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Phupong V. Management of PPROM AT 32 to 34 weeks. In: Desai SV, Tank P, eds. Handbbok on preterm prelabor rupture of membranes in a low source setting. New Delhi: Jaypee Brothers Medical Publishers Ltd, 2012: 39-46.

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ORIGINAL ARTICLES

Thai Journal of Obstetrics and Gynaecology
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EDITORIAL

At the beginning of New Year 2019, it's time for beginning good things. May this year bring happiness, new inspirations and new success to all members of Royal Thai College of Obstetricians and Gynaecologists (RTCOG).

Editor in Chief and managing staff will attended the Thai Journal Citation Index meeting: "**The 6th Editors' Workshop**" under the TCI-TRF-Scopus Collaboration Project on 26 March 2019 at Ambassador Hotel, Bangkok, Thailand. Editorial Board of TJOG looks forward to continuously raising the quality of the TJOG and prepare journal for submission to be index in an international index.

We would like to thank past RTCOG executive board, past editor in chief, editorial board and staff, reviewers, all members of RTCOG, and all researchers for their kind contribution and support to TJOG.

This first issue of TJOG 2019 contains many interesting articles. One special article is "**Particulate Matter 2.5 and Obstetric Complications**".

Prof. Vorapong Phupong, M.D.
Editor in Chief

Thai Journal of Obstetrics and Gynaecology
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SPECIAL ARTICLE

Particulate Matter 2.5 and Obstetric Complications

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ABSTRACT

Particulate matter (PM) is microscopic solid or liquid matter suspended in the atmosphere of Earth. The sources of PM can be natural or anthropogenic. The most common used for classification of PM is the size of PM. PM 2.5 influences general health problems. Inhalation of PM 2.5 also causes obstetric complications such as low birth weight, preterm delivery and stillbirth. Thus, pregnant women should avoid the exposure to PM 2.5 for prevention of these obstetric complications.

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Introduction

Particulate matter (PM) is microscopic solid or liquid matter suspended in the atmosphere of Earth[1, 2]. There have been many classifications of PM. The most common used for classification of PM is the size of PM.

PM 10 is defined as particles which pass through a size-selective inlet with a 50% efficiency cut-off at 10 µm aerodynamic diameter. PM10 corresponds to the "thoracic convention"[3].

PM 2.5 is defined as particles which pass through a size-selective inlet with a 50% efficiency cut-off at 2.5 µm aerodynamic diameter. PM 2.5 corresponds to the "high-risk respirable convention"[3].

The size of PM is very important. Only PM smaller than 10 µm can reach the alveoli. Larger PM are deposited higher up in the respiratory system and removed on the mucocilliary escalator, but may then be swallowed and subsequently absorbed through the gastrointestinal tract[2].

Sources of PM

Sources of PM can be natural or anthropogenic[1]. Natural sources include PM originating from volcanoes, dust storms, forest and grassland fires, living vegetation and sea spray. Anthropogenic sources include combustion within car engines, solid-fuel combustion in households, industrial activities (such as building, mining, manufacturing of cement, ceramics and bricks, and smelting), quarrying and mining[1].

Regulation

Due to the highly toxic health effects of particulate matter, most governments have created regulations. Each country has set standards for PM

10 and PM 2.5 concentrations. For example, United States has set standards for PM 2.5 concentrations: 35 μg/m^3 for daily average and 12 μg/m^3 for yearly average[4]. WHO has set standards for PM 2.5 concentrations: 25 μg/m^3 for daily average and 10 μg/m^3 for yearly average[5]. In Thailand, the standards for PM 2.5 concentrations are 50 μg/m^3 for daily average and 25 μg/m^3 for yearly average[6].

An air quality index (AQI) is used to communicate to the public how polluted the air currently is or how polluted it is forecast to become. As the AQI increases, an increasingly large percentage of the population is likely to experience increasingly severe adverse health effects[7].

The Air Quality Health Index or (AQHI) is a scale designed to help understand the impact of air quality on health. It has been used in Canada. It is a health protection tool used to make decisions to reduce short-term exposure to air pollution by adjusting activity levels during increased levels of air pollution. The AQHI also provides advice on how to improve air quality by proposing behavioural change to reduce the environmental footprint. The AQHI provides a number from 1 to 10$^+$ to indicate the level of health risk associated with local air quality. On occasion, when the amount of air pollution is abnormally high, the number may exceed 10[8]. Table 1 shows the AQHI Health Risk Categories[8].

Table 1. The AQHI Health Risk Categories[8].

Health Risk	AQHI	Health Messages	
		At Risk population*	General Population
Low	1–3	Enjoy your usual outdoor activities.	Ideal air quality for outdoor activities
Moderate	4–6	Consider reducing or rescheduling strenuous activities outdoors if you are experiencing symptoms.	No need to modify your usual outdoor activities unless you experience symptoms such as coughing and throat irritation.
High	7–10	Reduce or reschedule strenuous activities outdoors. Children and the elderly should also take it easy.	Consider reducing or rescheduling strenuous activities outdoors if you experience symptoms such as coughing and throat irritation.
Very high	Above 10	Avoid strenuous activities outdoors. Children and the elderly should also avoid outdoor physical exertion.	Reduce or reschedule strenuous activities outdoors, especially if you experience symptoms such as coughing and throat irritation.

* People with heart or breathing problems are at greater risk.

Effect of PM on health problems

The effects of inhaling PM that has been widely studied in humans and animals include respiratory diseases, cardiovascular disease, and obstetric problems. PM has an effect on health problems either acute or chronic effects. Acute health problems include lung inflammatory reactions, respiratory symptoms, adverse effects on the cardiovascular system, increased in hospital admissions, increased in mortality and increased in medication usage. Chronic health problems include increased in lower respiratory symptoms, reduction in lung function in children, increased in chronic obstructive pulmonary disease, reduction in lung function in adults, and reduction in life expectancy[9].

Effect of PM 2.5 on obstetric problems

There have been many studies regarding PM 2.5 and obstetric problems. Previous study showed that oxidative stress, deoxyribonucleic acid (DNA) methylation, mitochondrial DNA content alteration, and endocrine disruptions may all play an important role in PM 2.5 induced adverse effects to pregnant women and fetuses. In addition, PM 2.5 exposure can cause male reproductive toxicity, leading to associated adverse pregnancy outcomes[10]. Research evidence indicates that PM 2.5 has a potential to induce low birth weight (LBW), preterm birth (PTB), and stillbirth[10].

- ***Low birth weight***

Exposure to PM 2.5 during pregnancy may affect the growth and development of infants[11]. One study found that exposure to specific constituents of PM 2.5, especially traffic-related particles, sulphur constituents, and metals was associated with decreased birth weight. Inhalation of PM can trigger maternal oxidative stress, damage cells, cause inflammation and changes in the blood system, decrease placental blood flow, disrupt transplacental oxygenation, leading to poor growth of the fetus[12]. Previous studies found that exposure to PM 2.5 during pregnancy increased low birth weight infants[10, 13, 14]. Stieb DM, et al demonstrated pooled odds ratios for low birth weight ranged from 1.05 (0.99-1.12) per 10 μg/m^3 PM 2.5 to 1.10 (1.05-1.15) per 20 μg/m^3 PM 10 based on entire pregnancy exposure[15].

- ***Preterm delivery***

Previous studies demonstrated that exposure to PM 2.5 during pregnancy was associated with preterm delivery[10, 13, 14, 16, 17]. DeFranco E et al demonstrated that exposure to high levels of particulate air pollution, PM 2.5, in pregnancy is associated with a 19% increased risk of PTB; with greatest risk with high third trimester exposure[17]. Meta-analytic study found that the pooled odds ratio (OR) for PM 2.5 exposure (per 10 μg/m^3 increment) during the entire pregnancy on preterm birth was 1.13 (95 % CI 1.03-1.24) in 13 studies with a significant heterogeneity ($Q = 80.51$, $p < 0.001$). The pooled ORs of PM 2.5 exposure in the first, second and third trimester were 1.08 (95 % CI 0.92-1.26), 1.09 (95 % CI 0.82-1.44) and 1.08 (95 % CI 0.99-1.17), respectively[18].

- ***Stillbirth***

Some studies found that exposure to PM 2.5 during pregnancy was associated with stillbirth[10, 19]. DeFranco E et al found that exposure to high levels of PM 2.5 in the third trimester of pregnancy was associated with 42% increased stillbirth risk, aOR 1.42 (95% CI 1.06,1.91)[19].

Prevention of health problems from PM 2.5

The prevention of health problems from PM2.5 include minimizing the releasing of PM 2.5 especially from anthropogenic sources and avoiding the inhalation of PM 2.5.

Risk reduction behaviors of PM 2.5 include minimizing the times for opening windows in order to reduce the PM 2.5 exposure from outside, adjusting time of day or frequency that the physical exercise was done according to AQI, adjusting the physical exercise styles or amounts in relation to the AQI, wearing face masks when going outside in the haze, cleaning the mouths and noses after outdoor activities and using air purifiers when airing the room[20].

In conclusion, PM 2.5 can increase obstetric complications such as low birth weight, preterm delivery and stillbirth. Obstetric complications increase when exposure to PM 2.5 during pregnancy, the best way is prevention from PM 2.5 exposure. Pregnant women should avoid the exposure to PM 2.5 for prevention of these obstetric complications

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OBSTETRICS

Comparison of Vaginal pH between Bacterial Vaginosis and Non-bacterial Vaginosis in Preterm Labour

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ABSTRACT

Objectives: The aim of this study was to compare vaginal discharge pH between bacterial vaginosis (BV) and non-bacterial vaginosis in preterm labour.

Materials and Methods: An analytical cross-sectional study was carried out on patients admitted to the obstetrics ward of Prapokklao Hospital from June 2016 to January 2017. The main inclusion criterion was the presence of preterm labour without premature rupture of membranes or vaginal bleeding. Vaginal discharge was collected for pH measurement and Gram stain. The Nugent criteria from the University of British Columbia were used for BV diagnosis.

Results: The final analysis was based on data from 105 participants. The prevalence of BV was 71.4%. The mean of vaginal pH was 5.97±0.40 for the BV group and 5.20±0.36 for the non-BV group, $z=6.674$, $p < 0.001$.

Conclusion: Mean vaginal pH in the BV group was higher than in the non-BV group.

Keywords: Bacterial Vaginosis, Nugent criteria, Preterm labour, Vaginal pH.

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เปรียบเทียบค่าความเป็นกรดด่างของช่องคลอดในหญิงตั้งครรภ์ที่มีภาวะเจ็บครรภ์คลอดก่อนกำหนดที่มีและไม่มีภาวะติดเชื้อแบคทีเรียในช่องคลอด

จิรัชญา กลีบสุวรรณ์, จรรยา ธำรงวุฒิกุล, วัชรินทร์ เฉิดฉิ้ม

บทคัดย่อ

วัตถุประสงค์: *เพื่อเปรียบเทียบความเป็นกรดด่างของช่องคลอดในหญิงตั้งครรภ์ที่มาด้วยภาวะเจ็บครรภ์คลอดก่อนกำหนดที่มีและไม่มีภาวะติดเชื้อแบคทีเรียในช่องคลอด*

วัสดุและวิธีการ: *เป็นการศึกษาวิจัยเชิงวิเคราะห์แบบ cross-sectional ที่ห้องคลอด โรงพยาบาลพระปกเกล้า จังหวัดจันทบุรี ในหญิงตั้งครรภ์ที่มาด้วยภาวะเจ็บครรภ์คลอดก่อนกำหนดที่ไม่มีภาวะน้ำเดินก่อนกำหนด หรือเลือดออกจากช่องคลอด และรับไว้รักษาในโรงพยาบาลระหว่างเดือนมิถุนายน 2559 ถึงเดือนมกราคม 2560 โดยหญิงตั้งครรภ์ที่มาด้วยภาวะเจ็บครรภ์คลอดก่อนกำหนดทุกรายที่อยู่ในเกณฑ์คัดเข้าจะถูกเก็บสิ่งคัดหลั่งจากช่องคลอดเพื่อตรวจวัดค่าความเป็นกรดด่างและย้อมตรวจ Gram stain โดยใช้ Nugent criteria ของ University of British Columbia ในการวินิจฉัยภาวะติดเชื้อแบคทีเรียในช่องคลอด*

ผลการศึกษา: *หญิงตั้งครรภ์ที่มาด้วยภาวะเจ็บครรภ์คลอดก่อนกำหนดเข้าร่วมการศึกษาจำนวน 105 ราย ได้รับการวินิจฉัยว่ามีภาวะติดเชื้อแบคทีเรียในช่องคลอด 71.4% พบมีค่าเฉลี่ยความเป็นกรดด่างของช่องคลอดในกลุ่มที่มีและไม่มีการติดเชื้อแบคทีเรียในซ่องคลอด 5.97±0.40 และ 5.20±0.36 ตามลำดับ ($z=6.674$, $p < 0.001$)*

สรุป: *การศึกษานี้พบว่าค่าความเป็นกรดด่างในกลุ่มที่มีภาวะติดเชื้อแบคทีเรียในช่องคลอดสูงกว่ากลุ่มที่ไม่มีการติดเชื้อแบคทีเรียอย่างมีนัยสำคัญทางสถิติ*

คำสำคัญ: *การติดเชื้อแบคทีเรียในช่องคลอด, เกณฑ์ Nugent, เจ็บครรภ์คลอดก่อนกำหนด, ค่าความเป็นกรดด่างของช่องคลอด*

Introduction

Preterm labour is defined as regular contractions of the uterus that start before 37 weeks of pregnancy, resulting in changes in the cervix[1]. The preterm birth rate in Thailand was 10% in 2012[2] and regarded as a leading cause of both deficient maternal health and neonatal morbidity or mortality[1,3-4]. Based on five years of data from Prapokklao Hospital, it was reported that preterm births occurred at a rate of 6.23%. There are several risk factors of preterm labour, with previous studies reporting that vaginosis and cervicitis may have significant roles[5].

