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EDITORIAL

Intriguing Review and Topics in Sixth Issue of Thai Journal of Obstetrics and Gynaecology 2024

Vorapong Phupong, M.D., FRTCOG.*

** Editor in Chief, Thai J Obstet Gynaecol, The Royal Thai College of Obstetricians and Gynaecologists*

This sixth issue of Thai Journal of Obstetrics and Gynaecology 2024 contains many interesting articles. The special article is "Effects of cigarette smoking on pregnancy outcomes". The authors reviewed the effect of cigarette smoking on general and reproductive health, pregnant women and fetus, and the benefit of cigarette smoking cessation[1].

This issue also contains six original articles and two case reports. Anantaworapot et al performed a prospective study to assess variance between paired umbilical artery Doppler velocity indices in pregnancies at 18-37 weeks and found significant differences existed in pulsatility index, resistance index, and systolic/diastolic ratio between the two umbilical arteries[2]. Ali et al performed a randomized clinical trial to explore the value and safety of amniotomy after cervical ripening by Foley catheter balloon on termination of mid-trimester fetal death in utero. They found that performing amniotomy after using a Foley catheter balloon for cervical ripening during induction of mid-trimester fetal death in utero in a non-scarred uterus reduced the time to abortion as well as the oxytocin dose[3]. Puttakul et al performed a randomized control trial to evaluate the efficacy of dextrose-containing intravenous fluid and normal saline intravenous fluid in reducing labor duration in pregnant women. They found that dextrose-containing intravenous fluid administered during intrapartum may shorten total labor time especially active phase duration, without increasing maternal and neonatal complications[4]. Peetinarak et al performed a cross-sectional observational study to determine the prevalence and associated factors of vitamin D deficiency in Thai women with uterine fibroids. They found that the prevalence of vitamin D deficiency was 69.6% and there was no significant association between low serum 25-hydroxyvitamin D levels and the presence of uterine fibroids[5]. Nanthawong performed a single-blinded, randomized, controlled trial to evaluate the effectiveness of vibrational anesthesia in reducing pain and anxiety in the group receiving single rod contraceptive implant recipient (SRCI). The result showed that vibrational anesthesia during SRCI may reduce pain and anxiety among the recipients[6]. Manee et al performed a retrospective study to find the incidence and risk factors of obstetrics anal sphincter injuries (OASIS). The results revealed the incidence was 6% and the risk factors of OASIS were nulliparity, occiput posterior postition, forceps extraction, median episiotomy, residents and staffs (as the operators)[7].

Regarding case reports, Ayub et al reported an uncommon case of uterine arteriovenous malformation in woman presented with severe vaginal bleeding[8]. Ng et al reported a rare case of Fournier's gangrene in a pregnant woman with genital herpes and had long-term complications of Fournier's gangrene[9].

The RTCOG 39th annual meeting already held during 29 October - 1 November 2024 at Dusit

Thani, Pattaya, Chonburi, Thailand. The theme of the meeting was "Optimizing OBGYN". This meeting was successful with 1,200 delegates.

For the coming New Year 2025, we would like to extend our warmest wishes to members of Royal Colleague of Obstetricians and Gynaecologists, editorial board, reviewers, authors and families. We thank to all the authors, readers, reviewers, and editors for your contributions to Thai Journal of Obstetrics and Gynaecology this past year and look forward to receiving your invaluable contributions in 2025.

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SPECIAL ARTICLE

Effects of Cigarette Smoking on Pregnancy Outcomes

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ABSTRACT

Cigarette smoking increases several health risks, including maternal and neonatal adverse outcomes if smoking during pregnancy. Ectopic pregnancy, placenta previa, abruptio placenta, preterm premature rupture of membranes, low birthweight (less than 2,500 grams), intrauterine growth restriction, intrauterine fetal death, neonatal respiratory and gastrointestinal disease, need of transfer of newborn to a neonatal intensive care unit (NICU), and more than 7 days NICU admission of the newborn and neonatal infection have been reported to have increased risk in cigarette-smoking pregnant women. Risks of adverse pregnancy outcomes were found to be dose-dependent, with the highest risk found among heavy smokers (more than/equal to 20 cigarettes per day).

Keywords: cigarette, smoking, pregnancy.

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Introduction

Smoking is the human action of inhaling and exhaling the fumes of burning material. Several of these burned materials are derived from plants, such as marijuana, tobacco, etc. Most obstetricians are confused about and not familiar with some of these materials. Here, we define them as follows:

1. Marijuana: It is extracted from a plant in the Cannabaceae family. Its scientific name is Cannabis sativa and contains addictive chemical derivatives called cannabinoids, which act on the human body through cannabinoid receptors. It can reduce the occurrence of seizures, vomiting and inflammation, but it also increases risk of harm through both central nervous system stimulation and depression[1].

2. Tobacco: It is a plant whose scientific name is Nicotiana tabacum. Its addictive alkaloid derivative is nicotine, which has both a stimulative and tranquilizing psychoactive effect on humans[2]. Some of its psychoactive effects include improved

concentration and performance, relief of boredom and activated mood[3]. Tobacco products can be made in forms of cigars, pipe tobacco or chewing tobacco.

3. The cigarette is the most commonly used form of tobacco. It is comprised of tobacco, a filter and paper wrapping. When it is burned, people are exposed to more than 7,000 toxic chemical agents, such as carbon monoxide (CO), nicotine, tar, acetone, acetic acid, benzene, lead, methanol, toluene, etc. Moreover, more than 70 of these chemical agents are carcinogens[4].

Effect of cigarette smoking on general and reproductive health

Cigarette smoking increases several health risks, including risk of coronary health disease, stroke, chronic obstructive pulmonary disease (COPD) and malignancy[4]. Blood vessels are narrowed and thickened by cigarette smoking. These changes cause the heart rate to increase and clots to form[4]. Regarding the respiratory system, the airways and alveolar are damaged by cigarette smoking, leading to emphysema and chronic bronchitis. For asthmatic patients, cigarette smoking worsens symptoms and attacks occur more frequently[5]. Cigarette smoking causes an imbalance in bone turnover, leading to a lower bone mass and making bones prone to osteoporosis and fracturing more easily[6]. In terms of reproductive health, smoking makes pregnancy harder to achieve for both male and female smokers[7]. Cigarette smoking is associated with erectile dysfunction accompanied with a reduction in semen volume and total sperm count. Interestingly, semen quality is restored after the cessation of cigarette smoking[7].

Similarly, cigarette smoking is also associated with sub-fertility in female. More irregular or painful periods, low estrogen level have been reported[4].

Effect of cigarette smoking on pregnant women

The prevalence of cigarette smoking during pregnancy has been globally reported as around 1.7%[8]. Pathological harm to pregnant women and their babies from cigarette smoking is complex. It has been postulated that the mechanism occurs through disruption of fundamental processes such as proliferation, apoptosis and trophoblastic invasion during placental development and may also be caused by alteration of the vascularization and placental metabolism[9].

CO is an odourless and colourless gas. When pregnant women inhale and absorb it into their circulatory system, CO binds to haemoglobin instead of oxygen, forming carboxyhaemoglobin, which has a greater affinity than oxygen. In smokers, the level of carboxyhaemoglobin is higher than in non-smokers. The increased carboxyhaemoglobin concentration causes a shift to the left of the oxygen-haemoglobin dissociation curve. This shift to the left deprives the uterus, myometrium and fetoplacental unit of oxygen[10]. A chronic shift to the left of the oxygen-haemoglobin dissociation curve tends to result in chronic hypoxia, followed by fetal growth restriction and preterm birth[11].

It has been documented that the risks of many adverse pregnancy outcomes are linked to cigarette smoking, including ectopic pregnancy (odds ratio (OR) 1.77; 95% confidence interval (CI) 1.31, 2.22), placenta previa (OR 1.58; 95% CI 1.04, 2.12), abruptio placenta (OR 1.62; 95% CI 1.46, 1.77), preterm premature rupture of membranes (OR 1.7; 95% CI 1.18, 2.25), low birthweight (less than 2,500 grams) (OR 1.78; 95% CI 1.53, 2.08), intrauterine growth restriction (OR 1.83; 95% CI 1.64, 2.05), intrauterine fetal death (OR 1.98, 95% CI 1.01, 3.89), neonatal respiratory (OR 1.32; 95% CI 1.13, 1.56) and gastrointestinal disease (OR 1.63; 95% CI 1.11, 2.42), need of transfer of newborn to a neonatal intensive care unit (NICU) (OR 1.44; 95% CI 1.26, 1.63) and more than 7 days NICU admission of the newborn (OR 1.64, 95% CI 1.42, 1.90).(12,13) Risks of adverse pregnancy outcomes were found to be dose-dependent, with the highest risk found among heavy smokers (more than/equal to 20 cigarettes per day)[12].

In contrast, cigarette smoking has been shown to reduce preeclampsia risk[14,15]. Its protective role is explained by the reduction in anti-angiogenic protein production by the CO. Known anti-angiogenic proteins have been found to be linked to the pathogenesis of preeclampsia, including soluble fms-like tyrosine kinase-1 (sFlt-1) and soluble endoglin (sEng)[12]. However, the benefit of pre-eclampsia risk reduction should be balanced with the teratogenic effect.

Effect of smoking on the fetus

Nicotine stimulates the parasympathetic nervous system. It has effects on maternal and placental vessels and also passes through the placenta to affect fetal circulation. There are significant concerns regarding its effect on the fetal brain as the nicotine acts as neuroteratogen by binding to the nicotinic acetylcholine receptors in the fetal brain and interfering with fetal brain development. Some studies have postulated that it leads to cognitive, behavioural and emotional abnormalities during the childhood period[16]. The teratogenic effect of nicotine alone is difficulty determined because cigarette smoking contains more than 4800 different components. In utero smoking has been associated with some forms of birth defects, including limb reduction, gastroschisis, and oral clefts[17].

Particles of tar are contained in the burned cigarette smoke. This tar usually remains in the smoker's body. When it accumulates in the respiratory tract, it acts as a carcinogen. Moreover, heavy metals such as cadmium are also contained in the cigarette smoke. Cadmium passes through and accumulates in the placenta and has been reported to be associated with fetal growth restriction[11]. Mothers exposed to second hand smoking during pregnancy had significantly lower mean fetal birth weight, length, head circumference comparing to unexposed mothers[18].

Cigarette smoking cessation

All pregnant women should be asked about all types of tobacco or nicotine use at the preconception visit, the first prenatal visit, or subsequent visits. Pregnant smokers should be encouraged to stop smoking cigarettes and any forms of tobacco products as soon as possible. Cessation of cigarette smoking at any point in gestation improves maternal and fetal pregnancy outcomes. The greatest benefit has reported when cessation occurs before 15 weeks of gestation[19]. All types of tobacco, including e-cigarettes, vaping products, hookahs, lozenges, patches and gums should be avoided during pregnancy[19]. Psychological, behavioural and pharmacotherapy modality should be individually applied with pregnant women aiming for cigarette smoking cessation[20]. Nicotine replacement therapy is still controversial in regard to its efficacy and safety in cigarette smoking cessation usage[21].

Conclusion

In conclusion, awareness of cigarette smoking status during pregnancy should be raised, and cigarette smoking cessation should be encouraged among pregnant women, with the aim of reducing adverse pregnancy outcomes.

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OBSTETRICS

Difference between Paired Umbilical Arteries Doppler Velocimetry Indices in Singleton Pregnancy

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ABSTRACT

Objectives: To assess variance between paired umbilical artery Doppler velocity indices in pregnancies at 18-37 weeks.

Materials and Methods: We enrolled 450 women with singleton pregnancies, aged 18-37 weeks, between April 2023 and January 2024. They underwent Doppler transabdominal ultrasound to assess both umbilical arteries in a free-floating loop of umbilical cord. We recorded umbilical artery Doppler pulsatility index (PI), resistance index (RI), and systolic/diastolic (S/D) ratio for each umbilical artery.

Results: 418 women were analyzed. Mean PI, RI, and S/D ratio at each gestational age (18 - 37 weeks) significantly differed between paired umbilical arteries ($p < 0.05$). Discrepancies > 10% in PI, RI, and S/D ratio between the two umbilical arteries were observed in 48.6%, 23.9%, and 56.7% of cases, respectively. Discrepancy > 20% were observed in 12.7%, 2.6%, and 22% of cases, respectively.

Conclusion: Significant differences existed in PI, RI, and S/D ratio between the two umbilical arteries. As gestational age advances, there was a gradual decrease in the PI, RI, and S/D ratio. The mean difference in the S/D ratio between the two umbilical arteries tended to decrease as gestational age increased. Further considerations are necessary to determine whether the nomogram values, derived from measuring only one umbilical artery, should be based on higher or lower values, or if they should consider a specific relationship between the two umbilical arteries.

Keywords: paired umbilical arteries, pulsatility index, resistance index, systolic/diastolic ratio (S/D).

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ความแตกต่างระหว่างความเร็วดอปเปอร์เส้นเลือดแดงสายสะดือทารกในครรภ์แต่ละเส้นในหญิงตั้งครรภ์เดี่ยว

เอกพจน์ อนันตวรพจน์, ลัลธพร พัฒนาวิจารย์

บทคัดย่อ

วัตถุประสงค์: *ประเมินความแตกต่างระหว่างดัชนีความเร็วดอปเปอร์ของคู่เส้นเลือดแดงสายสะดือทารกในช่วงการตั้งครรภ์ที่อายุครรภ์ 18-37 สัปดาห์*

วัสดุและวิธีการ: *สตรีตั้งครรภ์เดี่ยวที่มีสุขภาพปกติอายุครรภ์ 18-37 สัปดาห์ จำนวน 450 รายระหว่างเดือนเมษายน 2566 ถึงเดือนมกราคม 2567 ถูกทำการวัดดอปเปอร์ของคู่เส้นเลือดแดงสายสะดือทารกในครรภ์ โดยวัดตำแหน่งสายสะดือบริเวณที่ลอยอิสระ ดัชนีดอปเปอร์ที่วัดได้แก่ ดัชนีการไหลเวียน ดัชนีความต้านทาน และสัดส่วนการไหลเวียนในช่วงบีบตัวและคลายตัว*

ผลการศึกษา: *จากผู้เข้าร่วมการวิจัยทั้งหมด 450 ราย วัดสำเร็จและตามผลการคลอดได้สำเร็จทั้งหมด 418 ราย ได้ถูกนำมาวิเคราะห์ข้อมูล พบว่าดัชนีการไหลเวียน ดัชนีความต้านทาน และสัดส่วนการไหลเวียนในช่วงบีบตัวและคลายตัวของคู่เส้นเลือดแดงสายสะดือในทุกอายุครรภ์ (ช่วง 18-37 สัปดาห์) มีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ ($p < 0.05$) ค่าดัชนีการไหลเวียน ดัชนีความต้านทาน และสัดส่วนการไหลเวียนในช่วงบีบตัวและคลายตัวที่ต่างกันมากกว่า 10 เปอร์เซ็นต์ อยู่ที่ร้อยละ 48.6, 23.9 และ 56.7 ตามลำดับ และค่าดัชนีการไหลเวียน ดัชนีความต้านทาน และสัดส่วนการไหลเวียนในช่วงบีบตัวและคลายตัวที่ต่างกันมากกว่า 20 เปอร์เซ็นต์ อยู่ที่ร้อยละ 12.7, 2.6 และ 22 ตามลำดับ*

สรุป: *พบความแตกต่างของดัชนีการไหลเวียน ดัชนีความต้านทาน และสัดส่วนการไหลเวียนในช่วงบีบตัวและคลายตัวของคู่เส้นเลือดแดงสายสะดืออย่างมีนัยสำคัญทางสถิติ ในอายุครรภ์ที่มากขึ้นพบว่าดัชนีทั้ง 3 จะมีค่าที่ค่อยๆ ลดลง นอกจากนี้ในอายุครรภ์ที่เพิ่มขึ้นค่าเฉลี่ยของความแตกต่างของสัดส่วนการไหลเวียนในช่วงบีบตัวและคลายตัวของคู่เส้นเลือดแดงสายสะดือยังค่อยๆ ลดลงด้วย จากข้อมูลการศึกษาพบว่าการนำค่าปกติที่มีการประเมินเส้นเลือดแดงสายสะดือทารกด้วยการใช้ค่าปกติของเส้นเลือดสายะสะดือเพียงค่าเดียว อาจต้องพิจารณาคำนึงถึงความแตกต่างระหว่างคู่เส้นเลือดแดงสายสะดืออีกเส้นด้วย เพื่อไปใช้ในดูแลทารกในครรภ์ต่อไป*

คำสำคัญ: *คู่เส้นเลือดแดงสายสะดือ, ดัชนีการไหลเวียน, ดัชนีความต้านทาน, สัดส่วนการไหลเวียนในช่วงบีบตัวและคลายตัว*

Introduction

There has been extensive investigation of the umbilical vessel in pregnancy. In 99% of cases, there are three umbilical vessels: two umbilical arteries and one umbilical vein[1]. These vessels play crucial roles in transporting nutrients, exchanging oxygen, and eliminating waste products from the fetus to the placenta. Utilizing Doppler velocity of the umbilical artery can aid in monitoring pregnancies, devising treatment plan, and determining the appropriate gestational age for delivery in cases of fetal growth restriction. This approach has the potential reduce postnatal mortality by up to 29%[2]. The recommended site for measuring Doppler velocity is at the free loop of the umbilical artery. Both the 2019 American College of Obstetricians and Gynecologists (ACOG) guidelines and the 2022 Society for Maternal-Fetal Medicine (SMFM) guidelines advocate for the use of Doppler velocity of the umbilical artery to assess fetal health during pregnancy[3, 4].

The circulation of the umbilical artery flows from the fetus to the placenta. Color Doppler enables assessment of blood flow velocity, which varies according to the heartbeat in systole and diastole. During systole, the blood velocity in the umbilical artery is high, as represented by an S waveform. Subsequently, the velocity gradually decreases during diastole, depicted by a D waveform. To derive the pulsatility index (PI), the resistance index (RI), and the systolic/diastolic (S/D) ratio, the values of S and D are calculated. The PI is calculated by dividing the difference between S and D by the means of S and D. The RI is obtained by dividing difference between S and D by S. S/D is determined by dividing S by D[5]. These measurements assist in assessing umbilical artery blood flow and are instrumental in diagnosing conditions associated with blood circulation.

The Doppler velocity of the umbilical artery in pregnancy serves as an indicator of fetal health. Typically, the umbilical arteries exhibit similar sizes since they are interconnected near their distal ends by Hyrtl's anastomosis. This anastomosis is typically situated near the entry points of arteries into the placenta, thereby ensuring equalized pressure values in both umbilical arteries[6]. However, each umbilical artery may provide different size or velocity values. Variations in vascular resistance, blood flow dynamics, and placental attachment sites can lead to differing Doppler velocity indices between the two arteries. Additionally, any asymmetry in the development or function of the placenta can contribute to these discrepancies[7-11]. Studies have reported differences between the two umbilical arteries in several Doppler velocity indices: up to 13.1% in the RI in low-risk pregnancies, and even up to 38%[7], and up to 16.7% in the PI[8]. Physicians typically measure the Doppler velocity at the free loop of one umbilical artery and subsequently utilize the obtained values to plan fetal care. Despite each umbilical artery in pregnancy providing different Doppler velocity values, the current nomogram for umbilical artery Doppler velocity indices has been derived from measuring only one umbilical artery[12, 13]. Therefore, our aim was to investigate the differences in the Doppler velocity indices of both umbilical arteries in low-risk singleton pregnancies. This endeavor may provide valuable information that could potentially lead to a revision of the current concept of the nomogram for umbilical artery Doppler indices.

Materials and Methods

Between April 2023 and January 2024, this prospective cross-sectional study recruited singleton pregnant women between 18 to 37 weeks of gestation at Rajavithi Hospital, Thailand. Four hundred fifty pregnant women who underwent prenatal visit care were enrolled. The eligibility inclusion criteria encompassed age ≥ 18 years, singleton low-risk pregnancy, and gestational age determined last menstrual period (LMP) and confirmed by ultrasonography of at least 18 weeks. Because the aim of this study was to evaluate low risk pregnancy. Women who had preexisting diabetes mellitus, gestational diabetes mellitus, thyroid disease, systemic lupus erythematosus, chronic hypertension, smoking, a single umbilical artery, umbilical cord abnormality, absent or reverse end-diastolic flow, fetal structural abnormalities and fetal genetic abnormalities were excluded. The study protocol received approval from the ethics committee of Rajavithi Hospital (No.

056/2566). Each participant provided informed consent prior to enrollment.

The participants underwent two-dimensional (2D) transabdominal ultrasound utilizing a GE Voluson S8 or S10 ultrasound machine equipped with a 2–5 MHz curved array transducer. Ultrasonography was performed by a single operator (PC), who was undergoing a maternal-fetal medicine fellowship and had been trained in umbilical artery Doppler measurements. Color Doppler ultrasound was employed to identify the paired umbilical arteries in the free-floating loop of the umbilical cord, with insonation optimized to be parallel to the vessel or at an angle of insonation not exceeding 30°. To confirm the measurement of each umbilical artery in this study, during the Doppler ultrasound examination, both umbilical arteries within a free-floating loop of the umbilical cord, lying parallel to each other, can be visualized simultaneously (Fig. 1). The pulsed-wave Doppler examination was conducted in the absence of fetal movement or breathing. Doppler ultrasound was performed three times consecutively for each vessel, capturing at least five uniform cardiac cycles during each session. The PI, RI, and S/D ratio were determined from the average of multiple flow velocity waveforms, each comprising a minimum of three consistent cardiac cycles. The measurement selected was the one exhibiting the most uniform wave with the lowest angle of insonation (Fig. 1). If each umbilical artery provided a different PI, then the artery with the higher PI was designated as "umbilical artery M," while the one with the lower PI was designated as "umbilical artery N." The scanning time was kept under 15 minutes for each woman. Additionally, it is important to note that Doppler ultrasound, while generally considered safe, can generate a thermal index that could potentially affect the fetus if not monitored and controlled properly. If ultrasound was unsuccessful, the patient was excluded from the study. Each participant underwent a single routine ultrasonographic examination, which included fetal standard biometry, estimated of fetal weight, and screening for fetal anomalies. The following maternal baseline characteristics were recorded: age, parity, and pre-pregnancy body mass index (BMI). The following pregnancy-related outcomes were recorded: route of delivery, gestational age of delivery, birth weight, sex of the baby, APGAR score, neonatal respiratory distress syndrome, and any obstetrical complications.

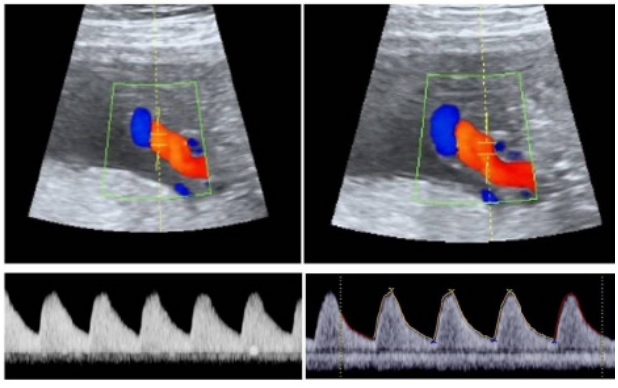

Fig. 1. Measurement the paired umbilical artery Doppler.

Statistical analysis

The sample size was calculated from the previous study[14] by using this formula.

$$n = \frac{(Z_{\alpha/2} + Z_{\beta})^2 \chi(\sigma_1^2+\sigma_2^2)}{(\mu_1 - \mu_2)^2}$$

n = sample size, $\alpha = 0.05$, $Z_{\alpha/2} = 1.96$, $Z_{\beta} = 0.842$, $\sigma 1 = 0.13$, $\sigma 2 = 0.15$, $\mu_1 = 0.74$, $\mu_2 = 0.70$

The subjects included 280 cases with a 30% drop-out rate, resulting in a total sample size of at least 400 cases per each umbilical artery Doppler with gestational age between 18 - 37 weeks.

Data analysis was conducted using SPSS version 22.0 for Windows (IBM Corp., Armonk, NY, USA). Categorical and continuous variables are presented as frequency, percentage, mean ± standard deviation (SD) or median (minimum–maximum). The normality of the data was assessed using the Kolmogorov–Smirnov test. Correlations between the PI, RI, S/D ratio, and gestational age were determined using Pearson's correlation analysis. A p value of < 0.05 was considered statistically significant. The intraclass correlation coefficient (ICC) was employed to evaluate the inter- and intra-rater reliability.

Results

A total of 450 singleton pregnant women were recruited in the study and underwent fetal umbilical artery Doppler measurements. Thirty-two women were excluded: 21 (4.6%) women were lost to follow-up, 10 (2.2%) women developed gestational diabetes mellitus, and 1 (0.2%) woman had a discordant umbilical artery Doppler pattern (one with a positive end-diastolic flow (EDF) and one with an absent EDF). Thus, 418 women were included in the analysis.

