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Editorial

COVID-19 and the Challenges for Academic Collaboration in Obstetrics & Gynaecology

Kok Hian TAN

Academic collaboration based on common interests and shared responsibilities amongst our Obstetrics and Gynaecology (O&G) community, is vital to raise and maintain the standard of education, research and academic activities for better O&G staff development and health care. This strong collaborative academic O&G landscape should be continually nurtured in Singapore and had been previously discussed in this journal.[1,2]

Coronavirus disease (COVID-19) is an infectious disease caused by a novel coronavirus SARS-CoV-2 first identified in Wuhan City, China, in December 2019. This virus which causes illnesses ranging from the common cough to more severe infections in humans, is spreading exponentially worldwide. Since its outbreak in Wuhan, Hubei China and 5 months into 2020, the world is facing an existential global health crisis from the COVID-19 pandemic. It had quickly infected millions of people worldwide (5,513,369 cases in over 200 countries with 346,868 deaths and 31,960 cases in Singapore with 23 deaths as of 24 May 2020).[3] It affected even more people through the necessity for lockdowns, movement controls, social distancing restrictions in many cities and countries in the world. Lives and livelihoods have been lost or affected severely globally.

The depth and intensity of impact from COVID-19 pandemic is far greater than that of the 2003 SARS outbreak and the 2009 H1N1 epidemic. There have been major disruptions to all aspects of social and economic activities as well as on healthcare including education, training, research and academic activities for Singapore healthcare. The need for safe social distancing and the imposition of extended period Circuit Breaker (a strict set of containment measures to prevent virus transmission with stay home orders and all non-essential workplaces closed from 7 April to 1 June 2020) in Singapore presented serious challenges to clinical care, healthcare education, training research and academic development activities. Meetings, congresses, conferences, learning sessions, face-to-face discussions and work gatherings locally and worldwide were postponed or cancelled.

Within this difficult conundrum, lies an opportunity to continue clinical care and academic activities through capitalizing on innovation and paradigm behavioural change. There is an urgent need to adapt, collaborate and rise to the challenge of balancing safe distancing for containing the pandemic; with optimal healthcare and the effective provision of healthcare training, education and research. This has led to greater use of digital technological platforms and more online & teleconferencing learning and teaching.

The past decade has allowed the development of a multitude of digital tools.[4] For example, my team initiated a regular public live webinar series on pregnancy issues (Pregnancy&Me: The World's First Dedicated Pregnancy Webinar Series 2009 to 2013) supported by KKH Corporate Communications and private enterprises. It fizzled

off after 2013, even the comparatively short-lived SARS work distancing then did not help. At that time, exactly a decade ago, the concept was too early and too cumbersome for many people, who were cozy to physical venue ambiance and close physical social interactions. Prolonged travel restrictions were unheard of (save for the brief period during SARS). Now with COVID-19 prolonged distancing and activity restrictions, these teleconferencing tools have become essential tools for collaboration, forged out of necessity and to remediate the consequences of the COVID-19 outbreak. Telemedicine, teleconferencing, and virtual classrooms become popular and take off as 2020 gamechanger for the way forward during COVID-19 and likely post COVID as well.

Our Singapore O&G community has risen up vigorously to the challenge of academic collaboration in the face of COVID-19 challenges. Education webinars were instituted quickly, both to fulfil the need, for rapid information about the COVID-19 pandemic with the concomitant affected management in O&G healthcare; and for the continual training and education for faculty and healthcare trainees and students.

Webinars conducted by our O&G faculty early in the pandemic and required close collaboration with the hospital departments and our O&G organizations. Serene Thain from the Department of Maternal Fetal Medicine, KK Women's and Children's Hospital; Mahesh Choolani from Division of Maternal Fetal Medicine Department of Obstetrics & Gynaecology, National University Hospital; and Tan Lay Kok & Yong Tze Tein from Department of Obstetrics and Gynaecology Singapore General Hospital collaborated as panel speakers in the Live Webinar on COVID-19: Management of Pregnancy and Birth in Women with Coronavirus disease (COVID-19) on 6 May 2020. The webinar was organised by the College of Obstetricians & Gynaecologists, Singapore (COGS) supported by the Academy of Medicine Singapore and Obstetrical & Gynaecological Society of Singapore.[5] Tan Lay Kok also collaborated with the Chapter of Neonatology, College of Paediatricians and Child Health Singapore (CPCHS) and Perinatal Society of Singapore, to share on Management & Outcome of Women with COVID-19 Infection in Pregnancy in the Lunchtime Webinar on 'Covid-19 infection in Pregnancy and Newborn' on 5 June 2020.[6]

Our local O&G faculty also collaborated with international bodies in global live webinars. We were early adopters of global liver webinars. Tan Lay Kok in collaboration with the International Society of Ultrasound in Obstetrics & Gynecology (ISUOG) shared Singapore experiences in French - Singapour : trucs et astuces de ceux qui ont évité la vague, in Coronavirus webinar (French): Risques, protection et gestion des maladies hosted in Paris on 21 April 2020[7]; and in collaboration with the Obstetrical and Gynaecological Society of Malaysia (OGSM) shared the Singapore Experience in the Intensive Course in Obstetric Emergencies (ICOE) 3rd Series: ICOE Panel Discussion GLOBAL PERSPECTIVE ON COVID-19 - OGSS Webinar hosted in Kuala Lumpur on 2 May 2020.[8] Tan Kok Hian in collaboration with World Health Organization (WHO), shared the Singapore experience in the first live webinar of the WHO patient safety webinar series: Patient safety implications during the COVID-19 pandemic - WHO Global Patient Safety Network Webinar hosted in Geneva on 8 May 2020.[9]

COVID-19 has imposed tough challenges on the training of medical students. When the Disease Outbreak Response System Condition (DORSCON) status in Singapore was first elevated to Orange on 7 February 2020, all clinical postings were suspended until further notice. In KKH O&G, it abruptly affected the batch of Lee Kong Chian (LKC) Medicine students doing O&G posting. To tackle the challenge, faculty were encouraged to be familiar with the teleconferencing protocols and to conduct the tutorials using teleconferencing platform. Students were provided with online video links for the mandatory procedures that they were required to watch e.g. Hysteroscopy, Laparoscopy, Vaginal delivery, C-Section and Hysterectomy; and with obstetrics and gynaecology case scenarios for

them to discuss with their tutors through teleconferencing. These tele-tutorials for case discussions were conducted regularly.

There has been active collaboration in academic guidelines and publications, promoted by the common need to share protocols and urgent information for better management of O&G patients in the COVID-19 environment. Serene Thain S, Mahesh Choolani M and Yong Tze Tein published the Committee Opinion on "Management of Pregnancy and Birth in Women with Coronavirus disease (COVID-19)" for the College of Obstetricians & Gynaecologists, Singapore on 20 April 2020.[10] Jill Lee was involved in ISUOG 'Interim Guidance on 2019 novel coronavirus infection during pregnancy and puerperium: information for healthcare professionals' article published in Ultrasound in Obstetrics & Gynecology journal.[11]

Information articles published included those of SingHealth group led by Tan Hak Koon on 'From the frontline of COVID-19 - how prepared are we as obstetricians?' in BJOG 2020;[12] and NUHS group led by Mahesh Choolani on 'Care of the pregnant woman with coronavirus disease 2019 in labor and delivery: anesthesia, emergency cesarean delivery, differential diagnosis in the acutely ill parturient, care of the newborn, and protection of the healthcare personnel' in American Journal Obstetrics & Gynecology 2020.[13]

COVID-19 requires safe distancing and as such almost all face-to-face physical venue meetings of the departments, hospitals, clusters, societies, academic organisations and MOH were converted to tele-meetings for almost the whole of 2020. Even the Duke-NUS Hippocratic Oath Ceremony for the graduating Class of 2020 was conducted virtually on 29 May 2020.

COVID-19 has inadvertently moved us towards greater use of Telemedicine and Tele-collaboration to overcome the challenges for academic clinical collaboration in O&G. In general, Telemedicine or Telehealth has 4 domains - Tele-collaboration; Tele-treatment; Tele-monitoring; and Tele-support. Tele-collaboration refers to interactions between (facility-based or mobile) onsite and remote healthcare professionals for clinical purposes e.g. referral, co-diagnosis, supervision or case review.[14] The distinguishing feature is that healthcare professionals are involved at both ends of the interaction and a patient may or may not be involved in the same Telemedicine interaction e.g. radiologist-clinician as well as consultant-junior-with patient situations. Tele-collaboration is used in many forms of remote specialty consultations e.g. Tele-radiology and Tele-pathology in current practice. It is expected that Tele-collaboration will become a strong pillar for future academic collaboration in Obstetrics & Gynaecology, even after COVID-19.

The academic determination and indomitable spirit of our O&G community to move on steadily despite challenges are admirable. Strong academic leadership in this endeavour is equally important.[15] We hope we can prevail. The legacy of our determination and innovation during COVID-19 will make a strong impact, strengthening our academic collaboration in Obstetrics & Gynaecology post COVID-19 for many years to come.

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An Unusual Presentation of a Missing Intrauterine Contraceptive Device: A Case Report and Literature Review

Cassandra PS Cheong, Karuna M Lional, Ann M Wright, Wei-Wei Wee-Stekly

ABSTRACT

Introduction: *Intrauterine contraceptive device (IUCD) is a safe and effective contraception. Uterine perforation is a rare but serious complication. The clinical presentation is variable.*

Case Summary: *We detail a case of a 41-year-old lady who had a uterine perforation and migration of IUCD into the peritoneal cavity which was successfully removed by laparoscopy. She first presented with abdominal pain. Plain abdominal radiograph revealed a retained IUCD over the right hemipelvis. She then recalled a history of IUCD insertion 5 years prior that was subsequently managed as an expulsion. Diagnostic laparoscopy was performed and the IUCD thread was seen at the right adnexa with its body embedded in adhesions. Purulent discharge was observed upon blunt dissection. The IUCD was successfully removed intact and whole laparoscopically.*

Conclusion: *When a patient presents with a missing IUCD thread, a complete workup should be performed to exclude uterine perforation and translocation before attributing it to expulsion. Laparoscopic removal is the preferred approach for surgical removal but patients should be adequately counselled regarding the potential risk of conversion to open surgery.*

Keywords: Intrauterine contraceptive device, IUCD, Expulsion, Migration, Laparoscopic removal

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INTRODUCTION

The intrauterine contraceptive device (IUCD) is the second most widely used contraceptive method [1]. While it is a safe and effective long acting reversible contraception, complications such as expulsion and infection do occur. A rare but serious complication is uterine perforation. This is estimated to occur in 2 in 1000 insertions [2]. When perforation occurs, the IUCD may remain in the peritoneal cavity or migrate to other abdominal or pelvic organs [3]. The clinical presentation is highly variable with some patients being asymptomatic, while other patients present with symptoms such as acute abdomen and urinary symptoms [4, 5]. We detail a case of a 41-year-old lady who had a uterine perforation and migration of IUCD into the peritoneal cavity which was successfully removed by laparoscopy.

CASE REPORT

Our patient is a 41-year-old Para 1 Chinese lady who presented with abdominal pain. She has previously

been well with no significant past medical history apart from a Caesarean section done many years ago. An X-ray of the Kidneys Ureters Bladder (XR KUB) performed as part of investigation for her presenting complaint revealed a retained IUCD over the right hemipelvis (Fig. 1). She was then referred to our tertiary Obstetrics and Gynaecology unit for further management. On further history taking, she recalled she had an IUCD inserted for contraception 5 years ago in another country where she was residing. However, during follow up examination one year after insertion, she was informed that no thread was seen at the cervix. A bedside ultrasound performed at that time failed to detect any IUCD within the uterus. She was thus informed that the IUCD has been dislodged and started on Yasmin for contraception since then. She complained of longstanding abdominal discomfort, with worsening of pain over the epigastrium and left lower quadrant over the past 2 weeks prior to presentation. This was associated with chronic diarrhea, but not related with menses. She has regular monthly menstrual cycles with normal flow and denied dysmenorrhea. The abdomen was soft on examination but mild tenderness was elicited over the epigastrium. Speculum and vaginal examination were unremarkable. There was no thread seen. An ultrasound of the pelvis was performed five days later and no IUCD was seen within the uterus. Instead, an extra-uterine IUCD was identified in the right adnexa (Fig. 2) with trace amount of fluid and mildly echogenic fat suggestive of surrounding inflammatory reaction (Fig. 3). This was consistent with the XR KUB done previously at presentation.

In view of her symptoms and the surrounding inflammation as a result of the retained IUCD, she was counselled for a Diagnostic Laparoscopy and removal of IUCD. We had an extensive discussion with her on the significant risks of bowel involvement which may warrant further repair procedures. She was also keen for tubal ligation at the same time as she had completed her family.

We proceeded with surgery as planned. First, we performed a diagnostic hysteroscopy that revealed a small old defect at the fundus (Fig. 4). Interestingly, the uterine cavity was intact and able to maintain hydrodistension. No IUCD was seen in the uterine cavity. Upon insertion of the laparoscope, an IUCD thread was seen in the right adnexa with its body embedded in adhesions between the uterovesical fold and the round ligament, just short of perforating the bladder wall (Fig. 5). The uterus, bilateral tubes and ovaries were normal. The bladder was drawn up to the right round ligament and filmy adhesions were seen along the right anterior abdominal wall. These adhesions were carefully dissected. Blunt dissection was performed along the right adnexa between the bladder and right round ligament to expose the IUCD. Upon dissection, purulent discharge was seen discharging from the abscess (Fig. 6). The IUCD was visualized and removed intact and whole (Fig. 7). The bladder integrity was confirmed with methylene blue instillation. Meticulous hemostasis was performed. No hemostatic agent was applied to avoid introduction of foreign material in the presence of an exposed abscess cavity. Bilateral tubal ligation was then performed and the abdomen closed in layers subsequently.