Bacterial vaginosis (BV) is the most common lower genital tract infection in women of reproductive age, resulting from a change in flora bacteria to mostly anaerobic bacteria. In pregnant women, BV is associated with preterm labour, early and late miscarriag, premature rupture of membranes, chorioamnionitis and low birth weight[6,7]. The incidence rate of BV in preterm labour is about 25.8%[8].

There are many criteria for the diagnosis of BV, including Amsel's criteria, Nugent's criteria and anaerobic culture[9-11]. Amsel's criteria is a simple bedside tool. However, a vaginal pH cut-off point of 4.5 may be unreliable because it is defined in the normal range of vaginal pH for pregnant women (3.5-6.0)[12]. Several studies have investigated vaginal pH change during pregnancy without infection, which showed consistently at 4.58 for within term delivery and 5.43 for preterm delivery[13]. No study has been conducted to determine the vaginal pH change with BV in pregnant women compared with non-BV. The Nugent scoring system and culture are inconvenient due to potential delays and high costs.

Accordingly, the aim of this study was to determine differences in vaginal pH between BV and non-BV patients in preterm labour.

Materials and Methods

This analytic cross-sectional study was carried out between June 2016 and January 2017 at Prapokklao Hospital, Chanthaburi, Thailand.

Sample size calculation

A pilot study conducted in February 2016 with 30 data records showed that the mean vaginal pH values for a BV group and a non-BV group of patients were 5.47 ± 0.54 and 5.18 ± 0.34, respectively. Sample size calculation was based on the difference in vaginal pH between the two groups. A one-tail test with 80% power was utilised for this purpose. The means vaginal pH from the pilot study were used for the calculation and giving at least 30 participants for each group. The results determined the chance for BV diagnosis at 0.6, requiring at least 45 samples for the BV group and 30 samples for the non-BV group.

The inclusion criteria for this study were women with singleton pregnancies and gestational age between 24^{+1} weeks to 36^{+6} weeks. The women had to have undergone routine ultrasonography (between 18^{+0} to 22^{+0} weeks), presenting with regular uterine contractions (4 times in 20 minutes or 8 times in 60 minutes) with cervical change in effacement ≥ 80% and dilation ≥ 1 cm. Exclusion criteria comprised premature rupture of membranes, vaginal bleeding, lack of understanding in Thai and last sexual intercourse within 72 hours. Consequently, 111 pregnant women were deemed eligible for the study. Six subjects were excluded because the Gram stain slides were lost and the patients delivered before recollection. As a result, 105 pregnant women actually participated in this study (Fig. 1).

After data and specimen collection, all preterm pregnancies were admitted to the labour room and treated following clinical guidelines for preterm labour. If cervical change advanced to the active phase of labour or spontaneous rupture of the amniotic membranes occurred, antibiotics for GBS prophylaxis was used in preparation for delivery. In cases diagnosed with BV, metronidazole at 1,200 mg/day was given for 7 days.

This study was approved by the Prapokklao Ethics Committee. Prior to enrollment, all eligible participants received information regarding the study and signed an informed consent form. The baseline characteristics of participants, antenatal data, vaginal

discharge for pH and Gram stain were collected and recorded.

Vaginal specimen collection procedure

A sterile dry speculum was inserted into the patient's vagina and 2 sterile cotton swabs were placed into the posterior fornix, one for aerobic culture (routine investigation in Prapokkloa Hospital) and another for Gram stain and pH measurement. All vaginal Gram stains were assessed for number of organisms and Clue cells in the required time by an official microbiologist, reviewed by the author and then checked for accuracy by a second official microbiologist for confirmation. Vaginal pH was measured using pH indicator paper with discrimination of 0.5. Vaginal discharge from the cotton swabs was placed on the pH indicator paper for 1 minute and read by 2 clinicians at the same time. Cervical change was assessed by training residents. Any conflicting opinions for Nugent score or pH level were resolved by mutual agreement. In some cases, a third opinion was sought.

Diagnosis of BV

Nugent criteria from the University of British Columbia were used for diagnosis in this study. Nugent scores of 4-6, which consisted of clue cells or a score of 7 or more, were reported as BV infection (Table 1)[14]

Allocation

This prospective study enrolled participants then diagnosed them as BV or non-BV prior to allocation into the two groups. The early period of this cross-sectional study identified a larger proportion of preterm patients with BV compared to non-BV, as evidenced by the ratio of 2.5 to 1 for BV to non-BV, at the end of the study period.

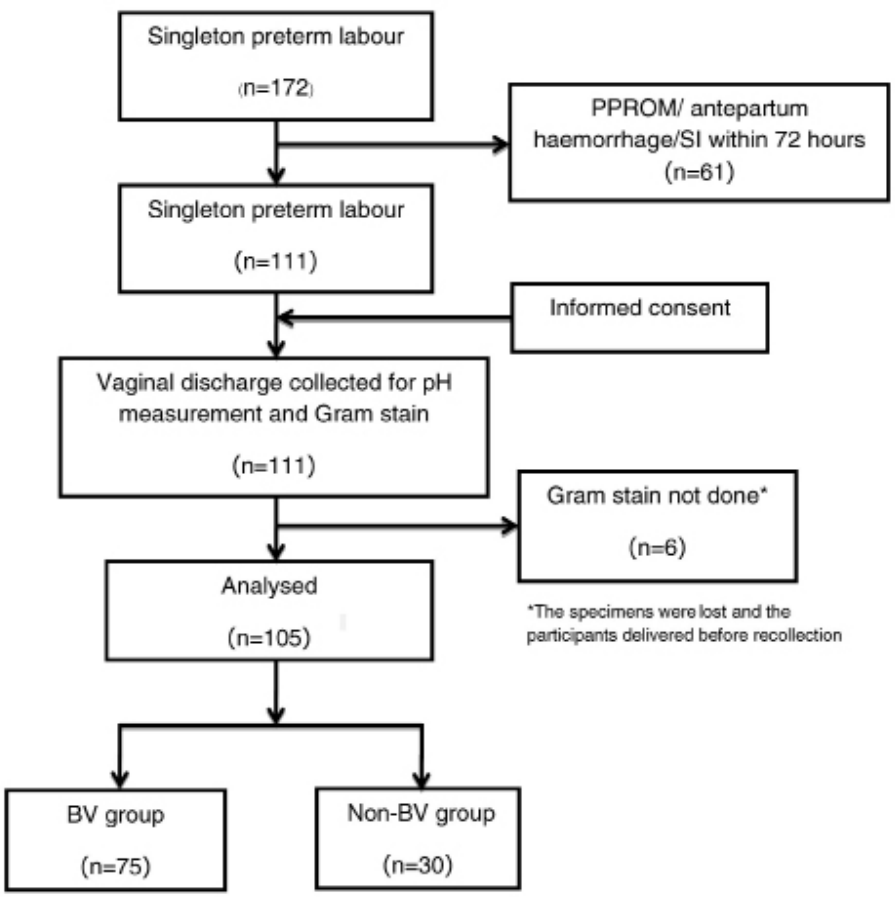

Fig. 1. The study flowchart.

Table 1. Laboratory interpretation of vaginal smears[14].

Gram positive rod*	Score	Small gram-variable CB, GNR*	Score	Curve gram-negative bacilli*	Score	Total score
≥ 30	0	0	0	0	0	
5 - 30	1	< 1	1	< 1	1	
1 - 4	2	1 - 4	2	1 - 4	1	
< 1	3	5 - 30	3	5 - 30	2	
0	4	≥ 30	4	≥ 30	2	

* number of organisms seen/100X objective, CB: curve bacilli, GNR: Gram negative rod

If N score is:	AND	Then Report
0 - 3 4 - 6	Clue cells NOT present	Smear NOT consistent with BV
4 - 6 ≥ 7	Clue cells ARE present	Smear consistent with BV

Statistical analysis

Baseline and antenatal characteristics among the two groups were analysed using percentage, mean, standard deviation (SD), exact probability test and independent t-test for maternal age and admission hematocrit. Differences in vaginal pH and gestational age between the groups were analysed using the Mann-Whitney U test because data had violation of normality assumption.

Results

In this study, 105 preterm labour pregnancies were enrolled and examined. The majority of patients had a high school level of education (59.1%), lived in Chanthaburi Province (89.5%) and were unemployed (45.7%). They had low and normal pre-gestational BMI at 32.4% and 39%, respectively. The BV and non-BV groups were similar for baseline and antenatal characteristics (Table 2).

Table 2. Baseline and antenatal characteristics.

Characteristics*	BV status		p value
	BV group (n = 75)	Non-BV group (n = 30)	
Pre-gestational overweight*	24 (32.0%)	6 (20.0%)	0.108
Nulliparous	30 (40.0%)	14 (40.7%)	0.662
Anaemia	35 (46.7%)	12 (40.0%)	0.665
Maternal age (years)**	25.6 ± 6.8	26.0 ± 7.2	0.723
Hematocrit (%)**	33.1 ± 3.9	34.2 ± 3.5	0.200
Gestational age (weeks)**	33.6 ± 3.0	32.7 ± 3.7	0.333†

* BMI ≥ 23.0 kg/m^2 (Asia), ** Mean ± SD, † Mann-Whitney U test

The prevalence of BV diagnosed utilising the Nugent criteria from University of British Columbia was 71.4%, while 29 cases (27.6%) had a Nugent score ≥7. Mean of vaginal pH in the BV group was higher than in the non-BV group (5.97±0.40 and 5.20±0.36, respectively, z=6.674, p < 0.001).

All diagnosed BV patients were orally treated with metronidazole and 48% delivered during the same visits comparable to 66.7% of non-BV patients (p = 0.129). The most common reasons for preterm deliveries included advanced cervical change, failure to inhibit following preterm labour practice guidelines, and fetal/maternal complications.

Discussion

BV during pregnancy is usually associated with a fishy-smelling discharge and is difficult to diagnose using Amsel's reproductive age standard criteria. The vaginas of pregnant women had a wider range of pH value than women who weren't pregnant. The three main causes of this phenomenon include a dramatic increase of the hormone circulated concentration from placental production[15], decreasing bacterial variety[16] and the reduction of vaginal lactobacilli producing lactate and H_2O_2[17]. In unnecessary cases, providing antibiotics can promote resistance to bacteria in the future.

The authors were interested in the changes of vaginal pH in preterm labour patients with BV. Thus, the study design invigilated confounding factors such as the premature rupture of amniotic membranes, bleeding from the genital tract and sexual intercourse within 72 hours. Our observations found that the prevalence of BV in pregnancy was higher than recorded at Siriraj Hospital (71.4% and 25.8%, respectively) because of different gestational age criteria and tools. The Siriraj Hospital study included gestational ages between 28^{+0}-36^{+6} weeks using the BVBlue test[8] (detection and measurement of microbial enzymes, sialidases: present among bacteria, viruses, mycoplasmas, fungi and protozoa)[18], whereas our study was conducted at gestational ages between 24^{+0} - 36^{+6} weeks using the Nugent criteria from University of British Columbia. However, the prevalence of BV was similar to the study by Siriraj and another study in Rio de Janeiro (27.6%, 25.8% and 28.1% respectively) if diagnosed by Nugent score ≥ 7[8,19]. Comparing the potential diagnostic tools, the BVBlue test is quick, easy and independent of personal skill, but it can be unspecified. In our opinion, standard benchmarks such as Amsel's criteria, Nugent score and bacterial culture may be more beneficial.