The mean ± SD maternal age and pre-pregnancy BMI were 29.91 ± 6.54 years and 23.46 ± 4.03 kg/m^2, respectively. Twenty-six (6.2%) women were classified as obese. Nearly half of the women (48.8%) were nulliparous. The mean ± SD gestational age at delivery was 38.63 ± 1.11 weeks. Most of them had a vaginal delivery (73%). The mean ± SD birth weight was 3037.52 ± 340.10 grams. Tables 1 and 2 provide the maternal characteristics and pregnancy outcomes, respectively.

Table 1. Maternal characteristics of the study population.

Characteristics	Total (n = 418)	
	n	%
Age (years)		
< 20	17	4.1%
20 - 35	312	74.6%
> 35	89	21.3%
Mean ± SD	29.91 ± 6.54	
Min - max	18 - 48	
BMI		
< 18.5	23	5.5%
18.5 - 22.9	196	46.9%
23 - 24.9	61	14.6%
25 - 29.9	112	26.8%
> 30	26	6.2%
Mean ± SD	23.46 ± 4.03	
Parity		
Nulliparous	204	48.8%
Multiparous	214	51.2%
Gestational age (weeks) Mean ± SD	27.47 ± 5.68	

SD: standard deviation, BMI: body mass index, n: number.

Table 2. Pregnancy outcomes of the study population.

	Total (n = 418)	
	n	%
Delivery route		
Vaginal delivery	305	73.0%
Cesarean section (CS)	113	27.0%
Indication of CS (n = 113)		
Previous CS	23	20.4%
Non-reassuring FHS	26	23.0%
Elective CS	35	31.0%
failed induction	10	8.8%
CPD	17	15.0%
Malpresentation	2	1.8%
Gestational age of delivery		
< 37	17	4.1%
≥ 37	401	95.9%
Mean ± SD	38.63 ± 1.11	
Neonatal gender		
Male	229	54.8%
Female	189	45.2%
Birth weight (gram)		
< 2,500	26	6.2%
≥ 2,500	392	93.8%
Mean ± SD	3037.52 ± 340.10	
Percentile		
AGA	404	96.7%
SGA	5	1.2%
LGA	9	2.2%
APGAR at 1 min		
≤ 7	10	2.4%
> 7	408	97.6%
Mean ± SD	8.54 ± 0.57	
APGAR at 5 min		
> 7	418	100%
Mean ± SD	9.53 ± 0.53	
RDS	13	3.1%
Developed FGR	4	1.0%
Preeclampsia	2	0.5%

SD: standard deviation, CS: cesarean section, CPD: cephalopelvic disproportion, AGA: appropriate for gestational age, SGA: small for gestational age, LGA: large for gestational age, APGAR: Activity-Pulse-Grimace-Appearance-Respiration score, RDS: respiratory distress syndrome, FGR: fetal growth restriction.

The mean "umbilical artery M" and "umbilical artery N" PI, RI, and S/D ratio for a gestational age of 18–37 weeks are shown in Table 3.

Table 3. Comparison the mean values of pulsatility index, resistance index, and systolic/diastolic between the two umbilical artery Doppler.

Gestational age (weeks)	n	Umbilical artery M	Umbilical artery N	Difference	p value
		Mean ± SD	Mean ± SD	Mean (95% CI)	
Pulsatility index (PI)					
18	18	1.366 ± 0.178	1.236 ± 0.185	0.152 (0.096, 0.208)	< 0.001*
19	18	1.356 ± 0.156	1.191 ± 0.115	0.130 (0.089, 0.171)	< 0.001*
20	30	1.356 ± 0.193	1.191 ± 0.176	0.164 (0.107, 0.222)	< 0.001*
21	19	1.348 ± 0.168	1.198 ± 0.143	0.150 (0.102, 0.198)	< 0.001*
22	20	1.271 ± 0.143	1.150 ± 0.170	0.120 (0.097, 0.144)	< 0.001*
23	22	1.253 ± 0.126	1.156 ± 0.111	0.097 (0.066, 0.128)	< 0.001*
24	20	1.163 ± 0.169	1.081 ± 0.149	0.182 (0.144, 0.220)	< 0.001*
25	18	1.155 ± 0.142	1.023 ± 0.123	0.132 (0.077, 0.187)	< 0.001*
26	17	1.151 ± 0.231	1.003 ± 0.232	0.149 (0.079, 0.219)	< 0.001*
27	18	1.142 ± 0.239	1.018 ± 0.169	0.124 (0.079, 0.169)	< 0.001*
28	28	1.138 ± 0.132	0.988 ± 0.097	0.150 (0.091, 0.209)	< 0.001*
29	20	1.103 ± 0.211	0.959 ± 0.167	0.144 (0.100, 0.188)	< 0.001*
30	23	1.076 ± 0.134	0.937 ± 0.083	0.139 (0.098, 0.180)	< 0.001*
31	18	1.068 ± 0.122	0.935 ± 0.115	0.132 (0.087, 0.178)	< 0.001*
32	28	1.015 ± 0.203	0.911 ± 0.153	0.104 (0.056, 0.152)	< 0.001*
33	30	0.967 ± 0.164	0.859 ± 0.150	0.108 (0.066, 0.150)	< 0.001*
34	19	0.955 ± 0.137	0.847 ± 0.103	0.108 (0.069, 0.146)	< 0.001*
35	18	0.942 ± 0.203	0.851 ± 0.216	0.091 (0.058, 0.124)	< 0.001*
36	17	0.929 ± 0.113	0.849 ± 0.112	0.081 (0.054, 0.107)	< 0.001*
37	17	0.883 ± 0.159	0.791 ± 0.177	0.092 (0.057, 0.128)	< 0.001*
Resistance index (RI)					
18	18	0.750 ± 0.051	0.702 ± 0.069	0.048 (0.020, 0.075)	0.002*
19	18	0.759 ± 0.047	0.716 ± 0.038	0.043 (0.025, 0.061)	< 0.001*
20	30	0.756 ± 0.045	0.720 ± 0.083	0.036 (0.000, 0.071)	0.048*
21	19	0.763 ± 0.053	0.718 ± 0.053	0.046 (0.034, 0.057)	< 0.001*
22	20	0.731 ± 0.048	0.690 ± 0.059	0.041 (0.032, 0.050)	< 0.001*
23	22	0.732 ± 0.048	0.697 ± 0.047	0.035 (0.020, 0.050)	< 0.001*
24	20	0.691 ± 0.055	0.634 ± 0.061	0.057 (0.045, 0.069)	< 0.001*
25	18	0.709 ± 0.052	0.662 ± 0.048	0.048 (0.026, 0.069)	< 0.001*
26	17	0.693 ± 0.080	0.639 ± 0.080	0.053 (0.024, 0.083)	0.001*
27	18	0.702 ± 0.080	0.660 ± 0.067	0.042 (0.029, 0.055)	< 0.001*
28	28	0.694 ± 0.038	0.646 ± 0.034	0.048 (0.030, 0.067)	< 0.001*
29	20	0.678 ± 0.079	0.622 ± 0.065	0.056 (0.040, 0.071)	< 0.001*
30	23	0.681 ± 0.053	0.622 ± 0.036	0.060 (0.042, 0.077)	< 0.001*
31	18	0.662 ± 0.046	0.617 ± 0.054	0.045 (0.027, 0.062)	< 0.001*
32	28	0.639 ± 0.079	0.603 ± 0.076	0.036 (0.022, 0.051)	< 0.001*
33	30	0.623 ± 0.060	0.570 ± 0.070	0.053 (0.033, 0.073)	< 0.001*
34	19	0.623 ± 0.066	0.583 ± 0.079	0.041 (0.024, 0.057)	< 0.001*
35	18	0.588 ± 0.074	0.568 ±0.102	0.020 (0.023, 0.063)	0.004
36	17	0.614 ± 0.051	0.575 ± 0.052	0.039 (0.030, 0.048)	< 0.001*
37	17	0.594 ± 0.066	0.546 ± 0.079	0.048 (0.030, 0.067)	< 0.001*

Table 3. Comparison the mean values of pulsatility index, resistance index, and systolic/diastolic between the two umbilical artery Doppler. (Cont.)

Gestational age (weeks)	n	Umbilical artery M	Umbilical artery N	Difference	p value
		Mean ± SD	Mean ± SD	Mean (95% CI)	
Systolic/diastolic(S/D)					
18	18	4.441 ± 1.116	3.679 ± 0.781	0.785 (0.378, 1.192)	0.001*
19	18	4.302 ± 0.811	3.600 ± 0.408	0.702 (0.359, 1.044)	< 0.001*
20	30	4.217 ± 0.744	3.546 ± 0.672	0.671 (0.479, 0.864)	< 0.001*
21	19	4.192 ± 1.031	3.408 ± 0.668	0.785 (0.378, 1.192)	0.001*
22	20	3.867 ± 0.684	3.341 ± 0.451	0.526 (0.281, 0.772)	< 0.001*
23	22	3.834 ± 0.672	3.346 ± 0.710	0.487 (0.385, 0.590)	< 0.001*
24	20	3.788 ± 1.211	3.006 ± 0.381	0.782 (0.219, 1.345)	0.009*
25	18	3.616 ± 1.080	3.060 ± 0.701	0.557 (0.307, 0.806)	< 0.001*
26	17	3.462 ± 0.882	2.923 ± 0.756	0.539 (0.222, 0.856)	0.003*
27	18	3.356 ± 0.697	2.814 ± 0.500	0.542 (0.411, 0.673)	< 0.001*
28	28	3.329 ± 0.442	2.852 ± 0.290	0.477 (0.257, 0.697)	< 0.001*
29	20	3.299 ± 0.863	2.733 ± 0.533	0.566 (0.368, 0.764)	< 0.001*
30	23	3.085 ± 0.488	2.675 ± 0.262	0.410 (0.235, 0.584)	< 0.001*
31	18	3.023 ± 0.434	2.660 ± 0.382	0.362 (0.235, 0.490)	< 0.001*
32	28	2.883 ± 0.577	2.579 ± 0.418	0.304 (0.144, 0.463)	0.001*
33	30	2.741 ± 0.651	2.439 ± 0.572	0.302 (0.173, 0.431)	< 0.001*
34	19	2.724 ± 0.882	2.475 ± 0.654	0.248 (0.074, 0.423)	0.008*
35	18	2.706 ± 0.487	2.426 ± 0.314	0.280 (0.141, 0.420)	< 0.001*
36	17	2.614 ± 0.360	2.393 ± 0.295	0.221 (0.129, 0.313)	< 0.001*
37	17	2.519 ± 0.420	2.288 ± 0.457	0.232 (0.136, 0.328)	< 0.001*

p value from paired t-test, * significant at p value < 0.05

SD: standard deviation, CI: confidence interval, n: number, PI: pulsatility index, RI: resistance index, S/D: systolic/diastolic

For each gestational age category included 17–30 measurements. Fig. 2, 3, and 4 display the mean PI, RI, and S/D ratio, respectively at each gestational age. Significant differences were observed in the PI, RI, and S/D ratio between the umbilical arteries ($p < 0.05$).

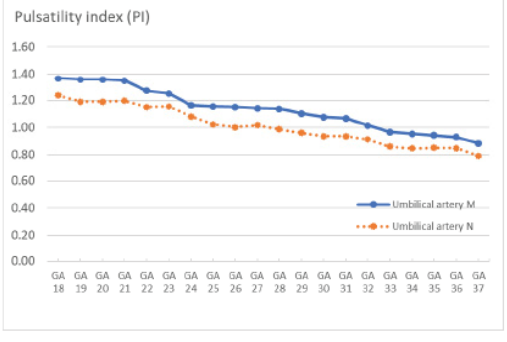

Fig. 2. Illustrating the graph depicting the values of pulsatility index (PI) for each umbilical artery Doppler measurement at different gestational ages.

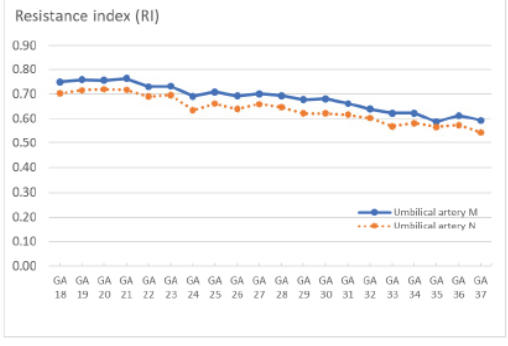

Fig. 3. Illustrating the graph depicting the values of resistance index (RI) for each umbilical artery Doppler measurement at different gestational ages.

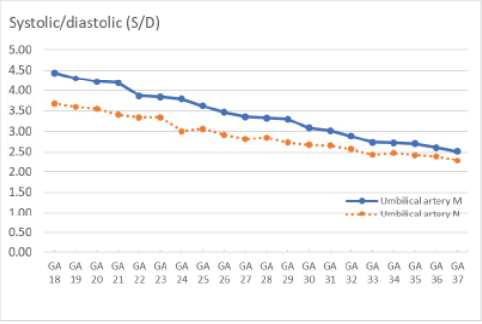

Fig. 4. Illustrating the graph depicting the values of systolic-diastolic (S/D) for each umbilical artery Doppler measurement at different gestational ages.

The mean percentage differences between the paired umbilical artery PI, RI, and S/D ratio are summarized in Table 4. Pregnancy outcomes associated with a difference of > 20% in the PI, RI, and S/D ratio are presented in Table 5.

The ICCs for the PI, RI and S/D ratio measurements indicated good agreement (Table 6). The intra-observer ICCs were as follows: 0.94 (95% confidence interval [CI] 0.89–0.96) for the PI, 0.91 (95% CI 0.88–0.97) for the RI, and 0.92 (95% CI 0.85–0.96) for the S/D ratio. The inter-observer ICCs were 0.93 (95% CI 0.87–0.96) for the PI, 0.91 (95% CI 0.86–0.95) for the RI, and 0.90 (95% CI 0.85–0.94) for the S/D ratio.

Table 4. The percentage difference of pulsatility index, resistance index, and systolic/diastolic values for each umbilical artery Doppler.

	Total (n = 418)	
	n	%
%diff PI		
≤ 5.0%	104	24.9
5.01-10.0%	111	26.6
10.01-15.0%	85	20.3
15.01-20.0%	65	15.6
> 20.0%	53	12.7
%diff RI		
≤ 5.0%	176	42.1
5.01-10.0%	142	34.0
10.01-15.0%	66	15.8
15.01-20.0%	23	5.5
> 20.0%	11	2.6
%diff S/D		
≤ 5.0%	92	22.0
5.01-10.0%	89	21.3
10.01-15.0%	85	20.3
15.01-20.0%	60	14.4
> 20.0%	92	22.0

%diff PI: percentage difference in the pulsatility index, %diff RI: percentage difference in the resistance index, %diff S/D: percentage difference in the systolic/diastolic ratio, n: number, PI: pulsatility index, RI: resistance index, S/D: systolic/diastolic

Table 5. Pregnancy outcomes associated with a difference of more than 20% in the values of PI, RI, and S/D of umbilical artery Doppler.

			%Diff PI					%Diff PI					%Diff PI				
	Total (n = 418)		> 20% (n = 53)		≤ 20% (n = 365)		p value	> 20% (n = 53)		≤ 20% (n = 365)		p value	> 20% (n = 53)		≤ 20% (n = 365)		p value
	n	%	n	%	n	%		n	%	n	%		n	%	n	%	
Delivery GA							0.146					1.000					1.000
< 37	17	4.1%	0	0%	17	4.7%		0	0%	17	4.2%		3	3.3%	14	4.3%	
≥ 37	401	95.9%	53	100%	348	95.3%		11	100%	390	95.8%		89	96.7%	312	95.7%	
Birth weight (gm)							0.060					1.000					0.228
< 2,500	26	6.2%	0	0%	26	7.1%		0	0%	26	6.4%		3	3.3%	23	7.1%	
≥ 2,500	392	93.8%	53	100%	339	92.9%		11	100%	381	93.6%		89	96.7%	303	92.9%	
Percentile							0.803					1.000					0.443
AGA	404	96.7%	53	100%	351	96.2%		11	100%	393	96.6%		89	96.7%	315	96.6%	
SGA	5	1.2%	0	0%	5	1.4%		0	0%	5	1.2%		2	2.2%	3	0.9%	
LGA	9	2.2%	0	0%	9	2.5%		0	0%	9	2.2%		1	1.1%	8	2.5%	
APGAR at 1 min							1.000					1.000					0.464
≤ 7	10	2.4%	1	1.9%	9	2.5%		0	0%	10	2.5%		3	3.3%	7	2.1%	
> 7	408	97.6%	52	98.1%	356	97.5%		11	100%	397	97.5%		89	96.7%	319	97.9%	
Complications																	
RDS	13	3.1%	2	3.8%	11	3.0%	0.674	0	0%	13	3.2%	1.000	3	3.3%	10	3.1%	1.000
FGR	4	1.0%	0	0%	4	1.1%	1.000	0	0%	4	1.0%	1.000	2	2.2%	2	0.6%	0.212
Preeclampsia	2	0.5%	1	1.9%	1	0.3%	0.238	0	0%	2	0.5%	1.000	1	1.1%	1	0.3%	0.392

p values from Fisher's exact test

%diff PI: percentage difference in the pulsatility index, %diff RI: percentage difference in the resistance index, %diff S/D: percentage difference in the systolic/diastolic ratio, N: number. Delivery GA: Gestational age of delivery, AGA: appropriate for gestational age, SGA: small for gestational age, LGA: large for gestational age, APGAR: Activity-Pulse-Grimace-Appearance-Respiration score, RDS: respiratory distress syndrome, FGR: fetal growth restriction.

Table 6. Intraclass correlation coefficients (ICC) for reliability in measurement of PI, RI, S/D (n = 45).

Measurement	Inter-rater Reliability		Intra-rater Reliability	
	ICC	95% CI of ICC	ICC	95% CI of ICC
PI	0.932	0.872 – 0.965	0.941	0.891 – 0.968
RI	0.914	0.864 – 0.951	0.912	0.882 – 0.967
S/D	0.902	0.846 – 0.943	0.922	0.852 – 0.959

%diff PI: percentage difference in the pulsatility index, %diff RI: percentage difference in the resistance index, %diff S/D: percentage difference in the systolic/diastolic ratio, n: number, PI: pulsatility index, RI: resistance index, S/D: systolic/diastolic

Discussion

Umbilical artery Doppler ultrasound examination is a valuable method to assess fetal well-being. Despite its wide use, the normal ranges for umbilical artery Doppler ultrasound indices are generally from one umbilical artery. In this prospective cross-sectional study, our aim was to evaluate the discrepancy between paired umbilical arteries in low-risk pregnancy. This endeavor might contribute to changes in normative values for umbilical artery Doppler ultrasound indices.

We demonstrated a relationship between three fetal umbilical artery Doppler indices (the PI, RI, and S/D ratio) and gestational age: All three decreased significantly as gestation advanced. This finding aligned with previous reports[8,15]. Studies examining paired umbilical arteries have indicated differences in size[9,16]. Subsequent investigations into the

structure and velocity flow of umbilical artery have become widespread. Hyrtl's anastomosis between the umbilical arteries occurs within the umbilical cord, within 3 cm of placental cord insertion, which facilitates flow between the two umbilical arteries[17, 18]. This mechanism helps balance or equalize the pressure in the arteries or bring them closer before entering the placenta, acting as a safety valve[6]. Hyrtl's anastomosis aids in redistributing blood from the fetal side to the placental side and serves as a buffer in cases where the placenta encounters issues, helping regulate blood pressure within the placental lobes[17, 19, 20].

However, umbilical artery Doppler velocity parameters such as the PI, RI, and S/D ratio vary at the fetal and placental ends[21], and both umbilical arteries might provide different Doppler velocity index values. Predanic and Perni[7] found significant discordance in the PI of two parallel umbilical arteries. Raio et al[11] showed that the RI was higher in a smaller artery than in a large artery (0.71 [0.59–0.8] versus 0.6 [0.48–0.75], $p < 0.01$). Dolkart et al[9] reported that the mean difference in the S/D ratio between two umbilical arteries was significant ($p < 0.001$). Predanic et al[16] found a higher overall maximum S/D ratio compared with the overall minimum S/D ratio (2.62 ± 0.58 versus 2.27 ± 0.40, respectively, $p < 0.001$). Our findings were similar to those studies. We observed a significant difference between small and large arteries regarding the PI, RI, and S/D ratio at a gestational age of 18-37 weeks.

Predanic and Perni[7] noted that the S/D ratio of both umbilical arteries differed by > 20% in 29% of cases, which aligned with our study. We found a discrepancy of > 10% between the two umbilical arteries regarding the PI, RI, and S/D ratio in 48.6%, 23.9%, and 56.7% of cases, respectively, while there was a discrepancy of > 20% in 12.7%, 2.6%, and 22% of cases, respectively. Notably, Cahill et al[22] reported that the paired umbilical arteries provided different PIs, with discrepancies of > 25%, reaching as high as 38%. However, we did not observe a significant increase in adverse perinatal outcomes in patients with umbilical artery discordance > 20%. The pregnancy outcomes did not differ when we compared the groups that had > 20% and ± 20% discrepancies between the umbilical arteries.

This study evaluated paired umbilical artery Doppler indices in low-risk pregnancies and showed significant differences. This finding was similar to the previous large high-risk pregnancy study (fetal growth restriction cohort) by Steller et al[8], which found that the overall discrepancy between the two umbilical artery pulsatility indices was 11.7%.

The strength of this study lied in the follow-up of all cases until delivery. We minimized selection bias by including all cases that had prenatal visits and met the inclusion criteria. Additionally, our study covered multiple gestational ages from 18 to 37 weeks. However, a limitation of the study was that all measurements were performed by a single operator.

Conclusion

In conclusion, our study revealed significant differences in the PI, RI, and S/D ratio between the two umbilical arteries. This suggests that several considerations need to be addressed regarding the determination of nomogram values derived from measuring only one umbilical artery. It prompts questions about whether these values should be based on higher or lower values, or whether they should reflect a specific relationship between the two umbilical arteries. Understanding these discrepancies is crucial for accurately assessing fetal health and identifying possible complications. Further research is warranted to explore these considerations and their implications for clinical practice.

Acknowledgments

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Potential conflicts of interest

The authors declare no conflicts of interest.

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OBSTETRICS

Effectiveness and Safety of Amniotomy after Cervical Ripening by Foley's Catheter Balloon on Induction of Mid-Trimester Fetal Death in Utero: A randomized clinical trial

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ABSTRACT

Objectives: To explore the value and safety of amniotomy after cervical ripening by Foley catheter balloon on termination of mid-trimester fetal death in utero.

Materials and Methods: The study was a randomized clinical trial conducted at Assiut Woman's Health Hospital, Egypt, from November 2021 to June 2023 on non-scared uterus women with mid-trimester fetal death in utero (18-26 weeks). Participants were subjected to Foley catheter balloon insertion and then assigned to group I: Amniotomy group or group II: No amniotomy group according to the randomization. The main outcome was the mean interval (hours) between Foley catheter balloon expulsion to complete abortion. The outcome variables were analyzed using an independent sample t-test, Mann-Whitney U, and Chi-square test.

Results: Sixty women were included in the study. The balloon expulsion to abortion time was shorter in the amniotomy group than the no amniotomy group with a statistically significant difference (6.89 ± 2.02 hours vs 9.22 ± 1.98 hours, $p < 0.001$). The mean dose of oxytocin was higher in the no amniotomy group than in the amniotomy group with a statistically significant difference (76.61 ±15.78 IU vs 57.55 ±16.88 IU, $p < 0.001$). No statistically significant differences were found between groups as regards the rate of complications.

Conclusion: Performing amniotomy after using a Foley catheter balloon for cervical ripening during induction of mid-trimester fetal death in utero in a non-scarred uterus reduced the time to abortion as well as the oxytocin dose and the procedure was relatively safe.

Keywords: amniotomy, bishop score, foley catheter, fetal death in utero.

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Introduction

The termination of abortion is an important issue that has many controversies[1]. The most common time of serious abortion-associated complications is the mid-trimester[2]. Missed abortion is one of the most common indications of termination of pregnancy in the mid-trimester[3].

Misoprostol and mifepristone are effective drugs for induction of abortion in the mid-trimester even with a scarred uterus[4, 5], but these drugs are now expensive, and non-available in some developing countries[6].

The effectiveness of Foley's catheter balloon on cervical ripping for mid-trimester pregnancy termination has been proved before[7, 8]. It can effectually shorten the time of the expulsion of the fetus[9, 10].

Amniotomy is an artificial rupture of the membranes. It is an ordinary obstetric practice used mainly in the induction of labor, with good results and less morbidity[11]. The obstetricians are used to combine amniotomy with other methods such as prostaglandins or oxytocin to induce labor in a woman with an unfavorable cervix[11, 12].

Despite plenty of studies that investigated the role of amniotomy in the induction of labor[13], the studies that addressed the role of amniotomy in the induction of mid-trimester fetal death in utero are very scarce in the literature.

So, we aimed in this study to examine the effectiveness and safety of amniotomy after cervical ripening by Foley catheter balloon on termination of mid-trimester fetal death in utero. To our knowledge, this is the first trial talks about this topic.