Postoperatively, she completed 24 hours of IV Ceftriaxone and IV Metronidazole and was discharged with oral Doxycycline and Metronidazole for a total of 2 weeks. Bacterial culture of the purulent discharge grew Escherichia coli and Streptococcus constellatus that were both sensitive to Ceftriaxone. She was discharged well and stable on day one postoperatively. During her outpatient review 3 weeks later, she remained well and had no more abdominal pain.

DISCUSSION

The intrauterine contraceptive device (IUCD) is the second most widely used contraceptive method. [1] The most common complication is expulsion, which occurs in 1 in 20 IUCD. However, a rare but serious complication is uterine perforation which occurs in 2 in 1000 cases. [2] There are two proposed theories on the mechanism of perforation – immediate traumatic perforation and a delayed perforation from gradual erosion through the myometrium. [6] Risk factors for perforation include breastfeeding [2], insertion within 6 months after delivery and clinician's inexperience. [7] When perforation occurs, the IUCD may remain in the peritoneal cavity or migrate to other abdominal or pelvic organs. A review by Mosley et al revealed that 48.1% of these perforated IUCD were found among pelvic organs with majority free within the pelvis, 46.5% were located within the abdominal cavity mostly embedded in the omentum or bowel and 5.4% involved both abdominal and pelvic organs. [3] There have also been numerous case reports regarding the various locations that a perforated IUCD was found in, including the caecum [8], sigmoid colon [9], uterovesical fold [10], bladder. There was even a

patient whose presenting complaint was an IUCD thread protruding from the anus from the IUCD that was embedded in the posterior rectal wall [11]. Regardless of the location of the IUCD, the WHO Scientific Group (1986) recommended that all perforated IUCD should be removed as soon as possible. [1] However, it is important to note that this recommendation might be guided by conventional IUCDs, which were commonly found in the shape of a ring, increasing the risk of intestinal obstruction. Rather, newer T-shaped devices used these days do not pose such a risk. [12] In fact, our patient only had vague abdominal discomfort for 4 years before worsening of pain 2 weeks prior to her presentation which lead to the discovery of her missing IUCD. This is consistent with other case reports of perforated IUCD resulting in abdominal abscess in current literature. Most patients remain well for the initial years and only present with delayed symptoms many years after. [5, 13,14] A recent retrospective review over a period of 14 years of intraperitoneal IUCDs also revealed that 43% were asymptomatic. [15] Yet, among these newer T-shaped devices, the factors which determine which cases would become symptomatic and which would remain asymptomatic remain poorly understood. Therefore, there is still no clear guidance with regards to the indication for removal of a perforated IUCD in an asymptomatic patient.

However, there are clear guidelines on the management of a missing IUCD thread. This has been clearly described in the Faculty of Sexual and Reproductive Healthcare (FSRH) Clinical Guidance for intrauterine contraceptive devices. When no thread is visible on speculum examination, it is imperative to first exclude pregnancy and advise alternative contraception. Then, an ultrasound of the pelvis should be arranged to determine if the device is located within the uterus. If no IUCD is seen within the uterus, an X-ray of the abdomen and pelvis should be performed. The visualization of an IUCD confirms a perforation and elective laparoscopic removal should be arranged. Failure to locate an IUCD in an adequate film indicates expulsion. [2] While plain radiographs are often sufficient to visualize these radio-opaque IUCDs, a computed tomography (CT) scan may occasionally be useful to assess the involvement of surrounding structures such as a in the case of bowel perforation. In cases with suspicion of bladder involvement, a cystoscopy may also be considered. [10] This would guide preoperative planning especially if additional support by general surgeons or urologists need to be arranged. A retrospective study among 1343 patients who had IUCD inserted postpartum found that among the 209 patients who had missing strings, there was only 1 case of perforation and translocation (0.48%). Majority of the cases (52.6%) were found to have string curled within the cervical canal. [16] Therefore, in a patient who presents with missing IUCD thread, it is important that a thorough workup is performed to adequately exclude perforation, before attributing it to expulsion.

Laparoscopic removal is often the first line technique for removal of a perforated IUCD. It is preferred as it is associated with a shorter recovery time and less postoperative pain. A systematic review of 30 studies was performed to compare laparoscopic and open approaches in the removal of a migrated IUCD. 93% of these cases had planned laparoscopy, of which 22.5% were eventually converted to open surgery. It was also found that the patients with IUCD related to both abdominal and pelvic organs had 57.1% rate of open surgery. [3] Therefore, while laparoscopy is a preferred approach in the removal of a migrated IUCD, its success is influenced by the location of the IUCD. Preoperative imaging should be performed to assess the potential complexity of the surgery and guide preoperative planning. When imaging suggests the possibility of involvement of other organs such as a bowel perforation, the gynaecologist should consider additional intraoperative support by the general surgeons. During consent-taking, the patient should be adequately counselled regarding the potential of conversion to open surgery and risk of injury to surrounding structures requiring additional repair procedures.

CONCLUSION

While uterine perforation is a rare complication, it has potentially serious complications. Therefore, when a patient presents with a missing IUCD thread, a complete workup should be performed to exclude uterine perforation and translocation before attributing it to expulsion. Laparoscopic removal is the preferred approach for surgical removal, but patients should be adequately counselled regarding the potential risk of conversion to open surgery. The gynaecologist should also consider engaging additional support from other specialties if other abdominal or pelvic organs are expected to be involved.

Figure 1: X-Ray Kidneys Ureters Bladder (XR KUB) – IUCD seen in right hemipelvis

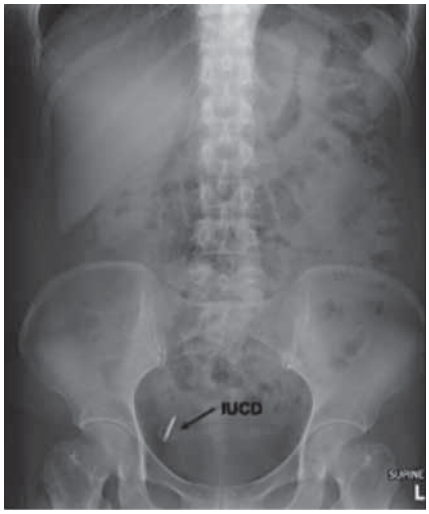

Figure 2: Pelvic ultrasound – extra-uterine IUCD in the right adnexal region

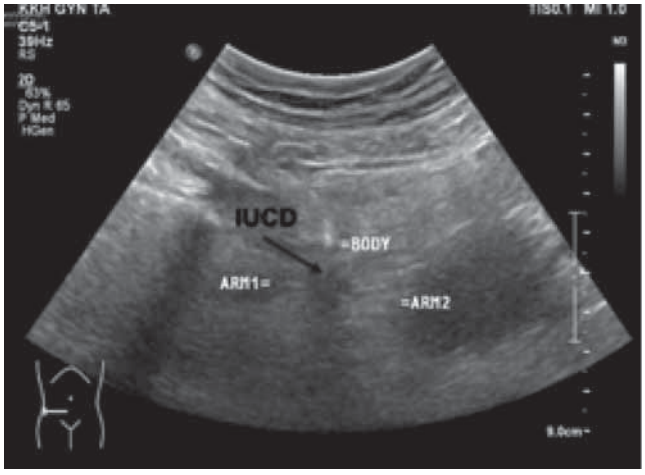

Figure 3: Pelvic ultrasound – extra-uterine IUCD in the right adnexal region with trace amount of fluid and mildly echogenic fat

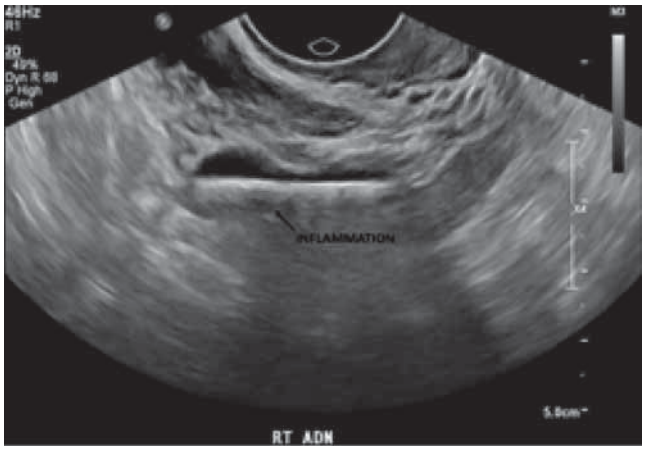

Figure 4: Hysteroscopic view – small defect seen at fundus

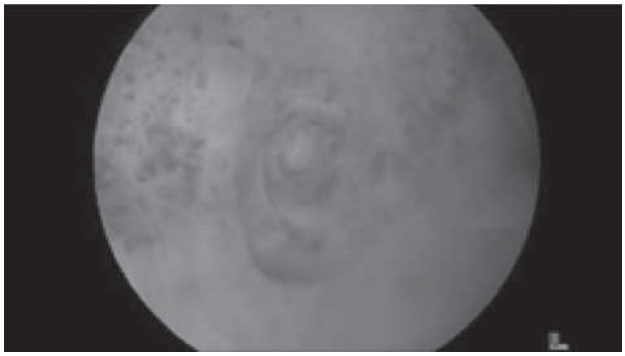

Figure 5: Laparoscopic view - IUCD thread in right adnexa with its body embedded in adhesions

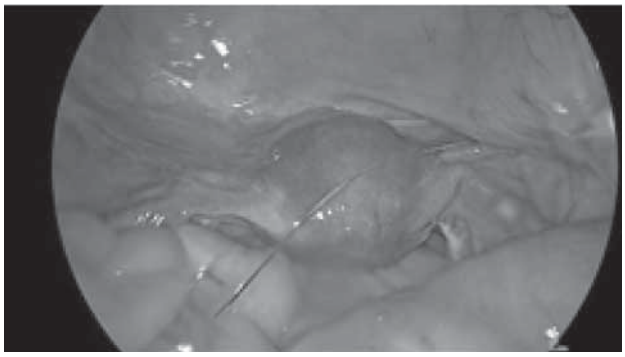

Figure 6: Laparoscopic view - Purulent discharge from the abscess upon dissection

Figure 7: Laparoscopic view – IUCD visualised and removed intact and whole

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Comparing Emotional, Relationship and Sexual Well-Being of Gynaecological Oncology Patients with a Matched Cohort in Singapore

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ABSTRACT

Introduction: *Gynaecological oncology patients experience a high burden of physical and emotional symptoms that can affect their psychological and relationship well-being, yet not much has been published on women in Asian countries like Singapore. The current study compares levels of psychological distress (depression, anxiety), relationship satisfaction and sexual disturbance between patients with gynaecological cancer and an ethnicity, age, and education-matched comparison group.*

Methods: *This is a cross-sectional study in which 104 gynaecological cancer patients and 223 women with no history of gynaecological cancer were recruited from a tertiary-level hospital in Singapore. Using propensity score matching, 87 pairs of patient-comparisons were compared on their self-reported symptoms of anxiety, depression, relationship satisfaction, and sexual disturbance.*

Results: *Patients reported significantly higher levels of sexual disturbance in contrast to their comparisons ($M = 18.94$ vs 14.54, $p = 0.002$) but not in anxiety, depression and relationship satisfaction. However, when we examined the subset of women below the median sample age (45 years), both depression scores ($M = 5.23$ vs 3.79, $p = 0.04$) and sexual disturbance scores ($M = 18.13$ vs 13.91, $p < 0.01$) in the patient group were significantly higher than the comparison group.*

Conclusion: *Sexual dysfunction is an important target to assess in gynaecological cancer patients to improve their quality of life and well-being. Women with gynaecological malignancies and who are younger are at higher risk of depression.*

Keywords: psychological distress, relationship satisfaction, sexual disturbance, gynaecological oncology, cancer

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INTRODUCTION

Gynaecological cancers affect approximately 16.3% of women worldwide.[1] Cancers of cervix and ovaries are the 5th and 7th commonest causes of death from cancer in Asian women, respectively.[2] In Singapore, the most common gynaecological cancers are uterine (6.9%), ovarian (5.4%) and cervical (3.1%) reported between 2011 and 2015.[3] Overall survival of patients with gynaecological cancers is improving due to earlier detection of cancer and more effective treatment.[4] However, there may be side effects from treatment, some being long-term, that can be unpleasant or debilitating to live with.[5] Maintaining good quality of life, means addressing psychological or emotional distress and sexual issues affecting patient.

A significant proportion of patients with gynaecological cancers have been known to report depressive symptoms, however the literature is mixed. Studies show that in 12%-25% of patients with gynaecological cancers have depression .[6] However in a study done in which anxiety and depression scores were compared between patients with cervical cancer and comparisons, depression scores in cervical cancer patients were even lower than the comparison group, leading them to conclude that cervical cancer patients showed relatively good mental health compared with healthy comparisons.[7]

Patients with gynaecological cancers have areas of body associated with femininity, sexuality and reproduction affected; hence the distress associated can impact not only the emotional well-being but also their relationship and sexual well-being.[8] Surgical treatment can affect sexual functioning by impairing the vascular supply or the innervation of the pelvic organs. The approximation of the surgical edges causes tension that may interfere with the range of motion during sexual intercourse.[9] Women who have intracavitary radiation implants for cervical cancer or endometrial cancer may be left with a shortened and stenosed vagina, which may lead to dyspareunia.[10] Hysterectomy also interferes with sexual response cycle, as the absence of rhythmic contractions of the uterus may prevent orgasm.[11] Oophorectomy or ovarian ablation due to radiation or chemotherapy also leads to vaginal dryness and thinning which results in dyspareunia.[11] Even though it is commonly expected that there is a risk of sexual difficulties in this group of patients, sexual well-being is often overlooked following gynaecological cancer diagnosis and treatment.[12]

We know that 80% of patients have difficulty discussing with their doctors about sexual problems and 85% of the doctors do not ask their patients about it.[13] This is especially so in the Asian context where talking about emotional symptoms and sexuality is difficult and may even be considered taboo. As such there is limited information on cancer patient's psycho-sexual well-being, and limited resources for support for emotional or sexual impairments. The aim of the study is to compare levels of psychological distress (depression, anxiety), relationship satisfaction, and sexual disturbance between patients with gynecological cancer to a comparison group matched for ethnicity, age and education level. We were also interested in examining risk factors that were associated with psychological distress.