The mean vaginal pH of both BV and non-BV groups were higher than the cut-off point for Amsel's criteria, but within the normal range for vaginal pH in pregnancy. However, the mean vaginal pH in the BV group was still significantly higher than in the non-BV group. This implied that changes in bacterial flora could elevate vaginal pH with the decrease in lactic acid from Lactobacillus species and increase susceptibility to infections due to the impairment of the natural protective mechanisms of the vagina. In our opinion, the cut-off point for Amsel's criteria used in preterm pregnancy may be higher than non-pregnant women.

Interestingly, vaginal pH in preterm labour may be affected by nationality. Royce, et al., reported that the vaginal pH and flora differed by race/ethnicity[20]. While the mean vaginal pH of all non-BV patients in our study was lower than the vaginal pH of all preterm deliveries recorded by Gleeson et al. (5.20 and 5.43, respectively)[13]. In our opinion, the effect of nationality on vaginal pH should be investigated and confirmed by further studies.

Our study compared vaginal pH between BV and non-BV patients by controlling the most common confounding factors that interfere with the acid-base value. However, there were some limitations. We used wide-range pH test papers to measure vaginal pH. Further, the sample size was too small for a diagnostic study.

Conclusion

Our study determined that vaginal pH in the BV group was higher than in the non-BV group. Further studies should investigate the diagnostic value of a new vaginal pH cut-off point using Amsel's criteria for

uncomplicated preterm labour.

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Potential conflicts of interest

The authors declare no conflict of interest.

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OBSTETRICS

Efficacy of Oral Isosorbide Mononitrate Sustained-release for Pre-induction Cervical Ripening in Term Pregnant Women in an Outpatient Setting: A randomized controlled trial

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ABSTRACT

Objectives: To compare the efficacy of 60 mg oral, sustained-release, isosorbide mononitrate (ISMN SR) with a control for improve pre-induction cervical ripening of term pregnant women in an outpatient setting.

Materials and Methods: In this randomized controlled, superiority trial, 36 women with uncomplicated singleton pregnancy at ≥ 39 weeks gestation and unfavorable cervix attending the antenatal care clinic at Khon Kaen Hospital were randomly assigned to (a) two oral 60 mg doses of ISMN SR every 24 h (n=18) prior to admission for induction of labor or (b) a control group (n=18). The primary outcome was the proportion of favorable cervix on admission. The secondary outcomes were (a) changes in the Bishop score, (b) time from admission to delivery, and (c) neonatal and maternal outcomes.

Results: Demographic characteristics were similar between the groups. The proportion of favorable cervix at 48 h after oral ISMN SR was significantly greater than the control group (0.61 vs 0.17, p = 0.008, RR = 7.85, 95%CI 1.65-37.40). The mean change in the Bishop score was significantly higher in the ISMN SR group than the control (6.05 vs 2.71, p = 0.022). The time from admission to delivery in the ISMN SR was also less than the control (10 vs 23 h, p = 0.002). However, there was no respective significant difference in the rate of cesarean section, maternal complications, or neonatal outcomes.

Conclusion: Our study provides evidence that pre-induction of cervical ripening with 60 mg of oral ISMN SR among outpatient, term pregnant women is effective and with no observed adverse outcomes.

Keywords: cervical ripening, isosorbide mononitrate SR, term pregnancy, induction of labor, outpatient setting

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การศึกษาประสิทธิภาพของการรับประทานยาไอโซซอร์ไบด์ โมโนไนเตรท เอสอาร์ เพื่อการกระตุ้นปากมดลูกให้พร้อมก่อนการชักนำคลอดในสตรีมีครรภ์ครบกำหนดแบบผู้ป่วยนอก

ชื่ณ เชาว์ตระกูล, ศุภศิริ หะยะกังฉัตร์, ทุมวดี ตั้งศิริวัฒนา

บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาประสิทธิภาพในการเตรียมความพร้อมของปากมดลูกก่อนการชักนำคลอดในสตรีตั้งครรภ์ที่มีอายุครรภ์ตั้งแต่ 39 สัปดาห์ ที่ได้รับประทานยา ไอโซซอร์ไบด์ โมโนไนเตรท เอสอาร์ (ISMN SR) 60 มก. เหนือกว่ากลุ่มควบคุมในรูปแบบผู้ป่วยนอก*

วัสดุและวิธีการศึกษา: *สตรีตั้งครรภ์อายุครรภ์ตั้งแต่ 39 สัปดาห์ และฝากครรภ์ที่ รพ.ขอนแก่น เข้าร่วมการวิจัยแบบผู้ป่วยนอก จำนวนทั้งหมด 36 คน ได้รับการสุ่มและแบ่งเป็น 2 กลุ่ม ได้แก่ กลุ่มที่ได้รับประทานยา ISMN SR 60 มก. จำนวน 18 คน และกลุ่มควบคุมจำนวน 18 คน จากนั้นนัดติดตามเพื่อวัดสัดส่วนความพร้อมของปากมดลูกและชักนำการคลอดหลังเข้าร่วมการวิจัย 48 ชม.*

ผลการวิจัย: *ลักษณะทางประชากรศาสตร์ไม่แตกต่างกันระหว่างกลุ่ม โดยกลุ่มที่ได้รับประทานยา ISMN SR มีสัดส่วนความพร้อมของปากมดลูกมากกว่ากลุ่มควบคุม ร้อยละ 61 และ ร้อยละ 17 ตามลำดับ ซึ่งมีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ (p = 0.008, RR = 7.85, 95%CI 1.65-37.40) นอกจากนั้นกลุ่มที่รับประทานยามีค่าเฉลี่ยความพร้อมของปากมดลูกเพิ่มขึ้นและลดระยะเวลาในการเริ่มนอนโรงพยาบาลจนถึงคลอดได้อย่างมีนัยสำคัญทางสถิติ (p = 0.022 และ 0.002 ตามลำดับ) อย่างไรก็ตามอัตราการผ่าตัดคลอด และภาวะแทรกซ้อนต่อมารดาและทารกทั้งสองกลุ่ม ไม่มีความแตกต่างกัน*

สรุป: *สตรีตั้งครรภ์ครบกำหนดที่ได้รับประทานยา ISMN SR 60 มก. มีประสิทธิภาพและความปลอดภัยในการกระตุ้นความพร้อมของปากมดลูกก่อนการชักนำการคลอดในสตรีตั้งครรภ์ครบกำหนดได้ในแบบผู้ป่วยนอก*

คำสำคัญ: *ความพร้อมของปากมดลูก, ไอโซซอร์ไบด์ โมโนไนเตรท เอสอาร์, สตรีตั้งครรภ์ครบกำหนด, การเหนี่ยวนำคลอด, ผู้ป่วยนอก*

Introduction

Post-term pregnancy is defined as a pregnancy with a gestational length of ≥ 294 days[1], which occurs in 17% of all births at Khon Kaen Hospital, and is associated with a respective increased rate of multiple maternal and fetal complications[2]. Elective labor induction plays an important role in reducing the risk of adverse outcomes without increasing the risk of operative delivery. According to The American College of Obstetricians and Gynecologists, elective induction may be considered for logistical or psychosocial reasons but not before 39 0/7 weeks of gestation[3].

To our knowledge, cervical ripening is one of the essential factors predicting success of labor induction. Favorable pre-induction cervix is a predictive factor of successful vaginal delivery[3].Various prostaglandin regimens, especially the PGE1 analogue (misoprostol), are commonly recommended for ripening the cervix[4]. Five percent of women, however, have uterine hyper-stimulation after administration of prostaglandin, causing changes in fetal heart rate[5]. For this reason, cervical ripening is conducted on an in-patient basis so that the fetus can be monitored during the process. Since serious maternal and fetal adverse events caused by prostaglandins have been observed, safer and cost-effective cervical-ripening agents have been sought for decades. The ideal cervical ripening agent would induce adequate cervical ripening (soft and thin) without causing uterine contractions[3]; as the lack of contractions obviates the need for fetal monitoring, and such an agent could be given on an outpatient basis. The advantages of outpatient cervical ripening include patient convenience, reduction of workload on labor and delivery units, and reduced hospitalization costs[6-9]. The 2017 Cochrane[10] report on different methods for the induction of labor in outpatient settings showed that it was feasible but that a trustworthy and effective protocol had not yet been established.

Nitric oxide donors (NODs) are free radical gases with a short half-life that acts as a relaxant for vascular or gastric smooth muscle and myometrium. In advanced term pregnancy, NODs are down-regulated in the myometrium but become up-regulated during the physiological process of cervical ripening[11,12]. Vaginal application of NODs is effective on pre-induction of the cervical ripening process of labor. NODs work directly through the stimulation of prostaglandin F2α and cyclooxygenase-2, releasing cytokines and inhibiting thromboxane-B2, which facilitates cervical ripening without any complications such as fetal distress[13]. A 2016 Cochrane review[14] confirmed that NODs can be a useful tool in the process of induction of labor causing favorable cervix compared to placebo. Thus, NODs are considered a fundamental mediator of cervical ripening in an outpatient setting since it is able to induce cervical ripening without causing uterine contractions or other maternal and fetal adverse effects of clinical importance[14,15].

Various studies have demonstrated that NODs for cervical ripening in an outpatient setting had a higher efficacy on vaginal isosorbide mononitrate (ISMN) than placebo and resulted in safe maternal and fetal outcomes[16-20]. Nevertheless, there were differences in drug form (sustained vs non-sustained release), dosage (2-3 doses), drug components (mono- vs di-nitrate) and time for assessment[16-20]. The drug application in most of the studies, moreover, used the vaginal route, which is more difficult to apply than oral administration. Haghighi, et al.[21] reported a statistically significant increase in the Bishop score for both the oral and vaginal isosorbide dinitrate (ISDN) (limited by first-pass metabolism) compared to the control group. Furthermore, the oral isosorbide mononitrate had a sustained release (ISMN SR), which means it has a longer duration of action than ISMN or ISDN and no first-pass metabolism limitation, for ripening cervix in term pregnancy in outpatient setting are absent. The aim of the current study was to evaluate the efficacy once-daily oral administration of 60 mg ISMN SR for cervical ripening prior to induction of labor in an out-patient term pregnancy setting.

Materials and Methods

This randomized controlled trial was conducted at the antenatal care clinic (ANC) at Khon Kaen Hospital, Thailand, between February and March,

2017. The Khon Kaen Hospital Institutional Review Board for Human Research reviewed and approved the study. All participants gave informed consent before being enrolled in the study.

We included pregnant women 18 years old and over at a gestational age of 39 weeks or more. This was a singleton pregnancy, cephalic presentation, with an unfavorable cervix (Bishop score of ≤ 6)[4]. We excluded pregnant women with a contraindication for vaginal delivery, labor pain, ruptured membranes, uterine scaring, pregnancy-induced hypertension or contraindication for ISMN administration (i.e., hypersensitivity or severe hypotension).

Eligible participants were randomized by computer-generated, block of four, and randomly assigned to two groups. Treatment packs containing 2 x 60 mg tablets of ISMN SR (Solotrate SR; ZydusCadila Healthcare Ltd, India) were prepared and numbered by the pharmacist. After each patient's baseline Bishop score was assessed and recorded by the first obstetric resident or staff, they were allocated-using sequentially numbered, sealed opaque envelopes (prepared by the second author who was not apprised of the Bishop score). Participants in study group were given two doses of 60 mg oral tablets of ISMN SR. The first dose was given at the ANC under direct supervision. The patients were instructed to take the second dose in 24 hours. The control group-with no intervention-was discharged after the antenatal care. All participants were asked to admit to the labor room 48 hours later. They had to return immediately if they felt any decrease in fetal movements, increased labor pains, vaginal bleeding, or sudden leakage of amniotic fluid.

Thirty minutes after drug administration, vital signs and a non-stress test were documented at the ANC before their being discharged. The dosage and the interval between the 2 doses was based on the pharmacokinetics of orally administered ISMN SR[22].

The Bishop score was recorded again on admission by one of the authors who were not a part of the investigation. This was thus a single-blind trial as the authors who assessed the Bishop score were not aware whether the participants were given oral ISMN SR or the control. Labor was induced by a 25-µg misoprostol vaginal suppository (Cytotec; Pfizer Inc, New York), which was inserted into the posterior fornix if the score was < 7 and without good uterine contraction. A repeated dose of misoprostol was administered 4 hours later if cervical ripening was insufficient or poor uterine contraction was observed. In those who had a Bishop score ≥ 7, a low-dose oxytocin infusion or 25-µg of misoprostol vaginal were used to augment labor. Induction failure was defined as the non-occurrence of the active phase of labor despite the 25-µg of misoprostol vaginal stimulation lasting at least 6 doses after induction of labor.