Materials and Methods

The study was a single-center, open-labeled randomized clinical trial. It was registered at Clinicaltrial.gov (NCT04906278) and was conducted from November 2021 to June 2023 at the Assiut Woman's Health Hospital, Egypt. Women who attended with the mid-trimester fetal death in utero were invited to participate. The Assiut Medical School Ethical Review Board approved the study protocol on October 26, 2021 (IRB approval number: IRB17101564).

Eligible participants

Women aged 18-40 years old with mid-trimester fetal death in utero (a fetus without a heartbeat prior to completion of 20 weeks 0 days gestation)[14]. The fetal death in utero was diagnosed using ultrasound by failure to find a cardiac pulsation in the fetus (all ultrasound examinations were performed by MK, a level 3 Ultrasonographer). We included singleton pregnancy from 18-26 weeks. Those women had unfavorable cervix (Bishop Score < 5) at the time of recruitment. However, we excluded women who delivered before by caesarian section or had a previous history of any type of uterine incision. The ultrasonography evidence of low amniotic fluid volume or low implanted placenta, history of rupture of fetal membranes, congenital fetal malformation, history or laboratory evidence of intrauterine infection, history suggestive of latex allergy, co-morbidities like severe anemia (Hb < 7g/dl), hypertension, diabetes, or coagulopathy were also exclusion criteria.

Randomization

Eligible women who gave their informed consent were randomized to either group I: the Amniotomy group or group II: No amniotomy group. A blocked randomization was done using https://www.sealedenvelope.com and a table of random numbers and codes was generated. Counseling for participation was done before recruitment. Allocation to any of the intervention arms could not be changed after randomization.

Intervention

The eligible women were subjected to history taking (including socio-demographic and obstetrics data) and body mass index assessment. Per-vaginal examination was done. A modified Bishop score was

used including dilatation, consistency, and effacement of the cervix. Each one scored 0 to 3 points. A score of 3 or less is considered to be an unripened cervix and a score more than 3 is considered a ripened cervix. Then, a two-dimensional trans-abdominal ultrasound examination using Mindry DP-10 Portable B/W, System, China was done to assess the condition of pregnancy.

Then the eligible women were subjected to Foley catheter balloon insertion. A 16F Foley catheter was inserted into the cervix and inflated with 40 ml of saline and it was pulled out to ensure the balloon covered the internal os. The catheter was fixed to the inner thigh with light traction[6].

The Foley catheter balloon was checked every 4 hours. Women were received, according to department policy, 2 gm IV cefotaxime (Cefotax, Egyptian International Pharmaceutical Industries Co. EPICO)[6]. If the catheter did not expulse within 24 hours; it was removed and was considered as a failure (those women were excluded from the final analysis). After the failure, those women were received vaginal misoprostol 400 mcg. This was repeated every 6 hours until cervical dilation occurred. After that, IV oxytocin was administered till complete abortion (according to our institutional protocol).

When the Foley catheter balloon fell out, the bishop score was assessed again. If the cervix remained unfavorable (< 2 cm dilated and not more than 30% effaced), this was considered a treatment failure, and those participants were also excluded from the study.

Amniotomy was successfully performed in all women in group I by toothed forceps immediately after Foley catheter balloon expulsion at the delivery room[11]. No amniotomy was done in group II.

After that, the uterine contractions in both groups were induced using an oxytocin infusion. The intravenous oxytocin infusion was administered as 50 IU oxytocin/ 500 ml saline / 30 mIU/minute every 6 hours till complete abortion occurred[16]. The uterine contractions were checked hourly and proper analgesia was given, if needed, till the expulsion of the fetus and placenta.

If severe bleeding or failure of complete expulsion of the placenta happened, the surgical intervention was done under general anesthesia. Women were observed for at least 12 hours after the termination of pregnancy and an ultrasound examination was performed before discharge. The women were followed-up, by telephone, 1week after abortion for the manifestations of post-abortive endometritis (abdominal tenderness, fever, and offensive vaginal discharge).

The study outcomes

The primary outcome was the mean interval (hours) between Foley catheter balloon expulsion to complete abortion. The secondary outcomes included the doses of oxytocin used to complete abortion and the rate of surgical removal of the placenta. The rate of complications like post-abortive bleeding (bleeding that needed additional uterotonics or surgical intervention) or post-abortive fever (oral temperature ≥ 38 c within first 24 hours on two separate occasions 6 hours apart), and post-abortive endometritis after 1 week was also reported.

Sample size

Ali et al reported that the mean time from catheter expulsion to complete abortion without amniotomy was 8.57 ± 2 hours[6]. Based on this study, we assumed that amniotomy may decrease this time by about 2 hours (6.57 ± 2 hours). So, using a two-sided chi-square (χ^2) test with α of 0.05, a total sample size of at least 60 patients in the 2 groups (30 in each

arm) will have 95% power to detect the difference in the time between amniotomy and no amniotomy group assuming that the rate of loss to follow-up 10% (Epi-info™, CDC, USA).

Statistical analysis

The data was collected and entered into the Microsoft Excel Database and analyzed using the Statistical Package for Social Science (SPSS Inc., Chicago, version 21). The Shapiro-Walik test was used first, to test the distribution of the variables. Normally distributed variables were expressed in means ± standard deviation and compared by independent sample t-test. While abnormally distributed variables were presented by medians and compared using means of non-parametric tests. Chi-square was used to compare proportions. The p value < 0.05 was considered statistically significant.

Results

Seventy-three women were counseled for participation. However, 13 women were excluded at the screening phase of the study. Sixty women consented to participate and were divided equally into two groups: group I (Amniotomy group) and group II (No amniotomy group) (Fig.1).

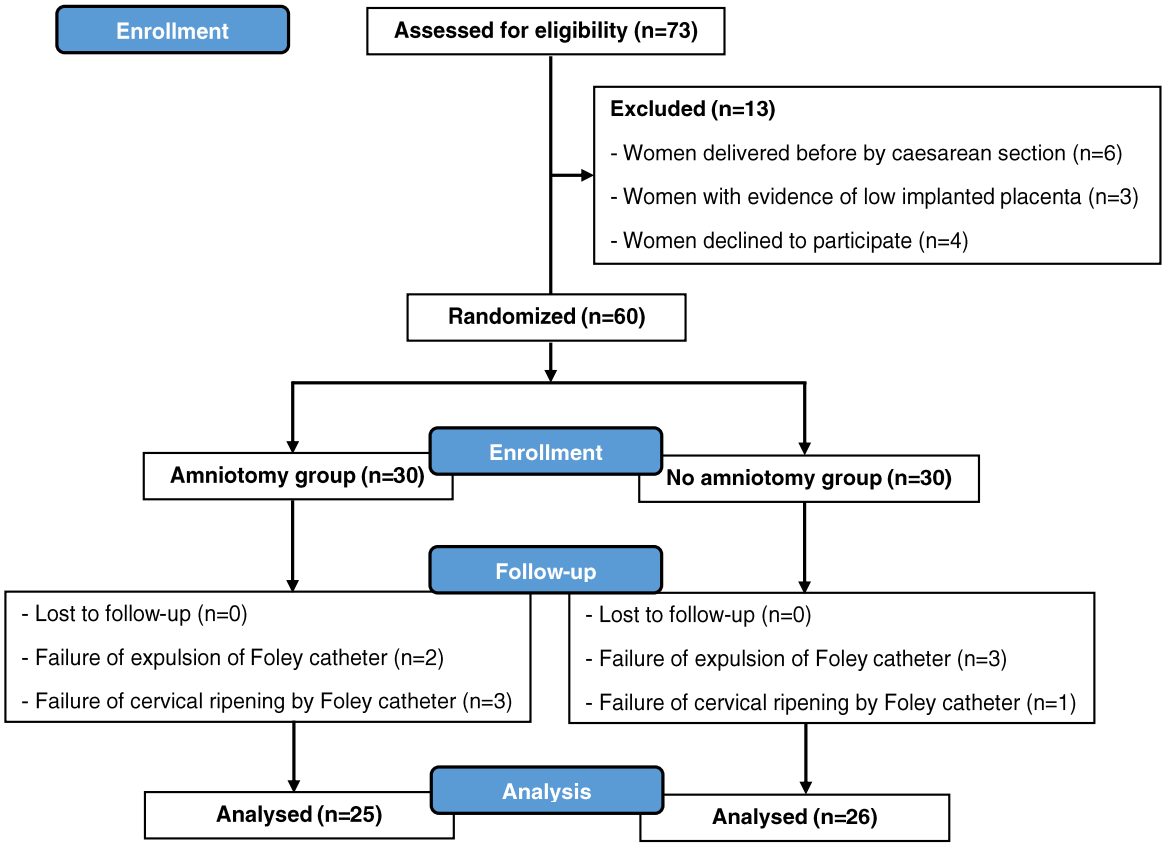

Fig. 1. Enrollment flowchart.

Table 1. Socio-demographic and obstetrics data of the women sharing in the study.

Personal data	Amniotomy group (n= 30)	No amniotomy group (n= 30)	p value
Age (years), mean ± SD	28.77 ± 7.13	30.13 ± 6.34	0.436
Residence, n (%)			0.158
Rural	11 (36.7)	16 (53.3)	0.134
Urban	19 (63.3)	14 (46.7)	
Level of education, n (%)			
Illiterate	8 (26.7)	10 (33.3)	0.581
Basic education	15 (50.0)	11 (36.7)	
Secondary or more	7 (23.3)	9 (30.0)	
BMI (kg/m^2), mean ± SD	26.33 ± 3.71	25.66 ± 3.52	0.474
Employment, n (%)	13 (43.3)	10 (33.3)	0.426
Parity, median (Range)	2.0 (0.0-6.0)	2.0 (0.0-7.0)	0.262
Number of living children, n (%)			0.460
0	3 (10.0)	4 (13.3)	
1	7 (23.3)	3 (10.0)	
2-3	12 (40.0)	11 (36.7)	
> 3	8 (26.7)	12 (40.0)	
History of previous abortion, n (%)	4 (13.3)	8 (26.7%)	0.197
Duration from last pregnancy (years), n (%)	4.0 (1.0-120.0)	6.0 (1.0-168.0)	0.519
< 1	8 (26.7)	4 (13.3)	
1-3	12 (40.0)	15 (50.0)	0.424
> 3	10 (33.3)	11 (36.7)	
Gestational age at the time of recruitment (weeks), mean ± SD	21.43 ± 2.58	22.23 ± 2.58	0.235

BMI: body mass index, n(%): number and percentage, SD: standard deviation

No statistically significant differences were noted between groups regards the socio-demographic and obstetrics data (Table 1). The mean gestational age of fetuses in this study was 21-22 weeks.

There are only three women (5%) had a previous history of Foley catheter balloon use for abortion induction. No statistically significant differences were found between groups as regards data before Foley catheter insertion (Table 2). The Foley catheter balloon successfully expulsed in 55 women in this study. The Bishop score after the expulsion was improved from before (median 1-1.5) to after (median 4). The time from balloon insertion to balloon expulsion was about 8 hours. No statistically significant differences were found in the data after Foley catheter balloon expulsion (Table 2).

As regards our primary outcome, the balloon expulsion to abortion time was shorter in the amniotomy group than the no amniotomy group with a statistically significant difference (6.89 ± 2.02 hours

vs 9.22 ± 1.98 hours, p < 0.001). The mean dose of oxytocin was higher in the no amniotomy group than in the amniotomy group with a statistically significant difference (76.61 ±15.78 IU vs 57.55 ±16.88 IU, p < 0.001). No statistically significant difference was observed regarding the number of women who needed analgesia (p = 0.296) or surgical placental removal in both groups (p < 0.001). The only reported complication in this study was the post-abortive bleeding in 3 women only (Table 3).

Table 2. Data before and after Foley catheter balloon expulsion.

	Amniotomy group (n= 30)	**No amniotomy group (n= 30)**	**p value**
Data before Foley catheter balloon expulsion			
Previous history of Foley catheter insertion, n (%)	2 (6.7)	1 (3.3)	1.000
Bishop score before Foley catheter insertion, median (range)	1.5 (0.0-3.0)	1.0 (0.0-3.0)	0.319
Need for analgesia after insertion, n (%)	4 (13.3)	7 (23.3)	0.317
Post-insertion bleeding, n (%)	2 (6.7)	4 (13.3)	0.671
Data after Foley catheter balloon expulsion			
Foley catheter balloon expulsion, n (%)	28 (93.3)	27 (90.0)	1.000
Bishop score after balloon expulsion, median (Range)	4.0 (0.0-6.0)	4.0 (0.0-6.0)	0.503
Cervical ripening after balloon expulsion, n (%)	25 (89.3)	26 (96.3)	0.611
Duration from insertion to balloon expulsion (hours), mean ± SD	7.93 ± 1.04	7.91 ± 0.82	0.926

SD: standard deviation, n(%): number and percentage

Table 3. The main study outcomes.

	Amniotomy group (n= 25)	**No amniotomy group (n= 26)**	**p value**
Balloon expulsion to abortion time (hours), mean ± SD	6.89 ± 2.02	9.22 ± 1.98	< 0.001*
Balloon insertion to abortion time (hours), mean ± SD	14.84 ± 2.37	17.14 ± 1.78	< 0.001*
Women needed analgesia, n (%)	8 (32)	5 (19.2)	0.296
The dose of oxytocin (IU), mean ± SD	57.55 ± 16.88	76.61 ± 15.78	< 0.001*
Surgical removal of placenta, n (%)	2 (8.0)	3 (11.5)	1.000
Post-abortive bleeding, n (%)	2 (8.0)	1 (3.8)	0.529
Post-abortive fever, n (%)	0 (0)	(0)	--
Post-abortive endometritis, n (%)	0 (0)	(0)	--

* Statistical significant difference (p < 0.05)
n (%): number and percentage, SD: standard deviation

Discussion

To our knowledge, this is the first study that talks about amniotomy and termination of mid-trimester fetal death in utero. The present work demonstrated that the amniotomy was safe and effectively decreased the interval between the expulsion of the Foley catheter balloon to complete abortion with fewer doses of oxytocin.

Induction of abortion in the mid-trimester is usually achieved by medical agents or by surgical methods like dilation and extraction (D&E)[17, 18]. Osmotic dilators are needed before D&E; where they are not available, a Foley catheter can be an alternative method to prepare the cervix[19, 20]. Transcervical Foley catheter is used to decrease the induction to labor/abortion interval[6, 21, 22].

Amniotomy is a safe and effective method to speed the process of labor. It is thought that amniotomy releases chemicals and hormones that induce uterine contraction and increases its power[13, 23, 25]. Despite many studies reporting the effectiveness of Foley catheter with medical treatment on induction of mid-trimester abortion[8, 25-27], no studies talked about Foley catheter and amniotomy.

In this study, we included only mid-trimester fetal death in utero because the termination of the mid-trimester living fetus is more difficult and takes more time[7]. The worry about uterine rupture in patients with one or more cesarean section scars during termination of mid-trimester abortion made us exclude those women from the study[8]. The mean of gestational age of fetuses in this study was 21-22 weeks, higher than other studies[6, 8, 27]. We chose this higher gestational age to allow easy and safe amniotomy. Most of the reports mentioned that a no.14 Foley catheter with a 40 mL balloon was suitable for mid-trimester abortion as we did[8, 28]. However, some preferred a larger size (no.18 Foley catheter[27].

The Bishop score was improved, in this study, after Foley catheter balloon expulsion. This fact was reported before[6, 8, 20, 29]. However, some reported no significant additional benefit[30]. The smaller gestational age and the less saline use in the Foley catheter balloon may be a cause of this result.

In this study, the Foley catheter balloon expulsed in about 91.5%. Foley catheter balloon expelled in all (100%) recruited women in many studies[6, 7, 26, 32]. However, all of them used misoprostol at the time or before the insertion of the Foley catheter. Fewer figures were previously reported (85% and 67%)[6, 33]. The smaller gestational age in their study (14-17 weeks) may be a reason for this difference.

The mean interval between Foley catheter balloon insertion and expulsion was 8 hours. We were on the same track with Ali et al[6]. A longer time was also reported in some studies (13 hours and 21 hours, respectively)[7, 29]. Moreover, they included women with smaller gestational ages from 13-24 weeks.

The time between insertion to abortion time was 14.84 ± 2.37 hours in the amniotomy group and 17.14 ± 1.78 hours in the no amniotomy group. Similar figures were noted in two studies (14.33 hours and 14.2 hours)[27, 31]. However, both of them used misoprostol with a Foley catheter. This means that amniotomy gives the same result without the need for misoprostol.

Some studies stated a much longer time (16.49, 38, 23.1, 19.76, 17.77, 16, and 20.11 hours)[6-9, 29, 30, 34, 35]. They included women with small gestational age or who underwent intended termination of living pregnancy, in addition, some were nulliparous women, and some of them used only a 30 ml Foley catheter balloon.

The dose of oxytocin needed to complete the abortion process was significantly lower in the amniotomy group (57.55 ± 16.88 vs 76.61 ± 15.78; respectively, $p < 0.001$). The amniotomy induces uterine contraction activity, increases the strength of contractions and subsequently decreases the oxytocin dose[36].

Both post-insertion pain and vaginal bleeding occurred in our study after Foley catheter balloon insertion. But they were not significant. Ercan reported that the rate of vaginal bleeding following the insertion of a Foley catheter balloon was about 7% which is almost near our figure (10%)[27]. It is recommended

to do an ultrasound assessment of the placental site before Foley catheter insertion[37]. We noticed that 10% of women needed surgical evacuation of the placenta. Velipasaoglu et al and Abo Bakr et al also reported near figures (10% and 8%, respectively)[8, 25].

In this study, the rate of post-abortive bleeding was 8 % and 3.8%, respectively, but it was not severe and stopped immediately after giving uterotonics. Near figures were also reported before (6.5%, 2%, 6.6%, and 8%)[8, 9, 27, 35].

A major strength of this study was its design as a randomized controlled trial with 95% power. In addition, this is the first study to address this issue. Moreover, a Foley catheter balloon was inserted by one investigator to decrease the interobserver errors. The small sample size and the heterogeneity of recruited women (different parity) may affect the results. We did not include women with previous caesarian sections was another limitation. Long-term complications were not studied.

Conclusion

The study proved that performing of amniotomy after using a Foley catheter balloon for cervical ripening during induction of mid-trimester fetal death in utero in a non-scarred uterus reduced time to abortion as well as oxytocin dose with very minimal complications.

Potential conflicts of interest

The authors declare no conflicts of interest.

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GYNAECOLOGY

Efficacy of Intravenous Dextrose-containing Fluid in Reducing Labor Duration of Pregnant Women: A randomized controlled trial

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ABSTRACT

Objectives: To evaluate the efficacy of dextrose-containing intravenous fluid and normal saline intravenous fluid in reducing labor duration in pregnant women.

Materials and Methods: In this randomized controlled trial, 164 low-risk term singleton pregnant women with gestational age of 37-42 weeks presenting with labor pain at Sanpasitthiprasong Hospital were equally randomized to receive either 1) dextrose-containing intravenous fluid 5% dextrose-containing in half-strength normal saline (5%D/N/2) or 2) normal saline (NSS) at a rate of 120 ml/hr. Primary outcome was total labor time, defined as duration during active phase plus second stage. Duration of latent phase, active phase, first stage and second stage of labor and maternal and neonatal outcomes were also assessed.

Results: Demographics, gestational age, cervical dilatation at the time of randomization and augmentation were comparable between the two groups. Total labor time was significantly shorter in dextrose group than NSS group (median 177.0, interquartile range 110.0, 258.0) and 206.5 (138.5, 298.3), p = 0.033). Active phase duration was significantly shorter in dextrose group (median 160.0 (100.0, 240.0) and 187.5 (127.3, 281.3), p = 0.029). There was no difference in latent phase, second stage, and third stage duration. Rates of cesarean delivery and maternal complications were comparable between the two groups. Transient tachypnea of the newborn was significantly higher in NSS group than dextrose group (29.3% and 9.8%, p = 0.002). There was no between-group difference in neonatal outcomes including birthweight, Apgar scores, and neonatal hypoglycemia.

Conclusion: Dextrose-containing intravenous fluid administered during intrapartum may shorten total labor time especially active phase duration, without increasing maternal and neonatal complications.

Keywords: Dextrose-containing intravenous fluid, intrapartum, total labor time, active phase duration.

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ประสิทธิภาพของการให้สารน้ำที่มีส่วนประกอบของน้ำตาลเด็กซ์โตรสทางหลอดเลือดดำในการลดระยะเวลาคลอดของสตรีตั้งครรภ์: การศึกษาแบบสุ่มมีกลุ่มเปรียบเทียบ

วนัชพร พุทธกูล, ปิยวดี วุฒิกรสัมมากิจ, ปริญญา ชำนาญ

บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาประสิทธิภาพของการให้สารน้ำที่มีส่วนประกอบของน้ำตาลเด็กซ์โตรสทางหลอดเลือดดำ เปรียบเทียบกับน้ำเกลือ ในการลดระยะเวลาคลอดของสตรีตั้งครรภ์*

วัสดุและวิธีการ: *การทดลองแบบสุ่มมีกลุ่มเปรียบเทียบในอาสาสมัครสตรีตั้งครรภ์เดี่ยวครบกำหนดที่มีความเสี่ยงต่ำ ขณะอายุครรภ์ 37 ถึง 42 สัปดาห์ จำนวน 164 ราย ซึ่งมาเข้ารับการรักษาที่ห้องคลอด โรงพยาบาลสรรพสิทธิประสงค์ ด้วยอาการเจ็บครรภ์คลอด โดยอาสาสมัครจะถูกแบ่งเป็น 2 กลุ่มเท่าๆ กัน โดยวิธีสุ่ม ได้แก่ กลุ่มที่ 1 ได้รับสารน้ำที่มีส่วนประกอบของน้ำตาลเด็กซ์โตรส 5% dextrose-containing in half-strength normal saline (5%D/N/2) และกลุ่มที่ 2 ได้รับสารน้ำเกลือ (normal saline; NSS) ในอัตรา 120 มิลลิลิตรต่อชั่วโมง โดยผลลัพธ์หลักคือระยะเวลาคลอด (total labor time) ซึ่งหมายถึงช่วง active phase รวมกับช่วงระยะที่สองของการคลอด (second stage of labor) รวมทั้งเก็บข้อมูลระยะเวลาช่วงปากมดลูกเปิดช้า (latent phase), active phase, ระยะที่หนึ่งและสองของการคลอด (first and second stage of labor) รวมทั้งภาวะแทรกซ้อนต่อมารดาและทารก เพื่อการวิเคราะห์*

ผลการศึกษา: *ข้อมูลทั่วไปของอาสาสมัคร, อายุครรภ์, การขยายตัวของปากมดลูก ณ เวลาที่เข้างานวิจัย และการได้รับยาเร่งคลอดไม่แตกต่างกันระหว่างกลุ่ม โดยพบว่าระยะเวลาคลอดสั้นลงอย่างมีนัยสำคัญในกลุ่มที่ได้รับสารน้ำที่มีส่วนประกอบของน้ำตาลเด็กซ์โตรส เปรียบเทียบกับกลุ่มที่ได้รับสารน้ำเกลือ (ค่ามัธยฐาน 177.0 นาที ในกลุ่มที่ได้รับสารน้ำที่มีส่วนประกอบของน้ำตาลเด็กซ์โตรสและค่ามัธยฐาน 206.5 นาทีในกลุ่มที่ได้รับสารน้ำเกลือ, p = 0.033) ระยะ active phase สั้นลงอย่างมีนัยสำคัญ ในกลุ่มที่ได้รับสารน้ำที่มีส่วนประกอบของน้ำตาลเด็กซ์โตรส (ค่ามัธยฐาน 160.0 นาที ในกลุ่มที่ได้รับสารน้ำที่มีส่วนประกอบของน้ำตาลเด็กซ์โตรสและค่ามัธยฐาน 187.5 นาที ในกลุ่มที่ได้รับสารน้ำเกลือ, p = 0.029) แต่ไม่พบความแตกต่างกันอย่างมีนัยสำคัญระหว่างกลุ่มของระยะปากมดลูกเปิดช้า (latent phase) และการคลอดระยะที่สองและสาม เช่นเดียวกันกับอัตราการผ่าตัดคลอด และภาวะแทรกซ้อนของมารดา ที่ไม่มีความแตกต่างกันระหว่างกลุ่ม อย่างไรก็ตามพบภาวะหายใจเร็วชั่วคราวของทารกแรกเกิด (transient tachypnea of newborn) ในทารกที่มารดาได้รับสารน้ำเกลือมากกว่ากลุ่มที่มารดาได้รับสารน้ำที่มีส่วนประกอบของน้ำตาลเด็กซ์โตรสอย่างมีนัยสำคัญ (ร้อยละ 29.3 ในกลุ่ม

NSS และร้อยละ 9.8 ในกลุ่มน้ำตาลเด็กซ์โตรส, p = 0.002) ส่วนผลลัพธ์ของทารกในด้านอื่นๆ ได้แก่ น้ำหนักแรกคลอด, คะแนน Apgar, และภาวะน้ำตาลในเลือดต่ำของทารก ไม่มีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ

***สรุป**: การให้สารน้ำทางหลอดเลือดดำที่มีส่วนประกอบของน้ำตาลเด็กซ์โตรสในช่วงเจ็บครรภ์คลอด ช่วยลดระยะเวลาคลอด โดยเฉพาะอย่างยิ่งระยะเวลาปากมดลูกเปิดเร็วได้ โดยไม่มีผลแทรกซ้อนต่อมารดาและทารกในครรภ์*

***คำสำคัญ**: การให้สารน้ำที่มีส่วนประกอบของน้ำตาลเด็กซ์โตรสทางหลอดเลือดดำ, ระยะคลอด, ระยะเวลาคลอด, ระยะปากมดลูกเปิดอย่างรวดเร็ว*

Introduction

According to stages of labor, the first and second stage of labor potentially affected successful vaginal delivery, decision of managements and neonatal outcomes[1]. From previous studies, many pregnant women who encountered the prolonged duration of labor, would have several adverse effects on pregnancy outcomes, such as increased risk of cesarean section from cephalopelvic disproportion[2], chorioamnionitis, neonatal intensive care unit (NICU) admission[3], neonatal asphyxia, postpartum hemorrhage[4]. In addition, prolonged labor might increase stress for pregnant women and her families.