METHODS

Participants

A cross-sectional study was conducted between October 2015 and December 2016. One hundred and four female gynaecological cancer patients and 223 women with no history of gynaecological cancer were recruited from a tertiary-level hospital in Singapore. Patients who present with a history of gynaecological cancer (ovarian, uterine/endometrial, cervical, vulvar, vaginal cancer) of all stages, were at least 21 years of age, currently living in Singapore and able to read and understand English were considered eligible. Eligibility criteria for comparison participants included females not having a history of gynaecological cancer, being at least 21 years of age, currently living in Singapore and able to read and understand English.

Procedures

Eligible patient participants as determined by nurses who were seen or treated in Gynaecology-Oncology Unit were approached to take part in a one-time 20-minute survey. All patient participants gave written informed consent. Comparison participants were recruited either via recommendation of patient participant or through the waiting room at the pharmacy of the study site. Comparison participants were exempted from signing informed consent as the survey was anonymized. The comparison participant version of the survey took 10-minutes to complete. Electronic data collection was conducted for both patient and comparisons using the platform Qualtrics using tablets. The study was approved by SingHealth Centralised Institutional Review Board (Reference number: 2015/2888).

Measures

Psychological distress. The Hospital Anxiety and Depression Scale [14] was used to measure psychological distress (defined as anxiety and

depression). The Hospital Anxiety and Depression Scale was originally designed for detecting clinically significant anxiety and depression in medical outpatients. There are 14 items in the Hospital Anxiety and Depression Scale, with seven items measuring anxiety symptoms and seven items measuring depressive symptoms. Participants reported their responses on a 4-point scale with higher scores indicating greater symptoms. The internal reliability of the overall scale and subscales has been reported to be good, with Cronbach's alpha for the Hospital Anxiety and Depression Scale - Anxiety Index ranging from 0.78 - 0.93 and Cronbach's alpha for the Hospital Anxiety and Depression Scale – Depression Index ranging from 0.82 - 0.90. A study conducted in Singapore validated the use of Hospital Anxiety and Depression Scale in cancer patients in Singapore and established cut-off score for depression to be score ≥ 7 and anxiety to be score ≥ 5.[15]

Relationship satisfaction. If participants indicated they were in a romantic relationship, the 4-item Dyadic Adjustment Scale-4[16] was used to measure participant's romantic relationship satisfaction. Participants responded to 3 items on a 6-point scale (1=all the time, 6=never) and 1 item on a 7-point scale (extremely unhappy-perfect) with higher scores indicating greater relationship satisfaction. The internal reliability (alpha 0.81-0.92) and construct validity of the measure has been shown to be good in its validation study. Cut-off scores to indicate clinically relevant relationship distress has been reported to be a score ≤ 12.

Sexual disturbance. The Arizona Sexual Experience Scale [17] was used to measure sexual disturbance. The Arizona Sexual Experience Scale is a 5-item validated measure. Items were reported on a 6-point scale with higher scores (ranging 5-30) indicating greater sexual disturbance in sexual drive, arousal, lubrication, ability to reach orgasm, and sexual satisfaction. The cut-off to indicate sexual disturbance is reported to be a score of ≥ 19, at least one item ≥ 5, or 3 items ≥ 4. In its validation report, reliability was good (alpha 0.80-0.89); convergent and discriminant validity was also

demonstrated. In this study, participants were given the option to skip this assessment if they wished.

Statistical Analytic Plan

Using propensity score matching (nearest neighbor matching), 87 pairs of patient-comparisons were matched based on ethnicity (Chinese, Malay, Indian, Other), age (+/- 5 years) and education (≤12 years of formal education or up to secondary school, >12 years of formal education) using Stata software. T-tests were used to examine the differences in scores of depression, anxiety, relationship satisfaction, and sexual disturbance. We also conducted post-hoc comparison analysis with a subgroup of our sample who are below the median sample age (≤45 years) consistent with the hypotheses that younger patients are expected to report more psychological distress. Subsequently, bivariate correlations and multi-variable linear regression analyses were conducted to examine factors that are associated with psychological distress. Significance was set at alpha <0.05. All statistical analyses were conducted using Statistical Package for the Social Sciences (SPSS) Version 24.

RESULTS

The study recruited 104 female gynaecological cancer patients and 223 women with no history of gynaecological cancer. Eighty-seven pairs of patient-comparisons were matched based on ethnicity, age, and education. Refer to *Table* 1 for study participant characteristics.

Comparison of outcomes between gynaecological cancer patients and matched comparisons

Patients reported significantly higher levels of sexual disturbance as indicated by difference in mean scores and proportion of those who met cut-off scores. Psychological distress and relationship satisfaction scores were not significantly different between the two groups (Refer to *Table 2*). A closer look at the items that capture sexual disturbance indicated that women in the gynaecological cancer group reported significantly higher disturbance in all the five stages of the sexual response cycle (Refer to *Table 3*). The most common problem was lack of sexual drive.

We further found that in women of 45 years of

age (median age in the sample) and below, the gynaecological cancer group reported higher scores than their matched comparisons in depression scores (t (89) = 2.11, p = 0.04) and sexual disturbance (t (51) = 2.78, p < 0.01). (Figure 1).

Factors associated with psychological distress in gynaecological cancer patients

Bivariate correlations were conducted to identify demographic characteristics (age, household income, whether patient had children under 21 years old), clinical characteristics (time since diagnosis, cancer stage,) and psychosocial factors (relationship satisfaction, sexual disturbance) that were associated with psychological distress (defined as the combination of depression and anxiety) in our sample of gynaecological cancer patients (n = 104). Age (r = -0.25, p = 0.01), days since diagnosis (r = -0.26, p = 0.01), and relationship satisfaction (r = -0.53, p < 0.001) were significantly associated with psychological distress and entered into subsequent multi-variable regression analysis. Household income, having children under 21 years old, cancer stage, and sexual disturbance were not associated with psychological distress.

Multi-variable linear regression results indicate that lower relationship satisfaction significantly predicted higher psychological distress, β = -0.55, t(101) = -4.52, p < 0.001, controlling for age and days since diagnosis. The model explained a significant proportion of variance in psychological distress scores, R^2 = 0.32, F(3,101) = 7.41, p < 0.001.

DISCUSSION

The aim of the study is to compare levels of psychological distress (depression, anxiety), relationship satisfaction, and sexual disturbance between patients with gynaecological cancers and their matched comparisons, and identify factors associated with psychological distress in gynaecological cancer patients.

Sexual disturbance is significantly higher in gynaecological cancers patients compared to comparisons matched for ethnicity, age and education level. Generally, gynaecological cancers patients reported sexual disturbance that on average occurred “quite a bit” while comparisons reported them to occur on average “sometimes”. The proportion of gynaecological cancer patients who met clinically relevant scores for sexual dysfunction was 68% vs 26% in the comparison group. Our findings are consistent with studies conducted in other parts of Asia - Hong Kong[18], China[19], and Malaysia[20] that have reported that sexual dysfunction sustained from treatment-related side effects can persist for many years into survivorship.[11, 21] Studies from US[22] and Europe[23] have also observed that sexual dysfunction was prevalent among gynaecological cancer survivors.

The gynaecological cancer patients reported greater problems in all aspects of sexual dysfunction measured: sexual drive, arousal, lubrication, orgasm and satisfaction. Lack of sexual drive was the most common sexual dysfunction being reported in our study. However, these findings contradict with certain previous studies that found sexuality were similar between cancer survivors and non-cancer women.[24] Literature on the most common sexual problem for gynaecological cancer patients was mixed, varying from vaginal dryness,[25] sexual desire,[20] orgasmic dysfunction[26] to pain.[25] The inconsistency could be due to the variations in assessment tools, treatment modalities and different diagnosis of gynaecological cancers, and direct comparison could not be made.

In examining a subset of younger women (age < 45) in our sample, we found that patients with gynaecological cancers reported more depressive symptoms and sexual disturbance than their matched comparisons. This finding reflect clinical observations and reports of recent studies that show younger survivors are more likely to suffer from psychological distress [27] and sexual dysfunction[28] compared to older gynaecological cancer survivors. Previous studies have reported that three-quarters of women below 45 years who were diagnosed with cancer are still interested in the prospect of bearing children.[29, 30] Potential loss of fertility from gynaecological cancer and treatments was an emotionally challenging experience and had a negative impact on both sexual function and psychological well-being,[29]

leading to emotional distress, anxiety, and depression in patients, in particular those in their reproductive years.

In examining factors associated with psychological distress (composite of depression and anxiety), poorer relationship satisfaction was found to be significantly associated with higher psychological distress, after controlling for age and time since diagnosis. This finding is also echoed in other studies which reported poor relationship satisfaction and predicted greater anxiety in gynaecological cancer women.[23, 31] The possible explanation could be that women confronted with the diagnosis and treatment of cancer had created intense emotional distress that may potentially drive partners apart and damage the relationship.[32] Women became anxious for fear of recurrence[24] or transmitting the cancer to their sexual partner [11, 18] if they resume sexual activity. Their reluctant to resume sexual intercourse may be interpreted as rejection or disinterest by their partner which can lead to deterioration of their relationship. Due to the feeling of guilt[33] or fear of losing their partners,[11] they feel the need to continue sexual intercourse primarily to satisfy their partners and to maintain the relationship[33] despite their own sexual difficulties. These experiences of physical and psychological trauma may result in poor relationship satisfaction. Furthermore, Asian women tend to hide their emotions [7] and are reluctant to discuss sexual issues with their partners.[31] Both cancer patients and their partners cope with adversity by self-silencing,[34] and this difficulty in communication creates more anxiety and depression between couples which can be detrimental to their marital relationship.[11]

Interestingly, our data demonstrated that sexual disturbance is not significantly associated with psychological distress, although it is found to be significantly different than the comparison group. This finding suggests that although sexual disturbance occurs more frequently in women with gynaecological cancers, they are not necessarily harmful. Patients may view sexual dysfunction as rather minor issue compared to a life-threatening disease and the side effects of treatment.[23] Furthermore, majority of the gynaecological survivors may have ceased sexual activities and perceive sex as an unimportant part of life.[35] The literature has noted Asian women to report relatively lower sexual activity[24] compared to their Western counterparts and higher probability of not resuming their sexual life after cancer treatment.[18, 26] Sexual dysfunction was possibly not a salient issue in our sample, and hence, not emotionally bothersome to patients.

Study limitations:

The current study has several limitations. Our samples were recruited from a single site, thus may not be representative of the general population. The study design was cross-sectional, therefore, the causal effects and temporal relationship cannot be established. We did not evaluate the psychiatric history, sexual function and relationship satisfaction before the diagnosis of the gynecological cancer for our patient sample, so an assumption we make is that the differences between the two groups are due to disease status. Additionally, nearly half of the patient sample did not complete the questions on sexual disturbance; the reason is unclear. Despite these limitations, we believe that our findings provide insight into an important clinical problem on psychosexual well-being in the long-term survivorship of gynaecological cancer women and can help in developing clinical management strategies to improve the psychosocial well-being of this population.

Clinical implications:

This study highlights the importance of assessing sexual function and psychosocial well-being of gynaecological cancer survivors. Given the high rates of sexual morbidity for younger gynaecological patients, there is a clear need for integration of sexuality into routine clinical care, i.e. providing information on fertility preservation and early referral to reproductive medicine facility when appropriate. The provision of psychosocial support services to couples is vital in improving communication on their sexual dysfunction and adaptation, which can help couples to cope more effectively with their relationship dissatisfaction. Timely management of sexual dysfunction may have a positive impact on the psychological well-being of young women diagnosed with

gynaecological cancer.