The primary outcome was the proportion of pregnant women who had favorable cervix on admission prior to induction of labor. The secondary outcomes included (a) the mean change in the Bishop score, (b) the time from admission to delivery, and (c) the mode of delivery. Other maternal outcomes, neonatal outcomes, and complications were recorded (presence or absence of tachycardia, hypotension, headache, nausea or vomit and dizziness, Apgar scores at 1 and 5 minutes and admission to the neonatal intensive care unit (NICU), uterine hyperstimulation, meconium-stained liquor, and postpartum hemorrhage).

This study used statistical test as superiority trial. The Chi-square test or Fisher's exact test was used as appropriate to analyze the categorical data (for proportion of favorable cervix, maternal, neonatal outcomes and complications). For continuous data, the Student t-test was used to assess the normal distribution continuous data while the Mann–Whitney U test was used to analyze the non-normal distribution continuous data.

Sample size in the current study was used for categorizing outcomes. This was based on a pilot study.

$$\text{N/ group} = \frac{(Z\alpha\sqrt{2pq} + Z\beta\sqrt{p1q1 + p2q2})^2}{(p1 - p2)^2}$$

p1 = Proportion of pregnant women who favorable cervix of ISMN SR group = 0.53

p2 = Proportion of pregnant women who favorable cervix of control group = 0.13

q1= 1 - p1	q2 = 1 - q2
α = 0.05	Zα = 1.64 (one-tailed test)
β = 0.8	Zβ = 0.84
p = (p1 + p2) / 2	q = 1 - p

We used a formula for testing an alpha of 0.05 and a power of 80%. The sample size in each group was 18 cases. $p < 0.05$ was considered statistically significant. Statistical analyses were performed using STATA 13 software.

Results

Thirty-six eligible women were enrolled into the study and were randomized to receive oral the ISMN SR treatment or the control (18 each) (Fig. 1). There were no significant differences in the maternal demographic and obstetric characteristics (i.e., maternal age, parity, gestational age, and baseline Bishop Score) between the two groups (Table 1).

The proportions of favorable cervix after 48 hours (Table 2) in the oral ISMN SR group (0.61) was significantly greater compared to the controls (0.17, p = 0.008, RR = 7.85, 95%CI 1.65-37.40). With respect to secondary outcomes (Table 2), there was significant increase in the change of the Bishop Score in the ISMN SR group (6.05 ± 2.71) compared to the control after 48 hours (3.72 ± 3.12, $p < 0.05$). The time from admission to delivery in the ISMNSR group was significantly shorter than the control group (10 vs. 23 hours, $p < 0.05$). The percentage of women who required misoprostol for secondary cervical ripening was significantly lower in the intervention group. The mode of delivery was similar between groups. The indication for cesarean delivery in both groups was failed induction.

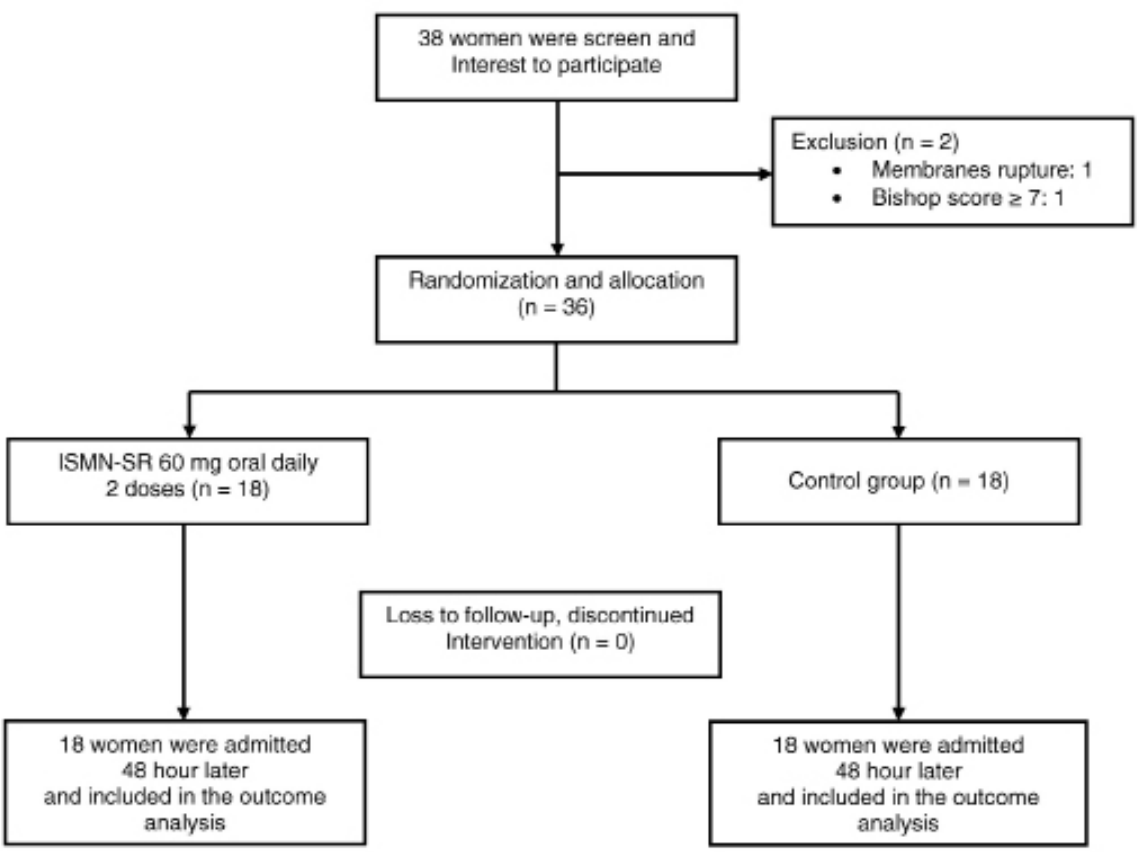

Fig. 1. Flow chart of the study participants.

Table 1. Demographic characteristics.

Characteristics	ISMN SR (n = 18)	Control (n = 18)
Age (years), mean (SD)	26.2 (3.9)	25.0 (5.2)
Parity		
Nulliparous, no. (%)	9 (50.0)	10 (55.6)
Multiparous, no. (%)	9 (50.0)	8 (44.4)
Gestationalage (days), mean (SD)	278 (4)	277 (3)
Baseline Bishop score		
0-1, no. (%)	15 (83.3)	16 (88.9)
2-3, no. (%)	3 (16.7)	2 (11.1)
4-6, no. (%)	0	0
BMI (kg/cm^2), mean (SD)	21.1 (1.9)	20.4 (2.0)

ISMN SR: isosorbide mononitrate sustained release, BMI: body mass index

Table 2. Primary and secondary outcomes.

Duration of delivery	ISMN SR (n = 18)	Control (n = 18)	p value
Primary outcome			
Favorable cervix, no. (%)	11 (61.1)	3 (16.7)	0.008
Secondary outcomes			
Change in Bishop score, mean (SD)	6.1 (2.7)	3.7 (3.1)	0.022
Time admission to delivery (hours), median (IQR)	10 (8,15)	23 (16,29)	0.002
Vaginal Delivery achieved in 24 hour, no. (%)	16 (88.9)	9 (50.0)	0.014
Routes of delivery			1.000
Vaginal delivery, no. (%)	17 (94.4)	17 (94.4)	
Cesarean section, no. (%)	1 (5.6)	1 (5.6)	
Use of misoprostol, no. (%)	7 (38.9)	15 (83.3)	0.008
Use of oxytocin, no. (%)	12 (66.7)	7 (38.9)	0.091

ISMN SR: isosorbide mononitrate sustained release

Table 3 shows no significant difference in birth weight and no cases of fetal distress or Apgar scores < 7 at 1 and 5 minutes, meconium at the time of ruptured membrane, or neonatal ICU admission between groups. There were no serious side effects of ISMN SR and none of the participants denied taking the second dose. The most common side effects experienced in the ISMN SR group were headache, which was relieved by oral analgesics. One woman (5.6%) in the ISMN SR group and 2 in the control group had uterine atony (11.1%), which did not develop into a postpartum hemorrhage. There were no cases of palpitation, uterine hyperstimulation, or changes in vital signs from the baseline that required treatment in either group.

Table 3. Maternal complications and neonatal outcomes.

Outcomes	ISMN SR (n = 18)	Control (n = 18)	p value
Maternal complications			
Uterine hyper-stimulation	0	0	1.000
Uterine atony, no. (%)	1 (5.6)	2 (11.1)	0.500
Headache, no. (%)	2 (11.1)	1 (5.6)	0.500
Nausea/ Dizziness, no. (%)	1 (6.7)	0	0.500
Palpitation, no. (%)	0	0	1.000
Neonatal outcomes			1.000
Neonatal birth weight (g), mean (SD)	3,145 (285)	3,173 (320)	0.695
Fetal non-reassuring, no. (%)	0	0	1.000
Meconium stained AF, no. (%)	0	1 (5.6)	0.500
Birth asphyxia (Apgar ≤ 7)			
At 1 min, no. (%)	0	1 (5.6)	0.500
At 5 min, no. (%)	0	0	1.000
Admission to NICU, no. (%)	0	0	1.000

ISMN SR: isosorbide mononitrate sustained release, AF: Amniotic fluid, NICU: neonatal intensive care unit

Discussion

In the present study, the superior efficacy of oral ISMN SR over the control was demonstrated by the cervix was favorable and the Bishop score had changed. This was consistent with Cochrane review 2016(14) as well as other studies on the use of vaginal ISMN SR administration for in-patients[23,24] and other out-patient vaginal NODs with a control group or placebo[16-18]. The reason for the high efficacy of nitric oxide in cervical ripening—apart from stimulation of prostaglandin F2α and cyclooxygenase-2, releasing of cytokines, and inhibiting of thromboxane-A2—is that it could facilitate an increasing level of physiologic cervical nitric oxide metabolites[13]. In contrast with Schmitz et al[19], and Bullarbo et al[20], studies, they reported that the change in the Bishop score was not significantly different. These could be explained by the dosage, drug form, and duration of action which were inadequate. About the route of drug administration: the first report, Haghighi et al., regarding the oral route of ISDN, similar results to our study, gave a significantly higher efficacy as defined by the mean change in the Bishop score over the control group[21]. Moreover, oral ISMN SR, suitable than oral ISDN, does not undergo first-pass metabolism.

The mean time from admission to delivery was also significantly shorter in the study group which was consistent with several previous studies[16,18,20,23,24]. Notwithstanding, Bollapragada et al[17], and Schmitz et al[19], found no significant reduction in the study group which might be explained by the use of low-dose ISMN and that most of their participants were beyond term which lowers nitric oxide metabolites in the cervical fluid[25].

The cesarean delivery rate was similar between groups, and in most recent outpatient studies comparing other NODs to placebo or control[16-20, 24].

The most common adverse effect in the study group was mild headache, which was found in other studies both outpatients[16-20] and inpatients[23, 24], and there were no major adverse effects in either the maternal or fetal hemodynamic. Oral ISMN SR

treatment in the present study induced neither uterine hyperstimulation nor abnormal fetal heart rate; as was observed in all of previous studies[21].

In the present study, most of the participants reported satisfaction with the oral route of administration and as an outpatient treatment. This is because of the advantage of not being hospitalized for cervical ripening and the simply route of administration which outweighed the minor adverse effects of the treatment as previously described[6, 8]. The oral ISMN SR prescription apparently results in a significant improvement in the proportion of favorable cervix for pre-induction and to a decrease in the usage of misoprostol, as well as a decrease in the length of induction for labor until delivery which are associated with a decrease in the risk of maternal and fetal adverse outcomes (from post-term pregnancy and side effect of other cervical ripening agent such as misoprostol)[6, 8]. The most important advantage was the convenience of drug administration.

Strengths of the study

The current study reduced bias by designing a randomized controlled trial and blinding the outcome to assessors. Our primary outcome was a statistically significant result from 30 participants; a number based on a pilot study with superior trial, and the known high efficacy of ISMN SR for cervical remodeling. There were no dropouts in the current study, suggesting a non-stressful and convenient process.

Conclusion

Sixty milligrams of oral ISMN SR administered at home is safe and effective for cervical ripening prior to induction of labor in term pregnant women without any evidence of maternal or fetal adverse outcomes.

Acknowledgements

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Potential conflicts of interest

The authors declare no conflict of interest.

