, p=0.007; per-protocol analysis: 0% vs 7%, p=0.01)[20]. However, a clinical trial in Thailand involving 331 women did not find any significant difference in the rate of IF between women taking TDF or placebo (0 vs 2%, p=0.12)[13]. This negative finding could be related to the low IF in both groups as a result of timely HBIg and vaccination and the inclusion of women with low viral loads[21].

The World Health Organization recommends the use of TDF in women with HBV DNA ≥200 000 IU/mL starting from 28 weeks of gestation until birth or even afterwards[7], in line with other international guidelines[22,23]. Under most circumstances, TDF treatment starting from 28 weeks can adequately suppress viral load before delivery. However, in women at high risk of preterm delivery or with a high baseline HBV DNA of ≥8 $\log_{10}$ IU/mL, TDF may be used in the early second trimester[24]. Early use of TDF should also be considered in women undergoing amniocentesis, as there is an increased risk of MTCT if the HBV DNA is ≥7 $\log_{10}$ copies/mL or ≥7 $\log_{10}$ IU/mL[25,26].

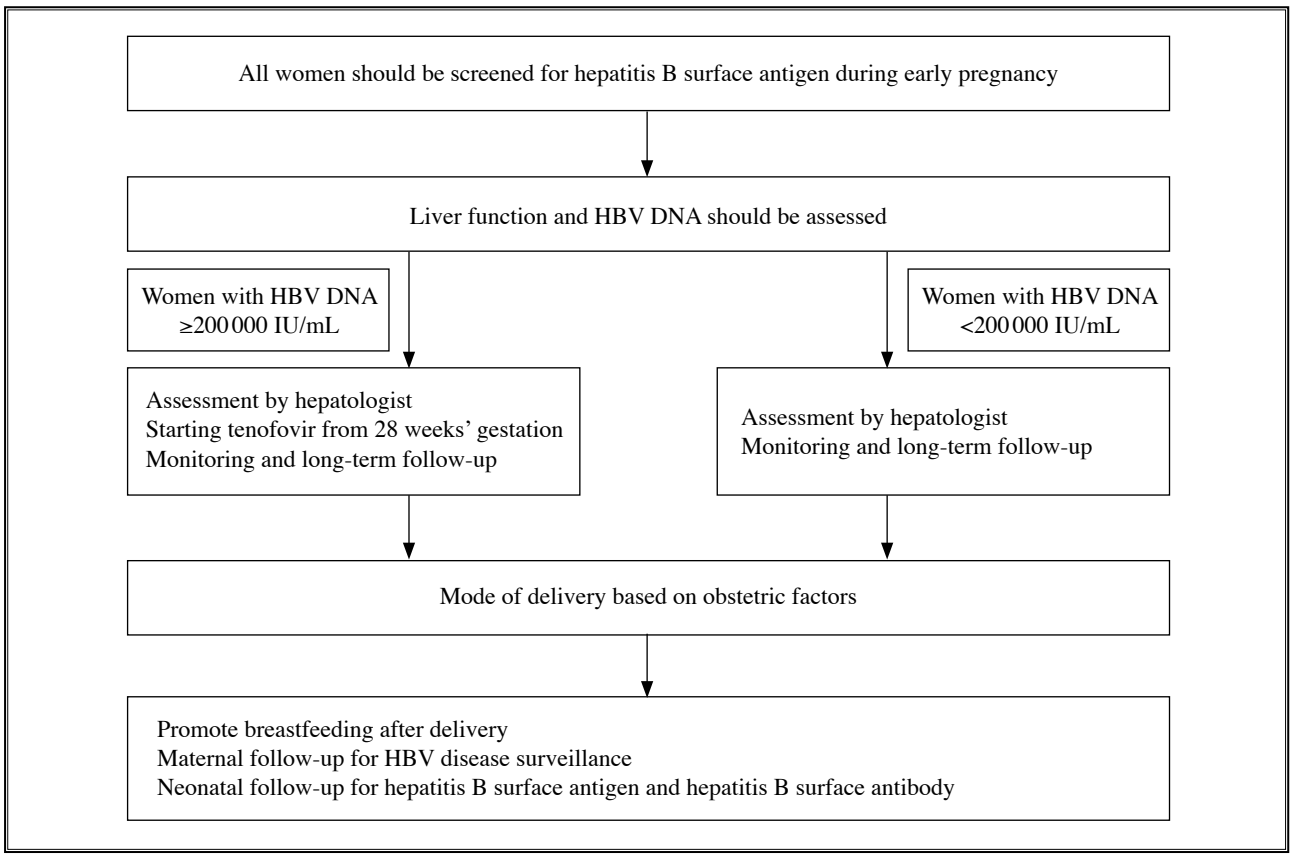

Figure. Clinical management algorithm for hepatitis B virus (HBV) carriers during pregnancy