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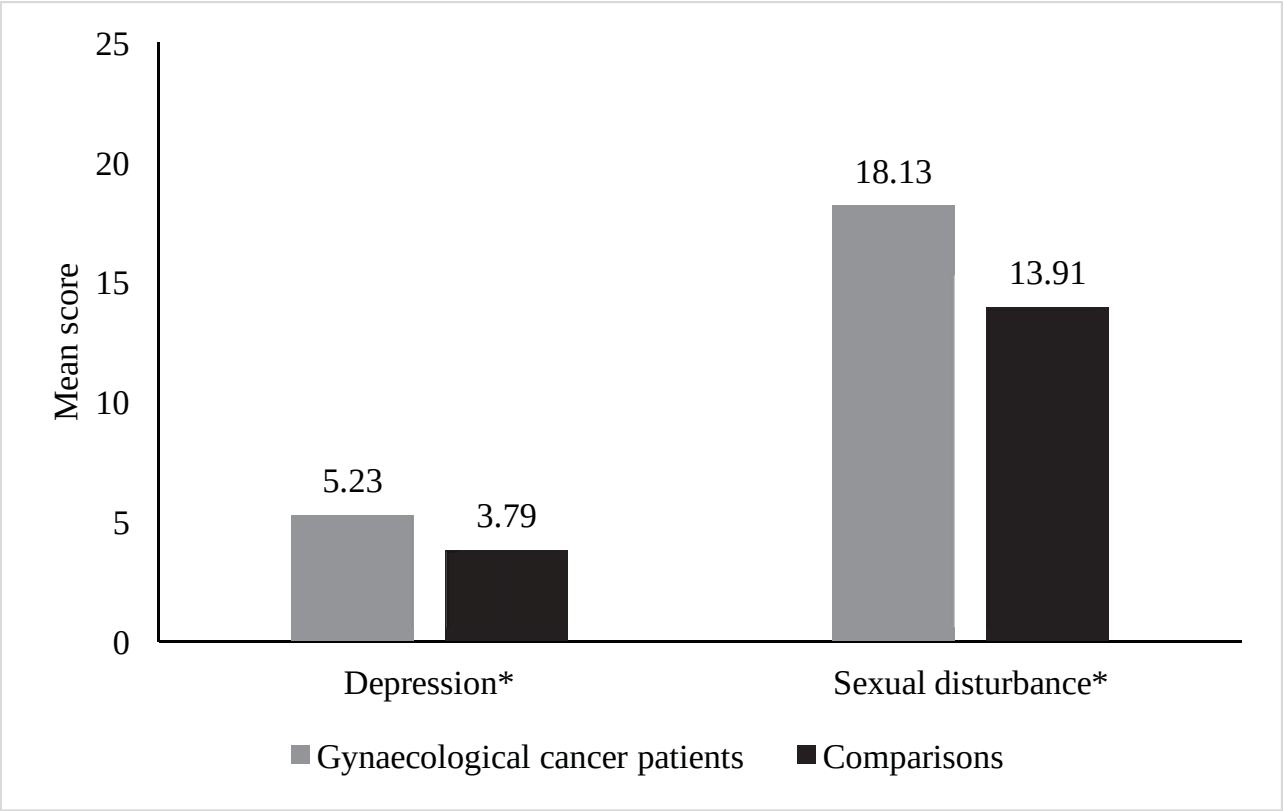
Patient consent for publication: Not required.

Data availability statement: Data are available upon reasonable request.

Figure 1. Comparison in depression and sexual disturbance scores in gynaecological cancer patients and comparisons matched for ethnicity, age, and education who are ≤ 45 years old



*Difference of $p < 0.05$

Table 1. Baseline demographics of study participants

Characteristics	Median ± Standard deviation / Count (%)		
	Gynaecological Cancer Patients (n=87)	Matched (n=87)	Comparisons
Age (years)	46.7 ± 11.8	42.7 ± 9.8	
Body Mass Index, BMI (kg/m2)	26.7 ± 7.6	25.4 ± 6.2	
Race			
Chinese	47 (54.0)	49 (56.3)	
Malay	23 (26.4)	24 (27.6)	
Indian	11 (12.6)	9 (10.3)	
Other	6 (6.9)	5 (5.7)	
Marital Status			
Married/in a romantic relationship	59 (67.8)	64 (73.6)	
Separated/Divorced	2 (2.3)	11 (12.6)	
Widowed	6 (6.9)	0 (0.0)	
Single and Never Married	20 (23.0)	12 (13.8)	
Education*			
Secondary and lower (≤12 years)	47 (54)	33 (37.9)	
Junior College/Polytechnic/ Diploma/Vocational / Technical Institute	21 (24.1)	28 (32.2)	
University and above	19 (21.8)	25 (28.7)	
Employment Status*			
Working full-time	45 (51.7)	52 (59.8)	
Working part-time	12 (13.8)	6 (6.9)	
Retired/Not working	13 (14.9)	6 (6.9)	
Homemaker	15 (17.2)	23 (26.4)	
Total monthly household income*			
Less than S$999	6 (6.9)	5 (5.7)	
S$1000 - $2999	23 (26.4)	24 (27.6)	
S$3000 - $4999	28 (32.2)	26 (29.9)	
S$5000 and above	28 (32.2)	32 (36.8)	
No. of children*			
0	29 (33.3)	18 (20.7)	
1	9 (10.3)	19 (21.8)	
2	26 (29.9)	23 (26.4)	
3 or more	15 (17.2)	27 (31.0)	

Characteristics	Median ± Standard deviation / Count (%)		
	Gynaecological Cancer Patients (n=87)	Matched (n=87)	Comparisons
No. of participants with children below 21 years	20 (23.0)	56 (64.4)	
Religion*			
Christian	13 (14.9)	20 (23.0)	
Buddhist/Taoist	27 (31)	21 (24.1)	
Muslim	24 (27.6)	24 (27.6)	
Hindu/Sikh	9 (10.3)	7 (8.0)	
Others	12 (10.7)	15 (17.2)	
Gynaecological cancer site			
Endometrial/uterine	34 (39.1)		
Ovarian	25 (28.7)		
Cervical	21 (24.1)		
Others	7 (8.0)		
Cancer stage*			
Stage I	54 (62.1)		
Stage II	7 (8.0)		
Stage III	15 (17.2)		
Stage IV	3 (3.4)		
Time since diagnosis	2ys ± 2.7ys		
Treatment modalities			
Surgery	70 (80.5)		
Chemotherapy	37 (42.5)		
Radiotherapy	22 (25.3)		
Hormone therapy	2 (2.3)		

* Data do not add up to 87 due to missing data

Table 2. Descriptive, number of clinically relevant cases and t-test results comparing gynaecological cancer patients and comparisons matched for ethnicity, age, and education

	Gynaecological Cancer Patients			Matched comparisons				
	N	Mean scores (Standard deviation)	Clinically relevant cases	N	Mean scores (Standard deviation)	Clinically relevant cases	*t*-test	*p*-value
Psychological distress (HADS)								
Depression	87	4.15 (3.38)	23%	87	3.56 (2.63)	15%	1.28	n.s.
Anxiety	87	6.07 (4.12)	59%	87	6.26 (3.75)	64%	-0.33	n.s.
Relationship satisfaction (DAS-4)	55	15.89 (4.66)	20%	64	15.27 (4.13)	20%	0.76	n.s.
Sexual disturbance (ASEX)	27	18.94 (5.98)	68%	59	14.54 (4.65)	26%	3.38	0.002

HADS = Hospital Anxiety Depression Scale, DAS-4 = Dyadic Adjustment Scale-4, ASEX = Arizona Sexual Experience Scale; Clinically relevant cases: psychological distress ≥ 13, depression ≥ 7, anxiety ≥ 5, relationship satisfaction ≤ 12, sexual disturbance ≥ 19 or at least 1 item ≥ 5 or 3 items ≥ 4.

Table 3. Comparisons in sexual disturbance between gynaecological cancer patients and comparisons matched for ethnicity, age, and education

Aspect of sexual function	Gynaecological Cancer Patients (n=27)	Matched Comparisons (n=59)	*t*-test	*p*-value
Drive	4.26 (1.71)	3.31 (1.28)	2.72	.01
Arousal	3.87 (1.43)	3.10 (1.15)	2.63	.01
Lubrication	3.96 (1.42)	2.76 (1.10)	3.87	<.001
Ability to reach orgasm	3.64 (1.28)	2.98 (0.97)	2.41	.02
Satisfaction	3.54 (1.43)	2.52 (0.97)	3.43	.001

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Incidence of Asymptomatic Bacteriuria in a Local Pregnant Population

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ABSTRACT

Introduction: *Asymptomatic bacteriuria occurs in 2 to 10% of pregnancies. Clinical guidelines recommend routine antenatal screening of asymptomatic bacteriuria due to its association with increased risk of pyelonephritis, preterm labor and low birth weight. Routine screening of asymptomatic bacteriuria is not practiced in our institution. There is no local study on the prevalence of asymptomatic bacteriuria. This is a pilot study that aims to define the local incidence of asymptomatic bacteriuria and its associated adverse outcomes in our population.*

Methods: *This is a retrospective study in a tertiary obstetrics and gynecology center in Singapore between October 2017 and August 2018. Urine dipstick for albumin, urine microscopy and urine culture with sensitivity were performed. A positive urine culture was defined when more than 10^5 bacteria per milliliters is present in a single voided midstream urine. Outcomes of interest were low birth weight, preterm delivery and admission for pyelonephritis.*

Results: *Fifty patients had antenatal urine studies performed during this period. Asymptomatic bacteriuria was detected in 6% (n = 3). None of these cases had complications of low birth weight, preterm delivery or admission for pyelonephritis. The BMI of patients with asymptomatic bacteriuria was found to be statistically significantly higher than the group without (28.7 ± 1.7 vs 22.9 ± 4.7 kg/m2, p = 0.04). There was no significant difference in outcomes between the group with asymptomatic bacteriuria and the group without.*

Conclusion: *The incidence of asymptomatic bacteriuria is consistent with international data. There were no adverse outcomes detected among these patients.*

Keywords: Asymptomatic bacteriuria, pregnancy, screening, urine culture

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INTRODUCTION

Asymptomatic bacteriuria is defined as the presence of more than 10^5 bacteria per millilitres of freshly voided urine specimen without symptoms of urinary tract infection. [1] This is estimated to occur in 2 to 10% of pregnancies. [2,3] Most clinical guidelines including the US Preventive Services Task Force (USPSTF), The Obstetrician and Gynaecologist (TOG), and The National Institute for Health and Care Excellence (NICE) recommend routine antenatal screening of asymptomatic bacteriuria due to its association with increased risk of pyelonephritis (up to 50%), preterm labor and low birth weight (<2500 grams). [4,5,6] However, these recommendations are based on earlier studies dating back to the period from the 1960s to 1980s. A recent multi-centre prospective cohort study in the Netherlands by Kazemier et al which showed

only 5% of women tested positive for asymptomatic bacteriuria. [7] While there was an increased risk of pyelonephritis in women with untreated asymptomatic bacteriuria, the absolute risk is low at 2.4%. The study was terminated early as the incidence of pyelonephritis was much less than expected. [7] A cost analysis study by Wadland et al concluded that screening of asymptomatic bacteriuria would be justified if the risk of asymptomatic bacteriuria is more than 2% and the risk of pyelonephritis with asymptomatic bacteriuria is more than 13%. [8]

At present, routine antenatal screening for asymptomatic bacteriuria is not practiced in our institution. There is no local study in Singapore to determine the local incidence of asymptomatic bacteriuria. This study aims to determine the local incidence of asymptomatic bacteriuria. This will help obstetricians in Singapore decide if routine screening for asymptomatic bacteriuria in local antenatal patients should be incorporated into routine clinical practice.

METHODS

We performed a retrospective cohort study in KK Women's and Children's Hospital, the largest tertiary obstetrics and gynecology center in Singapore. Urine studies to detect asymptomatic bacteriuria are not routinely performed by all clinicians in the institution. However, some clinicians offer urine screening for asymptomatic bacteriuria to their antenatal patients at booking visits. Antenatal patients with urine studies performed from October 2017 and August 2018 were identified. Patients with lower urinary tract symptoms, known abnormalities of the urinary tract, pre-existing diabetes, recent use of antibiotics within the last two weeks, current immunosuppressive therapy and retroviral disease were excluded.

Urine studies performed include urine dipstick for albumin, urine microscopy and urine culture and sensitivity. Urine microscopy was considered significant when 10 or more white cells per cubic millimeter are present or leukocyte esterase or nitrites are detected. A positive urine culture was defined when more than 10^5 bacteria per milliliters is present in a single voided midstream urine. Patients diagnosed with asymptomatic bacteriuria were treated with empirical antibiotics.

Clinical characteristics studied include maternal race, age, body mass index, gestational age at booking, and gestational age at urine studies. The outcomes of interest were low birth weight (defined as less than 2500 grams), preterm delivery (delivery before 37 weeks without another contributing cause) and admission for pyelonephritis.

RESULTS

During the 10-month period, there were 50 patients who had antenatal urine studies performed for asymptomatic bacteriuria screening identified from the database. 6% (n=3) of these patients had asymptomatic bacteriuria. None of these 50 cases had complications of low birth weight, preterm delivery or admission for pyelonephritis. The characteristics of these patients are described in Table I. There was no significant difference in maternal age, gestational age at urine studies or gestational age at booking visit between the group with asymptomatic bacteriuria and the group without. The average gestational age at booking visit and urine studies of this whole cohort were 12.1 and 12.5 weeks, respectively. However, the body mass index (BMI) of patients with asymptomatic bacteriuria was found to be statistically significantly higher than the group without (28.7 ± 1.7 vs 22.9 ± 4.7 kg/m2, p=0.04).

The three cases of asymptomatic bacteriuria are described in detail in Table II. Two of these cases booked early and had urine studies performed in the first trimester. Cephalexin was used to treat these cases. The last case was however a late booker. Interestingly, no white cells were detected on the urine microscopy in all three cases. The organisms isolated were *Escherichia coli, Enterococcus faecalis and Klebsiella pneumoniae*.

Outcomes of these patients were studied and are described in Table III. Eight patients (16%) were lost to follow up and three (6%) miscarried from the group without asymptomatic bacteriuria. Among the patients with asymptomatic bacteriuria, there

were no admissions for pyelonephritis. All 3 patients delivered at term, with a mean birth weight of 3400g. There was no significant difference in outcomes between the group with asymptomatic bacteriuria and the group without.

DISCUSSION

Asymptomatic bacteriuria is a common condition, found in up to 5% of healthy premenopausal women. [9] The most common organism isolated is Escherichia coli. In healthy individuals, asymptomatic bacteriuria has not been shown to be associated with significant adverse effects and hence, screening and treatment are not recommended. [9,10,3] However, the Infectious Disease Society of America (IDSA) recommends screening and treatment in the following groups of patients: pregnant women, before urological procedures in which mucosal bleeding is anticipated, and women with catheter-acquired bacteriuria that persists 48 hours after removal of indwelling catheter. [3] Mechanical obstruction by the gravid uterus, along with smooth muscle relaxation from the effects of progesterone, result in urinary stasis. This increases the risk of pyelonephritis complicating asymptomatic bacteriuria.