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OBSTETRICS

Percentage of Pregnant Women Reading the Maternal and Child Health Handbook and Associated Factors at Srinagarind Hospital

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ABSTRACT

Objectives: To evaluate the percentage of pregnant women who read the maternal and child health handbook (MCHH) at Srinagarind hospital, associated factors, attitudes toward the MCHH and to compare maternal knowledge between handbook readers and non-readers.

Materials and Methods: This was a cross-sectional study conducted from September 2016 to March 2017. All primigravida pregnant women who had been given the MCHH at least for one month previously were included. A questionnaire-based interview was conducted for evaluating the percentage of participants who read the MCHH and associated factors. "Read" meant the participants had read more than 50% of the MCHH's contents and at least four of the eight topics.

Results: Out of 317 pregnant women, 206 (65%) read the MCHH. The most read item was dietary recommendations (78.2 %). The two least read items were iodine deficiency disease and prevention of mother to child transmission of HIV (49.5 %). The participants who read the MCHH were 2.5 times more likely to pass the exam than who did not. The most influential factor affected the reading of the MCHH was "reading prior current pregnancy". The top two reasons for not reading the MCHH were choosing to receive the information from other sources and the style of the handbook not being attractive.

Conclusion: The percentage of participants who read the MCHH in Srinagarind Hospital was 65%. The factor that affected the reading of the MCHH was "reading prior current pregnancy". Moreover, women who read the MCHH had a more knowledge about pregnancy compared with those who did not.

Keywords: read, maternal and child health handbook, pregnant women

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ร้อยละของสตรีตั้งครรภ์ที่อ่านสมุดบันทึกสุขภาพแม่และเด็ก และปัจจัยที่เกี่ยวข้อง, โรงพยาบาลศรีนครินทร์

วรรณรัตน์ อัตถากร, ปิยะมาศ ศักดิ์ศิริวุฒโฆ

บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาจำนวนร้อยละของการอ่านสมุดบันทึกสุขภาพแม่และเด็กในสตรีตั้งครรภ์ที่มาฝากครรภ์ที่โรงพยาบาลศรีนครินทร์ รวมถึงปัจจัยที่สัมพันธ์กับการอ่าน ความคิดเห็นต่อสมุดฯ และเปรียบเทียบความรู้เกี่ยวกับการตั้งครรภ์ในสตรีตั้งครรภ์ที่อ่านกับไม่อ่านสมุดบันทึกสุขภาพแม่และเด็ก*

วัสดุและวิธีการ: *การศึกษาแบบ Cross sectional descriptive study ที่ทำการศึกษาในช่วงระหว่างเดือนกันยายน 2559 ถึง เดือนมีนาคม 2560 โดยศึกษาในสตรีตั้งครรภ์แรก ที่มาฝากครรภ์ที่ห้องฝากครรภ์ในโรงพยาบาลศรีนครินทร์และได้รับสมุดบันทึกสุขภาพแม่และเด็กที่ออกโดยกระทรวงสาธารณสุขไปแล้วอย่างน้อย 1 เดือน ทั้งนี้ใช้วิธีการตอบแบบสอบถามด้วยตนเอง แบบสอบถามและงานวิจัยได้ผ่านการพิจารณาจากสำนักงานคณะกรรมการจริยธรรมการวิจัยในมนุษย์มหาวิทยาลัยขอนแก่น การ "อ่าน" ในการศึกษานี้ คือ ผู้ทำแบบสอบถามประเมินตนเองว่า อ่านมากกว่าร้อยละ 50 ของเนื้อหาทั้งหมดในหัวข้อนั้นๆ และอ่านมากกว่าหรือเท่ากับ 4 หัวข้อจากทั้งหมด 8 หัวข้อ*

ผลการศึกษา: *จากอาสาสมัครผู้เข้าร่วมงานวิจัยจำนวนทั้งสิ้น 317 คน พบว่าสตรีตั้งครรภ์จำนวน 206 คน หรือคิดเป็นร้อยละ 65 ได้อ่านสมุดบันทึกสุขภาพแม่และเด็ก หัวข้อที่ได้รับการอ่านมากที่สุดคือ ข้อปฏิบัติการกินอาหารของหญิงตั้งครรภ์ (ร้อยละ 78.2) ส่วนสองหัวข้อที่ได้รับการอ่านน้อยที่สุดคือโรคจากการขาดไอโอดีน และการป้องกันการแพร่เชื้อเอชไอวีจากแม่สู่ลูก (ร้อยละ 49.5) อาสาสมัครในกลุ่มที่อ่านสมุดบันทึกสุขภาพแม่และเด็กทำแบบทดสอบผ่านเกณฑ์ที่กำหนดมากเป็น 2.5 เท่าเมื่อเทียบกับกลุ่มที่ไม่อ่านสมุดฯ ส่วนปัจจัยที่มีความสัมพันธ์กับการอ่านมากที่สุดคือ การเคยได้อ่านสมุดฯตั้งแต่ตอนก่อนตั้งครรภ์ ซึ่งสัมพันธ์กับการอ่านสมุดบันทึกสุขภาพแม่และเด็กที่มากขึ้นในขณะตั้งครรภ์ สาเหตุที่พบว่าทำให้สตรีตั้งครรภ์ไม่อ่านสมุดบันทึกสุขภาพแม่และเด็กมากที่สุดคือ การเลือกรับข้อมูลจากแหล่งความรู้อื่นมากกว่าและรองลงมาคือรูปเล่มไม่น่าสนใจ*

สรุป: *การอ่านสมุดบันทึกสุขภาพแม่และเด็กในสตรีตั้งครรภ์ที่มาฝากครรภ์ที่โรงพยาบาลศรีนครินทร์คิดเป็นร้อยละ 65 ส่วนปัจจัยที่มีความสัมพันธ์กับการอ่านมากที่สุดคือ การเคยได้อ่านสมุดฯตั้งแต่ตอนก่อนตั้งครรภ์ นอกจากนี้ยังพบว่าสตรีตั้งครรภ์ในกลุ่มที่อ่านมีความรู้เกี่ยวกับการตั้งครรภ์มากกว่ากลุ่มที่ไม่อ่าน*

คำสำคัญ: *การอ่าน, สมุดบันทึกสุขภาพแม่และเด็ก, สตรีตั้งครรภ์*

Introduction

Figures from the Department of Provincial Administration registration unit indicated that the population of Thailand in 2016 was 65,931,550 with a birth rate of around 704,000 people per year. The Maternal and Child Health Handbook (MCHH) was first published in 1985 to promote the health of pregnant women and children. Since then, the handbook has been periodically revised and updated to meet the evolving needs of both healthcare providers and users with the latest edition published in 2014. Contents include records of antenatal care examinations, information regarding the correct practices during pregnancy, pertinent information related to delivery, records of postpartum examinations, a child growth chart (weight and height) and child development and immunization records. The MCHH assists parents and healthcare providers to understand the importance of maternal, neonatal and child healthcare continuity. Using this handbook, parents can record their child's health details throughout the processes of pregnancy, delivery and child development. The MCHH is also useful as a reference document when a pregnant woman or child requires referral to another hospital[1].

However, despite the usefulness of the MCHH, insufficient data exists regarding the number of parents who read the handbook in Thailand, especially in the northeast of the country. A few studies were conducted to assess the number of pregnant women following MCHH guidelines in Central Thailand. They determined that the percentage of handbook readers was low[2].

This research project evaluated the percentage of pregnant women who read the MCHH, and also investigated associated factors including a comparison of the maternal knowledge of handbook readers and non-readers and also attitudes towards the MCHH by pregnant women who attended an antenatal care clinic at Srinagarind Hospital.

Materials and Methods

This cross-sectional study was conducted from September 2016 to March 2017. A total of 317 pregnant women were included and sample size was calculated using data collected by Aihara[2] in Kanchanaburi. Population proportion was 0.72 and precision errors of estimation were approximately 5%.

All primigravida pregnant women who attended the antenatal care clinic at Srinagarind Hospital, Khon Kaen University were given the MCHH at least one month before study recruitment. Pregnant women who could not read and write in Thai were excluded. After reading the information sheet, the subjects were required to give fully informed consent. A questionnaire developed based on the latest version of the MCHH was explained to the participants by nurses. The contents of the questionnaire consisted of four sections as follows:

1. Maternal characteristics (including gestational age, maternal age, education, marital status, occupation, residency, income, number of antenatal visits, gestational age of first antenatal care).

2. Topics were presented in the MCHH as eight main chapters. Answers include "read less than 50%," "read greater than or equal to 50%," "read 100%" and "did not read." Participants who answered "did not read" were asked to identify their sources of information regarding the subject matter.

3. Twenty questions concerning the contents of the MCHH were asked to test participants' knowledge after answering the second section. A result of "pass" indicated that participants had answered questions concerning four or more of the eight chapter topics successfully. Results were compared between participants who read the MCHH and those who did not.

4. Opinions concerning the MCHH.

When the participants had completed the questionnaire, logistic regression and multivariate analyses were performed using SPSS 19.0. The research protocol was reviewed and approved by the Khon Kaen University Ethics Committee, Faculty of Medicine.

The "read" group consisted of participants who had read more than 50% of the handbook or at least four of the eight chapters contained therein.

Results

A total of 317 pregnant women were included. Maternal characteristics are shown in Table 1. Mean gestational and maternal ages were 30.2 weeks and 29.1 years respectively. The majority of the women was married (96.8%) and had bachelor degrees or higher (53.6%). Most were civil servants (37.9%), lived in rural areas (53.9%) and had monthly incomes of less than 15,000 baht. The mean number of antenatal visits was seven and mean gestational age at the first antenatal care session was 10.3 weeks.

Table 1. Maternal characteristics (N 317).

Characteristic	Value
Gestational age (weeks): Mean ± SD	30.2 ± 7.1
Maternal age (years): Mean ± SD	29.1 ± 5.4
Education: n (%)	
Primary/ secondary school or lower	147 (46.4)
Bachelor degree or higher	170 (53.6)
Marital status: n (%)	
Married	307 (96.8)
Single/ Divorced/Widowed	10 (3.2)
Occupation: n (%)	
Student	5 (1.6)
Businessperson	58 (18.3)
Office employee	71 (22.4)
Agriculturist	15 (4.7)
Civil servant	120 (37.9)
Housewife	45 (14.2)
Others	3 (0.9)
Residency: n (%)	
Urban area	146 (46.1)
Rural area	171 (53.9)
Income: n (%)	
≤ 15,000 baht	190 (59.9)
> 15,000 baht	127 (40.1)
Number of antenatal visits: Mean ± SD	7 ± 3.1
Gestational age at first antenatal care session (weeks): Mean ± SD	10.3 ± 5.7

From the 317 pregnant women who participated, 206 (65%) had read the MCHH. The eight chapters in the MCHH were evaluated by the participants (Table 2). These included dietary recommendations, fetal development, maternal practices during pregnancy, thalassemia, maternal discomforts during pregnancy, family planning, iodine deficiency disease and prevention of mother to child transmission of HIV. The

most read chapter was dietary recommendations (78.2%). The two equally least read chapters were iodine deficiency disease and prevention of mother to child transmission of HIV (49.5%).

The third section evaluated participants' knowledge of the material contained in the handbook. Those who had read the MCHH were 2.5 times more likely to pass the exam than those who had not (OR: 2.5, 95%CI: 1.39 - 4.69, p = 0.002).

Many factors influenced whether or not the participants read the MCHH. Table 3 shows the results of the logistic regression and multivariate analyses. Factors included "reading prior to current pregnancy", "age", "education" and "income." The most influential factor was "reading prior to current pregnancy" (OR: 2.90, 95%CI: 1.40-6.02, p = 0.004) which was also associated with an increased rate of reading during pregnancy. Other factors were not related. The top three reasons for not reading the MCHH were choosing to receive the information from other sources, the style of the handbook not being attractive and being too busy (Table 4).

Table 2. Percentage of participants reading each chapter in the MCHH (N 317).

Chapter	Read n (%)
Dietary recommendations	248 (78.2)
Fetal development	238 (75.1)
Maternal practices during pregnancy	229 (72.2)
Thalassemia	199 (62.8)
Maternal discomforts during pregnancy	192 (60.6)
Family planning	184 (58.0)
Iodine deficiency disease	157 (49.5)
Prevention of mother to child transmission of HIV	157 (49.5)

Table 3. Factors determining reading the MCHH (N 317).