Role of caesarean section

With timely HBIg and HBV vaccination, the duration of membrane rupture and labour does not affect the IF rate even in women with high viral loads[27]. In a systematic review and meta-analysis involving 18 studies and 11 446 mother-and-child pairs, the rate of IF at the age of 6 months was similar between the vaginal delivery group and the caesarean section group (4.1% vs 3.3%)[28]. Therefore, caesarean section should not be routinely recommended to HBV carriers without obstetrical indications.

Clinical management algorithm

All women should be screened for HBsAg during early pregnancy. For women with positive HBsAg, liver function and HBV DNA should be assessed. HBV DNA quantification as early as before 22 weeks of gestation can be used reliably to predict the risk of IF and guide the use of antiviral treatment[29]. Women with high HBV DNA (>200 000 IU/mL) should be seen by a hepatologist to discuss the use of TDF after 28 weeks of gestation; whereas women with low HBV DNA should also be reminded to continue with long-term follow-up for surveillance of HBV complications (Figure).

Vaginal delivery should not be restricted, and caesarean section should be reserved for obstetric indications[28]. Hepatic flares can occur in women who stopped TDF after delivery, although they are mostly self-limiting and asymptomatic[13,20]. The timing of stopping TDF treatment post-delivery is controversial[30]; multidisciplinary care can facilitate smooth transfer of care for these women from obstetricians to hepatologists.

Breastfeeding should be promoted in HBV carriers irrespective of TDF use. The dosage of TDF exposed to breastfed infants was 0.01% to 0.04% of the recommended weight-adjusted therapeutic dose in infants (0.5% to 16% of the dosage experienced by fetuses via placental transfer)[31]. Therefore, women should be reassured that there is no contraindication of TDF use during breastfeeding[23,32,33]. For women not taking antiviral treatment, there is also no evidence that breastfeeding in HBV carriers increases the risk of MTCT after neonatal immunisation[34].

Conclusion

Timely HBIg and neonatal HBV vaccination lowers the IF rate and the prevalence of HBV in Hong Kong. Multidisciplinary care for pregnant carriers increases the awareness and continuation of HBV management after delivery. With prescription of TDF to pregnant carriers with high HBV viral loads, Hong Kong is expected to enter a new era of HBV eradication.

Declaration

The authors have no conflict of interest to disclose.

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Review Article

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Oocyte cryopreservation: a narrative review

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Oocyte cryopreservation is a method to preserve fertility for young cancer patients. Its indications have been extended to include the quarantine and storage of donor oocytes in egg donation programs, women with medical conditions that may culminate in premature ovarian insufficiency, and women who wish to safeguard fertility decline associated with ageing. In this review, we discuss the history of oocyte cryopreservation and its various clinical applications, with a focus on the safety of the procedure for cancer patients, especially those with hormone-dependent cancers such as breast cancers. We also discuss ethical considerations for women who are cryopreserving their oocytes to protect against age-related fertility loss, the optimal age to undergo oocyte cryopreservation, and the optimal number of oocytes to freeze. The risks associated with the procedure and potential risks to children born from cryopreserved oocytes are also addressed.

Keywords: oocyte cryopreservation; fertility preservation; cancer patients; ethical considerations; safety

History

Early attempts to cryopreserve human oocytes were hindered by a high incidence of aneuploidy and digynic polyploidy in the cryopreserved mammalian oocytes because of damage of the sensitive meiotic spindle at the metaphase II stage when mature oocytes were frozen. In 1986, a breakthrough was made using oocytes cryopreserved with the slow-freezing method[1]. However, oocyte survival on thawing was low, and safety of the children born from cryopreserved oocytes was a concern. In 2004, the ban on zygote and embryo cryopreservation in Italy provided an incentive to optimise oocyte cryopreservation. The first baby born from vitrified oocytes was reported in 1999[2]. The major obstacle restricting the clinical application of oocytes vitrification was the lack of an appropriate carrier. The introduction of Cryotop enabled an extremely rapid-cooling rate with minimal fluid volume and achieved an oocyte survival rate of >90% and the establishment of live births[3-5]. Vitrification is preferred to slow freezing, with higher rates of oocyte survival, fertilisation, embryo cleavage, and clinical pregnancy[6]. Comparisons between fresh and vitrified oocytes showed comparable oocyte survival and clinical pregnancy rates[7-9]. In view of the growing evidence on efficacy, the European Society for Human Reproduction and Embryology[10] and the American Society for Reproductive Medicine[11] affirmed that oocyte cryopreservation should no longer be considered as experimental in 2012 and 2013, respectively.