Intrapartum fluid hydration either oral or intravenous fluid has been reported to reduce labor duration due to glucose playing an important role in the muscle power, especially uterine muscle contraction[5]. Evidence from systematic review[6] indicated that intravenous fluid hydration with the rate of 250 ml/hour could reduce duration of labor in nulliparous women if a policy of no oral intake is applied. However, the effect of intravenous fluid administration still could not conclude in cesarean section rate and operative vaginal delivery rate[7].

Even intravenous fluid hydration was very essential for pregnant women during labor periods; however, there was no conclusion in deciding which type of intravenous fluid is suitable and safely given during labor[8]. The results from previous studies[9-20] were not concordant to determine types and rate of intravenous fluid given in beneficial effect of reducing labor duration. Most of previous studies[5, 9-11, 13, 14, 18, 19] could demonstrate the shorter labor time in dextrose-containing intravenous fluid administration but some studies[12,15, 17] demonstrated the contradicted results. Most previous studies[9, 10, 12-15, 19, 20] suggested that dextrose-containing fluid did not affect cesarean delivery rate, while more recent studies[16, 18] demonstrated the benefit in reducing cesarean section rate. However, the majority of these previous studies were conducted in western population and focused on nulliparous women which may not be generalized in clinical practice with both nulliparous and multiparous women. Therefore, the present study was aimed to investigate the effect of glucose-containing intravenous fluid compared with the normal saline intravenous fluid on labor duration and other maternal and neonatal outcomes in nulliparous and multiparous women giving birth at a tertiary hospital in northeastern Thailand.

Materials and Methods

Setting and study population

This was a two-arm parallel-group randomized controlled trial conducted in Sanpasitthiprasong Hospital during April 20th, 2023, to February 1st, 2024. This clinical trial was registered (TCTR20230605004) with http//: www.ClinicalTrials.in.th (Thai Clinical Trials Registry). After approval of institutional ethical committee (081/2566), singleton pregnant women, aged 18-45 years old, who came with labor pain at gestational age of 37 to 42 completed weeks, with

regular uterine contraction and a cervical dilatation of 3-5 cm., were invited to participate in the study. The pregnant women who had pregnancy-induced hypertension, gestational diabetes mellitus, underlying diseases such as renal, heart, or liver disorders, contraindication of vaginal delivery, and abnormal fetal status were excluded.

Randomization and interventions

After given written informed consent, a total of 164 participants were equally randomized to receive one of the two treatments: 1) received 5% dextrose-containing in half-strength normal saline (5%D/N/2) intravenous fluid and 2) received normal saline (0.9% NSS) intravenous fluid starting when participants entered active phase of labor at the same rate of 120 ml/hour. In this study, intravenous fluid was prohibited before randomization in all pregnant women. The randomized sequence generated by Microsoft Excel 2010. The allocated numbers were inserted into identical, opaque, and sealed envelopes placed in the labor room. The attending physicians or nurses opened envelopes to assign the participants to each group. Both types of fluid bottles were prepacked with opaque wrapping. The participants would receive the fluid according to the randomized sequence. The physicians and nurses who took care of the participants were blinded to the intervention. The two treatment groups received identical standard obstetric care included monitoring of fetal heart rate, observing uterine contraction, cervical progression every 2-4 hours, artificial rupture of membranes and augmentation in case of abnormal labor progression from poor uterine contraction and analgesic drugs administration when the participants had pain score of more than 5. To comply with standard practice, all participants were not allowed to eat or drink per oral during active phase. All participants in both groups were evaluated their blood glucose after 1 hour of receiving the intravenous fluid for safety concern of hypo- or hyperglycemic complication.

Data collection and outcome ascertainment

Data on baseline characteristics of participants were collected before allocation. These included age, occupation, education, marital status, income, gravidity, parity, nulliparous, gestational age (weeks), number of antenatal visits, gestational age at first antenatal visit, pre-pregnancy body mass index (BMI) and total weight gain. Data on cervical dilatation, and membrane status at randomization, augmentation with oxytocin and its duration, total volume of intravenous fluid administration were recorded. Primary outcome was total labor time, defined as the duration of active phase of first stage of labor plus the second stage of labor. Secondary outcomes were duration of each stage of labor such as latent, active phase of first stage of labor, second stage, and third stage of labor. Delivery outcomes such as route of delivery, indications for cesarean section and operative vaginal delivery, intrapartum and postpartum complications were recorded. In addition, neonatal outcomes, namely birthweight, Apgar scores at 1,5,10 minutes, and neonatal complications, such as respiratory distress, neonatal jaundice, sepsis, neonatal trauma, neonatal hypoglycemia, and NICU admission, were also recorded. Prolong latent phase was defined as duration from regular uterine contraction until cervical dilatation of 4 cm more than 8 hours and prolong active phase defined as duration from cervical dilatation of more than 4 cm to full dilatation being longer than 12 hours[21].

Statistical analysis

Sample size was calculated based on results from previous study by Swidan et al[13] which showed that the mean (standard deviation; SD) total duration of labor was 395.0 (172.4) minutes in dextrose-containing group and 487.0 (220.5) minutes in normal saline group. With the power of 80%, 2-sided type I error at 5%, and 10% addition for drop out, the sample size of 82 per group was required. An intention-to-treat analysis was done using SPSS version 17.0 (SPSS Inc., Chicago, IL, USA). The Kolmogorov-Smirnov normality test was used to determine the distribution of continuous data. Categorical data were reported

as number (percent) and continuous data were reported as mean ± SD and median (interquartile range; IQR) for normally- and non-normally distributed variables, respectively. Comparisons of outcomes between the two treatment groups were performed using chi-square test, student t-test and Mann-Whitney-U test for categorical variables, normally and non-normally distributed continuous variables, respectively. P value of < 0.05 was considered statistically significant.

Results

Fig. 1 shows enrollment, randomization, and follow-up of the study participants. From 391 pregnant women who met eligible criteria, 227 participants were excluded (139 declined to participate in this study and 88 met exclusion criteria). The final sample of 164 participants were equally randomized to receive either dextrose-containing in half-strength normal saline (5% D/N/2) or normal saline (NSS), at the same rate of 120 ml/hour. No participant was dropped out in this study. Delivery outcomes, maternal and neonatal complications were assessed in all participants.

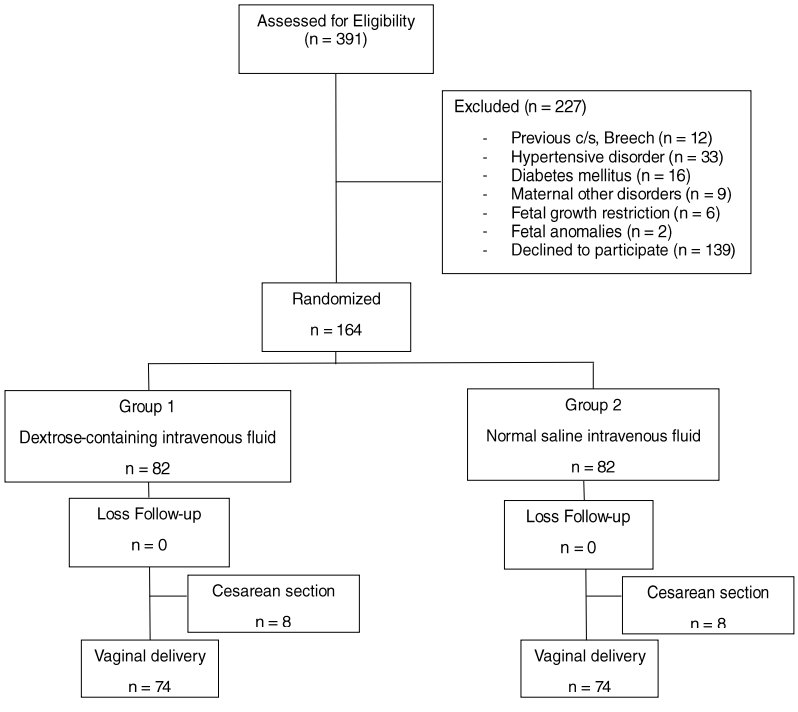

Fig. 1. Flow chart of participants recruitment.

Table 1 shows the baseline characteristics of participants, overall and by treatment groups. Among all participants, 81 (49.4%) were nulliparous with the median (IQR) gestational age of 39.0 (38.0, 39.0) weeks. The median (IQR) of cervical dilatation was 3.0 (3.0, 4.0) cm, and 29 (17.7%) had membranes ruptured at the time of randomization. Participants' age, occupation, education, marital status, and income were comparable between the two groups. Obstetric characteristics including gravidity, parity, nulliparous, gestational age, number of antenatal visits, gestational age at first antenatal visit,

prepregnancy BMI, total weight gain, cervical dilatation, and membrane status at the time of randomization were comparable between the two groups.

Table 1. Baseline characteristics of participants, overall and by treatment groups (n = 164).

	Total (n = 164)	Normal saline (n = 82)	Dextrose (n = 82)	p value*
Age (years), median (IQR)	26.0 (22.0, 30.0)	26.0 (22.0, 30.0)	26.0 (23.0, 30.3)	0.562
Occupation				0.505
No job, n (%)	43 (26.2)	26 (31.7)	17 (20.7)	
Student, n (%)	2 (1.2)	0 (0.0)	2 (2.4)	
Employee, n (%)	69 (42.1)	33 (40.2)	36 (43.9)	
Government official, n (%)	10 (6.1)	5 (6.1)	5 (6.1)	
Own-business, n (%)	31 (18.9)	14 (17.1)	17 (20.7)	
Medical personnel, n (%)	3 (1.8)	2 (2.4)	1 (1.2)	
Agriculturist, n (%)	6 (3.7)	2 (2.4)	4 (4.9)	
Education				0.553
Primary and secondary, n (%)	88 (53.7)	42 (51.2)	46 (56.1)	
Vocational, n (%)	33 (20.1)	15 (18.3)	18 (22.0)	
Bachelor, n (%)	39 (23.8)	22 (26.8)	17 (20.7)	
Master's degree or more, n (%)	4 (2.4)	3 (3.7)	1 (1.2)	
Marital status				0.587
Single, n (%)	15 (9.1)	8 (9.8)	7 (8.5)	
Married, n (%)	148 (90.2)	74 (90.2)	74 (90.2)	
Divorced, n (%)	1 (0.6)	0 (0.0)	1 (1.2)	
Income (baht), median (IQR)	10,000 (8,000, 15,000)	12,000 (8,000, 15,250)	10,000 (7,000, 15,000)	0.327
Gravidity, median (IQR)	2 (1, 2)	2 (1, 2)	2 (1, 2)	0.412
Parity, median (IQR)	0 (0, 1)	0 (0, 1)	0.5 (0, 1)	0.745
Nulliparous, n (%)	81 (49.4)	41 (50.0)	40 (48.8)	0.876
Gestational age (weeks), median (IQR)	39.0 (38.0, 39.0)	39.0 (38.0, 39.0)	39.0 (38.0, 40.0)	0.697
Number of antenatal visits, median (IQR)	10.0 (8.3, 12.8)	10.0 (8.0, 13.0)	10.0 (8.8, 12.3)	0.718
Gestational age at first antenatal visit, median (IQR)	10.0 (8.0, 13.0)	10.0 (7.0, 13.0)	10.0 (8.0, 13.0)	0.812
Pre-pregnancy body mass index (kg/m2), median (IQR)	20.7 (18.8, 24.0)	20.7 (18.9, 24.4)	20.7 (18.7, 23.6)	0.593
Total weight gain (kg), median (IQR)	13.0 (10.0, 17.0)	13.0 (10.0, 17.0)	12.5 (10.0, 16.0)	0.165
Cervical dilatation at randomization (cm), median (IQR)	3.0 (3.0, 4.0)	3.0 (3.0, 4.0)	3.0 (3.0, 4.0)	0.701
Effacement at randomization (%), median (IQR)	80 (70, 100)	80 (70, 100)	80 (70, 100)	0.275
Membrane status at randomization				0.072
Intact, n (%)	132 (80.5)	71 (86.6)	61 (74.4)	
Leakage, n (%)	3 (1.8)	2 (2.4)	1 (1.2)	
Ruptured, n (%)	29 (17.7)	9 (11.0)	20 (24.4)	
Pethidine administration, n (%)	7 (4.3)	2 (2.4)	5 (6.1)	0.246
Systemic blood pressure (mmHg), median (IQR)	120.0 (114.0, 127.0)	120.0 (114.0, 126.3)	120.5 (113.8, 127.0)	0.970
Diastolic blood pressure (mmHg), median (IQR)	76.0 (70.0, 80.0)	76.0 (70.0, 80.0)	76.5 (70.0, 80.0)	0.628
Pulse rate (beats/min), median (IQR)	90.0 (82.0, 100.0)	90.0 (81.5, 100.0)	91.0 (81.5, 100.0)	0.421

IQR: interquartile range

* p value for comparison between the two treatment groups, using chi-square test and Mann-Whitney-U test for categorical and non-normally distributed continuous variables, respectively

Table 2 shows duration of stages of labor, overall and by treatment groups. The duration of total labor was significantly shorter in dextrose-containing group than the normal saline group (median (IQR) of 177.0 (110.0, 258.0) minutes vs 206.5 (138.5, 298.3) minutes, respectively, p = 0.033). The duration of active phase of first stage of labor was also significantly shorter in dextrose-containing group than normal saline group. (median (IQR) of 160.0 (100.0, 240.0) minutes vs 187.5 (127.3, 281.3) minutes, respectively, p = 0.029). However, the median durations of latent phase, first stage, second stage, and third stage of labor were not significantly different between the two treatment groups. Prolonged latent phase was equally observed in both treatment groups (28.0% vs 24.4%, p = 0.594). There was no participant having prolonged active phase in both groups. The total intravenous fluid administration, augmentation with oxytocin and its duration were comparable between the two treatment groups.

Table 2. Duration of stages of labor, overall and by treatment groups (n = 164).

	Total (n = 164)	Normal saline (n = 82)	Dextrose (n = 82)	p value*
Total labor time[a] (minutes), median (IQR)	194.0 (124.0, 266.5)	206.5 (138.5, 298.3)	177.0 (110.0, 258.0)	0.033
(Active phase + Second stage)	300.0 (180.0, 480.0)	300.0 (180.0, 487.5)	300.0 (210.0, 480.0)	0.618
Latent phase, (minutes), median (IQR)	170.0 (115.0, 257.5)	187.5 (127.3, 281.3)	160.0 (100.0, 240.0)	0.029
Active phase[a], (minutes), median (IQR)	480.0 (350.5, 775.0)	457.5 (350.0, 815.0)	490.0 (370.0, 710.0)	0.885
First stage of labor[a], (minutes), median (IQR)	11.0 (7.0,16.0)	10.0 (8.0, 16.0)	11.0 (7.0, 16.0)	0.633
Second stage of labor[a], (minutes), median (IQR)	5.0 (4.0,8.0)	5.0 (4.0, 8.0)	5.0 (4.0, 8.0)	0.910
Third stage of labor[a], (minutes), median (IQR)	501.0 (369.0, 790.0)	473.5 (365.0, 839.5)	505.0 (385.0, 730.0)	0.888
First stage + Second stage + Third stage[a], (minutes), medain (IQR)	43.0 (26.2)	23.0 (28.0)	20.0 (24.4)	0.594
Prolong latent phase	73.0 (44.5)	33.0 (40.2)	40.0 (48.8)	0.271
Augmentation with oxytocin, n (%)	181.0 (90.8, 267.8)	120.0 (79.0, 242.0)	200.0 (129.0, 281.0)	0.057
Augmentation duration (min), median (IQR)	524.0 (339.0, 766.5)	539.0 (365.0, 751.5)	498.0 (316.0, 797.5)	0.383
Total fluid volume (ml), median (IQR)	524.0 (339.0, 766.5)	539.0 (365.0, 751.5)	498.0 (316.0, 797.5)	0.383

IQR: interquartile range

* p value for comparison between the two treatment groups, using chi-square test and Mann-Whitney-U test for categorical and non-normally distributed continuous variables, respectively

[a] Percentage of the outcome compared to total vaginal births in each treatment group.

Table 3 shows maternal outcomes overall and by treatment groups. Overall, 15 (9.1%) participants underwent Cesarean delivery, and 23 (14.0%) participants delivered by vacuum extraction with the remaining undergoing normal vaginal delivery. Overall, 9 (5.5%) participants had postpartum

hemorrhage, and there was no chorioamnionitis. When comparing the two treatment groups, there was no significant difference in routes of delivery, intrapartum and postpartum complications.

Table 3. Maternal outcomes, overall and by treatment groups (n = 164).

	Total (n = 164)	Normal saline (n = 82)	Dextrose (n = 82)	p value*
Route of delivery				0.259
Spontaneous Vertex delivery, n (%)	126 (76.8)	59 (72.0)	67 (81.7)	
Vacuum extraction, n (%)	23 (14.0)	15 (18.3)	8 (9.8)	
Cesarean section, n (%)	15 (9.1)	8 (9.8)	7 (8.5)	
Indication of vacuum extractiona				0.782
Fetal distress, n (%)	5 (21.7)	3 (20.0)	2 (25.0)	
Poor maternal effort, n (%)	18 (78.3)	12 (80.0)	6 (75.0)	
Indication for Cesarean sectionb				0.398
Fetal distress, n (%)	6 (40.0)	4 (50.0)	2 (28.6)	
Cephalopelvic disproportion, n (%)	9 (60.0)	4 (50.0)	5 (71.4)	
Intrapartum complications				0.301
Fetal distress, n (%)	10 (83.3)	6 (100.0)	4 (66.7)	
Shoulder dystocia, n (%)	1 (8.3)	0 (0.0)	1 (16.7)	
Failed vacuum extraction, n (%)	1 (8.3)	0 (0.0)	1 (16.7)	
Postpartum complications				
Postpartum hemorrhage, n (%)	9 (5.5)	3 (3.7)	6 (7.3)	0.304
Fourth degree perineum tear, n (%)	2 (1.2)	1 (1.2)	1 (1.2)	1.000
Perineum hematoma, n (%)	2 (1.2)	2 (2.4)	0 (0.0)	0.155
Blood glucose at 1 hour (mg%), median (IQR)	94.0 (86.0, 105.0)	91.0 (84.0, 97.0)	97.0 (89.3, 117.3)	< 0.001

IQR: interquartile range

* p-value for comparison between the two treatment groups, using chi-square test and Mann-Whitney-U test for categorical and non-normally distributed continuous variables, respectively

[a] Percentage of the outcome compare to total participants delivered by vacuum extraction in each treatment group

[b] Percentage of the outcome compare to total participants delivered by caesarean section in each treatment group

Concerning neonatal outcomes, the median infant birthweight was 3,042.5 grams and median Apgar scores at 1 and 5 minutes were 9, and 10, respectively (Table 4). There was no difference in birthweight, Apgar scores at 1, 5, and 10 minutes between the two groups. Respiratory distress was the most common neonatal complication (31.1%) with no significant difference between the two groups. Respiratory distress from transient tachypnea of newborn (TTNB) was significantly increased in normal saline group (29.3% in normal saline group vs 9.8% in dextrose-containing group, p = 0.002). There was no significant difference in other neonatal complications between groups.

Table 4. Neonatal outcomes, overall and by treatment groups (n = 164).

	Total (n = 164)	Normal saline (n = 82)	Dextrose (n = 82)	p value*
Birth body weight (grams), median (IQR)	3042.5 (2797.5, 3372.5)	3055.0 (2806.3, 3390.0)	3027.5 (2765.0, 3338.8)	0.579
Apgar score				
At 1 minute, median (IQR)	9 (9,9)	9 (9,9)	9 (9,9)	0.523
At 5 minutes, median (IQR)	10 (10,10)	10 (10,10)	10 (10,10)	0.322
At 10 minutes, median (IQR)	10 (10,10)	10 (10,10)	10 (10,10)	1.000
Respiratory distress, n (%)	51 (31.1)	30 (36.6)	21 (25.6)	0.129
Cause of respiratory distress, n (%)				
Delay adaptation, n (%)	14 (8.5)	6 (7.3)	8 (9.8)	0.576
TTNB, n (%)	32 (19.5)	24 (29.3)	8 (9.8)	0.002
Sepsis, n (%)	3 (1.8)	0 (0.0)	3 (3.7)	0.080
Pneumonia, n (%)	1 (0.6)	0 (0.0)	1 (1.2)	0.316
MAS, n (%)	1 (0.6)	0 (0.0)	1 (1.2)	0.316
Neonatal jaundice, n (%)	41 (25.0)	22 (26.8)	19 (23.2)	0.589
Sepsis, n (%)	3 (1.8)	0 (0.0)	3 (3.7)	0.080
Neonatal trauma, n (%)	16 (9.8)	11 (13.4)	5 (6.1)	0.114
Cause of neonatal trauma				
Caput succedaneum, n (%)	3 (1.8)	2 (2.4)	1 (1.2)	0.560
Cephalhematoma, n (%)	3 (1.8)	2 (2.4)	1 (1.2)	0.560
Subgaleal hematoma, n (%)	9 (5.5)	6 (7.3)	3 (3.7)	0.304
Scalp abrasion, n (%)	1 (0.6)	1 (1.2)	0 (0.0)	0.316
Fracture clavicle, n (%)	1 (0.6)	0 (0)	1 (1.2)	0.316
Neonatal hypoglycemia, n (%)	4 (2.4)	1 (1.2)	3 (3.7)	0.311
NICU admission, n (%)	9 (5.5)	5 (6.1)	4 (4.9)	0.732

TTNB: transient tachypnea of the newborn, MAS: meconium aspiration syndrome, NICU: neonatal intensive care unit, IQR: interquartile range
*p value for comparison between the two treatment groups, using chi-square test and Mann-Whitney-U test for categorical and non-normally distributed continuous variables, respectively.

Discussion

In this two-arm parallel group randomized controlled trial, dextrose-containing intravenous fluid had beneficial effect in shortening total labor time, especially active phase of labor. However, the duration of other stages of labor such as latent phase, first stage, second stage, and third stage of labor were not significantly different between dextrose-containing intravenous fluid and normal saline groups. There was no difference between groups in maternal and neonatal outcomes except for TTNB, which was observed more frequently in normal saline group.

Consistent with many previous studies[9-11,13, 16,18], our study showed the significant effect of dextrose-containing intravenous fluid to reduce the total labor time. However, some other studies[15, 17, 19] did not find this effect. The differences between these studies and our study may be explained by different types, concentration and administration rates of fluid, whether the mothers were allowed to eat or not. This may also be explained by the differences in participant's parity. That is, previous studies mainly investigated in nulliparous mothers, while our study included both nulliparous and multiparous. The reasons for the

beneficial effect of dextrose-containing intravenous fluid on duration of labor may be that glucose plays an important role in generating adenosine triphosphate (ATP), the major fuel to enhance effective contraction of uterine smooth muscle[6], especially during the period that the women had limited energy from nil-per-oral (NPO). It is possible that timing of dextrose-containing intravenous fluid administration may have impact on labor duration. A few studies[12,17] examining the effect of dextrose-containing intravenous fluid starting at different times when cervical dilatation ranged from 1 to 6 cm. showed negative results. However, to the best of our knowledge, there is no trial investigating head-to-head comparisons between different timing of dextrose-containing intravenous fluid, and this merits further studies.