Factor	Read MCHH	Crude OR (95% CI)	Adjusted OR (95% CI)
Reading prior to current pregnancy: n (%)			
Yes	201 (63.4)	2.69 (1.22-5.94)	2.90 (1.40-6.02)
No	98 (30.9)		
Unknown	18 (5.7)		
Age: Mean ± SD	30.2 ± 7.1	1.07 (0.97-1.17)	1.04 (0.96-1.13)
Education: n (%)			
Primary school/ secondary school or lower	147 (46.4)	1.74 (1.05-2.87)	0.59 (0.23-1.50)
Bachelor degree or more	170 (53.6)		
Income: n (%)			
≤ 15,000 baht	190 (59.9)	1.31 (0.78-2.20)	1.72 (0.68-4.35)
> 15,000 baht	127 (40.1)		

Table 4. Reasons for not reading the MCHH (N 317).

Reason	%
Choosing to receive the information from other sources	28.6
Style of the handbook was not attractive	22.7
Too busy	17.5
Already knew the contents of the MCHH	13.0
Too much detail or too many pages	8.9
Others	9.3

* Remark: participants could select more than one reason

Discussion

Pregnancy is one of the most important periods of women's lives. Pregnant women, their partners and their families hope for the health of both the mother and the infant. The MCHH plays an important role in improving the health of children and pregnant women in Thailand. Result from this study was similar to findings of previous studies[3–5] and determined that participants who read the MCHH had greater knowledge than those who did not.

Previous authors found a low incidence rate of reading the MCHH in Thailand and a survey conducted in 2005 determined this at only 14.3%[2]. In contrast, a study conducted in Japan in 1999 found the reading rate to be 98.3%[1].

In our study, the MCHH reading rate was 65%, higher than found in previous studies conducted in Thailand. The difference may be due to participants' attendance at parental classes held every morning at Srinagarind Hospital antenatal care clinic which emphasized the importance of reading the handbook. Factors that affected whether or not participants read the MCHH were also evaluated. Results showed that participants who read prior to their current pregnancy were 2.9 times more likely to read during their pregnancy. This finding differed from other authors. Kawakatsu[6] determined that maternal age, health knowledge and household wealth index were related to the rate of reading, while Mori[7] indicated that higher socioeconomic status affected usage of the handbook. Similarly, we found that a significant benefit of reading the MCHH was improved the knowledge regarding pregnancy.

We tested the participants' knowledge; results showed that those who had read the MCHH were more likely to pass the exam compared with those who had not. Pregnant women who read the MCHH had increased pregnancy knowledge. We strongly believe that improved knowledge will enhance maternal health awareness and encourage mothers to seek appropriate healthcare services before complications occur.

We also explored the reasons why pregnant women did not read the MCHH. The two most important reasons were cited as the ability to receive information from the internet or television and the style of the handbook was not attractive.

Our study explored each chapter topic in detail, whereas previous studies[2,8] only assessed results of reading the whole book. The most read chapter was dietary recommendations with least read as iodine deficiency disease and prevention of mother to child transmission of HIV. Healthcare providers or health stakeholders can use our data to better understand reasons why some chapters are read more than others and help to improve the quality of the handbook.

Pregnant women who had received the MCHH for at least one month were included in the study. However, no exact duration was specified. Pregnant women with access to the MCHH for many months had more time to read and study the chapters than others. Time of study may influence participants' knowledge of the material.

Further studies should focus on the relationship

between reading duration and maternal knowledge. In addition, studies should be conducted concerning alternative methods of transmitting maternal knowledge. Those women who did not read the handbook stated the reason as access to other data sources such as the internet or television.

Clinical applications of our results can promote the reading of the MCHH, not only for pregnant women but also non-pregnant women and family members, especially with regard to the chapters that had lower reading rates.

Conclusion

The percentage of participants who read the MCHH in Srinagarind Hospital was 65%. The most read chapter was dietary recommendations and the least read were iodine deficiency disease and prevention of mother to child transmission of HIV. The factor that most affected whether or not participants read the MCHH was "reading prior to current pregnancy." The two most important reasons given by pregnant women as to why they did not read the MCHH were that they received the information from the internet or television and that the style of the handbook was not attractive.

Potential conflicts of interest

The authors declare no conflict of interest.

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OBSTETRICS

Prevalence and Risk Factors of Birth Asphyxia among Elderly Gravidarum

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ABSTRACT

Objectives: To investigate the prevalence and risk factors of birth asphyxia in pregnancies with advanced maternal age.

Materials and Methods: This study involved a retrospective cohort with a nested case-controlled study. Data were collected at Rajavithi Hospital. The prevalence of birth asphyxia was investigated using a retrospective cohort study of cases from January 2012 to June 2016. Antepartum factors, intrapartum factors and postpartum and newborn factors were studied using a nested case-controlled approach that involved the random matching and analysis of the results according to these factors.

Results: The prevalence of birth asphyxia of advanced maternal age group in this study was 11.7%. The statistically significant risk factors included number of antenatal care (ANC) < 4 visits (adjusted OR 1.64, 95% CI 1.18-2.26), hypertensive disorders (adjusted OR 1.94, 95% CI 1.42 -2.65), placenta previa (adjusted OR 4.58, 95% CI 2.74-7.68), PROM > 18 hours (adjusted OR 3.71, 95% CI 1.98 – 6.98), non-cephalic presentation (adjusted OR 1.95, 95% CI 1.34-2.84), and non-reassuring intrauterine fetal status (adjusted OR 3.35, 95% CI 2.22-5.06). There were no significant risk factor at diabetes disorders (95%CI 0.84-1.42, p = 0.50), meconium stained amniotic fluid (95%CI 0.64-1.73, p = 0.830), administration of analgesic drug (95%CI 0.59-1.91, p = 0.839), and nuchal cord (95%CI 0.59-1.27, p = 0.453).

Conclusion: Birth asphyxia at Rajavithi Hospital was 11.7%. The statistically significant risk factors associated with birth asphyxia were number of ANC < 4 visits, hypertensive disorders, placenta previa, a PROM > 18 hours, non-cephalic presentation, and non- reassuring fetal status or fetal distress.

Keywords: birth asphyxia, advanced maternal age, risk factor.

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ความชุกและปัจจัยเสี่ยงสำหรับภาวะทารกแรกเกิดขาดออกซิเจนในหญิงตั้งครรภ์ที่อายุมากกว่าหรือเท่ากับ 35 ปี

อภิรักษ์ หงวนบุญมาก, สมบูรณ์ ศรศุกลรัตน์

บทคัดย่อ

วัตถุประสงค์: *การศึกษานี้มีวัตถุประสงค์เพื่อสืบค้นความชุกและปัจจัยเสี่ยงสำหรับภาวะทารกแรกเกิดขาดออกซิเจนในหญิงตั้งครรภ์ที่อายุมากกว่าหรือเท่ากับ 35 ปี*

วัสดุและวิธีการ: *การศึกษานี้เป็นชนิด retrospective cohort with nested case – controlled study ข้อมูลถูกเก็บรวบรวมที่ โรงพยาบาลราชวิถี ความชุกของภาวะทารกแรกเกิดขาดออกซิเจนศึกษาโดยใช้วิธี retrospective cohort study เก็บข้อมูลย้อนหลังตั้งแต่ มกราคม 2555 ถึง มิถุนายน 2559 และปัจจัยที่ศึกษารวมทั้งปัจจัยก่อนคลอด ปัจจัยระหว่างคลอด และปัจจัยหลังคลอดและทารก โดยใช้วิธี nested case – controlled จับคู่แบบสุ่ม และวิเคราะห์ข้อมูลตามแต่ปัจจัยที่ต้องการศึกษา*

ผลการศึกษา: *ความชุกของภาวะทารกแรกเกิดขาดออกซิเจนอยู่ที่ 11.7% ปัจจัยเสี่ยงที่มีความสัมพันธ์อย่างมีนัยสำคัญทางสถิติคือ การฝากครรภ์น้อยกว่า 4 ครั้ง (adjusted OR 1.64, 95% CI 1.18 - 2.26), ความดันโลหิตสูง (adjusted OR 1.94, 95% CI 1.42 – 2.65), ภาวะรกเกาะต่ำ(adjusted OR 4.58, 95% CI 2.74 – 7.68), ภาวะถุงน้ำคร่ำแตกก่อนการเจ็บครรภ์คลอดมากกว่า 18 ชั่วโมง (adjusted OR 3.71, 95% CI 1.98 – 6.98), ส่วนนำที่ไม่ใช่ศีรษะ (adjusted OR 1.95, 95% CI 1.34 – 2.84) และทารกในครรภ์มีภาวะ non reassuring หรืออยู่ในภาวะเครียด (adjusted OR 3.35, 95% CI 2.22 – 5.06) ไม่พบความสัมพันธ์อย่างมีนัยสำคัญทางสถิติในปัจจัย ภาวะเบาหวาน (95%CI 0.84 – 1.42, p = 0.50), ภาวะขี้เทาปนในน้ำคร่ำ (95%CI 0.64 – 1.73, p = 0.830), การได้รับยาแก้ปวดก่อนคลอด (95%CI 0.59 – 1.91, p = 0.839) และ ภาวะสายสะดือพันรอบศีรษะทารก (95%CI 0.59 – 1.27, p = 0.453).*

สรุป: *ภาวะทารกแรกเกิดขาดออกซิเจนในโรงพยาบาลราชวิถีอยู่ที่ร้อยละ 11.7 ปัจจัยเสี่ยงที่สัมพันธ์กับภาวะทารกแรกเกิดขาดออกซิเจนอย่างมีนัยสำคัญทางสถิติ ได้แก่ การฝากครรภ์น้อยกว่า 4 ครั้ง, ความดันโลหิตสูง, ภาวะรกเกาะต่ำ, ภาวะถุงน้ำคร่ำแตกก่อนการเจ็บครรภ์คลอดมากกว่า 18 ชั่วโมง, ส่วนนำที่ไม่ใช่ศีรษะ และทารกในครรภ์มีภาวะ non reassuring หรืออยู่ในภาวะเครียด*

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Introduction

Women with advanced maternal age is considered as a high risk for pregnancy, which seldom complicated with gestational diabetes and hypertensive disorders[1, 2] and result in delivery of a newborn with abnormal chromosome numbers[3] and birth asphyxia[4]. The World Health Organization (International Classification of Diseases)[5] has divided birth asphyxia into two categories: severe birth asphyxia, which is defined by a 1-minute Apgar scores between 1 and 3, and slight or moderate birth asphyxia, which is defined by an Apgar scores between 4 and 7.

According to data from the Ministry of Public Health, Thailand reported in 2010 showed that the incidence of birth asphyxia in Thai pregnant women was 22.8%[6]. Therefore, to prevent and reduce the incidence of birth asphyxia, the factors that affect the condition must be characterized. Most studies were conducted in all age group of pregnant women[7-9], and no study has specifically addressed birth asphyxia in advanced maternal age. Therefore, this study was conducted to investigate the prevalence and risk factors for birth asphyxia among pregnant women with advanced maternal age.

Materials and Methods

The report was a retrospective cohort study with nested case – controlled study. Data were collected at Rajavithi Hospital between January 2012 and June 2016. The inclusion criteria were as follows: pregnancy with age greater than or equal to 35 years, singleton pregnancy, and delivery at Rajavithi Hospital at a gestational age of 28 weeks or more with documented medical record. Birth with severe congenital abnormalities or birth weight less than 1,000 grams was excluded.

The collected data were divided into 3 groups; antepartum factors, intrapartum factors, and postpartum and newborn factors. Antepartum factors comprised of age, the number of antenatal visits (ANC), gravida, gestational age (GA), hypertensive disorders (preeclampsia with or without severe features, chronic hypertension and gestational hypertension), diabetes disorders (gestational diabetes mellitus and pregestational diabetes mellitus), fetal growth restriction, abnormal amniotic fluid index (AFI) (less than 5 cm or more than 24 cm) [10] and placenta previa.

Intrapartum factors comprised of fetal presentation, premature ruptured of the membranes for more than 18 hours (PROM > 18 h), chorioamnionitis, meconium stained amniotic fluid, intrauterine fetal status, pre-delivery morphine or pethidine treatment, cephalopelvic disproportion (CPD) and delivery route (spontaneous vaginal delivery group and cesarean section or operative vaginal delivery group). Postpartum and newborn factors comprised of a nuchal cord, the newborn birth weight.

The main study outcome was the Apgar scores, which was assessed by a pediatrician, pediatric resident or newborn nurse. The first objective was to assess the prevalence of the clinical factors using a retrospective cohort study of cases from January 2012 to June 2016, and the second objective was to assess the risk factor of birth asphyxia among advanced maternal age using a nested case-controlled approach by randomly matching by age of a birth-asphyxia group to a non-birth-asphyxia group (1:5 ratio) and analyzed the results according to the aforementioned factors. Furthermore, sub-group analysis of each age group was analyzed using univariate analysis method.