Asymptomatic bacteriuria is estimated to occur in about 2 to 10% of pregnancies. [2,3] This is consistent with the local Singaporean incidence of 6% found in our study. Most clinical guidelines recommend routine antenatal screening for asymptomatic bacteriuria due to the association with increased risk of pyelonephritis (up to 50%), preterm labour and low birth weight (<2500 grams). [4,5,6] However, among the cases of asymptomatic bacteriuria detected in our study, there was no adverse outcome such as those described. This could be attributed to the prompt treatment of asymptomatic bacteriuria with antibiotics in two out of three cases. The remaining case did not receive antibiotics, as this patient was a late booker at 30 weeks and subsequently defaulted follow up until delivery. This is consistent with findings by Kazemier et al in Netherlands. [7] Our lack of observed adverse outcomes may be due to our small study population. However, our study serves as a pilot study for future studies on asymptomatic bacteriuria in Singapore.

Interestingly, the BMI of patients with asymptomatic bacteriuria was found to be significantly higher than the group without. This was statistically significant ($p = 0.04$). A review of current literature revealed mixed opinions with regards to the effect of BMI as a risk factor of asymptomatic bacteriuria or urinary tract infection. Several other retrospective analyses on asymptomatic bacteriuria in pregnancy failed to detect any significant difference in BMI between these two groups of patients. [11,12,13] However, a large observational study in Australia found that women with a BMI $\geq$ 35 kg/m2 had a significantly higher risk of urinary tract infection compared to those with normal BMI. [14] Asymptomatic bacteriuria was not discussed. Future studies such as a large epidemiological prospective cohort studies may potentially guide us in determining the effect of raised BMI as a risk factor for asymptomatic bacteriuria.

With a larger population, we would be able to determine the true incidence of asymptomatic bacteriuria in the local population and in turn, assess the risk of adverse outcomes. Studies such as randomized controlled trials comparing the effects of screening and treatment of asymptomatic bacteriuria could also guide our decision on whether this should be incorporated into management of our local antenatal population. However, many might question the need for screening especially in terms of its cost-effectiveness. As our study found that the risk of asymptomatic bacteriuria is 6% with risk of pyelonephritis lower than 13%, further cost analysis studies need to be performed for this population. It is likely based on Wadland et al's study that screening for asymptomatic bacteriuria is not cost effective in our population. [8]

Other possible adjuncts to the much more costly urine culture include the urine dipstick and urine microscopy. However, among all the cases with asymptomatic bacteriuria in our study, their urine microscopy test was negative for white blood cells. The value of urine dipstick as an alternative to urine culture was compared in a

recent cross-sectional study in Iran. The nitrite test had a high specificity of 100% but a low sensitivity of 37%; while the leucocyte esterase test had a high sensitivity of 100% but a low specificity of 65%. [15] In Taiwan, antenatal urine screening is routinely performed using urinalysis as part of the National Health Insurance program. In a retrospective analysis by Lai et al, asymptomatic pyuria was associated with preterm delivery, low birth weight and lower APGAR score. [13] However, an important weakness pointed out by the authors was that there was no information on whether these patients had any lower genital tract infection. [13] Lower genital tract infections such as bacterial vaginosis are well established to be associated with preterm birth [16], and this could have resulted in the pyuria as well. Likewise, a review article on eight studies comparing the use of rapid urine screening alone or in combination against urine culture concluded that no test is a sufficiently accurate alternative to urine culture. [17] Urine culture remains the gold standard for detection of asymptomatic bacteriuria. [2,5]

Our study was limited by its small sample size which was insufficiently powered to determine the incidence of complications in patients with asymptomatic bacteriuria. A larger study population is necessary to determine the true incidence of asymptomatic bacteriuria and neonatal outcomes. Moreover, the diagnosis of asymptomatic bacteriuria in our study was based on a single urine culture. Up to 80% of women have true bacteriuria after a single urine culture. The diagnostic accuracy increases to 95% after 2 consecutive cultures positive for the same organism. [2,3,18] However, this is unlikely to be feasible in our clinical practice due to the cost of urine cultures and difficulty in patients' compliance with repeated visits. Nevertheless, this is the first local study on the incidence of asymptomatic bacteriuria in our antenatal population. It encourages further studies and discussions onto whether urine screening for asymptomatic bacteriuria in pregnancy should be performed, if at all. If the risk of adverse outcomes is truly low, then perhaps it is justified to continue our current practice of not screening for asymptomatic bacteriuria in pregnancy. In addition, the subjects in our study were culturally and socioeconomically diverse, which is representative of the larger population in this multiracial country.

To date, the screening of asymptomatic bacteriuria is controversial. Rather, the fundamental question lies in whether asymptomatic bacteriuria does in fact need to be treated. A systematic review by Angelescu et al concluded that the reduction in incidence of pyelonephritis in women who received treatment with antibiotics was based on data collected more than 50 years ago, whereas recent statistics reveal that there is actually no significant difference. [1] Kazemier et al found no significant difference in the proportion of women who developed pyelonephritis, preterm birth (less than 34 weeks) or both between asymptomatic bacteriuria-positive women who were untreated or received placebo and asymptomatic bacteriuria-negative women. [7]

CONCLUSION

The incidence of asymptomatic bacteriuria in our study is 6%, consistent with international data. However, there was no adverse outcome among these patients. Larger adequately powered studies are needed to provide more information on the true incidence and guide recommendations on the role of routine screening for asymptomatic bacteriuria in our antenatal population. Randomized controlled trials evaluating the benefits and risks of screening of asymptomatic bacteriuria will also be useful in guiding future local practice.

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Table I. Characteristics of Patients with and without Asymptomatic Bacteriuria

Characteristics	Asymptomatic Bacteriuria $n = 3$ (Mean ± SD)	No Asymptomatic Bacteriuria $n = 47$ (Mean ± SD)	*P*
Age (years)	29.7 ± 6.5	29.2 ± 4.3	0.851
Gestational age at urine studies (weeks)	15.4 ± 12.9	12.3 ± 6.2	0.721
Gestational age at booking visit (weeks)	14.4 ± 13.6	11.9 ± 6.3	0.787
BMI (kg/m^2)	28.7 ± 1.7	22.9 ± 4.7	**0.04**
Race			
Chinese	1 (33.3%)	21 (44.7%)	
Malay	1 (33.3%)	14 (29.8%)	
Indian	1 (33.3%)	3 (6.4%)	
Others	0	9 (19.1%)	

Table II. Cases of Asymptomatic Bacteriuria

Case	Age (years)	Gravida/Para	GA at booking (weeks)	GA at urine studies (weeks)	BMI (kg/m^2)	White Cell Count on Urine Microscopy/ mm^3	Epithelial Cell on Urine Microscopy/ mm^3	Organism on urine culture ($>10^5$ count)	Treatment	GA at delivery (weeks)	Birth Weight (g)
1	23	G1P0	7.0	10.0	27.0	0	2	*E. coli*	Cephalexin	39.3	3092
2	30	G2P1	30.1	30.1	28.6	0	0	*E. faecalis*	Nil	38.7	3410
3	36	G3P1	6.0	6.0	30.5	0	2	*K. pneumoniae*	Cephalexin	37.9	3698

(GA: Gestational age, BMI: Body Mass Index)

* Cephalexin dose: 500mg three times per day for 5 days

Table III. Observed outcomes in patients with and without asymptomatic bacteriuria

Outcome	Asymptomatic Bacteriuria $n = 3$ (Mean ± SD)	No Asymptomatic Bacteriuria $n = 36$ (Mean ± SD)	*P*
Pyelonephritis	0	0	
Gestation age at delivery (weeks)	38.6 ± 0.7	37.6 ± 4.7	0.714
Birth Weight (g)	3400.0 ± 303.1	3065.4 ± 324.1	0.093

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Induction of Labour – a Review of the Indications

Claudia Ren Hwee TONG, Tony Yew Teck TAN

ABSTRACT

Induced labour has poorer outcomes when compared to spontaneous labour. Outcomes of induction of labour (IOL) and expectant management (EM) should be compared against each other as these are the two options available. EM may result in spontaneous labour or in IOL at a later gestation. IOL at full term is associated with decreased caesarean section rates, pre-eclampsia, perinatal death, stillbirth, meconium aspiration syndrome and neonatal morbidity risks as compared to EM. The widely accepted indications for IOL include prolonged pregnancy (≥ 41 weeks), advanced maternal age (age ≥ 40 or age ≥ 35 at 39 weeks), gestational diabetes mellitus at 38-40 weeks, hypertensive disorders in pregnancy (37-39 weeks), large for gestational age (37-38 weeks), and small for gestational age (36-38 weeks). More recently, IOL at 39 weeks for low risk nulliparous women has been shown to reduce the risk of caesarean section, gestational hypertension, andneonatal respiratory morbidity.

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INTRODUCTION

Induction of labour (IOL) is increasingly common, occurring in at least 20% of deliveries in developed countries. With the recent ARRIVE trial (A Randomized Trial of Induction Versus Expectant Management) showing that IOL at 39 weeks for low risk nulliparous women reduces the risk of caesarean sections (CS) , gestational hypertension, and neonatal respiratory morbidity [1], the rate of IOL is set to increase further. This review seeks to discuss indications of IOL in both low and high-risk pregnancies by comparing the outcomes of IOL and expectant management (EM).

SHOULD OUTCOMES OF IOL BE COMPARED TO OUTCOMES OF EM OR SPONTANEOUS LABOUR?

IOL has poorer outcomes when compared to spontaneous labour. These include higher rates of CS [2], increased analgesia use during labour and increased utilization of precious labour ward resources.

However, induced labour and spontaneous labour are not true options available for the patient.

At any one gestation, one can choose IOL or EM. For patients managed expectantly, they may subsequently progress on to spontaneous labour or be induced for other indications at a later gestation (see **Fig. 1a**). In a recent randomized controlled trial (RCT) comparing IOL and EM in nulliparous women at 39 weeks, half of the patients managed expectantly underwent IOL later for prolonged pregnancy, decreased fetal movement and hypertensive disorders of pregnancy. [3]

Comparing outcomes of induced labours against those of spontaneous labours (see **Fig. 1b**) is easily done by retrospective studies of labour ward admissions. Comparing outcomes of IOL against that of EM is more challenging. Such an evaluation is best achieved by a large RCT comparing the short- and long-term outcomes to the mother and the fetus / neonate / child for each indication. Meta-analyses of available RCTs are the next best method for such an evaluation. IOL should then be offered when the risks of EM to the mother and/or fetus exceed the risks associated with IOL.

POSSIBLE REASONS FOR OBJECTIONS TO IOL

There are 4 main objections to routine IOL. Firstly, many believe that IOL increases the risk of CS. Secondly, some may think that labour would start naturally when the fetus is ready, therefore IOL is unnatural and would increase the risk of neonatal morbidity. Thirdly, there are concerns that IOL would utilize precious busy labour ward resources and increase the cost of medical care. Lastly, patients who wish to have minimal intervention during labour would probably not accept an offer of an IOL. These are the main concerns that will be considered in this review.

IOL FOR LOW RISK PATIENTS

Our discussion in this section focuses on IOL in term low-risk pregnancies, particularly at 39 weeks. As a clarification, we do not support routine IOL in early term low-risk pregnancies (i.e. at 37+0-38+6 weeks).

There is overwhelming evidence to suggest that non-medically indicated deliveries at early term leads to greater risk of adverse outcomes in neonates and infants compared to delivery at 39 weeks. [4] The Consortium of Safe Labor included a large retrospective cohort study (N=233,844) which showed greater risk of respiratory morbidities in infants delivered at 37 weeks as compared to 39 weeks. [5] Another study from the Eunice Kennedy Shriver National Institute of Child Health and Human Development showed that even neonates delivered just short of the 39-week mark, i.e. at 38+4 to 38+6 weeks of gestation, still sustained significantly greater risk of morbidity. [6]

IOL at 39 weeks for low risk nulliparous women decrease the risk of CS

The main reservation most obstetricians have about IOL in low risk pregnancies is that it is associated with a higher CS rate when compared with spontaneous labour. However, IOL actually lowers CS rate when rightly compared with EM. A meta-analysis (N=9217) of RCTs of IOL versus EM showed a 18% relative reduction in CS rate.[7] A more recent Cochrane meta-analysis (N=12,479) comparing IOL vs EM at or beyond term similarly showed that IOL reduced the rates of CS. [8] This is contrary to many obstetricians' belief about induced labour.

More discerning academics would note that both meta-analyses include the large (N=3,407) Canadian Multicenter Post-Term Pregnancy Trial in 1992 which could have skewed the results of CS rate in favour of IOL. [9] A drawback in that study design was the restriction of prostaglandin use in the EM group if IOL was required later up to 44 weeks as the authors felt that the rates of fetal distress were inherently higher in that group. Hence the rate of prostaglandin use was significantly lower in the EM group, which could explain the higher rates of CS in the EM group.