The benefit of dextrose-containing intravenous fluid on active phase duration, oxytocin use, and risk of prolonged labor remains inconclusive. Our study showed consistent results with a few previous studies[11,13] suggesting that dextrose-containing intravenous fluid significantly reduced active phase duration for approximately 27.5 minutes. However, many other studies[9, 14, 15, 20] showed no such benefit. This inconsistency was observed regardless of rates of intravenous fluid administration (varying rates in different studies ranging from 120 to 250 ml/hours). Of note, dextrose-containing intravenous fluid did not impact on the second stage duration in our study. This may be because the second stage of labor was relatively short and therefore the impact of dextrose-containing intravenous fluid may be modest. Our study found no difference in oxytocin use and augmentation time between groups which was consistent with many previous studies[11-13, 15, 17]. However, other studies[10, 20] found less oxytocin use in dextrose group. While some studies[9, 10, 13, 16] showed the effect of dextrose-containing intravenous fluid on reducing prolonged labor, other studies[15, 17, 19] failed to demonstrate such benefit. Of note, no participants in our study had prolonged labor, hence we could not demonstrate the difference between groups in the risk of prolonged labor. The reason for the benefit of dextrose-containing intravenous fluid on this outcome may be likely similar to that of total labor time. However, further research is needed to explore other mechanisms underpinning the impact of dextrose-containing fluid on these outcomes.

Despite its likely benefit on duration of labor, the dextrose-containing intravenous administration has been consistently reported to have no effect on cesarean delivery rate and other maternal outcomes (chorioamnionitis, postpartum hemorrhage, and severe perineal tear). Many previous studies[5, 9, 10, 12-17, 19, 20] showed that cesarean section rate did not differ between mothers receiving dextrose- and non-dextrose-based intravenous fluid. This is confirmed by a recent meta-analysis[18] of 7 trials which suggested a trend toward a reduction in rate of cesarean section in dextrose-group, but the pooled relative risk reduction did not reach statistically significant.

Among all neonatal outcomes, only outcome that was different between normal saline and dextrose-containing group was TTNB. Although there was no previous study mentioning about this outcome, our study revealed higher risk of TTNB in normal saline group than dextrose-containing group. This might be explained by certain cellular level pathophysiology mechanisms. TTNB results from delayed lung fluid clearance. With the onset of labor, maternal epinephrine and glucocorticoid activate the epithelium sodium channel (ENaC) on the apical membrane of type II pneumocytes which creates the osmotic gradient to absorb fluid into the pulmonary circulations[22]. However, human birth is associated with many inflammatory processes, and correlated with many cytokines and chemokines[23]. TNF- α is one of these proinflammatory mediators, which can downregulate ENaC expression in alveolar epithelium cells[24]. It is possible that prolonged labor time, which was observed in normal saline group, would probably result in an increase in TNF- α, hence downregulation of ENaC receptors and compromised reabsorption

process in the neonatal lungs. Consistent with many previous studies[12-15,17-19], our study found no difference in other neonatal outcomes such as Apgar scores, neonatal hypoglycemia, jaundice, pneumonia, sepsis, birth trauma and NICU admission. However, a study by Shafaie et al[16] reported a statistically significant lower Apgar score at 1 min in dextrose-containing group (8.8 in dextrose group vs 9.0 in ringer lactate solution group). However, such a difference in Apgar score was likely to be of no clinical significance.

This study was a well-designed randomized controlled trial, with double blinding (both participants and caregivers). The outcomes were completely investigated without drop out of participants. The participants (both pregnant women and fetuses) were safely monitored to prevent the inadvertent events such as random blood sugar testing, electronic fetal monitoring, and standard obstetric care. This study is among the first to examine in the effect of dextrose-containing intravenous fluid on duration of labor in both nulliparous and multiparous, so the results can be generalizable to all low-risk pregnant women, not limited to only nulliparous mothers. However, our study had a number of limitations. Firstly, our study focused mainly on comparison of dextrose versus non-dextrose containing intravenous fluid supplements, while there were also a number of other approaches to fluid supplementation that have reportedly been effective in reducing labor time; for example, ringer lactate solution[25], oral fluid supplement[26], and anticholinergic agents[27]. Secondly, the onset of labor to determine duration of latent phase of first stage of labor depended largely on mother's recall. Thirdly, our study did not include specific certain groups such as teenage under 18 years old, pregnancy induced hypertension, gestational diabetes mellitus, and other high-risk pregnant women. Therefore, the generalizability of our findings to these high-risk groups may be limited. Lastly, this study only compared normal saline with 5% dextrose-containing fluid at a fixed rate of 120 ml/hour, further studies on different types, concentration and administration rates of intravenous fluid may be needed.

Conclusion

Dextrose-containing intravenous fluid administered during intrapartum may help shorten total labor time especially active phase duration, without increasing in maternal and neonatal complications.

Potential conflicts of interest

The authors declare no conflicts of interest.

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GYNAECOLOGY

Prevalence of Vitamin D Deficiency in Thai Women with Uterine Fibroids

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ABSTRACT

Objectives: To determine the prevalence and associated factors of vitamin D deficiency in Thai women with uterine fibroids.

Materials and Methods: A cross-sectional observational study was conducted on 181 Thai women aged 21-49 diagnosed with at least one uterine fibroid with a diameter of 10 mm or greater by ultrasound. The volume of uterine fibroids was calculated using the ellipsoid volume formula. Serum concentrations of 25-hydroxyvitamin D (25(OH)D), parathyroid hormone, and calcium were measured. Then, the participants were stratified into three groups according to their vitamin D status.

Results: The prevalence of vitamin D deficiency in Thai women with uterine fibroids was 69.6%. The mean serum concentrations of 25(OH)D, parathyroid hormone, and calcium were 18.8 ± 5.8 ng/ml, 47.9 ± 17.8 pg/ml, and 9.2 ± 0.5 mg/dl, respectively. Neither serum 25(OH)D levels nor serum calcium levels were significantly associated with total uterine fibroid volume (crude mean difference (MD) = -0.01, 95% confidence interval (CI) = -0.02, 0.2, p = 0.949, crude MD = -0.19, 95%CI = -0.48, 0.1, p = 0.193, respectively). However, there was a significant association between serum parathyroid hormone (PTH) levels and total uterine fibroid volume (Adjusted MD = -0.02, 95%CI = -0.06, -0.001, p = 0.006).

Conclusion: Although a high prevalence of vitamin D deficiency was observed among Thai women with uterine fibroids, no significant association was found between low serum 25(OH)D levels and the presence of uterine fibroids.

Keywords: Vitamin D deficiency, 25-hydroxyvitamin D, uterine fibroids.

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ความชุกของภาวะวิตามินดีบกพร่องในหญิงไทยที่เป็นเนื้องอกกล้ามเนื้อมดลูก

ดวงฤดี ปีตินารักษ์, วริษา สิริสุวรรณทัศน์

บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาความชุกและปัจจัยที่เกี่ยวข้องกับภาวะวิตามินดีบกพร่องในหญิงไทยที่เป็นเนื้องอกกล้ามเนื้อมดลูก*

วัสดุและวิธีการ: *การศึกษานี้เป็นการศึกษาเชิงพรรณนาภาคตัดขวางในหญิงไทยจำนวน 181 คน ที่มีอายุ 20-49 ปี ที่มาเข้ารับการรักษาที่โรงพยาบาลราชวิถีตั้งแต่เดือน มิถุนายน 2562 ถึงเดือนมีนาคม 2563 ซึ่งได้รับการวินิจฉัยว่ามีเนื้องอกกล้ามเนื้อมดลูกอย่างน้อยหนึ่งก้อนและมีขนาดมากกว่าหรือเท่ากับ 10 มิลลิเมตรจากการทำอัลตราซาวด์ จากนั้นนำขนาดก้อนเนื้องอกมดลูกมาคำนวณหาปริมาตรโดยใช้สูตรปริมาตรทรงรี และเก็บเลือดตรวจเพื่อหาระดับความเข้มข้นของวิตามินดี (25-hydroxyvitamin D; 25(OH)D) , พาราไทรอยด์ฮอร์โมน และแคลเซียม*

ผลการศึกษา: *จากผู้เข้าร่วมงานวิจัยจำนวน 181 คน พบค่าความชุกของภาวะวิตามินดีบกพร่องในหญิงไทยที่เป็นเนื้องอกกล้ามเนื้อมดลูกคิดเป็นร้อยละ 69.6 ค่าเฉลี่ยระดับความเข้มข้นของวิตามินดี (25-hydroxyvitamin), พาราไทรอยด์ฮอร์โมน และแคลเซียม คือ 18.8 ± 5.8 นาโนกรัม/มิลลิลิตร, 47.9 ±17.8 พิโกกรัม/มิลลิลิตร และ 9.2 ± 0.5 มิลลิกรัม/เดซิลิตร ตามลำดับ โดยไม่พบความสัมพันธ์อย่างมีนัยสำคัญทางสถิติระหว่างลอการิทึมของปริมาตรรวมเนื้องอกกล้ามเนื้อมดลูกกับระดับซีรัม 25-hydroxyvitamin D (crude mean difference (MD) = -0.01, 95% confidence interval (CI) = -0.02, 0.2, p = 0.949) และระดับซีรัมแคลเซียม (crude MD = -0.19, 95%CI = -0.48, 0.1, p = 0.193) อย่างไรก็ตาม พบความความสัมพันธ์อย่างมีนัยสำคัญทางสถิติระหว่างลอการิทึมของปริมาตรรวมเนื้องอกกล้ามเนื้อมดลูกกับระดับซีรัมพาราไทรอยด์ฮอร์โมน (Adjusted MD = -0.02, 95%CI = -0.06, -0.001, p = 0.006).*

สรุป: *แม้ว่าจะพบอัตราภาวะวิตามินดีบกพร่องสูงในหญิงไทยที่มีเนื้องอกกล้ามเนื้อมดลูก แต่ไม่พบความสัมพันธ์อย่างมีนัยสำคัญระหว่างระดับความเข้มข้นของวิตามินดีในเลือดที่ต่ำกับการมีเนื้องอกกล้ามเนื้อมดลูก*

คำสำคัญ: *เนื้องอกกล้ามเนื้อมดลูก, ภาวะวิตามินดีบกพร่อง, ระดับวิตามินดีในเลือด*

Introduction

Uterine fibroids are monoclonal tumors of smooth muscle cells of the myometrium. It has been recognized that it is the most common benign tumor of the uterus in reproductive women[1]. A study found that the incidence of fibroids among African American women by age 35 was 60%, and it was over 80% by age 50[2]. Moreover, a previous study revealed that the incidence of uterine fibroids among Asia women was around 20 to 40%[3]. Symptoms of uterine fibroids range from asymptomatic to many symptoms that interfere with the quality of life, such as abnormal uterine bleeding, abdominal pain, and compressive symptoms[2, 3]. Although the etiology of uterine fibroids is still unclear, molecular biology studies of these tumors suggested a relationship between uterine fibroids and several factors, including hormones, genetics, and growth factors, especially transforming growth factor β3 (TGF β3)[2]. Recently, many studies have noted that vitamin D deficiency was another risk factor for uterine fibroid development[4-8].

Vitamin D is a group of steroid compounds, soluble in fats, which impact several parts of the human body through their receptors, which can be found in various organs, including musculoskeletal, nervous and immune systems, as well as myometrium and uterine fibroid tissue. It has been noted that vitamin D affects cell proliferation and differentiation, inhibiting angiogenesis and stimulating apoptosis[1]. Many studies reported that vitamin D has an effect against the growth of uterine fibroids by inhibiting TGF β3, resulting in a decreased extracellular matrix (ECM) and uterine fibroid volume[1, 9].

Nationwide reports in Thailand revealed that the prevalence of vitamin D deficiency ranged from 9% to 32%[10-12]. However, no study identified the prevalence of vitamin D deficiency among Thai women with uterine fibroids. Therefore, this study aimed to evaluate this prevalence and associated factors of vitamin D deficiency in Thai women diagnosed with uterine fibroids.

Materials and Methods

Sample size

This cross-sectional observational study was conducted between June 2019 and March 2020 in both the outpatient and inpatient gynecologic departments of Rajavithi Hospital, Bangkok, Thailand. This study was approved by the Institutional Review Board (IRB) of Rajavithi Hospital, and written informed consent was obtained from participants. The sample size was calculated using an infinite population proportion formula[13] based on the previous study by Paffnoni et al[6], which reported the prevalence of vitamin D deficiency in women with uterine fibroid at 63%; alpha values and accepted error were set at 0.05 and 12.5%, respectively. The sample size required was 149 participants. The 20% addition for dropouts was included; therefore, the total number of participants was 179.

Participants

Women aged 20-49 years diagnosed with at least one uterine fibroid with a diameter of 10 mm or greater confirmed by ultrasound were recruited into this study. Women with one or more of the following conditions were excluded: history of previous myomectomy, chronic systemic disease, malignancy, adenomyosis, pregnancy, lactation, menopausal women, abortion, and pregnancy loss in the past six months, oral contraceptive / hormonal agents utilization in the past three months, history of vitamin D or calcium replacement in the past three months. The clinical characteristics of each patient were recorded. Blood samples of 25-hydroxyvitamin D [25(OH)D], parathyroid hormone (PTH), and calcium were collected and measured on the same day of the ultrasound examination.

Measurement

Ultrasonography was performed by experienced gynecologist staff using a GE Voluson S8 ultrasound machine fitted with a 2-4 MHz endovaginal probe for the transvaginal scan and a 4-9 MHz convex probe for the abdominal scan. The sonographic appearance of fibroids was defined as symmetrical, well-defined, hypoechoic, and heterogeneous masses.

A fibroid with more than 50% of its diameter bulging out of the uterine contour line was defined as a subserous fibroid. Intramural fibroids were those lining mostly within the uterine shape. Fibroids distorting the uterine cavity were defined as submucosal type. The volume of uterine fibroids was calculated by the ellipsoid volume formula (a x b x c x 0.523), where a is height, b is width, and c is depth[7].

Assay

25(OH)D levels were analyzed using the cobas e602 autoanalyzer (Roche Diagnostics, Thailand) with the electrochemiluminescence immunoassay (ECLIA) technique. The sensitivity of this assay is 3 ng/mL, and the coefficient of variation is less than or equal to 5.94%[12]. Serum levels of 25(OH) D were categorized into three different groups according to the Endocrine Society Clinical Practice Guideline recommendations, including vitamin D deficiency (below 20 ng/mL), vitamin D insufficiency (21-29 ng/mL), and vitamin D sufficiency (30-100ng/mL)[14].

Serum PTH levels were measured by cobas e602 autoanalyzer (Roche Diagnostics, Thailand) with chemiluminescent technique (coefficient of variation is 1.94%). Serum PTH levels between 15-65 pg/ml are defined as a normal range. Additionally, serum calcium levels were analyzed by cobas c702 autoanalyzer (Roche Diagnostics, Thailand) with a colorimetric assay technique (coefficient of variation is 1.8%), and a normal range is noted between 8.6 -10 mg/dl.

Statistical analysis

Data analysis was performed using Statistical software SPSS version 25 (SPSS Inc, Chicago, IL, USA). As appropriate, descriptive analysis was performed using means ± standard deviation (SD), percentage, median, and interquartile range. Categorical data were analyzed using chi-square and Fisher's exact test as appropriate. For continuous data with normal distribution, student t-test and one-way analysis of variance (ANOVA) test were performed, while Mann-Whitney U-test and Kruskal-Wallis test were performed for continuous variables with non-normal distribution. The factors associated with the presence of uterine fibroids were analyzed using univariate and multivariate logistic regression analysis, as well as Pearson correlation. A p value < 0.05 was considered statistically significant.

Results

A total of 183 Thai women diagnosed with at least one uterine fibroid with a diameter of 10 mm or greater participated in this study. Two women were excluded due to incomplete laboratory results. The baseline characteristics of participants are revealed in Table 1. The age of participants ranged from 21 to 49 years (mean age, 41.3 ± 5.7 years). Also, the mean body mass index (BMI) was 24.5 ± 4.8 kg/m^2. Regarding uterine fibroids, the diameter of uterine fibroids ranged from 1 cm to 20 cm, and the mean total fibroids volume was 53.8 cm^3. The most common type of uterine fibroids in our study was intramural fibroids, and dysmenorrhea (35.4%) was the most common symptom, followed by abnormal uterine bleeding (34.8%). Moreover, the mean levels of serum 25(OH)D, calcium, and PTH were 18.8 ± 5.8 ng/ml, 9.2 ± 0.5 mg/dl, and 47.9 ± 17.8 pg/ml, respectively.

Table 1. Baseline characteristics of patients with uterine fibroids.

Variables	Total (n = 181)
Age (years), mean (SD)	41.3 (5.7)
BMI (kg/m^2), mean (SD)	24.5 (4.8)
Parity, median (min-max)	0 (0-4)
Age at menarche (years), mean (SD)	13.2 (1.5)
Family history of uterine fibroids (%)	28 (15.5)
Education (%)	
Primary school or less	19 (10.5)
Secondary school	40 (22.1)
University or more	122 (67.4)
Working (%)	
Indoor	141 (77.9)
Indoor and outdoor	36 (19.9)
Outdoor	4 (2.2)
Sunscreen using (%)	
No	32 (17.7)
Yes	149 (82.3)
Uterine fibroids	
Amount, median (min-max)	1 (1-9)
Maximal size (cm), median (min-max)	4.9 (1.0-20.0)
Total volume (cm^3), median (min-max)	53.8 (0.4-4,190.5)
Type of uterine fibroids (%)	
Submucous	6 (3.3)
Intramural	108 (59.7)
Subserous	28 (15.5)
Mixed	39 (21.5)
Asymptomatic (%)	48 (26.5)
Symptoms (%)	133 (73.5)
Abnormal uterine bleeding*	63 (34.8)
Dysmenorrhea	64 (35.4)
Urinary symptoms	51 (28.2)
Gastrointestinal symptoms	31 (17.1)
Others	7 (3.9)
Laboratory	
Serum vitamin D level (ng/ml), mean (SD)	18.8 (5.8)
Serum calcium level (mg/dl), mean (SD)	9.2 (0.5)
Serum PTH level (pg/ml), mean (SD)	47.9 (17.8)

BMI: body mass index, SD: standard deviation, PTH: parathyroid hormone

*Abnormal uterine bleeding is defined as bleeding from the uterine corpus that is abnormal in duration, volume, frequency, and/or regularity according to FIGO AUB system 2018[15]

The participants were stratified into three groups according to their vitamin D status defined by the Endocrine Society Clinical Practice Guideline recommendations: vitamin D deficiency referred to as serum 25(OH)D level below 20 ng/ml, insufficiency as 25(OH)D serum level of 21-29 ng/ml, and sufficiency as a 25(OH)D serum of 30-100 ng/ml[14]. It was revealed that the prevalence of vitamin D deficiency among Thai women with uterine fibroids was 69.6% (Table 2). No significant differences

regarding age, BMI, family history of uterine fibroids, number, type, and total volume of uterine fibroids were observed among the three groups. Nevertheless, the prevalence of vitamin D deficiency was significantly higher in women with indoor work (p = 0.035) and sunscreen use (p = 0.045). The three groups had no significant differences concerning serum calcium and PTH.

Table 2. Comparison between factors and serum vitamin D levels.

Variables	Vitamin D deficiency (n = 126)	Vitamin D insufficiency (n = 44)	Vitamin D sufficiency (n = 11)	p value
Age (years), mean (SD)	40.7 (6.1)	42.2 (4.7)	43.9 (3.8)	0.100[a]
BMI (kg/m^2), mean (SD)	24.3 (4.8)	24.6 (4.8)	26.7 (4.5)	0.267[a]
Parity, median (min-max)	0 (0-4)	0 (0-3)	2 (0-3)	0.133[b]
Age at menarche (years), mean (SD)	13.2 (1.5)	13.1 (1.7)	12.6 (1.6)	0.314[a]
Family history of uterine fibroids (%)	21 (16.7)	6 (13.6)	1 (9.1)	0.743[c]
Working (%)				0.035*, [c]
Indoor	103 (81.7)	33 (75.0)	5 (45.5)	
Indoor and outdoor	22 (17.5)	9 (20.5)	5 (45.5)	
Outdoor	1 (0.8)	2 (4.5)	1 (9.1)	
Sunscreen using (%)				0.045*, [c]
No	20 (15.9)	7 (15.9)	5 (45.5)	
Yes	106 (84.1)	37 (84.1)	6 (54.5)	
Uterine fibroids				
Amount, median (min-max)	1 (1-5)	1 (1-6)	1 (1-9)	0.682[b]
Maximal size (cm), median (min-max)	4.9 (1.0-20.0)	4.4 (1.0-17.0)	5.6 (1.5-7.2)	0.953[b]
Type (%)				0.745[c]
Submucous	5 (4)	1 (2.3)	0 (0)	
Intramural	72 (57.1)	30 (68.2)	6 (54.5)	
Subserous	19 (15.1)	6 (13.6)	3 (27.3)	
Mixed	30 (23.8)	7 (15.9)	2 (18.2)	
Symptoms (%)				0.401[c]
Asymptomatic	35 (27.8)	12 (27.3)	1 (9.1)	
Symptomatic	91 (72.2)	32 (72.7)	10 (90.9)	
Serum calcium (mg/dl) , mean (SD)	9.2 (0.56)	9.3 (0.5)	9.23 (0.39)	0.523[a]
Serum PTH (pg/ml), mean (SD)	49.01 (17.80)	43.9 (18.49)	50.63 (13.93)	0.235[a]

BMI: body mass index, SD: standard deviation, PTH: parathyroid hormone

*Significant difference among 3 groups at p < 0.05, [a] ANOVA test, [b] Kruskal-Wallis test, [c] Chi-square test

From univariate and multivariate logistic regression analysis, there was no association between the uterine fibroids volume and clinical characteristics, including age, BMI, family history of leiomyoma, and symptoms. Also, neither serum 25 (OH)D levels nor serum calcium levels were associated with the uterine fibroid volume (crude mean difference (MD) = -0.01, 95% confidence interval (CI) = -0.02, 0.2, p = 0.949, crude MD = -0.19, 95%CI = -0.48, 0.1, p = 0.193, respectively). Surprisingly, we found a statistically significant association between the uterine fibroids volume and serum PTH levels (Adjusted MD = -0.02,

95%CI = -0.06, -0.001, p = 0.006). One unit increase in serum PTH would downsize the volume of uterine fibroids.

Furthermore, correlation analysis revealed that there was no correlation between the logarithm of the total uterine fibroids volume and both serum 25(OH) D levels (r = 0.05, p = 0.899) and serum calcium levels (r = 0.098, p = 0.192). However, a statistically significant negative correlation between the logarithm of total uterine fibroids volume and serum PTH levels was observed in our study (r = - 0.172, p = 0.020).

Discussion

In gynecologic conditions, it has been noted that uterine fibroids are the most common benign tumor of the uterus affecting reproductive women. Although a relationship exists between uterine fibroids and various factors, including genetics, hormones, growth factors, etc., their etiology is still unclear[2]. Recently, it has been demonstrated that hypovitaminosis D was correlated with a high prevalence of uterine fibroids, ranging from 63.3% to 100%[4, 6, 8]; additionally, some authors reported that serum vitamin D levels are inversely correlated with the severity of uterine fibroids[6, 7]. Many previous studies have revealed that vitamin D deficiency was another factor involved in uterine fibroids development as its effect is able to inhibit the growth of uterine fibroids by inhibiting TGF β3, leading to decreasing the ECM of uterine fibroids[1, 9].

Our study was the first cross-sectional observational study in Thailand, aiming to determine the prevalence and associated factors of vitamin D deficiency in Thai women with uterine fibroids. Our study revealed that the prevalence of vitamin D deficiency among Thai women diagnosed with uterine fibroids was 69.6%, and the mean serum vitamin D level was 18.8 ng/ml, aligned with previous studies. A case-control study of 384 Italian women reported that the mean serum 25(OH)D3 was significantly lower in women having leiomyomas than that of the control group (18 ± 7.7 ng/ml vs 20.8 ± 11.1 ng/ml, respectively p = 0.010). Also, they documented that the prevalence of vitamin D deficiency in women with uterine leiomyoma was 63.3%[6]. Although they found a trend toward a relationship between low vitamin D serum levels and having more than three uterine fibroids (p = 0.08), our results did not find a difference between low serum vitamin D levels and the number of uterine fibroids.

Additionally, our study's mean serum 25(OH)D level was congruent with the results obtained by Sabry et al[7]. Their cross-sectional observational study was conducted on 154 premenopausal Egyptian women to identify whether low serum vitamin D levels correlate with an increased risk of uterine fibroids. They revealed that lower serum 25(OH)D levels were significantly associated with the occurrence of uterine fibroids (p = 0.001); the mean serum 25(OH)D level in their study was 19.7 ± 11.8 ng/ml. However, we did not find a significant association between low levels of serum vitamin D and the occurrence of uterine fibroids. Moreover, they found a statistically significant inverse correlation between serum 25(OH)D levels and total uterine fibroids volume (r = -0.31; p = 0.02). Unfortunately, our study revealed no correlation between low serum 25(OH)D and total uterine fibroids volume.

In addition, our results followed a similar trend to the previous study by Kaplan et al[4]. Their cross-sectional observational study on 124 Turkish women reported that there was no relationship between vitamin D levels and the size, volume, location, and number of uterine fibroids. Nonetheless, they found a significant correlation between vitamin D deficiency and traditional clothing style, low education, and being housewives. It has been recognized that a variety of factors, such as outdoor activities, sunlight exposure, season, clothing, etc, affect vitamin D levels. This present study also found the similar fashion that indoor working and sunscreen utilization were significantly associated with vitamin D deficiency[5].