Sample size calculation for prevalence study was used infinite population proportion formula to calculated prevalence of birth asphyxia and used two independent proportions formula to calculated case – controlled study. Total sample size for prevalence study was 2,700 subjects. Total sample size for case – controlled study was 337 subjects in case group and 1,685 subjects in controlled group. The protocol of this research was reviewed and approved by the Ethic Committee of Rajavithi Hospital.

Statistical analysis

Data were analyzed using the SPSS version 17.0 statistical software with descriptive statistics

reported as the percentage, average, standard deviation, median, minimum, and maximum. A comparative analysis of the qualitative data for the relationship between the different factors associated with asphyxia in newborns was performed using the chi-square test or Fisher's exact test. The quantitative data were analyzed using Student's t-test or the Mann-Whitney U test with a p value less than 0.05 indicating statistical significance. After a univariate analysis and selection of variables with statistical significance, a multivariate analysis was performed using Binary Logistic Regression.

Results

A total of 3,193 cases of pregnant women with advance maternal age were enrolled in the study. Antepartum data showed median maternal age was 37 years and gravida was 2. Median gestational age was 38 weeks and 22% and 10.3% were complicated by diabetes and hypertensive disorders respectively. During intrapartum period, 92.9% were cephalic presentation, but only 45.6% were delivered by spontaneous vaginal delivery. One-minute Apgar scores ≤ 7 was as high as 11.7% of total deliveries (Table 1).

Table 1. Baseline characteristics of pregnant women with advanced maternal age.

Factors	Total (n = 3,193)
Antepartum	
Age (years), median (IQR)	37.0 (3.0)
Number of ANCs, mean (SD)	8.7 (4.1)
Gravida, median (IQR)	2.0 (1.0)
Gestational age (weeks), median (IQR)	38.0 (2.0)
Hypertensive disorders (%)	329 (10.3)
Diabetes disorders (%)	702 (22.0)
Abnormal amniotic fluid index (%)	51 (1.6)
Placenta previa (%)	66 (2.9)
Fetal growth restriction (%)	21 (0.9)
Intrapartum	
Cephalic presentation (%)	2,966 (92.9)
PROM > 18 hours (%)	57 (1.8)
Chorioamnionitis (%)	12 (0.4)
Non-reassuring fetal status or fetal distress	165 (5.2)
Meconium staining (%)	173 (5.4)
Administration of analgesic drug (%)	104 (3.3)
CPD (%)	308 (9.6)
Spontaneous vaginal delivery (%)	1,456 (45.6)
Postpartum and newborn	
Apgar score ≤ 7 at 1 min (%)	373 (11.7)
Nuchal cord (%)	330 (10.3)
Birth weight (grams), mean (SD)	2,985 (10.5)

Number of ANCs : number of Antenatal care visits
PROM : Premature rupture of membranes
CPD : Cephalopelvic disproportion

To analyze factors associated with low one-minute Apgar scores, 373 pregnant women delivered baby with Apgar scores ≤ 7 were compared with the control group that Apgar scores > 7 with ratio 1:5 matched by age. A total of 1,865 pregnant women were chosen in further analysis showed in Fig. 1.

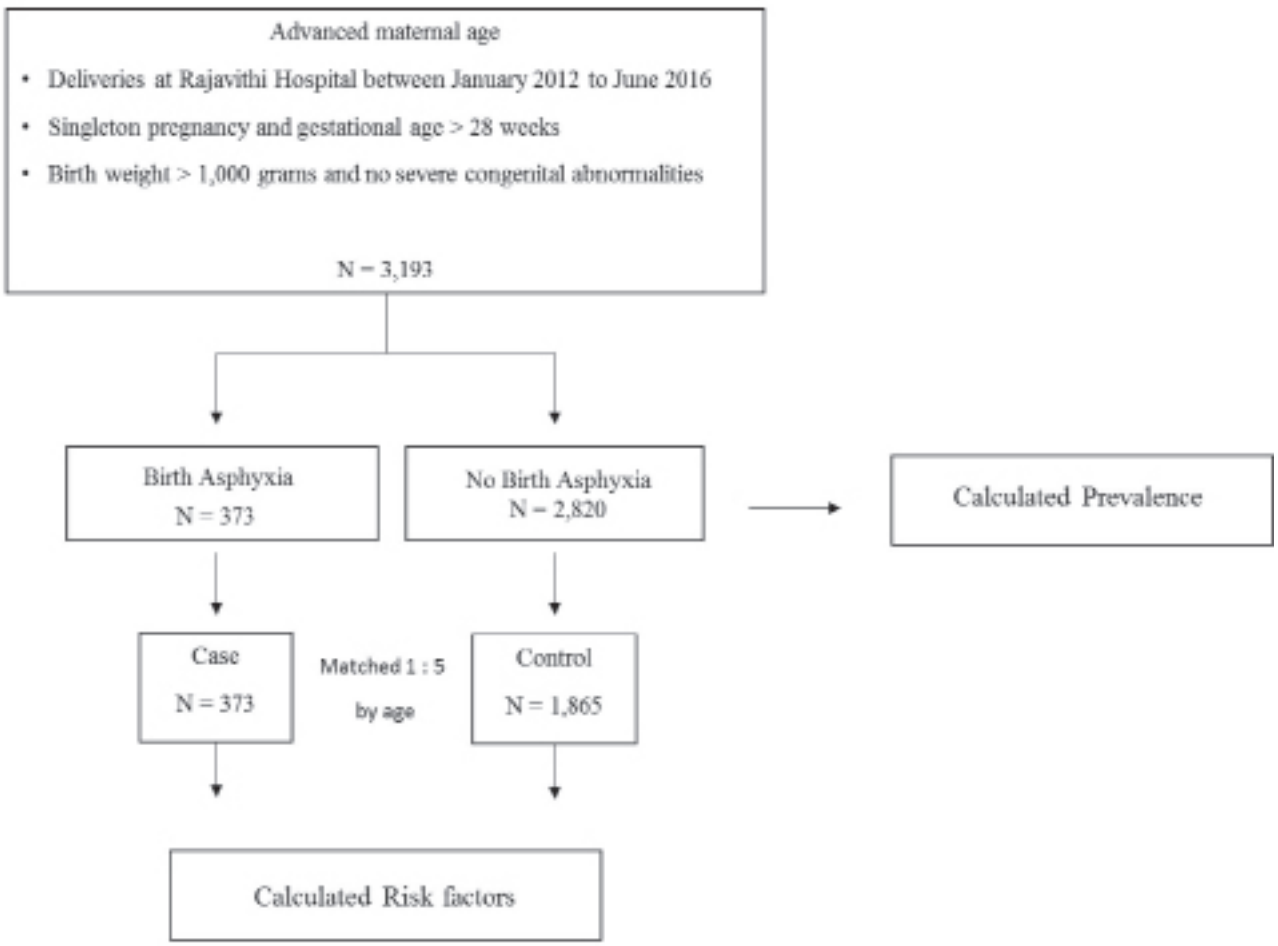

Fig. 1. Flow diagram of study participants.
Advanced maternal age : pregnant women with age ≥ 35 years
Case group : birth asphyxia; Apgar score at 1 minute < 7
Control group : no birth asphyxia; Apgar score at 1 minute ≥ 7
Computer randomly selected to case group and control group and matched by age

The antepartum factors that were statistically significantly associated with birth asphyxia were number of ANC < 4 visits (odds ratio (OR) 1.66, 95% CI 1.21- 2.27), gestational age ≥ 37 weeks (OR 0.42, 95% CI 0.34-0.53), hypertensive disorders (OR 1.95, 95% CI 1.44-2.64), placenta previa (OR 4.16, 95% CI 2.53-6.86), abnormal AFI (OR 2.15, 95%CI 1.05-4.39) and fetal growth restriction (OR 4.64, 95% CI 1.96-11.01). The intrapartum factors that were statistically significant associated with birth asphyxia were PROM > 18 hours (OR 3.59, 95% CI 1.95-6.61), non-cephalic presentation (OR 2.13, 95% CI 1.49-3.05), non- reassuring fetal status or fetal distress (OR 3.35, 95% CI 2.24-5.01), chorioamnionitis (OR 5.03, 95% CI 1.01-25.03), CPD (OR 0.59, 95%CI 0.37-0.94) and vaginal delivery (OR 2.11, 95% CI

1.66-2.68). The newborn factors, birth weight was associated with birth asphyxia with statistical significance (mean difference 430.6, 95%CI 37.9-493.2) (Table 2).

Table 2. Univariate analysis of factors associated with birth asphyxia (Apgar scores at 1 minute < 7).

Factors	Case group (Apgar at 1 min < 7) (n = 373)		Control group (Apgar at 1 min ≥ 7) (n = 1,865)		OR	95% CI	p value
Antepartum factors							
Age ≥ 40 years	85	(22.8)	425	(22.8)	1.00	0.77,1.30	1.000
Number of ANCs < 4	60	(16.1)	193	(10.3)	1.66	1.21,2.27	0.001
Gravida > 1	297	(79.6)	1,522	(81.6)	0.88	0.67,1.16	0.307
GA ≥ 37 weeks	189	(50.7)	1,320	(70.8)	0.42	0.34,0.53	0.001
Hypertensive disorders	68	(18.2)	191	(10.2)	1.95	1.44,2.64	< 0.001
Diabetes disorders	91	(24.4)	425	(22.8)	1.09	0.84,1.42	0.50
Abnormal AFI	11	(2.9)	26	(1.4)	2.15	1.05, 4.39	0.032
Placenta previa	29	(7.8)	37	(2.0)	4.16	2.53,6.86	< 0.001
Fetal growth restriction	10	(2.7)	11	(0.6)	4.64	1.96,11.01	< 0.001
Intrapartum factors							
PROM > 18 hours	18	(4.8)	26	(1.4)	3.59	1.95,6.61	< 0.001
Non-cephalic Presentation	47	(12.6)	118	(6.3)	2.13	1.49,3.05	< 0.001
Non-reassuring fetal status/fetal distress	42	(11.3)	68	(3.6)	3.35	2.24, 5.01	< 0.001
Chorioamnionitis	3	(0.8)	3	(0.2)	5.03	1.01,25.03	0.028
Meconium stained AF	20	(5.4)	95	(5.1)	1.06	0.64,1.73	0.830
Administration of analgesic drug	14	(3.8)	66	(3.5)	1.06	0.59,1.91	0.839
CPD	21	(5.6)	172	(9.2)	0.59	0.37,0.94	0.024
Vaginal delivery	113	(30.3)	892	(47.8)	2.11	1.66,2.68	< 0.001
Postpartum and newborn factors							
Nuchal cord	34	(9.1)	194	(10.4)	0.86	0.59,1.27	0.453
	mean	**(SD)**	**mean**	**(SD)**	**MD**	**95% CI**	**p value**
Birthweight (gm), mean(SD)	2,620.6	(814.8)	3,051.2	(497.8)	430.6	37.9,493.2	< 0.001

Number of ANCs < 4: number of ANC < 4 visits
GA: Gestational age, AFI: Amniotic fluid index
PROM: Premature rupture of membranes, AF: Amniotic fluid
CPD: Cephalopelvic disproportion
MD: Mean difference
Matched case group (birth asphyxia; Apgar score at 1 minute < 7) and control group (no birth asphyxia; Apgar score at 1 minute ≥ 7) ratio 1:5
Case group and control group were randomly matching by age
Compared :age 35 – 40 and ≥ 40 years, number of ANC < 4 and ≥ 4 visits, gravida 1 and >1, GA ≤ 37 and > 37 weeks, normal AFI (5 – 24 cm) and abnormal AFI (< 5 cm or > 24 cm), cephalic presentation and non-cephalic presentation, reassuring fetus and non-reassuring fetal status or fetal distress, spontaneous vaginal delivery and cesarean section or operative delivery.

After multivariate analysis, placenta previa was the strongest risk factor associated with birth asphyxia (adjusted OR 4.58, p < 0.001) and the second was non- reassuring fetal status or fetal distress (adjusted OR 3.35, < 0.001). Other significant factors were number of ANC < 4 visits (adjusted OR 1.64, p = 0.003), hypertensive disorders (adjusted OR 1.94, p < 0.001), PROM > 18 hours (adjusted OR 3.71, p < 0.001), non-cephalic presentation (adjusted OR 1.95, p < 0.001) (Table 3).

Additionally, calculation for the relationship between number of the significant risk factors after multivariate analysis (a total of 6 significant risk factors) and birth asphyxia found that advanced maternal age group would have a birth asphyxia rate of 11.6% if there were no associated risk factors; this rate was close to the overall prevalence of birth asphyxia in pregnancies with advanced maternal age. However, any one of these factors was present, the probability of having asphyxia would increase to 23.4%. If two factors were present, the rate would increase to 39.7%, and 3 or more factors would increase the rate to 60% (Table 4).