Oocyte cryopreservation

Controlled ovarian stimulation is the first step. Among the various protocols adopted from in vitro fertilisation (IVF) treatment cycles, the antagonist protocol is preferred because of its flexibility and shorter duration. Treatment is initiated in the early follicular phase of a spontaneous or combined oral contraceptive pill-induced menstrual cycle with daily injections of follicle-stimulating hormone. Daily gonadotropin releasing hormone (GnRH) antagonist injections are added on day 6 (fixed protocol) or when the leading follicles are ≥14 mm in diameter (flexible protocol), in order to prevent premature luteinising hormone surge. An ovulation trigger injection is administered when the leading follicle exceeds 18 mm in diameter. An GnRH agonist is almost always used to minimise the risk of ovarian hyperstimulation syndrome (OHSS). The oocytes are then retrieved by aspirating these follicles under transvaginal ultrasound guidance.

Clinical applications

In the early days, oocyte cryopreservation was largely reserved for women undergoing gonadotoxic chemotherapy or radiotherapy. As the technology evolves, it has become the standard protocol for cryopreserving donor oocytes to establish egg banks. Indications for oocyte cryopreservation have further been extended to include medical conditions other than cancers and to those who wish to delay childbearing for various reasons – often known as social reasons, elective oocyte cryopreservation,

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age-related fertility loss, or elective fertility preservation (EPP).

Fertility preservation for cancer patients

Cancer treatments often have detrimental effects on female fertility when involving irradiation to the pelvic organs, surgical removal of the ovaries, or systemic gonadotoxic agents. The extent of damage to the ovarian function depends on the type and dose of chemotherapeutic agent used, the patient's age, and the ovarian reserve at baseline. Alkylating agents such as cyclophosphamide are the most gonadotoxic, causing depletion of the primordial follicle pool, and thus compromising the ovarian reserve[12,13].

Advances in cancer treatments have substantially improved patient survival. Professional organisations such as the American Society for Reproductive Medicine[14] and the American Society of Clinical Oncology[15] recommend oncologists to discuss with their patients the impacts of chemotherapy on fertility during cancer treatment planning and refer patients to reproductive specialists to discuss the possibility of fertility preservation. Despite this, only 3036 (44%) of 6976 patients in the United States were counselled regarding the risk of infertility associated with chemotherapy[16].

In cancer patients undergoing ovarian stimulation for oocyte cryopreservation, there is a concern that supra-physiological levels of oestrogen during ovarian stimulation may stimulate growth of hormone-dependent cancers such as breast cancers. The addition of an aromatase inhibitor in combination with gonadotropins has been proposed. Letrozole is an aromatase inhibitor that effectively reduces the peak oestradiol level and does not affect the oocyte yield[17,18]. It is usually administered orally starting on the second or third day of a spontaneous cycle until the day of ovulation trigger, and then restarted after oocyte retrieval until menstruation returns[19]. Final egg maturation is achieved with a GnRH agonist instead of the conventional human chorionic gonadotropin. GnRH agonist triggering results in significantly decreased oestradiol level on the day of retrieval and a faster drop of oestradiol levels in subsequent days[20]. GnRH agonist also reduces the risk of OHSS.

Breast cancer patients who underwent combined letrozole-gonadotropin ovarian stimulation showed no significant difference with controls in terms of short-term recurrence rate and relapse-free survival[21], as well as longer term follow-up of 5 (range, 1-13) years[22] and 6.3 years (range, 3 months to 23.6 years)[23].

For cancer patients, there is a time constraint before the commencement of chemotherapy or radiotherapy. Novel ovarian stimulation protocols can shorten the time interval to oocyte retrieval. The random-start protocol[24] initiates ovarian stimulation at the time of patient presentation rather than waiting for spontaneous menstruation. It is equally effective as conventional start protocol in terms of the total number of mature oocytes retrieved, oocyte maturity rate and fertilisation rate, irrespective of whether the stimulation is started in the late follicular phase or the luteal phase[25-28].