The recently published ARRIVE trial involving 6,106 women from 41 hospitals in the US clearly showed that IOL in low risk nulliparous women at 39 weeks 0 days to 39 weeks 4 days gestation had a lower CS rate when compared to EM till 40 weeks 5 days to 42 weeks 2 days gestation (18.6% vs 22.2%, RR 0.84 [0.76=0.93]). (1) The reduction in CS rate for IOL in

these nulliparous women was similar in women with favourable and unfavourable cervixes. This is another counter-intuitive finding as most clinicians believed failed IOL to be more a problem with nulliparous women with unfavourable cervixes. Such women are more likely to remain undelivered with EM and continue to have a high rate of CS after IOL later. In addition, the ARRIVE trial also showed that IOL at 39 weeks in nulliparous women reduced the risk of pre-eclampsia and gestational hypertension when compared to EM (9.1% vs 14.1%, RR 0.64, 95% CI 0.56-0.74).

It is important to note that strict criteria were followed in this trial including accurate dating before 20 weeks, use of cervical priming methods before IOL for unfavourable cervixes and allowing a long time after rupture of membranes and oxytocin use for the patient to get into active phase of labour, defined as cervix ≥ 5-6 cm dilated. The latter criterion reduced the number of "failed IOL" that required CS. In a separate observational study involving 10,677 women, it was found that 8.6% of women were still in latent phase at 12 hours after IOL. At 15 hours, however, only a small minority (3.6%) of nulliparous women remained in latent phase. [10] The definition for failed IOL was therefore proposed to be the failure to reach the active phase of labour (cervical dilatation ≥ 5-6 cm) only after at least 15 hours of oxytocin and rupture of membranes. If labour wards were to adopt this definition, unnecessary CS can be avoided, and the CS rate could be further reduced.

Thus far, most of the available data discussed are for nulliparous women, or for mixed groups of nulliparous and multiparous women. Indeed, there is paucity of randomised controlled trials (RCTs) looking at IOL versus EM in low risk multiparous women. CS after IOL for multiparous women is known to be low at about 4%. [11] It is not clear if IOL vs EM would result in an even lower rate of CS in low risk multiparous women.

IOL from 39 weeks decreases the risk of neonatal morbidity and perinatal mortality

Neonatal outcomes (e.g. NICU admissions, respiratory morbidity) in early term births at 37-38 weeks are poorer than those of full-term births at 39-41 weeks [12], and hence IOL should be avoided before 39 weeks.

At 39 weeks, IOL significantly reduces neonatal respiratory morbidity (3.0% vs 4.2%, RR 0.71, 95% CI 0.55-0.93) (1) and meconium stained liquor (4.0% vs 13.5%, RR 0.32, 95% CI 0.18 - 0.57). [13] IOL at or beyond term vs EM also reduces the risk of meconium aspiration syndrome (RR 0.77, 95% CI 0.62 - 0.96, N=7,781 infants in 11 trials). [8]

IOL at or beyond term vs EM is associated with fewer perinatal deaths (RR 0.33, 95% CI 0.14-0.78), fewer stillbirths (RR 0.33, 95% CI 0.11-0.96), and lower rates of APGAR scores < 7 at 5 minutes (RR 0.70, 95% CI 0.50-0.98). [8] The reduction in stillbirths with IOL is not surprising as large observational data have shown an increase in prospective stillbirth risks from 38-39 weeks (see **Fig. 2**). [14, 15, 16] In the ARRIVE trial, whilst the primary outcome measure of perinatal composite (which includes perinatal death and perinatal morbidity) was not statistically significant in the same trial (4.3% vs 5.4%, RR 0.80 [95% CI 0.64-1.00]), there was nevertheless a 20% reduction in the risk in the IOL group. This is probably due to a small difference of 5 days in the median gestational age at delivery for both the IOL and EM groups (39.3 weeks vs 40.0 weeks, p<0.001). If EM was more persistently pursued till a later gestation in the ARRIVE trial, it would be reasonable to expect that the difference in the better outcomes of IOL and the poorer outcomes of EM would have widened further.

Indeed, IOL at 39 weeks may well reduce stillbirth in this and the next pregnancy. A previous CS (compared to previous vaginal birth) increases the risk of stillbirth (OR 1.14-1.56) and unexplained stillbirth (OR 1.47-2.34). [17, 18, 19] As IOL reduces the risk of CS in this pregnancy, one could argue that it would also reduce the risk of stillbirth in the next pregnancy.

Hence, while EM may seem more natural and allow a higher chance for the pregnancies to go into spontaneous labour, it is clearly not a safer option for the fetuses/neonates when compared to IOL.

IOL would utilize more labour ward resources but may not increase the cost of care

IOL at 39 weeks for low risk nulliparous women

results in a longer median stay in labour ward compared to EM (median of 20 hrs stay vs 14 hrs, $p < 0.001$) but a shorter stay in the hospital after delivery.[1] Hence widespread adoption of routine IOL could potentially place additional strain on busy labour wards.

This, however, does not translate to an increased cost of the IOL strategy when compared to the EM strategy. In adopting the EM strategy, it has been noted that there were more readmissions, more visits to the antenatal clinics, and more intensive antenatal monitoring with ultrasound scans and cardiotocographs. Indeed, economic analyses showed either similar or lower costs for the IOL strategy when compared to the EM strategy. [20, 21, 22] By reducing the CS rate, IOL is likely to reduce the overall cost of care.

IOL may not be acceptable to some patients but patients who have had induced labours reported better satisfaction

Interestingly, 73% of the eligible women had declined to participate in the ARRIVE trial. [1] We can only speculate that some of these women may have a desire for non-intervention for the labour and hence declined randomization. With the new findings, it is not yet clear how patients would choose if properly counselled on the risks of IOL versus EM at 39 weeks.

However, among the women who underwent IOL in the ARRIVE trial, they generally reported less pain and more perceived control during delivery. [1] In another trial, the majority of women who were allocated to the IOL arm (74%) also wished to be allocated to the same trial arm again, twice the proportion for the group allocated to the EM arm. [23]

IOL FOR HIGH RISK PATIENTS

Prolonged pregnancy ≥ 41 weeks

This is a common occurrence affecting about 10% of all pregnancies.

Risks of EM after 41 weeks

EM after 41 weeks is associated with increased risks of a bigger baby (e.g. macrosomia, CS from poor progress of labour, shoulder dystocia and anal sphincter tear) [13], placental deterioration (e.g. stillbirth, fetal distress requiring CS during labour, meconium-stained liquor and meconium aspiration syndrome, cerebral palsy) and maternal hypertensive disorders in pregnancy. [24, 25]

As such, standard management during EM in prolonged pregnancy requires increased frequency of visits to the obstetrician, with serial monitoring with CTG and AFI in many centres' protocols. This consumes more medical resources, creates more anxiety for patients (and obstetricians), and unfortunately still results in cases of "unexplained" stillbirths.

Outcomes of IOL vs EM

The largest single RCT (N=3,407) done on this topic was the Canadian Multicenter Post-Term Pregnancy Trial Group in 1992. IOL was shown to have a lower rate of CS (21.2% vs 24.5%, p=0.03), especially the rate of CS from fetal distress (5.7% vs 8.3%, p=0.003).(9)

Subgroup analysis in the Cochrane meta-analysis in 2018 compared IOL after 41 completed weeks of gestation to EM. IOL resulted in fewer perinatal deaths and lower rates of NICU admission. [10]

Term Premature Rupture of Membranes (Term PROM)

PROM complicates about 8% of term pregnancies.

Risks of EM

With EM, 50% of term PROM patients would have delivered within 33 hours, and 95% delivered within 94-107 hours of membrane rupture.[26] However, EM may also lead to increased risks of maternal and neonatal infection, prolonged hospitalization and may also increase risks of fetal distress resulting from possible cord prolapse or placental abruption. [27]

Outcomes of IOL vs EM

The first and largest RCT on term PROM patients was the Term PROM Study (N=5,041) [28] which

showed no difference in rates of CS (10.1% vs 9.7%, Odds Ratio 1.0, 95% CI 0.8-1.4) and neonatal infection (2.0% vs 2.8%, Odds Ratio 0.7, 95% CI 0.4-1.2) between IOL and EM for term PROM pregnancies. However, IOL with oxytocin led to a significantly lower incidence of clinical chorioamnionitis compared with EM (4.0% vs 8.6%, p<0.001), an advantage which IOL has over EM. Also, women were more likely to have positive experiences after IOL when compared to EM. ([28, 29]

More recently, the Cochrane review of 23 trials exploring IOL versus EM in term PROM pregnancies (N=8615) also demonstrated that IOL decreased the risk of maternal infection i.e. chorioamnionitis and endometritis (RR 0.49, 95% CI 0.33-0.72) and risk of early-onset neonatal sepsis (RR 0.73, 95% CI 0.58-0.92). [30] In addition, EM tends to prolong hospitalization and increase healthcare costs as well. [31]

Suspected Small for Gestational Age (SGA) Fetus at Term

SGA fetuses are defined as fetuses with AC or EFW measuring less than the 5th or 10th centile. This occurs in 5-10% of all pregnancies and is a concern because it may indicate a hostile intrauterine environment for the fetus with deteriorating placental function.

Risks of EM

In suspected mild to moderate SGA fetuses at term, EM till 38-39 weeks may reduce the risk of respiratory morbidity at 37 weeks but expose the fetuses to possibly further deteriorating placental function, potentially increasing the risks of perinatal morbidity, mortality and possibly neurodevelopmental difficulties in childhood. [32]

Outcomes of IOL vs EM

The DIGITAT trial (Disproportionate Intrauterine Growth Intervention Trial at Term) [33] explored the outcomes related to IOL versus EM in 650 singleton pregnancies beyond 36 weeks with suspected IUGR. IOL was associated with a significant reduction in neonates born with birth weight below the third centile (12.5% vs 30.6%, difference in mean -18.1%, 95% CI -24.3 to -12.0). In terms of maternal morbidity, there was also a reduction in progression to pre-eclampsia with IOL (3.7% vs 7.9%, difference in mean -4.2%, 95% CI -7.7 to -0.6). IOL is also not associated with increased CS rates, neonatal morbidity and subsequent neurodevelopmental or behavioural problems in the children [32, 33]. EM beyond 38 weeks, however, has been shown to lower NICU admission rates. [33, 34]

SGA fetuses with absent or reversed end-diastolic flow on umbilical artery Doppler should undergo CS as soon as possible while SGA fetuses with normal umbilical artery flow or present end-diastolic flow can be offered IOL and monitored closely with Doppler studies and CTG. [35]

Suspected Macrosomia

Macrosomia can either be defined as birth weight > 4000g regardless of gestational age, or when the estimated AC or estimated fetal weight (EFW) is >= 95th centile. This complicates about 5% of all pregnancies.

Risks of EM

Macrosomia is associated with poorer obstetric outcomes affecting both the mother and child, including emergency CS, shoulder dystocia, maternal anal sphincter tears, as well as neonatal intensive care unit (NICU) admission. [36] With EM, the fetal weight typically gains 200 to 300 grams further per week, and hence increases the rates of the aforementioned risks.

Outcomes of IOL vs EM

A RCT in 2015 (N=818) [37] found that IOL at 37-38 weeks in pregnancies with suspected macrosomia reduced the incidence of significant shoulder dystocia (8/407 or 2% in IOL group vs 25/411 or 6% in the EM group, RR 0.32, 95% CI 0.12-0.85), and was associated with a higher rate of spontaneous vaginal delivery (59% vs 52%, RR 1.14, 95% CI 1.01-1.29). There was no difference in the rate of CS rate or neonatal morbidity.

Meta-analyses involving 4 RCTs (N=1190) comparing IOL at or near term for suspected fetal macrosomia versus EM showed a reduction in shoulder dystocia

(RR 0.60, 95% CI 0.37-0.98) and birth fractures (RR 0.20, 95% CI 0.05-0.79). [38, 39]

Maternal Obesity

Maternal obesity is defined similarly as for non-pregnant individuals when the pre-pregnancy body mass index (BMI) is ≥30. [40] Up to 30% of pregnant women in some developed countries are obese.

Risks of EM

Maternal obesity increases the risk for gestational diabetes, gestational hypertension, pre-eclampsia, CS and delivery of a macrosomic baby [41, 42, 43], and EM would further increase these risks. Obesity is also associated with fetal growth restriction, preterm birth, stillbirth and even fetal death. [44]

Outcomes of IOL vs EM

In a prospective controlled study (N=1,927), IOL in nulliparous obese women compared to nulliparous women with normal BMI led to a doubling of the risk of emergency CS (p<0.006),[45] suggesting that IOL in obese patients is associated with higher risks.

There are no RCTs performed that studied IOL versus EM with maternal obesity as a sole indication. A recent study using modelled retrospective cohort data [46] showed that IOL at 39 weeks vs EM for obese nulliparous women reduced CS rates (35.9% vs 41.0%, p < 0.05, adjusted OR 0.82, 95% CI 0.77-0.88), severe maternal morbidity (5.6%vs 7.6%, p < 0.05, adjusted OR 0.75, 95% CI 0.65–0.87) and NICU admission rates (7.9% vs 10.1%, p < 0.05, adjusted OR 0.79, 95% CI 0.70–0.89). For the morbidly obese (BMI >=40 kg/m2) women, IOL vs EM also reduced the risk of CS for multiparous women at term (5.4% vs 7.9%, adjusted OR 0.64, 95% CI 0.41-0.98). [47]

A subgroup analysis in the ARRIVE trial showed that IOL versus EM in women with BMI >=30 had a lower CS rate (RR 0.89, 95% CI 0.79-1.00) although it was not statistically significant. [1]

Advanced Maternal Age

Advanced maternal age (AMA) at pregnancy poses an issue as it increases risk of CS and preterm delivery (48), and is associated with a 65% increase in stillbirth risk. [49, 50]

Risks of EM

In addition, the risk of stillbirth increases with gestational age after 39 weeks, and this uprising trend is more prominent in older women (see **Fig. 2**). For instance, the risk of stillbirth at 39 weeks for a 40-year-old woman is more than double the risk for a 30-year-old lady with a post-term pregnancy at 41 weeks' gestation. [14]

Outcomes of IOL vs EM

In the 35/39 trial [3] with a small number of participants (N=619), the outcomes of IOL and EM at 39 weeks were compared for women aged 35 and above with an uncomplicated singleton pregnancy. IOL was also not associated with increased CS rates (32% in IOL group vs 33% in EM group; RR 0.99, 95% CI 0.87-1.14) or rates of instrumental vaginal delivery (38% in IOL group vs 33% in EM group; RR 1.30; 95% CI 0.96-1.77). The trial however was not sufficiently powered to show reduction in the risk of term stillbirth in AMA. IOL for advanced maternal age at 39 weeks is already a common indication in many centres.