Besides, it has been documented that obesity and vitamin D status have a complex relationship. Several studies have highlighted the inverse relationship between hypovitaminosis D and

obesity[16-20]. The plausible mechanisms have been proposed, including decreased sun exposure, negative feedback from 1,25-dihydroxyvitamin D3, sequestration in adipose tissue, and volumetric dilution[21]. Although our study revealed no association between BMI and the occurrence of uterine fibroids, our findings had a similar trend with this inverse relationship. The mean BMI in our study was 24.5 ± 4.8 kg/m^2, which is in the range of overweight according to the Asian-Pacific cutoff points[22]. Also, it has been stated that the Asian population has a higher level of body fat percentage than Australian-Caucasians at the same BMI. This may be an explanation for low levels of 25(OH)D in our study; since vitamin D is a fat-soluble vitamin, it might be sequestered in adipose tissue or diluted in volumetric form in our overweight population.

Interestingly, we found a significant negative correlation between serum PTH levels and uterine fibroids volume (r = - 0.172, p = 0.020). One unit increase in serum PTH would reduce the risk of occurrence of uterine fibroid. Our findings were aligned with the study by Ciavattini A et al[8] Their study aimed to determine the effect of vitamin D supplementation in women with hypovitaminosis D and small-burden uterine fibroids. Similarly, they found a negative correlation but failed to obtain a statistical significance between serum PTH and the total volume of fibroids (r = - 0.02, p = 0.76). A previous study reported that parathyroid hormone-related protein (PTHrP) expression in fibroid tissue was higher than in normal myometrium, and their expression may potentially regulate fibroid growth or differentiation through autocrine or paracrine mechanisms[23]. Additionally, it has been noted that vitamin D deficiency is associated with an elevation of serum PTH levels; unfortunately, our results did not carry this association. The convincing reason for this finding may stem from unchanged serum calcium levels in our data.

This study had certain limitations. While experienced gynecologic ultrasonologists performed all the ultrasound scans using a standard technique to assess uterine fibroids, subjective variability remains. Additionally, the lack of serum albumin to correct serum calcium levels was another limitation in this study.

Conclusion

There was a high prevalence rate of vitamin D deficiency among Thai women with uterine fibroids, albeit no significant association was found between low serum 25(OH)D and uterine fibroids. Further prospective cohort studies are required to explore the causality between leiomyomas and vitamin D deficiency and to shed light on the potential intervention of vitamin D supplementation in uterine fibroids.

Acknowledgments

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Potential conflicts of interest

The authors declare no conflicts of interest.

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GYNAECOLOGY

The Efficacy of Vibrational Anesthesia in Reducing Pain and Anxiety among a Single Rod Contraceptive Implant Recipient: A single-blinded randomized controlled trial

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ABSTRACT

Objectives: To evaluate the effectiveness of vibration anesthesia in reducing pain and anxiety in the group receiving single rod contraceptive implant recipient (SRCI).

Materials and Methods: This study was a single-blinded, randomized, controlled trial. Forty-five women were randomly assigned to the experimental group and forty-five women to the control group. The control group had SRCI using the standard method. However, the experimental group received vibrational anesthesia during the implantation. The study variables were general information, the numeric rating scale, and the state-trait anxiety inventory (STAI) form Y-1 questionnaire.

Results: The median pain score of the experimental group was 2 (1-2), while that of the control group was 4 (3-4). There was a statistically significant difference ($p < 0.01$) in the pain scores. Thirty-six cases (80.0%) in the experimental group showed low anxiety levels compared to no cases in the control groups ($p < 0.01$). No adverse events were reported.

Conclusion: Vibrational anesthesia during SRCI may reduce pain and anxiety among the recipients.

Keywords: vibrational anesthesia, single rod contraceptive implant recipient, pain, anxiety.

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ประสิทธิภาพของการระงับความรู้สึกแบบสั่นสะเทือนเพื่อลดความเจ็บปวดและความวิตกกังวลในกลุ่มที่มารับบริการฝังยาคุมกำเนิดแบบแท่งเดียว: การทดลองปกปิดทางเดียวแบบสุ่มและมีกลุ่มควบคุม

น้ำผึ้ง นันทวงศ์

บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาประสิทธิภาพของการระงับความรู้สึกแบบสั่นสะเทือนเพื่อลดความเจ็บปวดและความวิตกกังวลในกลุ่มที่มารับบริการฝังยาคุมกำเนิดแบบแท่งเดียว*

วัสดุและวิธีการ: *การศึกษานี้เป็นการทดลองแบบสุ่มและมีกลุ่มควบคุมโดยปกปิดทางเดียว โดยใช้วิธีการสุ่มเข้ากลุ่มทดลอง 45 ราย และกลุ่มควบคุม 45 ราย กลุ่มควบคุมได้รับวิธีการฝังยาคุมกำเนิดแบบมาตรฐาน กลุ่มทดลองได้รับการประยุกต์ใช้การระงับความรู้สึกแบบสั่นสะเทือนระหว่างรับบริการฝังยาคุมกำเนิด ตัวแปรในการศึกษาได้แก่ ข้อมูลทั่วไป คะแนนความเจ็บปวด visual analog scale (VAS) และแบบสอบถามความวิตกกังวลขณะเผชิญ (The state-trait anxiety inventory (STAI) form Y-1)*

ผลการศึกษา: *เมื่อเปรียบเทียบระหว่างกลุ่มพบว่าค่ามัธยฐานคะแนนของความเจ็บปวดของกลุ่มทดลอง 2 (1-2) และกลุ่มควบคุม 4 (3-4) พบแตกต่างกันอย่างมีนัยสำคัญทางสถิติ ($p < 0.01$) และความวิตกกังวลขณะเผชิญระดับต่ำ กลุ่มทดลอง 36 ราย (ร้อยละ 80.0) และกลุ่มควบคุม 0 ราย พบความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ ($p < 0.01$) ไม่พบเหตุการณ์ไม่พึงประสงค์ด้วยวิธีการระงับความรู้สึกแบบสั่นสะเทือน*

สรุป: *การระงับความรู้สึกแบบสั่นสะเทือนอาจจะมีประสิทธิภาพในการลดความเจ็บปวดและความวิตกกังวลในกลุ่มที่มารับบริการฝังยาคุมกำเนิดแบบแท่งเดียว*

คำสำคัญ: *การระงับความรู้สึกแบบสั่นสะเทือนฝังยาคุมกำเนิดแบบแท่งเดียว, ความเจ็บปวด, ความวิตกกังวล*

Introduction

Due to its greater efficacy and consistency than oral contraceptives, the American College of Obstetricians and Gynecologists (ACOG) recommends long-acting reversible contraception as an effective method of birth control, particularly for adolescents[1]. It provides all women with long-term contraception and can also be used by those women, who cannot use hormonal contraception which contains estrogen. Implants are more convenient than oral contraceptives because they require no maintenance for up to three years[2]. In accordance with the universal health coverage policy of Thailand, family planning services are free, and free access to contraceptive implant services for all health rights is promoted. Services are accessible at any facility within the network of the National Health Security Office[3]. However, the Bureau of Reproductive Health has reported that only 2.4% of teenage mothers actually use contraceptive implants, whereas 55.2% of postpartum women do use them[4]. According to Inoue, women are more likely to generate negative opinions after hearing about subdermal implants from others[5]. Within the Australian setting, it is necessary to explore interventions in order to improve informed awareness of the implant's benefits and drawbacks, such as enhancing access to supportive contraceptive counseling. Additionally, further investigations should explore avenues that can be used to enhance a woman's sense of control over the device.

Typically, receiving contraceptive implant services can be mildly painful, but some individuals may experience significant anxiety[6]. This can also negatively impact mental health, causing psychological symptoms, such as having a phobia of needles and/or suffering other emotional consequences. Long-term consequences of needle phobia include an avoidance of healthcare facilities and a failure to comply with needle-related procedures[7]. Anxiety and depression are also possible[8]. A large body of clinical evidence has demonstrated that pain can cause psychological abnormalities that can affect behavior and mental health, with anxiety being the most prevalent abnormality that is caused by pain[9].

Vibratory anesthesia, which is widely recognized as an effective method for relieving pain and anxiety, is utilized in various healthcare settings. It is utilized when performing dermatological biopsies and injectable cosmetic treatments, as well as employed in the fields of pediatrics and dentistry[10,11]. Vibratory anesthesia is a highly efficient and widely accepted technique for distraction[12]. It is considered to be psychological in nature, since it distracts the patient and causes brain cells to transmit the vibration[13]. This muddles the perception of pain signals, leading to a "masking of pain's impact"[14].

Vibrant anesthesia has not been studied to reduce pain and anxiety in patients undergoing single-rod contraceptive implant services, which could potentially change their experiences. Therefore, the objective of this study was to evaluate the effectiveness of vibration anesthesia in reducing pain and anxiety among individuals receiving single-rod contraceptive implants.

Materials and Methods

This research was conducted at the Family Planning Unit and the Postpartum Ward of Chaiyaphum Hospital between February and July 2023. It was a single-blind randomized controlled trial (RCT) that was certified by Chaiyaphum Hospital with Ethics number 009/2023 (February 9, 2023). Additionally, the clinical trial research was registered in Thailand's Clinical Trials Registry (Thai Clinical Trials Registry: TCTR) with the registration number of TCTR20230217006. The inclusion criteria were women between 18-49 years of age, who had received single rod contraceptive implant recipient (SRCI). The exclusion criteria were the women, who had received the service of removing a SRCI and inserting a new one at the same time. Furthermore, within 6 hours before beginning the study, the volunteers should not have received any painkillers.

After obtaining written informed consent, the procedure details were disclosed to the participants and the consent forms were signed by those

volunteers, who were willing to participate in the study. It was a randomized 1:1 randomization process using the block randomization method with the block size of 5. The experimental group received 2% lidocaine without adrenaline and vibrational anesthesia to reduce pain and anxiety in the group receiving SRCI, while the control group received treatment in accordance with the standard use 2% lidocaine without adrenaline. The volunteers monitored the effectiveness of the care to reduce pain and anxiety only once and this was carried out immediately after receiving a single rod contraceptive implant. However, in order to reduce any bias that could occur, this study was masked to the evaluators, with only 1 person performing the numeric rating scale (NRS) interview and anxiety assessment form Spilberger's state anxiety inventory (STAI) formY-1 Thai version.

For this study, the researcher used a tool called the NRS to measure pain levels. The NRS uses numbers from 0 to 10 to show how much pain a person is feeling. A score of 0 means no pain, while a score of 10 means very severe pain. Patients simply had to point to the number that matched their level of pain. The Thai version of Spilberger's state anxiety inventory [STAI] form Y[15], which was created by Nonthasak et al (1991), consists of 20 items (10 positive statements and 10 negative statements). The scale, which was used for estimation, has four levels. The positive items were rated from 4 points (none) to 1 point (the most), while the negative items were scored from 1 point (the most) to 4 points (none). The total scores ranged from 20 to 80, which were interpreted comparatively. Anxiety levels were classified as low (20-40 points), moderate (41-60 points), and high (61-80 points). The reliability coefficient (C) was 0.85, encompassing the full range of scores from the lowest 20 to the highest 80. Regarding interpretation, a high overall score corresponded to high anxiety, while a low score indicated low anxiety. (Fig. 1)

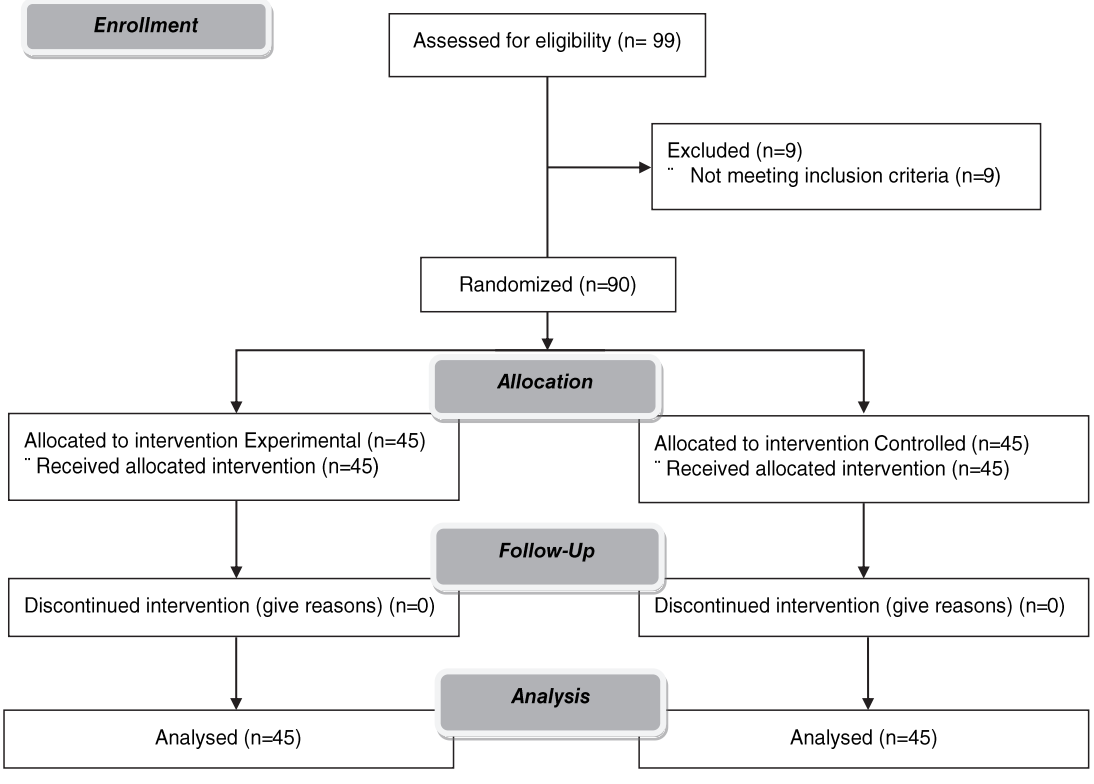

Fig. 1. The consort flow chart of randomization.

Vibrational anesthesia device (VAD) of application filed by Blaine Labs Inc. S/N:65373-009969 is a medical innovation created by medical professionals, which was approved for safety by the Food and Drug Administration (FDA) of the United States (USA) and is shown in Fig. 2. This device has been extensively examined in diverse research domains like cosmetic medicine and dentistry, while its effectiveness has been documented in international journals[11].

The manner in which it is utilized is as follows: 1. clean the VAD with a cotton ball moistened with disinfectant alcohol (70% ethyl alcohol), 2. Place the vibrational anesthesia device 2 inches under a sterile drape, as shown in Fig. 3., 3. Pressing and holding down this tool is necessary during and after usage. Pressing the pause button is the way to stop working. Vibration equipment will be used in this experiment for two periods: before the anesthetic injection and throughout the implantation process, 4. wipe the VAD with a cotton ball, which has been moistened with disinfectant alcohol (70% ethyl alcohol), and 5. finally, keep the VAD in the toolbox.

The experimental group was treated with a contraceptive implant using vibration anesthesia for 5-10 minutes, whereby the operative physician placed the VAD about 2 inches from the implant area, starting from the beginning of the contraceptive implant process until the end as shown in Fig. 2-4.

Fig. 2. The vibrational anesthesia device from Blaine Labs

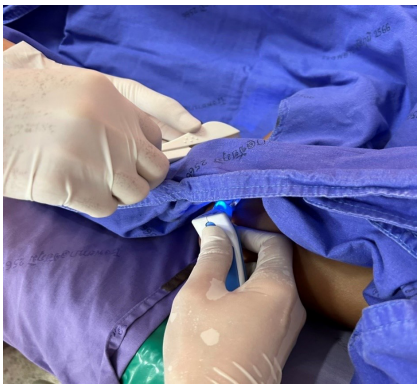

Fig. 3. Demonstrating the process of SRCI by placing the device under a sterile drape.

SRCI: single rod contraceptive implant recipient

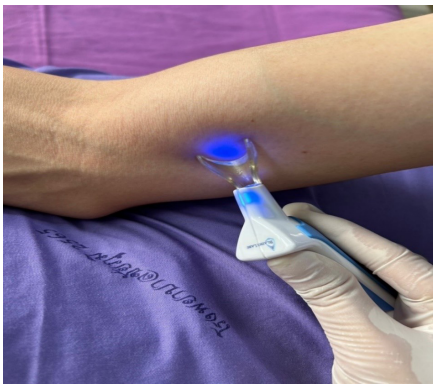

Fig. 4. Demonstrating the positioning of the device by pressing and holding it on the patient's skin.

The number of samples was calculated based on a study by Mapaisankit et al[16], which employed the formular of randomized controlled trial for continuous data. The mean in the treatment group = 3, the mean in control group = 2.4, the standard deviation (SD) in the treatment group = 1, the SD in the control group = 1 with the power of 80% and with an alpha level of 0.05. The calculated sample size was determined to be 45 patients for each group.

Statistical analysis was conducted on all the data using the STATA 10.1 program. Descriptive statistics: mean and standard deviations for continuous data that was normally distributed, median and interquartile range (IQR) for continuous data that was not normally distributed, and frequencies and percentages for categorical data were calculated. The chi-square test or the Fisher exact test was used to compare the experimental group and the control group with regard to the categorical data, while the independent t-test and the Mann-Whitney-U test were employed to compare the quantitative variables that were not normally distributed.

Results

Baseline characteristics between the standard contraceptive implant group and the dermal vibration application group are shown in Table 1. There were no significant differences.

Table 1. The Baseline characteristics.

Variables	Controlled (n = 45)	Experimental (n = 45)	p value
Age (years) (median, IQR)	27 (24-33)	28 (24-32)	0.96[a]
BMI (kg/m^2) (median, IQR)	25.05 (21.27-27.79)	24.3 (20.95-26.57)	0.27[a]
Underlying disease (n, %)			0.27[b]
- No	39 (86.67)	35 (77.78)	
- Yes	6 (13.33)	10 (22.22)	
Marital status (n, %)			0.76[c]
- Married	30 (66.67)	33 (73.33)	
- Divorced	3 (6.67)	2 (4.44)	
- Separated	1 (2.22)	2 (4.44)	
- Single	11 (24.44)	8 (17.78)	
Highest educational level (n%)			0.97[c]
- Primary school	1 (2.22)	1 (2.22)	
- Junior high school	4 (8.89)	5 (11.11)	
- High school	14 (31.11)	12 (26.67)	
- Diploma /associate	15 (33.33)	17 (37.78)	
- Bachelor's degree	11 (24.44)	10 (22.22)	
Income (median, IQR)	12,000 (9,000-20,000)	15,000 (10,000-20,000)	0.23[a]
Gravida (n, %)			0.21[c]
0	6 (13.33)	8 (17.78)	
1	20 (44.44)	23 (51.11)	
2	15 (33.33)	14 (31.11)	
3	4 (8.89)	0 (0)	
Use of contraception (n, %)			0.20[b]
- Never	18 (40.0)	24 (53.33)	
- Have used	27 (60.0)	21 (46.67)	

BMI: body mass index, IQR: interquartile range.

[a] Wilcoxon rank sum test, [b] chi square, [c] Fisher's exact test, significant $p < 0.05$*

A comparison of the pain severity scores between the standard contraceptive implantation group and the dermal vibration application group is shown in Tables 2 and 3. For the single-blinded group, the median pain scores of the experimental group were 2[1-2], and those of the control group were 4[3-4]. There was a statistically significant difference ($p < 0.01$) in the pain scores. Thirty-six cases (80.0%) in the experimental group showed low anxiety levels compared to none in the control groups ($p < 0.01$). Furthermore, no adverse events were reported.

Table 2. A comparison of the pain scores between the group that had received the standard single rod contraceptive implant recipient recipient services and those who had undergone vibration anesthesia.

Pain scores	Controlled (n = 45)	Experimental (n = 45)	p value
0	0 (0)	1 (2.22)	< 0.001[b]
1	3 (6.67)	19 (42.22)	
2	3 (6.67)	18 (40.0)	
3	12 (26.67)	4 (8.89)	
4	19 (42.22)	3 (6.67)	
5	8 (17.78)	0 (0)	
median (IQR)	4 (3-4)	2 (1-2)	< 0.001[a]

IQR: interquartile range

[a] Wilcoxon rank sum test, [b] Fisher's exact test, significant $p < 0.05$*

Table 3. A comparison of the anxiety levels between the group that had received the standard single rod contraceptive implant recipient single rod contraceptive implant recipient services and those who had undergone vibration anesthesia.

Levels of anxiety	Controlled (n = 45)	Experimental (n = 45)	p value
Anxiety			< 0.001[b]
- Low	0 (0)	36 (80.0)	
- Moderate	44 (97.78)	9 (20.0)	
- High	1 (2.22)	0 (0)	
mean ± SD	50.62 ± 4.59	35.26 ± 5.66	< 0.001[a]

SD: standard deviation

[a] student t- test, [b] Fisher's exact test, significant $p < 0.05$*

Discussion

Birth control implants are highly effective and suitable for women regardless of age or pregnancy history. This includes those women, who have never been pregnant, have been infected with HIV, have recently undergone an abortion, or who are undertaking breastfeeding to limit pregnancy[17]. They are 100 times more effective than the injections and pills, which are commonly used, and are 360 times[17] more effective than using condoms. Consequently, under the universal health coverage policy, family planning services are freely available in Thailand[3]. However, despite these advantages, the Bureau of Reproductive Health found that only 2.4% of teenage mothers were found to be using birth control implants, with 55.23%[4] opting for birth control pills postpartum.

Jacobstein et al[17] recommended that in order to encourage women to consider birth control implants, the women should be provided with informed choice, counseling, anticipatory guidance, the management of side effects, prompt removal services, and follow-up appointments. Counseling and effective management of any side effects are particularly crucial in facilitating the women's decision making processes regarding their treatment options.

This study placed emphasis on the importance of thoughtful counseling to aid clients in selecting methods, discussing their characteristics, and in dispelling myths and misconceptions, as well as in providing anticipatory guidance regarding the common side effects of implants[17], such as mood changes, headaches[18], and localized pain at the implant area[19], all of which are crucial. Research has shown that pain contributes to mental disorders, and affects behaviors and the mind, with anxiety being a common disorder that is associated with pain. Local pain at the insertion site is a typical complication, which occurs in approximately 2% to 3% of cases and is typically resolved by the end of the 3rd month[20]. Efforts to mitigate insertion pain, such as using ethyl chloride spray[16], have been explored and do show promise. Additionally, techniques like vibrating sensation (dermal vibration) have been recognized as effective treatments for pain and anxiety.

This study aimed at investigating the effectiveness of vibrational anesthesia in alleviating pain and anxiety among individuals receiving a single-rod contraceptive implant. The results of the study revealed that there had been a significant difference in median pain scores between the experimental group 2[1-2] and the control group 4[3-4], with a p value < 0.01. However, a lack of prior research on its use exists, specifically in individuals, who have undergone birth control implant services, which complicates the process of making direct comparisons with similar studies. Nevertheless, vibrational anesthesia has demonstrated efficacy in other fields, such as reducing patient discomfort during cosmetic botulinum toxin injections[21]. This finding aligned with previous dental studies, which have shown the effectiveness of vibrational instruments for pain control[22,23]. Vibrational anesthesia, which is considered a distraction technique, is widely accepted[12] and highly effective. These operate within the psychological realm, in which the vibrating devices distract the patients and cause confusion with regard to transmitting pain signals within the brain[13]. This phenomenon leads to a "masking of pain effects"[14] and contributes to its efficacy in pain management.

The study revealed a significant difference in anxiety levels between the experimental group, in which anxiety was low in 36 cases (80.0%), and in the control group in which no cases of common anxiety were reported ($p < 0.01$). It's important to note that fear and anxiety may influence the intensity of pain. Research has indicated that heightened patient anxiety may exacerbate both the duration and severity of pain[24].

The strength of the study was to evaluate the results of using a non-invasive device to reduce pain and anxiety in those receiving single-rod contraceptive implants. Using 80% power, the sample size was determined, and the pain and anxiety questions were asked to a single assessor after the patient's visit. Yet, our study had some limitations. First due to the nature of this study, subjects could not be blinded. Volunteers were able to feel the vibrations, which is why this happens. Although vibration is very effective in reducing pain, many factors are involved, and more studies need to be conducted in order to determine the effectiveness of vibration in pain control. This stems from the fact that these devices run on batteries. Over time, the frequency and intensity of vibration may change for each patient. Moreover, in this study, data on anxiety scores was not collected before the experiment.

Furthermore, different operators may choose to use various vibrational tools. In addition, future studies should focus on coverage that will offer women opportunities to gain access to SRCI, which should cover informed choice, counseling, anticipatory

guidance, the management of side-effects, prompt removal services, and follow-up appointments.