The number of oocytes retrieved is important in determining the probability of the patient having a successful live birth in the future. Cancer patients do not have much time to undergo repeated ovarian stimulation and oocyte retrieval cycles. The double stimulation or DuoStim protocol combines conventional follicular phase stimulation together with luteal phase stimulation, so that two oocyte retrieval procedures can be performed within the same ovarian cycle, maximising the total number of oocytes that can be retrieved for an individual patient[28-33]. The oocytes collected from the luteal phase stimulation have comparable rates of fertilisation, blastulation, euploid embryo, and pregnancy after embryo transfer, compared with oocytes collected from the follicular phase stimulation in IVF patients[33]. Because of the low utilisation rate of cryopreserved oocytes in cancer patients, data regarding pregnancy and live birth rates from these two novel ovarian stimulation protocols are scarce and inconclusive. Nonetheless, the European Society of Human Reproduction and Embryology recognised these as options when there is urgency in cryopreserving oocytes[34].

Other medical indications

Other medical and iatrogenic conditions causing premature ovarian insufficiency include autoimmune, genetic and epigenetic, environmental, metabolic, and gynaecological conditions (Table). The impact of endometriotic cysts (both the occurrence and removal) on the ovarian reserve is often overlooked. Women with endometriomas have a faster depletion of ovarian follicles and early (premature) ovarian insufficiency. It is pertinent that doctors looking after these women discuss or refer these women to an appropriate specialist who can offer the option of fertility preservation including oocyte or embryo cryopreservation.

Oocyte donation programmes

Oocyte donation is an alternative to adoption for women with premature ovarian failure who desire to bear

Table. Medical conditions other than cancer for oocyte cryopreservation

Iatrogenic
Surgery
Radiotherapy
Chemotherapy
Chromosomal and genetic aberrations
BRCA gene carriers before prophylactic oophorectomy
X chromosome abnormality: 45X, 47XXX
Fragile X premutation
Autoimmune ovarian damage
Autoimmune diseases requiring chemotherapy
Systemic lupus erythematosus
Rheumatoid arthritis
Environmental factors
Viruses
Chemical agents
Radiation
Metabolic diseases
Diabetes type 1
Galactosaemia
17-OH deficiency
21-OH deficiency
Endometriosis
Endometrioma
Endometrioma surgery

children[35]. It can be used to treat women with age-related infertility owing to the reduction in the number and the quality of oocytes or simply diminished ovarian reserve. Women who are carriers of a known genetic disease who wish to avoid passing the abnormality to the next generation can also benefit from oocyte donation.

In the early days, fresh donor oocytes were used, and the menstrual cycles of the donor and the recipient had to be synchronised to allow transfer of the resultant (fresh) embryo in the same cycle. In addition, donor oocytes cannot be quarantined for infectious diseases such as HIV. Cryopreserved oocytes can be quarantined for the incubation period and kept in an oocyte bank[8]. Recipients can have the embryos replaced at their 'convenience'. Oocytes from a pool of donors can be allocated to more than one recipient, potentially improving the efficiency and reducing the cost and waiting time of oocyte donation programmes.

Oocyte donation programmes enable study of the efficacy of the oocyte cryopreservation process, as frozen and fresh oocytes can be compared with regard to their capacity to be fertilised, cleaved, implant, and ultimately the live birth rate. The oocyte survival rate was reported to be 92% on thawing, with a comparable ongoing pregnancy rate between vitrified and fresh oocytes (43.7% vs 41.7%) in a single-centre prospective randomised study[8]. However, the Society for Assisted Reproductive Technology reported a lower live birth rate in recipients of cryopreserved donor oocytes (43.2% vs 49.6%)[36]. A follow-up study reporting two additional years (2103-2015) of the national outcome data using the same database[37] confirmed a lower live birth rate per recipient cycle started (39.7% vs 51.1%) and per embryo transfer (45.3% vs 56.4%), despite a similar number of embryos transferred. Reasons for the lower live birth rates in the US remain speculative. It may be attributable to the allotment of oocytes from one donor to several recipients rather than giving the entire cohort to a single recipient in order to reduce cycle costs for each recipient. However, it is impossible to evenly divide a cohort based on quality. This explains cancellation in recipient cycles where all allocated oocytes fail to survive the thawing process. Although this may lower the live birth rate per recipient cycle started, it should not affect the live birth rate per embryo transfer. Another possible explanation may be related to the freezing and thawing process in each centre. It can negatively affect the developmental potential of an oocyte and that of the subsequent embryo. Vitrification technique is difficult to master, as is the thawing process[7-9,36-38]. Embryologists in different centres may not have the same level of skill and experience. Finally, donor selection by commercial donor oocyte banks may not be as rigid as selection for fresh donor cycles by fertility centres.