PROPER CONDUCT OF IOL

A proper conduct of IOL would involve cervical priming with cervical membrane sweep [51], intracervical balloon catheter [52] and/or use of prostaglandin E1 or E2 [53], followed by intravenous oxytocin with or without rupture of membranes. Use of intravenous oxytocin without prior cervical priming leads to a lower rate of successful vaginal delivery within 24 hrs. [54]

Oxytocin has a short plasma half-life of 3-6 minutes, with uterine response occurring within 3-5 minutes, and steady levels in plasma by 40 minutes. If 10 IU of oxytocin was diluted in 500 ml of normal saline or dextrose 5% with normal saline (equivalent to 20 mU/ml), 1 mU/min is equivalent to an infusion rate of 3 ml/hr. IV oxytocin can be started at 0.5-2 mU/min (or 1.5-6 ml/hr), and increased at an arithmetic sequence of 1-2 mU/min (or 3-6 ml/hr)

every 15-40 minutes until regular contractions lasting about 60-90 seconds every 2-3 minutes is established or till a maximum of 40 mU/min (or 120 ml/hr) unless uterine hyperstimulation (more than 5 contractions in 10 minutes) or fetal distress occurs. If the cervix has not dilated beyond 5-6 cm after at least 15 hours of oxytocin and rupture of membranes, failed IOL may be diagnosed. [10]

Once the labour is in the active phase, consideration should be given to either discontinue or reduce the dose of oxytocin. Continuation increases the risk of CS (14.3% vs 8.6%, RR 1.67, 95% CI 1.25-2.23), uterine hyperstimulation (12.4% vs 4.7%, RR 2.59, 95% CI 1.70-3.93) and non-reassuring fetal heart rate (19.2% vs 12.5%, RR 1.55, 1.18-2.02) compared to discontinuation of oxytocin. [55]

CONTRAINDICATIONS TO IOL

The contraindications to labour induction are generally similar to the contraindications for vaginal delivery. These include previous uterine rupture, previous major uterine surgery, placenta and vasa previa, abnormal fetal lie or presentation, as well as anatomical abnormalities of the uterus or pelvis. [56] Previous uterine scars are also a relative contraindication to induction as the risk of uterine rupture increases with IOL compared to spontaneous labour.

CONCLUSION

In summary, outcomes of IOL versus EM should be used to determine the merits of IOL, and not the outcomes of induced vs spontaneous labours. With the increasing evidence supporting IOL vs EM for both low and high-risk patients, the option of IOL should now be offered routinely to all patients without a uterine scar from 39 weeks. A careful discussion of the pros and cons of both IOL and EM should be done with the patients and their partners. IOL should be avoided for pregnancies < 39 weeks unless there are high risk factors like macrosomia, SGA fetus, gestational diabetes and gestational hypertension / pre-eclampsi

FIGURE LEGENDS:

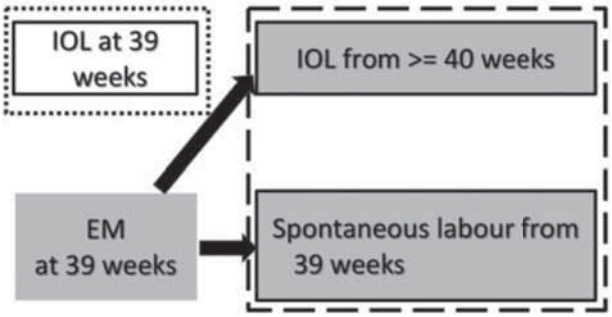

Figure 1a.

Options for Managing a Patient at 39 weeks' Gestation: Induction of labour (IOL) vs Expectant Management (EM). EM at 39 weeks may result in spontaneous labour from 39 weeks or IOL from 40 weeks onwards for other obstetric indications (see the dashed box). The outcomes of EM at 39 weeks should be compared with the outcomes of IOL at 39 weeks (see dotted box).

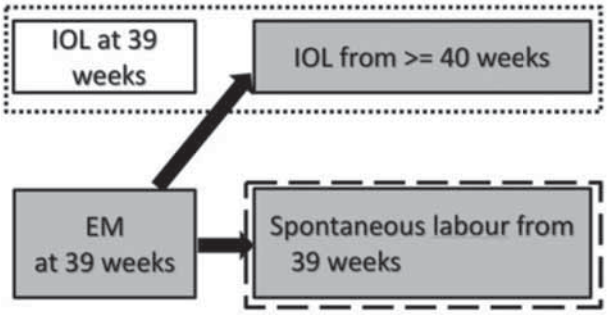

Figure 1b.

The comparison between induced labour (see dotted box) and spontaneous labour (see dashed box) is flawed as this would have incorrectly included the IOL cases from 40 weeks onwards that resulted from EM into the initial group for IOL at 39 weeks.

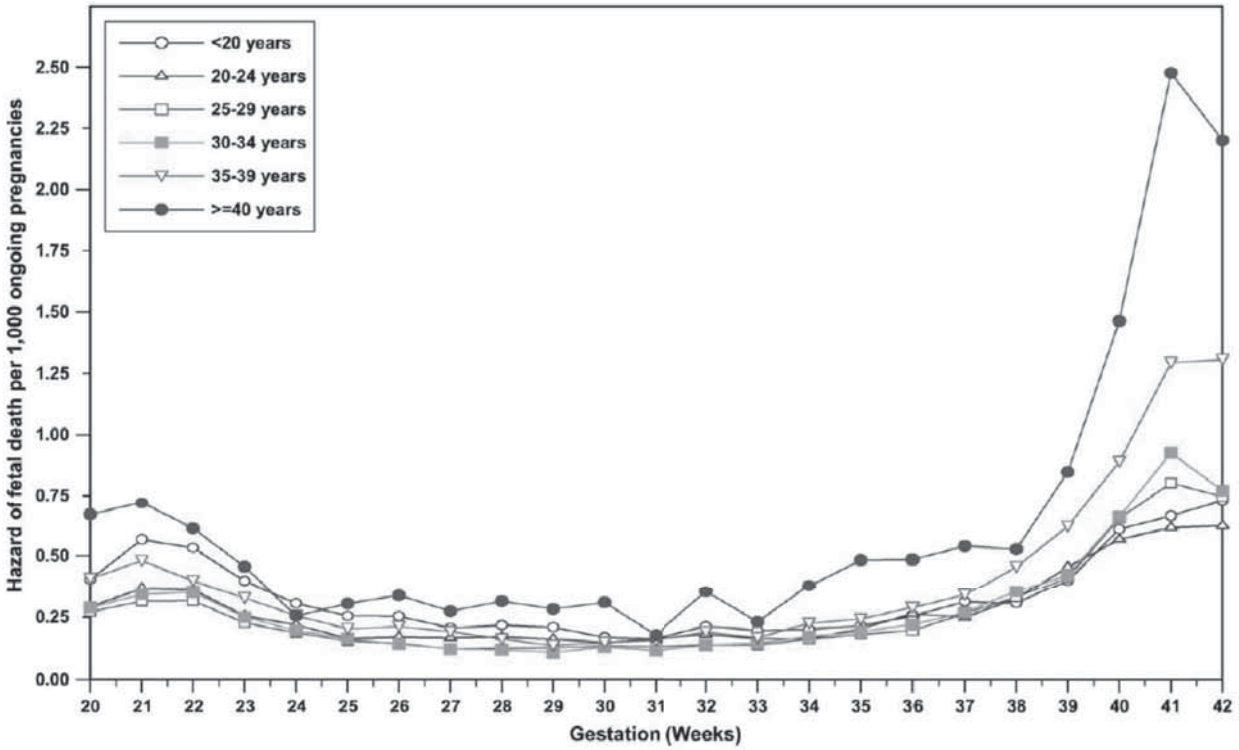

Figure 2.

This shows the prospective risk of stillbirth for ongoing pregnancies from Reddy et al (14). The risk of antepartum stillbirth increases from 38-39 weeks onwards and that the risk of antepartum stillbirth increases with maternal age.

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Ruptured Isthmocele: Myometrial Niche or Fascial Covering? An Unusual Cause for Irregular Bleeding and Potential Long Term Gynaecological Complication of Caesarean Section

Mohamed Siraj SH, Ann Wright

ABSTRACT

Introduction: *Scar rupture is a well-recognised obstetric complication after previous caesarean section and the incidence of both scar ectopic pregnancy and a morbidly adherent placenta in subsequent pregnancy is increasing but now it is becoming clear that scar problems may also be responsible for a number of gynaecological complaints and should be included in the differential diagnosis of women presenting after an operative delivery. We present the first case of a ruptured isthmocele in a non-gravid uterus and attempt to explain its aetiology.*

Case Summary: *We report the case of a grand multipara who presented acutely with pain, fever and anaemia and who had a history of prolonged postmenstrual spotting with previous four successful vaginal births following caesarean section (VBAC). After extensive investigation she was found to have a deficient scar with disruption of the overlying fascial layer. The redundant fascia was excised and the uterine defect repaired with complete resolution of her symptoms.*

Conclusion: *In this age of increasing caesarean section it is important to include the diagnosis of ruptured isthmocele or disrupted scar fascia associated with underlying myometrial deficiency in women with otherwise unexplained gynaecological symptoms presenting after caesarean section.*

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INTRODUCTION

The rate of caesarean delivery now exceeds 30% in a lot of the developed world. As a result, the rate is rising of caesarean scar defect—the presence of a "niche" at the site of the caesarean scar—with a reported prevalence of between 24 and 70% in a random population of women with at least one caesarean delivery [1] and an estimated one in three of caesarean delivery patients developing symptoms from this defect [2]. While scar rupture is a well-recognised and feared complication in subsequent pregnancy, gynaecological complications such as utero-peritoneal fistula, niche, and isthmocele which lead to less dramatic symptoms such as irregular bleeding and pelvic pain are less well known and are currently underdiagnosed and therefore remain untreated. We report a case of 'niche' rupture in an attempt to raise clinical

awareness of this important condition when faced with unexplained gynaecological symptoms after caesarean section.

CASE REPORT

A 31-year-old Malay grand multipara presented with a two-day history of lower abdominal pain and tenderness associated with fever on day two of menses, having had post menstrual spotting since the normal delivery of her last child eighteen months previously. She had had four successful vaginal births after a primary Caesarean section for breech in 2010, with a cerclage being placed in the last two pregnancies because of two mid trimester miscarriages. Her haemoglobin at presentation was 5.9g/dl.

An initial pelvic ultrasound scan revealed a 4.3cm fluid collection with internal echoes anterior to the lower uterus and very thin myometrium in the area of her scar. A subsequent MRI revealed a 5 x, 5 x3.3cm lobulated cystic structure in continuity with the endometrial cavity extruding anteriorly at the level of the previous scar. A diagnosis of scar defect was made. (Figure1)

After a blood transfusion and with intravenous antibiotic cover, she underwent hysteroscopy which showed ballooning of an isthmocele which a laparoscopy, being performed at the same time, confirmed had ruptured and was bleeding. Because of the associated inflammation and the position of the defect, being at very low in the pelvis and close to the bladder base, a decision was made to open to allow better access for repair.

At laparotomy the endoscopic findings were confirmed. The isthmocele was opened laterally from the point of rupture and the myometrial fibres of the lower uterus just above the cervix were identified and pulled up with Littlewood forceps. The bladder was dissected free and the isthmocele resected with removal of all the redundant tissue which was sent for histopathology. The defect was then repaired in two layers with vicryl and the visceral peritoneum closed over the repair. (Figure2)

Histological examination of the tissue removed shows strips of fibrofatty tissue coated by a layer of fibrin admixed with an inflammatory infiltrate consisting of neutrophils, lymphocytes and macrophages (Figure 3A and 3B). The inflammatory cells are seen extending into the underlying fatty tissue. A focus shows inflamed scar tissue consisting of hyalinized fibrous tissue with scattered aggregates of inflammatory cells (see picture 3C).

She was reviewed three months later and reported compete resolution of her symptoms. A pelvic scan showed obliteration of the niche.

DISCUSSION

As the caesarean section rate (CSR) continues to increase, concern regarding the association between caesarean delivery and long-term maternal morbidity is growing. In the USA the CSR rose from 21.2 to 32.8% between 1990 and 2011. In the Netherlands, which has one of the lowest CSR in the developed world, it still increased from 7.4 to 15.8% during the period 1990–2008 [3]. While the obstetric-related morbidities of previous caesarean section have been comprehensively reported, the gynaecological complications are less well known.

Caesarean scar defects have been described for 20 years, and laparoscopic repair has been performed for over 15 years [4, 5]; yet patients may have pain, bleeding, and infertility for years before they find a physician who is familiar with the diagnosis, let alone with the treatment of this myometrial defect or isthmocele.