Conclusion

Vibrational anesthesia was a safe and effective method for contraceptive implant services. It significantly reduced pain and anxiety. No adverse events were reported

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Potential conflicts of interest

The authors declare no conflicts of interest.

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The Incidence and Risk Factors of Obstetrics anal Sphincter Injuries at King Chulalongkorn Memorial Hospital during 2017-2019

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ABSTRACT

Objectives: To study the incidence and risk factors of obstetrics anal sphincter injuries (OASIS) during 1 January 2017 to 31 December 2019

Materials and Methods: A retrospective study of all pregnant woman with vaginal delivery (6,714 cases) at King Chulalongkorn Memorial Hospital during 2017-2019 were conducted. We collected the data of all pregnant women who delivered in our hospital since 1 January 2017 to 31 December 2019, using International Classification of Diseases, Tenth Revision (ICD 10) codes for data extraction and review. The case group comprised of pregnant women with an OASIS (third- degree and fourth-degree perineal laceration). The control group comprised of pregnant women delivered vaginally without OASIS.

Results: The incidence of OASIS was 6% (403/6,714). The significant risk factors are nulliparity vs multiparity (adjusted odds ratio (aOR) 3.0, 95% confidence interval (CI) 2.3-4.0, $p < 0.01$), obesity vs normal BMI (aOR 0.5, 95%CI 0.3-0.7, $p < 0.01$), forceps extraction vs spontaneous delivery (aOR 4.5, 95% CI 3.1-6.5, $p < 0.01$), occiput posterior vs occiput anterior position (aOR 2.3, 95%CI 1.2-4.3, $p = 0.01$), median episiotomy vs no episiotomy (aOR 2.3, 95%CI 1.3-4.3, $p = 0.01$), staff vs nurses (aOR 11.1, 95%CI 5.0-25.0, $p < 0.01$), residents vs nurses (aOR 13.3, 95%CI 5.9-30.2, $p < 0.01$), and medical student vs nurses (aOR 3.5, 95%CI 1.3-9.6, $p = 0.01$).

Conclusion: The risk factors of OASIS were nulliparity, occiput posterior postition, forceps extraction, median episiotomy, residents and staffs (as the operators). The protective factors were obesity and nurses. Preventive strategies for these factors are advocated.

Keywords: incidence, median episiotomy, nulliparity, obstetric anal sphincter injuries, risk factors.

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อุบัติการณ์และปัจจัยเสี่ยงของการบาดเจ็บของหูรูดทวารหนักในสูติศาสตร์ในโรงพยาบาลจุฬาลงกรณ์ปี พ.ศ.2560-2562

ธนพัฒน์ มณี, สุวิทย์ บุณยะเวชชีวิน, ปุริม เรือนภู่, กีรติ เชียงทอง, พริมา มนูสุข

บทคัดย่อ

วัตถุประสงค์*: เพื่อศึกษาอุบัติการณ์ และปัจจัยเสี่ยงของการเกิดการฉีกขาดของฝีเย็บหลังคลอดระยะที่ 3 และ 4 ในหญิงตั้งครรภ์ (OASIS)*

วัสดุและวิธีการ*: เก็บรวบรวมข้อมูลของหญิงตั้งครรภ์คลอดธรรมชาติทุกคน (6,714 คน) ที่โรงพยาบาลจุฬาลงกรณ์ ระหว่างปี พ.ศ 2560-2562 ผ่านเวชระเบียนอิเล็กทรอนิกส์ ได้ทำการรวบรวมข้อมูลของสตรีตั้งครรภ์ที่คลอดที่โรงพยาบาล ตั้งแต่วันที่ 1 มกราคม พ.ศ. 2560 ถึง 31 ธันวาคม พ.ศ. 2562 โดยใช้รหัส ICD 10 ในการคัดเลือกและทบทวนข้อมูล กำหนดให้กลุ่มที่ต้องการศึกษาได้แก่สตรีที่มีภาวะOASIS(การฉีกขาดของฝีเย็บหลังคลอดระยะที่ 3 และ 4) โดยกลุ่มเปรียบเทียบประกอบด้วยสตรีตั้งครรภ์ที่คลอดโดยไม่มีภาวะ OASIS*

ผลการศึกษา*: การศึกษาพบว่าอุบัติการณ์ของการเกิดการฉีกขาดของฝีเย็บหลังคลอดระยะที่ 3 และ 4 ในหญิงตั้งครรภ์ (OASIS) จำนวน 403 คนจาก 6,714 คน คิดเป็นร้อยละ 6 โดยพบว่าปัจจัยเสี่ยงที่มีนัยสำคัญทางสถิติได้แก่ สตรีที่ไม่เคยคลอดบุตร [adjusted odds ratio (aOR) 3.0, 95% confidence interval (CI) 2.3-4.0, p < 0.01] ภาวะอ้วน (aOR 0.5, 95%CI 0.3-0.7, p < 0.01) การช่วยคลอดด้วยคีม (aOR 4.5, 95%CI 3.1-6.5, p < 0.01) ศีรษะในท่าท้ายทอยเฉียงหลัง (aOR 2.3, 95%CI 1.2-4.3, p = 0.01) การตัดฝีเย็บแนวกลาง (aOR 2.3, 95%CI 1.2-4.3, p = 0.01) อาจารย์แพทย์ (aOR 11.1, 95%CI 5.0-25.0, p < 0.01) แพทย์ประจำบ้าน (aOR: 13.3, 95%CI 5.9-30.2, p < 0.01) และนักศึกษาแพทย์ (aOR: 3.5, 95%CI 1.3-9.6, p = 0.01)*

สรุป*: ในการศึกษานี้พบว่าปัจจัยเสี่ยงของการเกิดการฉีกขาดของฝีเย็บหลังคลอดระยะที่ 3 และ 4 ในหญิงตั้งครรภ์ (OASIS) ได้แก่ สตรีที่ไม่เคยคลอดบุตร ทารกในท่าศีรษะเฉียงหลัง การช่วยคลอดด้วยคีม การตัดฝีเย็บแนวกลาง แพทย์ประจำบ้าน และอาจารย์แพทย์ ส่วนปัจจัยป้องกันได้แก่ ภาวะอ้วนและพยาบาลผู้ทำคลอด ควรหาแนวทางป้องกันในผู้มีปัจจัยเสี่ยงเหล่านี้*

คำสำคัญ*: อุบัติการณ์, การตัดฝีเย็บแนวกลาง, สตรีที่ไม่เคยคลอดบุตร, การฉีกขาดของฝีเย็บหลังคลอดระยะที่ 3 และ 4, ปัจจัยเสี่ยง*

Introduction

Obstetric perineal laceration is one of the most common maternal complications during vaginal delivery and it is classified by Sultan's classification of perineal trauma according to its depth[1]. There are four categories included in the classification: 1st, 2nd, 3rd, and 4th degree laceration. Obstetric anal sphincter injuries (OASIS) are defined as third-degree and fourth-degree perineal laceration[2]. Of all obstetric perineal laceration, OASIS has greater impacts on maternal morbidities such as blood loss, puerperal pain, wound disruption, infection rate, and particularly fecal incontinence in the long term[2]. The incidence of OASIS in the general populations ranges from 0.3 to 4.5%[3-7] and the risk of recurrence is higher and varies between 5.1 to 10.7%[8]. In 2015, Royal college of obstetricians and Gynecologists (RCOG)[9] published the green top guidelines for management of third- and fourth-degree tears and identified the risk factors of OASIS which included Asian ethnicity, nulliparity, birth weight greater than 4 kg, shoulder dystocia, occiput posterior position, prolonged second stage of labor, and instrumental delivery. Since Asian ethnicity is the risk factor for OASIS and there is no published data of the prevalence and risk factors of OASIS in Thai pregnant woman. The aims of this study were to study the incidence and risk factors of OASIS at King Chulalongkorn Memorial Hospital during 2017-2019.

Materials and Methods

After Institutional Review Board (IRB) approval, a retrospective study was conducted at King Chulalongkorn Memorial, a tertiary center in Bangkok, Thailand. We collected the data of all pregnant women who delivered in our hospital since 1 January 2017 to 31 December 2019, using International Classification of Diseases, Tenth Revision (ICD 10) codes for data extraction and chart review. The inclusion criteria were pregnant woman with vaginal delivery in this hospital during 2017-2019, having third- and fourth-degree perineal laceration, singleton pregnancy, pregnancy with more than 22 weeks of age, and birth weight more than 500 g. The exclusion criteria were multiple gestation with vaginal delivery and cases with incomplete data. The case group comprised cases with an OASIS (third- degree and fourth-degree perineal laceration). The degree of perineal laceration was classified according to Sultan's classification of perineal trauma[1]. The control group comprised cases without OASIS. The diagnosis was made immediately following delivery, after exposure of the anal sphincter using digital vaginal and rectal examination. The maternal and obstetric characteristics studied were age, parity, second stage of labor, body weight, height, body mass index, total weight gain during pregnancy, episiotomy type, use of operative vaginal deliveries, degree of perineal laceration, neonatal factors including fetal presentation, birth weight, sex, and level of operator.

Statistical analysis

The descriptive data analysis was represented as mean ± standard deviation (SD) and percentage. The comparative data analysis used chi square for categorical data and student t-test for continuous data to estimate the risk significance ($p < 0.05$) and crude odds ratio. The significant risk factors were analyzed again with multivariate logistic regression model to evaluate the adjusted odds ratio. All data was entered and analyzed using SPSS version for window (version 28.0, SPSS Inc., Armonk, NY, USA).

Results

Of 7,171 cases with vaginal delivery since 1 January 2017 to 31 December 2019 extracted by ICD 10 codes (Fig. 1), 96 women were excluded from the study (67 women had newborn with birth weight less than 500 g or less than 22 weeks of gestational age, 27 women with multiple gestation and 2 women with cesarean delivery), and the total missing or incomplete data of 361 cases were excluded. Of 6,714 cases, 338 cases had third-degree perineal laceration, and 65 cases had fourth degree perineal laceration. The incidence of OASIS was 6.0% (403/6,714).

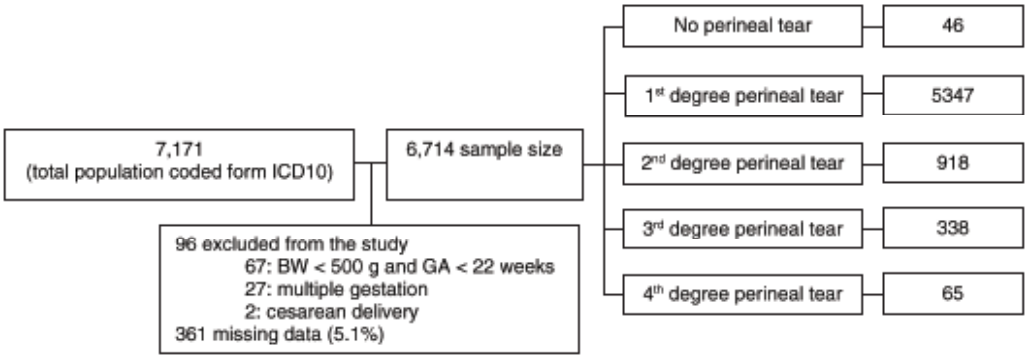

Fig. 1. Population flow.

From the bivariate analyses (Table 1), the OASIS was higher among pregnant women with higher gestational age (38.3 ± 1.4 vs 38.0 ± 1.7 years), higher weight gain (14.0 ± 5.0 vs 13.2 ± 4.8 kgs), nulliparous (80.9% vs 53.2%), lower body mass index (21.0 ± 3.2 vs 21.7 ± 4.1 kg/m^2), occiput posterior (6.7% vs 0.4%), forceps extraction (23.6% vs 2.6%), vacuum extraction (1.7% vs 0.6%), median episiotomy (52.1% vs 21.3%), staffs as operator (24.3% vs 8.5%), residents as operator (71.5% vs 57.2%), and the second stage of labour 60-120 minutes (0.7% vs 0.2%) and > 120 minutes (3% vs 0.4%) (Table 1).

Table 1. Baseline characteristics (n = 6,714).

Variables	No OASIS n = 6,311	OASIS n = 403	p value
Age	29.1 ± 6.0	29.8 ± 5.7	0.68
< 35 years old	5,018 (79.5%)	317 (78.7%)	
≥ 35 years old	1,293 (20.5%)	86 (21.3%)	
Gestational age	38.0 ± 1.7	38.3 ± 1.4	0.01
Birth weight ≥ 4 kg	72 (1.1%)	5 (1.2%)	0.86
Birth weight < 4 kg	6,239 (98.9%)	398 (1.2%)	
Weight gain	13.2 ± 4.8	14.0 ± 5.0	<0.01
Parity			<0.01
Nulliparous (0)	3,358(53.2%)	326(80.9%)	
Multiparous (≥ 1)	2,953(46.8%)	77(19.1%)	
Height	158.8 ± 5.7	158.3 ± 5.5	0.80
< 140 cm	-	-	
≥ 140 cm	6,310 (100%)	403 (100%)	
Body mass index	21.7 ± 4.1	21.0 ± 3.2	< 0.01
< 18.5kg/m^2 (underweight)	1271 (20.1%)	85 (21.1%)	
18.5-22.9 kg/m^2 (normal)	3159 (50.1%)	226 (56.1%)	
23-24.9 kg/m^2 (overweight)	805 (12.8%)	53 (13.2%)	
≥ 25kg/m^2 (obesity)	1,076 (17%)	39 (9.6%)	
Sex			0.42
Male	3,299 (52.3%)	219 (54.3%)	
Female	3, 012 (47.7%)	184 (45.7%)	
Presentation			< 0.01
Cephalic			
Occiput anterior	6,265 (99.3%)	376 (93.3%)	
Occiput posterior	28 (0.4%)	27 (6.7%)	
Breech	18 (0.3%)	-	
Shoulder dystocia			0.72
No shoulder dystocia	6,309 (100%)	403 (100%)	
Shoulder dystocia	2 (0.0%)	-	
Operative vaginal delivery			< 0.01
Spontaneous labor	6,016 (96.8%)	301 (74.7%)	
Forceps extraction	164 (2.6%)	95 (23.6%)	
Vacuum extraction	41 (0.6%)	7 (1.7%)	
Type of episiotomy			< 0.01
No episiotomy	610 (9.7%)	12 (3%)	
Median episiotomy	1,344 (21.3%)	210 (52.1%)	
Mediolateral episiotomy	4,357 (69.0%)	181 (44.9%)	
Level of operator			< 0.01
Residents	3,607 (57.2%)	288 (71.5%)	
Nurses	1,493 (23.7%)	6 (1.5%)	
Medical student	674 (10.7%)	11 (2.7%)	
Staff	537 (8.5%)	98 (24.3%)	
The second staged labor			
< 60 minutes	6,278 (99.5%)	388 (96.3%)	
60-120 minutes	10 (0.2%)	3 (0.7%)	
>120 minutes	23 (0.4%)	1 2(3%)	

Data presented as mean ± standard deviation, n (%)

By using multiple logistic regression model, the risk factors that associated with OASIS were nulliparity vs multiparity (adjusted OR 3.0, 95%CI 2.3-4.0, p < 0.01), obesity vs normal BMI (adjusted OR 0.5, 95%CI 0.3-0.7, p < 0.01), forceps extraction vs spontaneous delivery (adjusted OR 4.5, 95%CI 3.1-6.5, p < 0.01), occiput posterior vs occiput anterior position (adjusted OR 2.3, 95%CI 1.2-4.3, p = 0.01), median episiotomy vs no episiotomy (adjusted OR 2.3, 95%CI 1.3-4.3, p = 0.01), median episiotomy vs mediolateral episiotomy (adjusted OR 2.0, 95%CI 1.6-2.6, p < 0.01), the levels of operators (staff vs nurses) (adjusted OR 11.1, 95%CI 5.0-25.0, p < 0.01), the levels of operators (staff vs medical student) (adjusted OR 3.3, 95%CI 1.6-6.3, p = 0.01), the levels of operators (residents vs nurses) (adjusted OR 13.3, 95%CI 5.9-30.2, p < 0.01), the levels of operators (residents vs medical student) (adjusted OR 3.8 95% CI 1.3-9.6, p = 0.01), and the levels of operators (medical student vs nurses)(adjusted OR 3.5, 95% CI 1.3-9.6, p = 0.01). (Table 2)

Table 2. Secondary outcomes (n= 6,714).

Variables	Univariate analysis for risk factors of OASIS		Multivariate analysis for risk factors of OASIS	
	p value	Crude OR (95%CI)	p value	Adjusted OR (95%CI)
Gestational age	0.01	1.1 (1.0-1.2)	-	-
Weight gain	< 0.01	1.1 (1.0-1.1)	-	-
Body mass index				
Underweight vs normal	0.61	0.9 (0.7-1.2)	-	-
Overweight vs normal	0.60	0.9 (0.7-1.3)	-	-
Obesity vs normal	< 0.01	0.5 (0.4-0.7)	< 0.01	0.5 (0.3-0.7)
Nulliparity vs multiparity	0.01	3.7 (2.9-4.8)	< 0.01	3.0 (2.3-4.0)
Fetal presentation				
OP vs occiput anterior presentation	< 0.01	16.1 (9.4-27.5)	0.01	2.3 (1.2-4.3)
Breech vs occiput anterior presentation	0.30	0.9 (0.9-1.0)	-	-
OVD				
Forceps extraction vs no OVD	< 0.01	11.8 (8.9-15.5)	< 0.01	4.5 (3.1-6.5)
Vacuum extraction vs no OVD	0.01	3.5 (1.5-7.8)	-	-
Type of episiotomy				
Median vs no episiotomy	< 0.01	7.9 (4.4-14.3)	0.01	2.3 (1.6-4.3)
Mediolateral vs no episiotomy	0.01	2.1 (1.2-3.8)	-	-
Median vs mediolateral episiotomy	< 0.01	3.8 (3.1-4.6)	< 0.01	2.0 (1.6-2.6)
Level of operator				
Staff vs residents	< 0.01	2.3 (1.8-2.9)	-	-
Staff vs nurses	< 0.01	50 (20.0-100.0)	< 0.01	11.1 (5.0-25.0)
Staff vs medical student	< 0.01	22.2 (5.8-20.0)	0.01	3.3 (1.6-6.3)
Residents vs nurses	< 0.01	19.9 (8.8-44.7)	< 0.01	13.3 (5.9-30.2)
Medical student vs nurses	< 0.01	4.1 (1.5-11.0)	0.01	3.5 (1.3-9.6)
Residents vs medical student	< 0.01	4.9 (2.7-9.0)	< 0.01	3.8 (2.1-7.1)
The second staged labor				
60 -119 mins vs < 60 mins	0.01	49 (1.3-17.7)	-	-
> 120 mins vs < 60 mins	< 0.01	8.4 (4.2-17.1)	-	-

OASIS: obstetric anal sphincter injuries, BMI: body mass index, OP: occiput posterior, OVD: operative vaginal delivery, OR: odd ratio, CI: confidence interval.

For nulliparous subgroup analysis, the incidence of OASIS in nulliparous group was 8.8%. The occiput posterior, median episiotomy and staffs and residents as the operator were higher in the OASIS group. The second stage of labor, height and shoulder dystocia were not included in the analysis due to the lack of sample or small sample in the reference group (Table 3).

Table 3. Baseline characteristics for nulliparity.

Variables	No OASIS (n = 3,358)	OASIS (n = 326)	p value
Age	27.4 ± 5.9	29.3 ± 5.6	< 0.01
< 35 years old	3,358 (100%)	326 (100%)	
≥ 35 years old	-	-	
Gestational age	37.9 ± 1.9	38.3 ± 1.4	0.02
Birth weight ≥ 4kg	11 (0.3%)	1 (0.3%)	0.95
Birth weight < 4 kg	3347 (99.7)	325 (99.7%)	
Weight gain	13.3 ± 4.8	14.1 ± 5.0	< 0.01
Height			-
< 140 cm	-	-	
≥ 140 cm	3,358 (100%)	326 (100%)	
Body mass index	21.14 ± 3.8	20.75 ± 3.1	< 0.01
< 18.5kg/m^2 (underweight)	842 (25.1%)	77 (23.6%)	
18.5-22.9 kg/m^2 (normal)	1,703 (50.7%)	184 (51.2%)	
23-24.9 kg/m^2 (overweight)	356 (10.6%)	43 (13.2%)	
≥ 25kg/m^2 (obesity)	457 (13.6%)	22 (6.7%)	
Sex			0.76
Male	1,780 (53.1%)	177 (54.3%)	
Female	1,578 (46.9%)	149 (45.9%)	
Presentation			
Cephalic			
Occiput anterior	3,327 (99.1%)	303 (92.9%)	
Occiput posterior	19 (0.6%)	23 (7.1%)	
Breech	12 (0.4%)	-	
Shoulder dystocia			-
No shoulder dystocia	3,357 (100%)	326 (100%)	
Shoulder dystocia	1 (0%)	-	
Operative vaginal delivery			< 0.01
Spontaneous labor	3,196 (95.2%)	233 (93.1%)	
Forceps extraction	128 (3.8%)	86 (5.8%)	
Vacuum extraction	34 (1%)	7 (1.1%)	
Type of episiotomy			< 0.01
No episiotomy	119 (3.5%)	5 (1.5%)	
Median episiotomy	813 (24.2%)	177 (54.3%)	
Mediolateral episiotomy	2,426 (72.3%)	144 (44.2%)	
Level of operators			< 0.01
Residents	2,071 (61.7%)	231 (70.9%)	
Nurses	608 (18.1%)	3 (0.9%)	
Medical student	351 (10.5%)	5 (1.5%)	
Staff	328 (9.8%)	87 (26.7%)	
The second staged labor			-
< 60 minutes	3,358 (100%)	326 (100%)	
60-120 minutes	-	-	
> 120 minutes	-	-	

Data presented as mean ± standard deviation, n (%). OASIS: obstetric anal sphincter injuries

The significant factors of OASIS in nulliparity (Table 4) were included in adjusted analyses by multiple logistic regression model, the factors that associated with OASIS in the nulliparous subgroup were: obesity vs normal body mass index (BMI) (adjusted OR 0.4, 95%CI 0.2-0.6, p < 0.01), occiput posterior postition vs occiput anterior postition (adjusted OR 2.3, 95%CI 1.1-4.7, p = 0.02), forceps extraction vs spontaneous delivery (adjusted OR 4.6, 95%CI 3.2-6.8, p < 0.01), median episiotomy vs mediolateral episiotomy (adjusted OR 2.0, 95%CI 1.5-2.7, p < 0.01), the level of operators (staff vs nurses) (adjusted OR 16.7, 95%CI 5.0-5.00, p < 0.01), the level of operators (staff vs medical student) (adjusted OR 5.6, 95%CI 2.1-14.3, p < 0.01), the level of operators (residents vs nurses) (adjusted OR 17.7, 95%CI 5.6-55.9, p < 0.01) and the level of operators (residents vs medical student) (adjusted OR 4.4, 95%CI 1.6-12.1, p < 0.01).

Table 4. Subgroup analysis for nulliparity.

Variables	Univariate analysis for risk factors of OASIS		Multivariate analysis for risk factors of OASIS	
	p value	Crude OR (95%CI)	p value	Adjusted OR (95%CI)
Gestational age	< 0.01	1.1 (1.0-1.21)	-	-
Weight gain	0.02	1.0 (1.0-1.1)	-	-
BMI				
Underweight vs normal	0.74	1.1 (0.8-1.4)	-	-
Overweight vs normal	0.67	1.0 (0.8-1.6)	-	-
Obesity vs normal	< 0.01	0.5 (0.3-0.7)	< 0.01	0.4 (0.2-0.6)
Fetal presentation				
OP vs occiput anterior presentation	< 0.01	13.3 (7.2-24.8)	0.02	2.3 (1.1-4.7)
Breech vs occiput anterior presentation	0.28	0.9 (0.9-0.9)	-	-
OVD				
Forceps extraction vs no OVD	< 0.01	9.2 (6.8-12.5)	< 0.01	4.6 (3.2-6.8)
Vacuum extraction vs no OVD	0.06	2.15 (0.9-4.9)	-	-
Type of episiotomy				
Median vs no episiotomy	< 0.01	5.2 (2.1-12.9)	-	-
Mediolateral vs no episiotomy	0.46	1.4 (0.6-3.5)	-	-
Median vs mediolateral episiotomy	< 0.01	3.7 (2.9-4.6)	< 0.01	2.0 (1.5-2.7)
Level of operator				
Staff vs residents	< 0.01	2.4 (1.8-3.1)	-	-
Staff vs nurses	< 0.01	50 (16.7-100.0)	< 0.01	16.7 (5.0-50.0)
Staff vs medical student	< 0.01	20.0 (7.7-50.0)	< 0.01	5.6 (2.1-14.3)
Residents vs nurses	< 0.01	22.6 (7.2-70.9)	< 0.01	17.7 (5.6-55.9)
Residents vs medical student	< 0.01	7.8 (3.2-19.1)	< 0.01	4.4 (1.6-12.1)
Medical student vs nurses	0.13	2.9 (0.7-12.2)	-	-

OASIS: obstetric anal sphincter injuries, BMI: body mass index, OP: occiput posterior, OVD: operative vaginal delivery, OR: odd ratio, CI: confidence interval.