Cryopreserved donor oocytes offer advantages over fresh ones. These include simplified access to a larger pool of oocytes particularly for ethnic minorities, ability to transport frozen oocytes over long distances thereby reducing the need for reproductive tourism and lowering the cost per treatment cycle. Although cryopreservation of donor oocytes has become a routine practice for some IVF centres, the American Society for Reproductive Medicine does not recommend routine donor oocyte banking until clinical data on safety and equivalent efficacy of oocyte cryopreservation become available[39].

Elective fertility preservation

Women's fertility declines with age[40,41], and the decline accelerates after the age of 35 years. The decline is due to reduction in oocyte quantity and quality[42],

reflected by an increased miscarriage rate[43] and a higher risk of carrying a fetus with chromosomal abnormalities[44]. However, a study using shared oocytes between the donors and recipients showed that oocyte recipients had comparable pregnancy and delivery rates to their donors[45], indicating that uterine or endometrial factors do not seem to be reduced in women of advanced reproductive age, and that the age-related decline in fertility can be largely overcome by using younger oocytes.

When women of advanced reproductive age fail to conceive, they have the option to undergo IVF with donor oocytes. If they have previously cryopreserved their own oocytes, they can use their own oocytes for IVF and have their own genetic offspring. Compared with using donor oocytes, elective oocyte cryopreservation may potentially reduce the cost of multiple cycles of IVF. Thus, EPP may offer a solution to prevent unavoidable age-related infertility.

Ethical issues

Society is divided on whether oocyte cryopreservation should be made available to women who wish to postpone child-bearing. This issue can be examined from the perspectives of autonomy, beneficence, non-maleficence, and justice.

Oocyte cryopreservation enhances women's reproductive autonomy by enabling them to decide whether, when, and with whom they wish to start a family. It allows them to divert their energies towards alternative life goals such as education and career plans and not to rush to start a family because of the biological clock pressure. Reproductive autonomy is further enhanced by granting women, particularly single women, the control of their destiny. To generate embryos, the couple has to be legally married and those contributing the gametes will have a stake. Conflicts may ensue when the partner changes his mind and decides against having children, or when they separate, divorce, or posthumously. The Hong Kong Human Reproductive Technology Ordinance prohibits the transfer of embryos to persons who are not the parties to a marriage (Cap.561 Part III Section 15-5). It prohibits the posthumous use of embryos and any stored embryos have to be disposed of when the partner passes away. Furthermore, oocytes are generally not afforded the same status as embryos. The latter may conjure emotional or religious connotations upon disposal. Cryopreserving oocytes thus provides a more flexible option for single women and for those who prefer not to generate and then cryopreserve embryos[46].

Women have a narrower reproductive window than men; their optimal fecundity spans less than two decades and is drastically reduced 5 to 10 years before the menopause. Historically, women had to choose between childbearing or education and career development. This biological inequity can be partially offset by oocyte cryopreservation. Women can pursue other life goals or career plans without losing their natural reproductive potential and/or before they are able to find a suitable partner. Oocyte cryopreservation can thus foster gender equality[47].

In regard to beneficence, oocyte cryopreservation, strictly speaking, is not fertility preservation; rather it preserves gametes for future attempts at reproduction. There is no guarantee that one or more live births will result from the cryopreserved oocytes. In fact, it may do harm by giving women a false sense of security so that they may delay childbearing until it is too late.

The process is not without risks (non-maleficence)[47]. Controlled ovarian stimulation can lead to severe OHSS and its attendant complications. Oocyte retrieval is painful and invasive; it can be complicated by substantial internal haemorrhage and pelvic infection. These can result in infertility and even mortality. Nonetheless, if society accepts oocyte donors to undergo a medical intervention for no personal benefit, there is no reason why the same risks become unacceptable when a woman chooses to cryopreserve her own oocytes. Current adoption of the antagonist (stimulation) protocol, use of a GnRH agonist ovulation trigger and withholding embryo transfer can practically reduce the risk of severe OHSS to near zero[48].