In the past decade several articles have described a defect that can be seen on ultrasound at the site of the caesarean section scar, known as a 'niche' [6, 7, 8] A niche is defined as a triangular anechoic structure at the site of the scar or a gap in the myometrium of the anterior lower uterine segment at the site of a previous caesarean section and is best diagnosed after menses when the endometrial stripe is thin. Niche prevalence depends on the method used for evaluation and the population being investigated. In non-pregnant women the scar is visible with transvaginal ultrasonography (TVU) and contrast sonohysterography using either saline (saline infusion sonohysterography, SIS) or gel (gel instillation sonohysterography, GIS). Magnetic resonance imaging (MRI) can also aid in diagnosis. When viewed hysteroscopically, a concave defect in the anterior uterine wall is often visible. A niche is present in 64.5% of women 6–12 weeks after caesarean section, when examined by GIS [3].

The size of the niche varies depending on the number of vaginal births after caesarean section. With each VBAC, there is progressive thinning of the

scar and deepening of the niche with formation of fibrosis and loss of contractility. Large niches are those with a residual myometrium with thickness of <50% of that of the adjacent myometrium and these have been associated with gynaecological symptoms, in particular post- menstrual spotting and anaemia due to an accumulation of blood in the reservoir-like niche [3].This blood may become infected causing inflammation and potential rupture, as in our case Patients with a caesarean scar defect also experience pelvic pain, vaginal discharge, dysmenorrhea, and dyspareunia. Secondary infertility is common, likely due to accumulated blood degrading the quality of sperm and cervical mucus.

While spontaneous scar rupture is a well-recognised complication in pregnant women who are attempting vaginal delivery after caesarean section we describe the first cases in the literature of scar rupture in a non –gravid uterus Our patient did have many risk factors including four VBACs and cerclage placement, all of which would have led to progressive myometrial thinning, a large niche and finally an isthmocele with no included myometrium.

CONCLUSION

The case aims to raise awareness of this unusual complication and highlights the importance of a high index of suspicion for diagnosis and treatment of a scar related issue in women presenting with gynaecological symptoms after caesarean section to prevent sepsis and life threatening bleeding.

Figure 1 Laparoscopic view of the ruptured myometrial defect/fascial defect with US and MRI Images

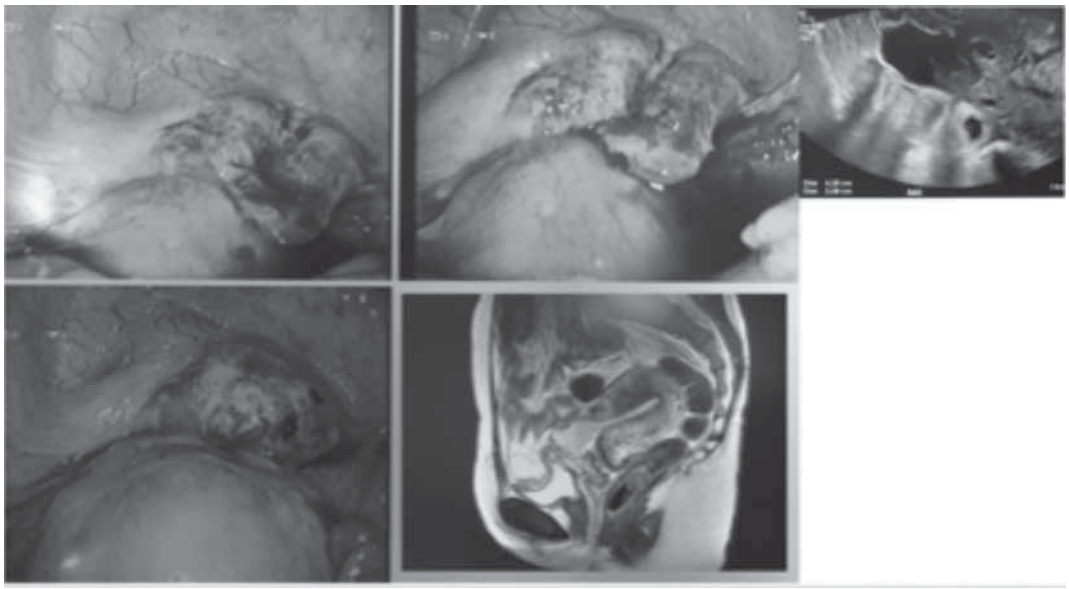

Figure 2 Intraoperative images of the myometrial defect and resection of the isthmocele. Repair of the myometrial defect.

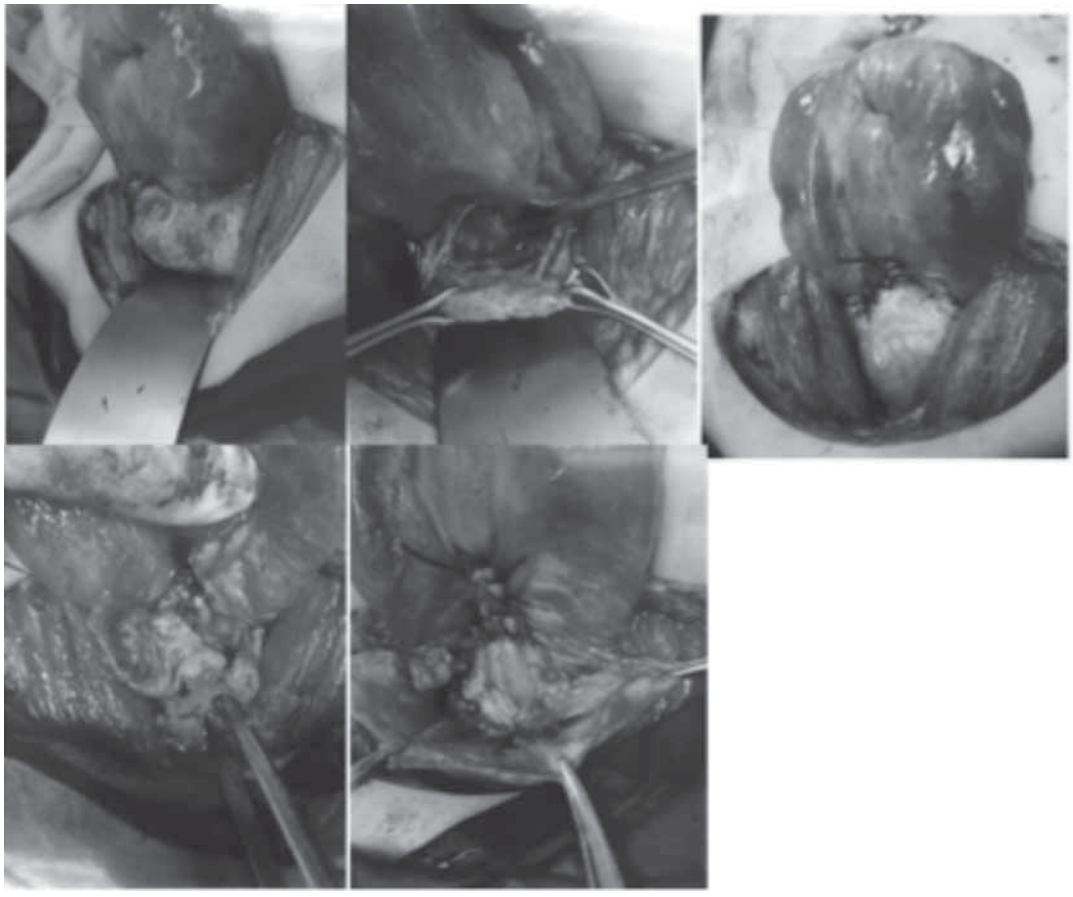

Figure 3A shows the strips of inflamed tissue exhibiting surfaces coated with a layer of fibrin admixed with inflammatory cells (red box). Areas of inflamed fibrosis can be seen (portion of area marked by a black box) (hematoxylin and eosin 40x magnification).

Figure 3B shows the magnified area demarcated by the red box seen in picture 3A. Inflammatory cells composed predominantly of lymphocytes and macrophages with some neutrophils seen sprinkled within the layer of fibrin coating the strips of tissue (hematoxylin and eosin, 200x magnification).

Figure 3C shows a higher magnification of an area demarcated by the black box in Figure 3A. There is inflamed scar tissue composed of pink bundles of hyalinized fibrous stroma with aggregates acute and chronic inflammatory cells (Hematoxylin and Eosin, 200x magnification). (Acknowledgement; AdeleP C Wong for supplying H/P image)

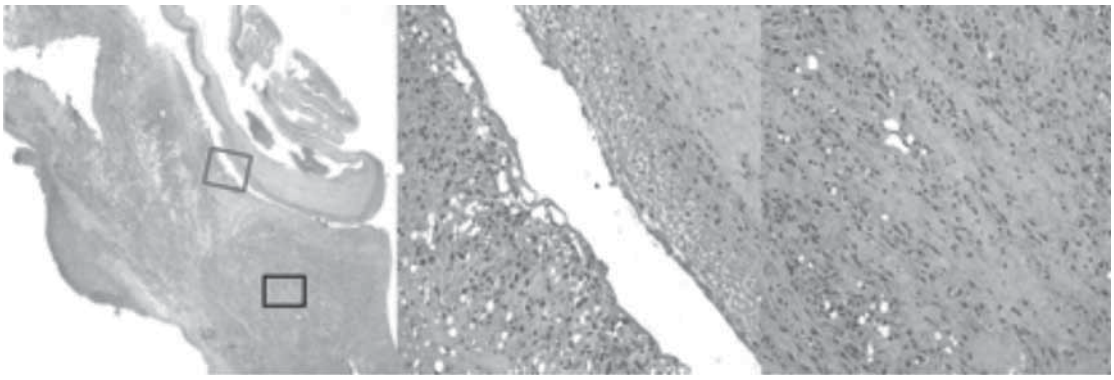

Figure 3A **Figure 3B** **Figure 3C**

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Events

OGSS Educational Night 2019

10 July 2019, Aura @ National Gallery Singapore

Dr Tony Tan presented a talk on "Implementing Maternal Immunization Guidelines and benefits for Mother & Child"

OGSS Members (L-R): Dr Tan Eng Kien, Dr Serene Thain, Dr Lim Min Yu, Dr See Tho Kai Yin

1st year residents from NUHS and SingHealth provided the entertainment for the evening

OGSS Members (L-R): Dr Alex Ooi, Dr Khong Chit Chong, Dr Lee Seong Tuck

OGSS Members (L-R): Dr Serene Thain, Dr Celene Hui, A/Prof Han How Chuan, Dr Suresh Nair, Mrs Han

OGSS Members (L-R): Dr Hong Sze Ching, Dr Natalie Chua, Dr Heng Tung Lan, Mrs Fong, Mrs Lee, Dr Lee Keen Whye, Dr Jessie Poon, Dr Caroline Khi, Dr Arthur Tseng

OGSS Annual Oration 2019

8 November 2019, Regent Hotel Singapore

OGSS President, Dr Timothy Lim Yong Kuei presented Orator, Dr Sudha Nair with a gold plated medal as a token of appreciation

Orator, Dr Sudha Nair presenting a talk on "Silent Wish - The Impact of Domestic Violence on Children"

SS Ratnam Book Prize Winner, Ms Kellynn Oen Qi Xuan

SS Ratnam Book Prize Winner, Mr Wong Hong Zhe Gabriel

SS Ratnam Book Prize Winner, Mr Shawn Sanjay Rajoo

Sitting (L-R): Dr Serena Koh, Dr Tan Yin Ru, Dr Tiffany Wong, Dr Jonathan Han
Standing (L-R): Dr Celene Hui, Dr Julian Kang, Dr Lee Shi Hui, Dr Grace Cheah, Dr Cheryl Lim, Dr Amelia Chua, Dr Selina Chin

Guests, doctors and administrative staffs of NUHS Department of O&G

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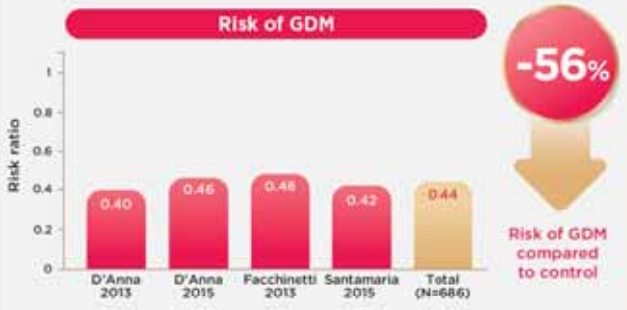
GDM*: Gestational Diabetes Mellitus

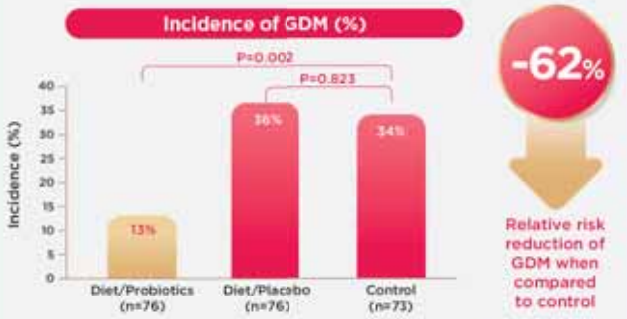
Myo-inositol and probiotics are promising non-pharmacologic agents to reduce the risk of GDM.[2-4]

MYO-INOSITOL[3]



All intervention groups consisting of pregnant women at risk of GDM received 400µg folic acid + 4g of myo-inositol. GDM rate was significantly reduced in the intervention groups.

PROBIOTICS[4]



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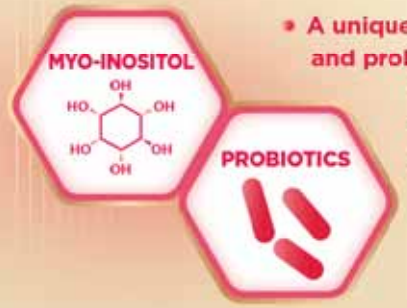

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