Discussion

In this study, the prevalence of OASIS was 6.0%, which was higher than previously reports[3-7]. The incidence of OASIS was 0.32% in Hong Kong[3], 0.34% in Croatia[6], 1.2% in France[7], 2.1% in India[5], and 4.5% in America[4]. This can be explained by the high prevalence of episiotomy and high prevalence of median episiotomy in our center. The incidence of OASIS varies according to the episiotomy protocol (selective/ routine use) of each center and country policy. The risk factors of OASIS in this study were nulliparity, occiput posterior presentation, forceps extraction, median episiotomy, residents and staff (as the operators). The protective factors were obesity and nurses. Our findings were similar to the previous reports4 except for the median episiotomy. The median episiotomy is still utilized in our center because of its advantages such as less perineal pain, less blood loss, quick episiotomy repair, and for cosmetic purposes. Due to the increasing risk of OASIS by median episiotomy, many guidelines suggest avoiding this episiotomy technique[9-11]. Our study confirmed the significance of the median episiotomy as the risk factor of OASIS in both total

population and in nulliparous subgroup. Hospital policy and campaign to avoid median episiotomy is now going at our center after the result of this study was recognized.

In nulliparous subgroup analysis, we found that risk factors of OASIS were occiput posterior postition, forceps extraction, median episiotomy, and staff. In contrast to other studies[3-7], we found that the obese pregnant women were less likely to experience OASIS compared to the normal BMI pregnant women. Due to the degree of obstetric perineal laceration classified by the depth, it could be explained that the obesity was a protective factor for OASIS because obese women posed thicker subcutaneous layer. Moreover, OASIS was more common when the residents and staff were the operators. This could be explained by the fact that they were responsible for more difficult or high-risk cases, compared to the nurses and medical students. Similar to the other studies, nulliparity and operative vaginal deliveries were shown to be the common risk factors[3-7]. Contrary to the study in India[5], shoulder dystocia was not identified as the risk factor of OASIS in our population. This can be explained by the very low incidence of shoulder dystocia (only 2/6,714 cases) at King Chulalongkorn Memorial Hospital.

After nulliparity subgroup analysis, we found the higher incidence of OASIS (8.8%) than the total population (6.0%), which was similar to the other reports[4, 5, 7]. The other risk factors (occiput posterior position, forceps extraction, and median episiotomy) were found to be common in both nulliparous subgroup and in the total population group in this study. The high prevalence of OASIS in our center should be recognized, concerned, and solved. OASIS represents a morbidity encountered after vaginal delivery. This problem should be raised concern by the delivery room personnel. Many intrapartum measures can be taken to decrease the risk of occurrence. The preventive strategies of OASIS such as perineal massage at the antenatal period, Kegel exercise at the antenatal period, intrapartum warm compression, manual protection of perineal during crowning, restrict episiotomy, and avoid median episiotomy are now being conducted at our center. These OASIS preventive strategies are advocated in every hospital to avoid the short term (infection, wound breakdown, perineal pain, urinary retention, and defecation problems) and long term sequelae (dyspareunia and sexual dysfunction) that can worsen quality of life of women.

The strength of this study

Our study included the total population during 2017-2019. This represents the real prevalence of OASIS. The high percentage of complete data enabled analysis of the multiple risk factors to produce reliable results.

Limitation of this study

Due to the retrospective cohort design, there was lack of some data such as the perineal protection, angle of episiotomy, and subtype of the third-degree laceration. Due to the single hospital study design, the result of this study is unable to represent the other hospitals in different parts of Thailand. The nation-wide study is advocated for further evaluation of OASIS prevalence in Thailand for finding national prevention program for OASIS in the future.

Conclusion

The risk factors of OASIS were nulliparity, occiput posterior position, forceps extraction, median episiotomy, residents and staffs (as the operators). The protective factors were obesity and nurses. Preventive strategies for these factors are advocated.

Potential conflicts of interest

The authors declare no conflicts of interest.

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CASE REPORT

Severe Uterine Hemorrhage Resulting from Uterine Arteriovenous Malformation: A catastrophic scenario

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ABSTRACT

Background: Abnormal uterine bleeding (AUB) is often challenging to diagnose in the emergency department (ED) due to its various causes. Uterine arteriovenous malformation (AVM) is a rare but significant gynaecological emergency that is frequently missed. It typically manifests as sudden and heavy vaginal bleeding, posing a potential life-threatening risk that requires immediate attention.

Case: A 40-year-old, para 3-0-0-3, woman presented to the ED with severe vaginal bleeding. Despite rapid resuscitation, she experienced hemodynamic instability. Uterine AVM was suspected based on colour Doppler pelvic ultrasound and later confirmed by angiography. Successful treatment was achieved with uterine artery embolization with complete resolution of the bleeding.

Conclusion: This case highlights the importance of early recognition and rapid resuscitation in treating uterine AVM with multidisciplinary team approach as a life-saving measure. Transcatheter arterial embolization is highly effective and preferred for preserving fertility in women. Timely intervention is crucial in managing this gynaecological emergency.

Keywords: uterine arteriovenous malformation, color Doppler ultrasonography, embolization, computed tomography angiography, hysterectomy.

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Introduction

Uterine arteriovenous malformation (AVM) is an uncommon vascular disorder primarily seen in women of reproductive age, characterized by severe per vaginal bleeding. The rarity of this condition not only underscores its clinical complexity but also accentuates the urgency, as delayed diagnosis can lead to a critical and life-threatening state. Colour Doppler ultrasonography is readily accessible, non-invasive, and highly effective diagnostic tool. Early resuscitation and uterine artery embolization, facilitated through angiography, offer a proactive approach, particularly for women desiring fertility preservation, potentially obviating the need for conventional hysterectomy. We report a case of uterine AVM in our emergency department (ED) with massive per vaginal bleeding, emphasizing the importance of early AVM recognition and highlighting prompt resuscitation as a crucial life-saving intervention.

Case Report

A 40-year-old, para 3-0-0-3, woman presented at ED with sudden onset of heavy per vaginal bleeding, experiencing a flow heavier than her usual menstrual flow. The bleeding was accompanied by blood clots and flooding, and associated with suprapubic pain. Her previous deliveries were uneventful with normal vaginal delivery. While in the ED, she experienced another episode of escalating vaginal bleeding and started to exhibit signs of drowsiness and paleness. Her vital signs deteriorated with episodes of hypotensive and tachycardia. The estimated blood loss amounted to three liters. There was no mass palpable per abdomen, and the vaginal examination was unremarkable. Transabdominal ultrasonography revealed a blood clot at the cervix, with present of minimal free fluid in the pouch of Douglas. A urine pregnancy test was negative. Treatment included fluid resuscitation, packed cell transfusion, and the administration of intravenous tranexamic acid.

An urgent pelvic ultrasound with color Doppler (Fig. 1) revealed bulky uterus with increased vascularity and multidirectional flow with presence of prominent vessels displaying dilated vessels adjacent to the left side of the uterine fundus. These vessels appeared to be connected to the left iliac artery. A diagnosis of uterine AVM was initially suspected and later confirmed through computed tomography angiography (CTA) of the abdomen and pelvis. The CTA revealed multiple tortuous and prominent vessels within the uterus, indicating the presence of a vascular malformation (Fig. 2). Successful treatment was achieved through bilateral uterine artery embolization, effectively halting any further vaginal bleeding (Fig. 3).

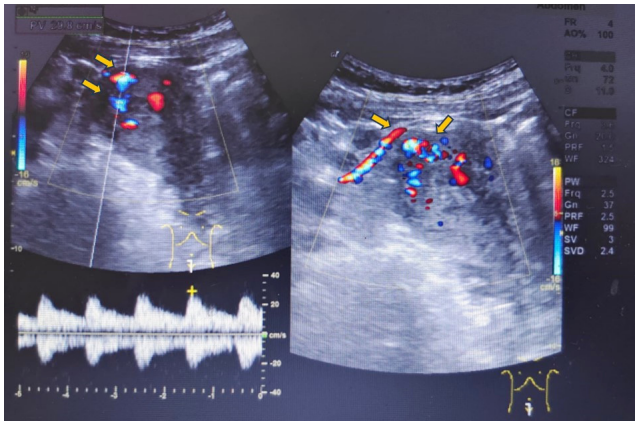

Fig. 1. An ultrasound pelvis showed increase vascularity on colour Doppler with dilated vessels that appear connected with left internal iliac artery.

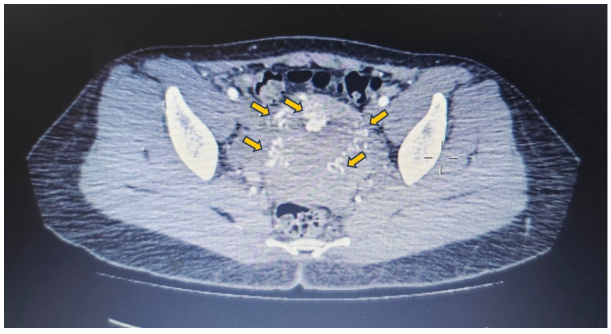

Fig. 2. A computed tomography angiography abdomen and pelvis showed multiple tortuous prominent uterus vessels represent vascular malformation.

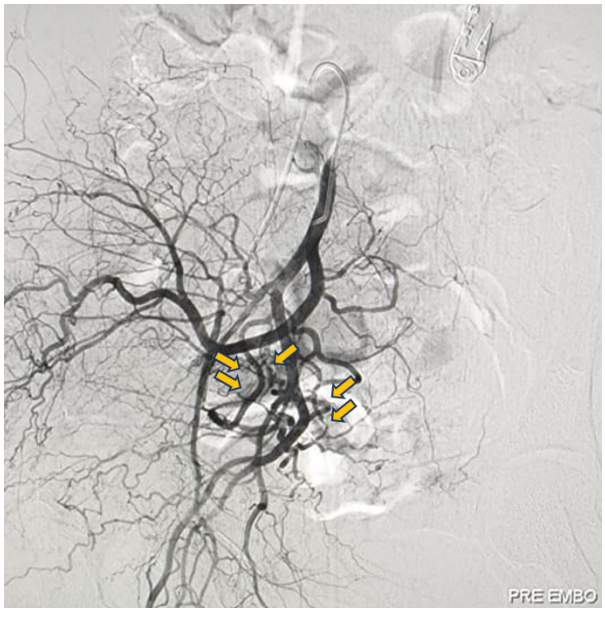

Fig. 3. Procedure of uterine artery embolization: Presence of dilated tortuous vessels arising from bilateral uterine artery suggestive of arteriovenous malformation at the uterus.

She has been discharged well post-procedure and resumed normal menstruation during regular follow-up over the past two years. This case report highlights our successful experience with a patient having this uncommon gynecological condition in our center. This case also emphasizes in the absence of widely agreed-upon guidelines for managing symptomatic uterine AVM, it is important to adopt a multidisciplinary approach with individualized management.

Discussion

Uterine AVM is a seldom encountered yet potentially life-threatening condition whenever not promptly recognized and addressed, can result severe morbidity and even mortality[1]. In a study involving 959 patients, sonographically evident uterine AVM were discovered in 5.2% of women following dilatation and curettage, and in 0.22% of women after delivery. However, only one AVM (0.1%)

within the study population was considered clinically significant[2]. A hypothesis of uterine AVM is part of the same pathological process within the spectrum of abnormal invasive placental disorders. In the context of previous trophoblastic processes, vascular malformations may resemble AVM but not in fact to be considered as true AVM[3].

In case of acute vaginal bleeding, the list of potential differential diagnoses should be routinely encompassing conditions like ectopic pregnancy, miscarriage, and uterine corpus and cervical malignancies[4]. However, ones should not disregard the possibility of rare occurrence of uterine AVM. Uterine AVM can lead to abrupt and extensive vaginal bleeding, potentially causing hemodynamic instability necessitates blood transfusion and/ or emergency hysterectomy[5]. While the common age range affected was between 20 and 40 years old, the youngest reported case of congenital uterine AVM occurred in a seven-month-old infant, necessitating a total hysterectomy due to recurrent intractable vaginal bleeding[6].

AVM can be categorized into congenital and acquired forms, with the latter being more prevalent. Congenital AVMs are very rare and are thought to arise from anomalies in the embryological development of primitive vascular systems[7]. On the other hand, acquired AVM are frequently linked to iatrogenic uterine trauma, such as dilatation and curettage or caesarean section, although they can also be associated with normal vaginal birth or malignancy[8, 9]. In this case, the patient's CTA results with absence of prior uterine trauma strongly suggest the presence of a congenital AVM, the rarer type.

Various diagnostic imaging modalities, including Doppler ultrasonography, contrast enhanced CTA, magnetic resonance imaging (MRI), and conventional angiography, can be employed for the identification of uterine AVM[10]. However, ultrasonography stands out as a preferred diagnostic method due to its attributes, eg cost-effectiveness, speed, simplicity, and non-invasiveness. As demonstrated in this case, transabdominal pelvic ultrasonography provides valuable insights into uterine abnormalities, and color Doppler imaging can unveil heightened vascularity and dilated vessels, characteristics signs of AVM.

The management of uterine AVM depends on multifactorial such as patient's hemodynamic condition, the extent of the bleeding, patient's age, and future fertility intentions[11]. Managing uterine AVM is challenging necessitate multidisciplinary approach[12]. Initial treatment focuses on stabilizing the patient's hemodynamic status and halting the bleeding. Historically, hysterectomy was the primary treatment choice. Given that uterine AVM is frequently diagnosed in women of childbearing age, angiographic embolization has rendered hysterectomy no longer the sole imperative solution[13]. In this particular case, the rapid resuscitation with initiation of fluid and blood products, and intravenous tranexamic acid played a crucial role in stabilizing the patient's hemodynamic status. Nonetheless, the definitive treatment for uterine AVM often involves the successful performance of transcatheter embolization of the anomalous vessels, uterine artery embolization effectively closed off the irregular vascular connections, resulting in the cessation of abnormal bleeding. Repeat embolization is feasible and recommended for recurrence symptomatic uterine AVM, emphasizing the importance of both clinical and imaging follow-up[14]. A systematic review analysing fertility after uterine artery embolization suggested that pregnancy rates were similar to age-adjusted rates in the general population, with similar rates of complications[15]. Medical management with either combined oral contraceptives pills or medroxyprogesterone acetate is effective in completely or partially resolving uterine AVM. Subsequent pregnancies in this population are feasible and are not at higher risk for perinatal complications[16]. Based on literature search, the scarcity of reported cases has led to the absence of universal treatment guidelines for uterine AVM. Hence, detailed discussions with multidisciplinary specialists including gynecologists, vascular surgeons, and radiologists could facilitate the

development of guidelines for the personalized management of AVM[17].

Conclusion

This case emphasizes the significant of early identification and prompt resuscitation as life-saving measures in uterine AVM treatment. Transcatheter arterial embolization stands out as a highly effective and preferred method for preserving fertility in women. In the absence of widely agreed-upon guidelines for managing symptomatic uterine AVM, it is crucial to adopt a multidisciplinary approach and provide personalized patient care.

Potential conflicts of interest

The authors declare no conflicts of interest.

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CASE REPORT

Fournier's Gangrene in a Pregnant Woman with Genital Gerpes: A case report

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ABSTRACT

Genital herpes is a viral infection caused by herpes simplex virus. Most of the literature on genital herpes in pregnancy focused on the transmission of the herpes simplex virus to the newborn and the majority of disseminated genital herpes had been reported as encephalitis, hepatitis and pneumonia. In this case report, the genital herpes was complicated with secondary infection and disseminated rapidly through the perineal subcutaneous tissue which is also known as Fournier's gangrene. In females, Fournier's gangrene is rare, and it is even rarer in pregnant women. There are only a few cases reported worldwide. To our best knowledge, this is the first case of genital herpes in pregnancy that progressed to Fournier's gangrene. This case report also highlighted the long-term complications of Fournier's gangrene.

Keywords: Fournier's gangrene, genital herpes, pregnancy, vaginal stenosis, colostomy, sexual dysfunction, hematocolpos, hematometra.

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Introduction

Genital herpes and Fournier's gangrene (FG) are two distinct medical conditions and there are no reports of them occurring simultaneously in a pregnant woman. Genital herpes is a viral infection caused by herpes simplex virus (HSV) that can affect the genital and anal areas. During pregnancy, there are concerns about the transmission of HSV to the baby during childbirth[1]. FG is a medical emergency characterized by rapidly progressive necrotizing fasciitis of the perianal and genitourinary area with high mortality. FG is a polymicrobial synergistic soft tissue infection, with a mixture of gram-positive, gram-negative bacteria and aneroboic organisms. The most commonly cultured organisms are Escherichia coli, Streptococci, Staphylococci, Bacteroides and Pseudomonas[2]. Compared to males, FG is less common in females as the vagina allows the drainage of pelvic secretion and contents[3]. There is a lot of literature focusing on the acute management of FG. Early detection, intensive fluid resuscitation, systemic antibiotics, extensive wound debridement, wound care and nutritional support are the key components of FG management[4]. Our case report highlighted the long-term complications and consequences of FG: vaginal stenosis causing sexual dysfunction, genital tract outflow obstruction leading to hematocolpos and hematometra, and the need for lifelong colostomy.

Case report

A 28-year-old diabetic obese lady at 31 weeks of pregnancy presented with complaints of blisters over the perineal region, associated with worsening itchiness and pain for the past one week. Examination revealed a 3 cm ulcer at the posterior fourchette involving bilateral labia minora and labia majora (Fig. 1). Multiple vesicles were seen at the perianal region which subsequently erupted and turned into ulcers with pus discharge (Fig. 2). A diagnosis of genital herpes with secondary infection was made and confirmed with serum HSV polymerase chain reaction test. She was started on intravenous acyclovir and intravenous ampicillin /sulbactam. On day 3 of admission, she went into labor, and an emergency cesarean section was performed. A 1.6 kg baby girl was delivered and admitted to the neonatal intensive care unit for neonatal HSV infection.

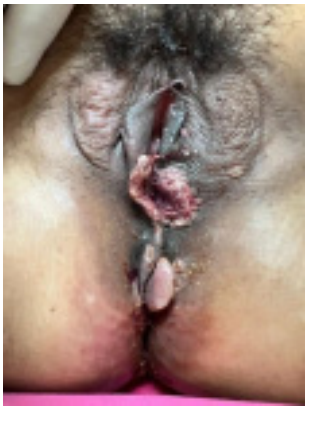

Fig. 1. Genital herpes with ulceration.

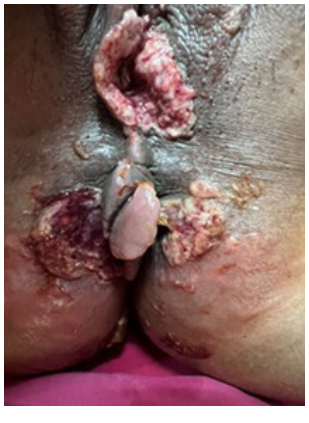

Fig. 2. Worsening of genital herpes wound with secondary infection.

The perineal and perianal wounds expanded and worsened despite medical treatment and dressings. The patient went into severe sepsis with acute kidney injury and respiratory distress on day five of admission. She was intubated and a decision for wound debridement and colostomy was made to

prevent wound contamination from fecal soiling. Full dehiscence of the anal triangle with complete destruction of the external and internal anal sphincter muscles extending into the ischiorectal fossa was noted intraoperatively. Anteriorly, extensive wound debridement was carried out till the level of the clitoris, removing all the pus collection and necrotic tissue over the vulvar and vagina (Fig. 3). The diagnosis of Fournier gangrene was confirmed with histopathology examinations reporting obliterative endarteritis, arteriolar thrombosis and necrotic areas. Perineal tissue cultures grew a mixture of gram-positive and gram-negative microorganisms. The antibiotic was changed to intravenous piperacillin/ tazobactam and clindamycin. The perineal wound was left open and healed through secondary intention (Fig. 4).

She made an uneventful recovery after 3 weeks of intensive care unit stay.

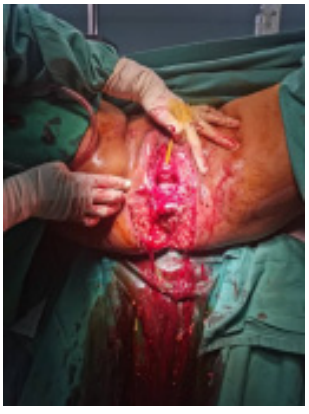

Fig. 3. Surgical debridement of the Fournier's gangrene.

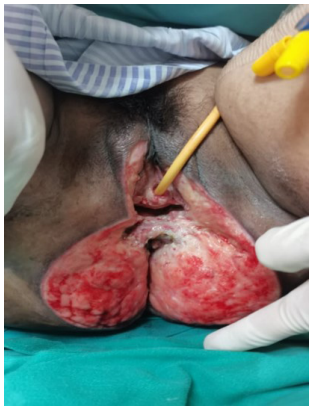

Fig. 4. Secondary healing of the perineal wound.

However, at 6 months follow-up, the patient revealed that she had no menstrual flow, and she was unable to consummate with her husband. She experienced severe pain and bleeding during sexual intercourse which traumatized her. Her vagina and anus were obliterated and stenosed with well-healed scared tissue (Fig. 5). She was scheduled for vaginoplasty and vaginal recanalization by urogynecologists and plastic surgeons.

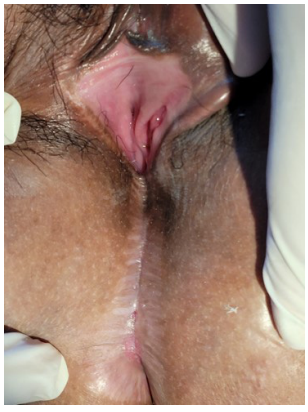

Fig. 5. Vaginal and anal stenosis.

Discussion

Genital herpes in pregnancy can progress to FG if it is not managed appropriately. Obesity, diabetes mellitus, and pregnancy itself, which is an immunomodulatory event, predispose patients to FG[5]. Blisters and ulcers in genital herpes serve as an entry port for secondary infection. Furthermore, the proximity of the anal opening lead to wound contamination with feces. This highlights that besides antiviral treatment; perineal hygiene is an important part of genital herpes management. Worsening of the perineal wound needs to seek immediate medical attention and FG needs to be suspected.

FG is a clinical diagnosis with the hallmark of severe pain, erythema, subcutaneous crepitation, purulent discharge and gangrene in the genitalia and perianal tissue.

Laboratory parameters are non-specific and imaging tests may aid in determining the origin and the extension of the gangrene[6].

Broad-spectrum antibiotics, early wound debridement and aggressive resuscitation are the mainstay of treatment for FG. Antibiotic therapy used needs to cover gram-positive, gram-negative, and anaerobic organisms which are usually associated with Fournier gangrene. The combination of a third-generation cephalosporin, aminoglycoside, penicillin, and metronidazole has traditionally been used as triple therapy antibiotic coverage. However, in pregnancy, aminoglycoside (Food and Drug Administration (FDA category D) is usually avoided and replaced with piperacillin/tazobactam, vancomycin or carbapenems (FDA Category B)[7]. For pregnant women whose condition deteriorates, timely delivery of the baby is important to enhance maternal resuscitation.

Colostomy has a contentious role in the treatment of FG. Although it minimizes fecal contamination and promotes wound healing, it is associated with increased mortality, exposing the patient to further surgical operations and the possibility of anastomosis breakdown[8]. Colostomy was performed in our case due to extensive anal sphincter damage. Vaginal stenosis and sexual dysfunction are long-term complications of FG that are rarely discussed. Patients may be embarrassed to admit that they are unable to consummate with their spouse. According to the diagnostic and statistical manual of mental disorders fifth edition (DSM-5), this will fall under the category of genito-pelvic pain/penetration disorder (GPPD)[9]. Information on sexual function needs to be checked during follow-up. Radiation therapy, vaginal surgery, and trauma are the most common causes of vaginal stenosis; to the best of our knowledge, this is the first case of vaginal stenosis following FG. Vaginal estrogen therapy, early vaginal dilatation, and wound dressing, in our opinion, would prevent vaginal scarring and stenosis. Furthermore, genital tract outflow obstruction will lead to hematometra, hematocolpos and retrograde flow of menstruation into the abdominal cavity, causing severe abdominal pain. Vaginal recanalization and reconstruction are the solutions to these complications. These procedures require expertise, such as urogynecologists and plastic surgeons.

Conclusion

Genital herpes in pregnancy should not be treated lightly as it can progress to FG in the presence of risk factors. FG is a life-threatening condition that requires urgent treatment to prevent the rapid spread of infection and tissue necrosis. The management of FG in pregnancy is complex. A multidisciplinary approach and timely delivery of the baby are important to improve maternal resuscitation and outcomes. Not only the physical health but also the psychological well-being of patients with FG needs to be taken care of. Long-term complications including sexual dysfunction and lifelong colostomy should be addressed and monitored in patients with FG.

Potential conflicts of interest

The authors declare no conflicts of interest.

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