Delaying childbearing until women are in their fifth decade or beyond may also do more harm than good, because older women have more obstetric and neonatal complications[49]. Their offspring may face negative psychosocial consequences of being born to a mother of advanced age, and may lose a parent relatively early in his/her life. Children as caregivers are more likely to suffer from depression and behavioural problems, and they have less time for school activities and to make friends. They live in constant fear of losing one or both parents[50]. The long-term impact of early (before the age of 18 years) parental death has shown a negative impact in adulthood with regards to trust, relationships, self-esteem, loneliness, and isolation[51].

In terms of justice, oocyte cryopreservation is expensive and often not covered by health insurance and thus not every woman has access to this option, although Apple and Facebook offer EPP to their women employees

as health benefits. There are social, racial and ethnic disparities in women's access to this option[52]. It is also important that women are not pressured into delaying childbearing just because their company is providing insurance coverage for oocyte cryopreservation, and that they will not be considered as non-committal to their career if they choose to have children early rather than cryopreserving their oocytes and defer motherhood to a later age[46], thereby undermining the whole concept of reproductive autonomy.

Optimal age for EPP

The conception rate, natural or via reproductive technology treatment, diminishes rapidly with advancing maternal age. This is largely due to the age-related decline in the quantity and quality of oocytes in a woman's ovaries. In a study of associations between maternal age and the prevalence of embryonic aneuploidy in over 15000 consecutive trophectoderm biopsies, the lowest risk was seen in women in their mid to late twenties, and the risk of having no euploid embryo was lowest in women aged 26 to 37 years[53].

In a retrospective analysis of IVF patients, the chance of having a live birth for each fresh oocyte reduced gradually from 8.67% for women aged <30 years to 7.33% for those aged 35 to 37 years, and then rapidly to 1.06% for those aged ≥43 years. In women who used their autologous cryopreserved oocytes, the chance of having a live birth showed a similar downward trend[54]. In another retrospective study of women who underwent EPP, the live birth rate was significantly higher at the age cutoff of 35 years (50% [95% CI=32.7-67.3] vs 22.9% [95% CI=14.9-30.9])[55].

Younger women may be able to maximise the number of 'good quality' oocytes for storage, but they may be less likely to use these oocytes in the future. The procedure and expense of oocyte cryopreservation may become unnecessary if they never have to use these oocytes. Cryopreserving oocytes at a later age may yield fewer and poorer-quality oocytes per cycle, and women may need multiple cycles to bank an adequate number of oocytes to have a reasonable chance of a live birth and this increases the cost. Using a mathematical model, in women who plan to delay childbearing until the age of 40 years, oocyte cryopreservation before the age of 38 years reduces the cost to achieve a live birth[56]. In a decision-tree model, the highest probability of live birth is seen when oocyte cryopreservation is performed at the age of <34 years (>74%), and that oocyte cryopreservation versus no action has the largest benefit at the age of 37 years and is most cost-effective[57]. However, there is little benefit to cryopreserve oocytes for younger women aged 25 to 30 years, because they may not need to use these oocytes in the end. Nonetheless, young women at risk of premature ovarian insufficiency should be counselled of the option of oocyte cryopreservation at an earlier age.

In Hong Kong, the Council on Human Reproductive Technology specifies that "the maximum storage period for gametes or embryos stored for patients' own use in a reproductive technology procedure should not exceed 10 years" (Chapter X, Para 10.7). This means that for women younger than 32 years, their cryopreserved oocytes would have to be disposed of before the age of 42 years, thereby defeating the intention of EPP. Therefore, the optimal age for EPP – at least in Hong Kong – is between 33 and 37 years of age.

Optimal number of oocytes to freeze

Every vitrified-warmed oocyte has a 5% to 7.4% chance of a live birth with an overall efficiency of 6.4%[54]. The number of oocytes required varies with the woman's age at the time of cryopreservation. In a study of IVF outcome using vitrified oocytes, in women aged ≤35 years, the cumulative live birth rate increased sharply from five (15.4%) to eight (40.8%) oocytes, with an 8.4% gain for each additional oocyte banked, and the rate of increase plateaued at 10 to 15 oocytes (85.2%)[55]. This contrasted with a milder increase for women aged >36 years, their cumulative live birth rate was 5.1% (5 oocytes) and 19.9% (8 oocytes), reaching a plateau of 35.6% with 11 oocytes[55]. For women aged <38 years, 15 to 20 oocytes should be frozen to produce a 70% to 80% chance of having at least one live birth; and 25 to 30 oocytes should be frozen for women aged 38 to 40 years to produce a 65% to 75% chance of having at least one live birth[54]. Based on a mathematical model, women aged 34, 37, or 42 years, each with 20 mature oocytes frozen, are expected to have a 90%, 75%, and 37% chance of having at least one live birth, respectively; and 10, 20, and 61 oocytes should be frozen to produce a 75% likelihood of having at least one live birth[58]. All these studies are of single-centre, retrospective, and have not been validated or reproduced. In a study from Reprogenetics regarding the euploidy rates in donor egg cycles among 42 fertility clinics in the United States, the average euploidy rate per centre ranged from 39.5% to 82.5%, whereas the mean expected rate of euploidy was 68.4%. The implication of these findings is that centre-specific assisted reproductive technology practices and outcomes can vary considerably, including oocyte cryopreservation[59].

Safety for women

The risks associated with oocyte cryopreservation involve controlled ovarian stimulation and oocyte retrieval. The risks of oocyte retrieval include pelvic infection, internal bleeding, inadvertent damage to other intra-abdominal organs, and ovarian torsion. OHSS is the most serious complication. OHSS can be classified as mild, moderate, severe, and critical[60]. Mild and moderate OHSS is characterised by abdominal pain, enlarged ovaries, and weight gain, with an incidence of 3% to 6%; it can be managed conservatively, as it is self-limiting and generally resolves upon resumption of menstruation. Severe and critical OHSS can occur in 1% to 3% of IVF cycle. These women have fluid retention in the form of ascites and sometimes pleural effusion, massive ovarian enlargement, haemoconcentration and oliguria, and venous thrombo-embolism. It is potentially life-threatening and worsens by an ensuing pregnancy following fresh embryo transfer. The rise in endogenous human chorionic gonadotropin can exacerbate its symptoms and duration. Elective cryopreservation of embryos can prevent OHSS[61,62]. Women who are cryopreserving oocytes will not have embryo transfer, and hence late-onset OHSS can be avoided. A systematic review and meta-analysis demonstrated a significantly lower incidence of OHSS in the GnRH antagonist protocol compared with the GnRH agonist protocol (OR=0.59, 95% CI=0.42-0.82)[63]. The risk can be further reduced with the concomitant use of a GnRH agonist for final oocyte maturation instead of the traditional human chorionic gonadotropin. A Cochrane review showed that the incidence of moderate to severe OHSS was significantly lower in the GnRH agonist trigger group compared with the human chorionic gonadotropin group (OR=0.10, 95% CI=0.01-0.82)[64]. Therefore, the antagonist stimulation protocol coupled with GnRH agonist trigger is recommended, as it minimises the risk of OHSS.

Safety for children

In the early days of oocyte cryopreservation, there were concerns about the risk of meiotic spindle damage leading to an increased aneuploidy and digynic triploidy in the subsequent embryos derived from cryopreserved oocytes. The aneuploidy rate by fluorescence in situ hybridisation showed that the percentage of embryos with aneuploidy in the cryopreservation group was comparable to that observed in the controls[65]. A review of over 900 live births derived from cryopreserved oocytes also showed no increased risk of congenital anomalies, compared with the general population[66]. In a retrospective study of 2252 live babies born from cryopreserved oocyte in the Italian National Register, only 0.9% had congenital malformations reported[67].

Despite these, the safety of long-term cryopreservation of oocytes is lacking. Cryopreserving oocytes for up to 4 years did not seem to affect the IVF success outcomes[68]. The euploid rate of blastocysts was similar to those derived from fresh oocytes, after a median of 3.5 years (maximum, 6 years)[69]. There is no study reporting the long-term follow-up of children born with oocyte cryopreservation, especially when the oocytes are cryopreserved for a prolonged period.

Conclusion

Oocyte cryopreservation is an option for women with various medical conditions to preserve fertility. It is also widely applied in oocyte donation and has been extended to women who wish to preserve their fertility against age-related fertility loss. As the number and quality of oocytes decrease with advanced reproductive age, women who wish to cryopreserve oocytes should preferably consider this procedure before 37 years of age. The procedures of ovarian stimulation and egg retrieval are generally safe for women. The safety of children born from cryopreserved oocytes is reassuring, but the long-term outcome is lacking.

Declaration

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