Table 3. Multivariate analysis of factors associated with birth asphyxia (Apgar score at 1 minute < 7).

Factors	Adjusted OR	95% CI	p value
Number of ANCs < 4	1.64	1.18,2.26	0.003
Hypertensive disorders	1.94	1.42,2.65	< 0.001
Placenta previa	4.58	2.74,7.68	< 0.001
PROM > 18 hours	3.71	1.98,6.98	< 0.001
Non-cephalic presentation	1.95	1.34,2.84	< 0.001
Non- reassuring fetal status or fetal distress	3.35	2.22,5.06	< 0.001

Table 4. Factors associated with birth asphyxia (Apgar score at 1 minute < 7).

Risk factors	Total	Birth asphyxia (n = 373)	
		n	%
No risk factor	1,494	174	11.6
1 risk factor	603	141	23.4
2 risk factors	131	52	39.7
≥ 3 risk factors	10	6	60.0

Factors : a total of 6 significant risk factors after multivariate analysis

Discussion

Prevalence of birth asphyxia among pregnancy with advanced maternal age at Rajavithi hospital was 11.7%. When this statistic was compared to the data from 2000 to 2002[11], the results revealed prevalence of birth asphyxia was 7.6%. Additionally, when the incidence was compared with data from other tertiary care centers[12], the incidence of birth asphyxia in term pregnancies was 4.4%.The incidence was also higher than the target and indicators of the state Department of Health, Ministry of Public Health, Thailand, which had set the incidence of birth asphyxia at less than 30 per 1,000 live births[13].

The antepartum factors that were associated with

birth asphyxia included number of ANC < 4 visits, gestational age < 37 weeks, hypertensive disorders, placenta previa, and fetal growth restriction. The association between number of ANC < 4 visits and hypertensive disorders with birth asphyxia was consistent with previous studies[7, 8,14] that had identified antepartum factors associated with birth asphyxia. Moreover, studies previously conducted in Thailand[15, 16] revealed that hypertensive disorders was associated with birth asphyxia. However, few studies have examined placenta previa and fetal growth restriction factors. Additionally, the studies conducted in pregnancies with advanced maternal age that often focused on diabetes disorders. Previous study revealed that diabetes disorders were associated with birth asphyxia[15]. However, in this study showed that factors associated with diabetes disorders were not related to birth asphyxia.

The intrapartum risk factors that were associated with birth asphyxia were a PROM > 18 hours, non-cephalic presentation, non- reassuring fetal status or fetal distress, chorioamnionitis, CPD and vaginal delivery. Other studies[15-17] have shown that fetal distress and cesarean delivery were associated with birth asphyxia, which was consistent with our study. CPD was also associated with birth asphyxia[16]. Furthermore, a non-cephalic presentation was previously shown[12] to be associated with birth asphyxia.

Although some studies[12,15] have shown that meconium stained amniotic fluid was associated with birth asphyxia, this study did not do so. This discrepancy may be due to awareness, focus, close monitoring and active management by the clinicians.

Regarding the newborn factors, birth weight was associated with birth asphyxia. For cases with lower newborn birth weights than the control group, a nuchal cord was not statistically significantly associated with birth asphyxia, which was inconsistent with a previous report of a confirmed association between a nuchal cord and birth asphyxia[12]. Additionally, the factor associated with birth asphyxia can be applied to women who are classified as advanced maternal age.

Until now, no study has examined the risk factors that are associated with birth asphyxia in pregnancies with advanced maternal age. This study included a large population size that could provide insight into the different contributions of various factors. The limitation of this study involved its retrospective nature, which may have introduced an information bias in the data recording that could not be mitigated ahead of time. However, the credibility of this study was supported by its use of a nested case control that was implemented by pairing the case group with the control group at a ratio of 1:5. Regarding clinical application, the factors associated with a birth asphyxia risk can be used as an initial screening to search for vulnerable groups who may be at risk for severe birth asphyxia and who may be good candidates for counseling. Moreover, if a pregnant woman has the above risk factors, she can be identified as having a possibility of experiencing birth asphyxia, and the risk factors can be defined as clear objectives for clinical treatment.

Conclusion

The prevalence of birth asphyxia in advanced maternal age was 11.7%, and the statistically significant risk factors associated with this condition were number of ANC < 4 visits, hypertensive disorders, placenta previa, a PROM > 18 hours, non-cephalic presentation, and non- reassuring fetal status or fetal distress.

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Potential conflicts of interest

The authors declare no conflict of interest.

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GYNECOLOGY

Prevalence of Anxiety and Depression in Infertile Women in Siriraj Hospital by using Thai Hospital Anxiety and Depression Scale

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ABSTRACT

Objectives: To identify the prevalence of anxiety and depression in infertile women at Siriraj Hospital using Thai Hospital Anxiety and Depression Scale (Thai HADS) and to identify the risk factors of anxiety and depression.

Materials and Methods: All the patients who attended at infertile clinic during July 2016 to February 2017 received the questionnaires that consisted of demographic information and Thai HADS questionnaire. The consent occurred when the participant gave the questionnaires back after completing. Potential risks were compared by Chi square and analysis of variance test.

Results: From 500 questionnaires, 421 were returned. The mean age was 36.5 years old and 61.3% had income ≥ 50,000 baht. Previous treatment failure was 71.3% (300/421) which 59% (177/300) had treatment failure ≥ 3 times. The prevalence of anxiety and depression were 13% and 3%, respectively. Factors that significantly lead to anxiety were duration of infertility 5 years or more, previous infertility treatment failure, previously failed in vitro fertilization (IVF) and the number of treatment failure ≥ 3 times. The relative risks of anxiety were 1.88, 2.37, 1.72 and 2.61, respectively

Conclusion: Prevalence of anxiety and depression in infertile women at Siriraj Hospital by using Thai HADS was 13% and 3%. Duration of infertility ≥ 5 years, previous treatment failure, previously failed IVF and the number of treatment failure ≥ 3 times increased anxiety significantly.

Keywords: infertility, anxiety, depression, HADS, Thai HADs

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ความชุกของภาวะวิตกกังวลและซึมเศร้าของผู้ป่วยหญิงที่มีบุตรยากในโรงพยาบาลศิริราช โดยใช้แบบสอบถาม Hospital Anxiety and Depression Scale ฉบับภาษาไทย

วริษฐา สกุลแสงประภา, จปรัฐ ปรีชาพานิช, สมสิญจน์ เพ็ชรยิ้ม

บทคัดย่อ

วัตถุประสงค์: *เพื่อทราบถึงอัตราความชุกของภาวะวิตกกังวลและซึมเศร้าในผู้ป่วยหญิงที่มีบุตรยากของ รพ.ศิริราช โดยใช้แบบสอบถาม Hospital Anxiety and Depression Scale ฉบับภาษาไทย และปัจจัยเสี่ยงที่ทำให้เกิดภาวะวิตกกังวลและซึมเศร้าในผู้ป่วยที่มีบุตรยาก*

วัสดุและวิธีการ: *ผู้ป่วยหญิงที่เข้ารับการรักษาในคลินิกผู้มีบุตรยาก ในช่วงเดือนกรกฎาคม 2559 ถึงกุมภาพันธ์ 2560 จะได้รับแบบสอบถามซึ่งประกอบด้วย ส่วนที่เป็นข้อมูลพื้นฐาน และแบบสอบถาม Hospital Anxiety and Depression Scale ฉบับภาษาไทย ซึ่งให้ผู้ป่วยกรอกแบบสอบถามด้วยตนเอง หากผู้ป่วยส่งแบบสอบถามคืนจะถือว่าเป็นการให้ความยินยอมเข้าร่วมในงานวิจัยนี้ ในส่วนของการประเมินปัจจัยเสี่ยง ได้ใช้วิธีการทางสถิติ คือ Chi square และ ANOVA test*

ผลการศึกษา: *จากแบบสอบถาม 500 ฉบับ ได้รับการส่งคืน 421 ฉบับ โดยอายุเฉลี่ยของผู้เข้าร่วมวิจัยคือ 36.5 ปี และร้อยละ 61.3 มีรายรับมากกว่าหรือเท่ากับ 50,000 บาทต่อเดือน ร้อยละ 71.3 (300/421) ของผู้เข้าร่วมวิจัยเคยประสบความล้มเหลวในการเข้ารับการรักษาผู้มีบุตรยาก ซึ่งในจำนวนนี้พบว่า ร้อยละ 59 (177/300) เคยล้มเหลวในการรักษามาแล้วมากกว่าหรือเท่ากับ 3 ครั้ง โดยความชุกของภาวะวิตกกังวลและซึมเศร้า คือ ร้อยละ 13 และ 3 ตามลำดับ โดยปัจจัยเสี่ยงที่สัมพันธ์กับการเกิดภาวะวิตกกังวลอย่างมีนัยสำคัญทางสถิติคือ การอยู่ในภาวะการมีบุตรยากตั้งแต่ 5 ปีขึ้นไป, ประวัติการเคยประสบความล้มเหลวในการรักษาเรื่องมีบุตรยาก, ประวัติการเคยประสบความล้มเหลวในการรักษาโดยวิธี IVF และการประสบความล้มเหลวในการเข้ารับการรักษาเรื่องมีบุตรยากตั้งแต่ 3 ครั้งขึ้นไป*

สรุป: *ความชุกของภาวะวิตกกังวลและซึมเศร้าของผู้ป่วยหญิงที่มีบุตรยากใน รพ.ศิริราช โดยใช้แบบสอบถาม Hospital Anxiety and Depression Scale ฉบับภาษาไทย คือ ร้อยละ 13 และ 3 ตามลำดับ การอยู่ในภาวะการมีบุตรยากตั้งแต่ 5 ปี ขึ้นไป, ประวัติการเคยประสบความล้มเหลวในการรักษาเรื่องมีบุตรยาก, ประวัติการเคยประสบความล้มเหลวในการรักษาโดยวิธี IVF และการประสบความล้มเหลวในการเข้ารับการรักษาเรื่องมีบุตรยากตั้งแต่ 3 ครั้งขึ้นไป เป็นปัจจัยเสี่ยงที่มีนัยสำคัญทางสถิติที่นำไปสู่ภาวะวิตกกังวล*

คำสำคัญ: *การมีบุตรยาก, วิตกกังวล, ซึมเศร้า, HADS, Thai HADS*

Introduction

Infertility defined as failure to conceive after 12 months of unprotected intercourse. Many ways to treat infertility include conventional methods such as providing advice about timing of intercourse, preventing miscarriages, ovulatory stimulation and/or to repair reproductive organ and more advanced method using assisted reproductive technology (ART). During treatment, patient could face with many steps of the treatment process, medication side effects, the high costs of treatments and undesirable outcomes. These may lead them to develop psychiatric problems[1]. According to the study in ART clinic in Taiwan, 40.2% of patients had a psychiatric disorder, which were generalized anxiety disorder (23.2%), major depressive disorder (17.0%), and dysthymic disorder (9.8%)[2].

Anxiety is one of the psychological stresses. Study in Iran showed that anxiety levels in those who failed to conceive were slightly higher than those who got pregnant[3]. In the study, the infertile participants had relatively elevated stress levels which prolactin and cortisol levels were higher than in the fertile group. The rising level of cortisol can delay the LH surge[4] and associated with significantly lower progesterone levels[5]. According to the study in Guatemala, elevated gonadotrophins and decreased midluteal progesterone levels could impaired the ovulation and luteinization, which result in lower chances of successful implantation[5]. In addition, psychological stress has been reported to affect the outcome of infertility treatment[3].

There are several ways to detect anxiety and depression such as self-rating depression scale (SDS), Zung depression scale (ZDS), Zung anxiety scale (ZAS), state trait anxiety inventory (STAI), Beck depression inventory (BDI), mini-international neuropsychiatric interview (MINI) and also hospital anxiety and depression scale (HADS). All of these, HADS has been shown to have satisfactory psychometric properties. HADs was originally developed in 1983 by Zigmond et al(6) and has been used worldwide. HADS was translated in to Thai version and was used in cancer patients to study the validity of the questionnaire by comparing to the diagnosis of the psychiatrist. The sensitivity and specificity to detect anxiety were 100% and 86%, respectively. For the sensitivity and specificity of depression were 85.7% and 91.3%, respectively. Hence, the Thai version of HADS[7] was chosen to use in the present study.

There were substantial amount of researches that studied about the stress, anxiety and depression in the infertile couple. Most studies performed in the western but few studies in the Asia[8-10]. The objectives of this study were 1) to identify the prevalence of anxiety and depression in infertile women at Siriraj hospital by using a Thai version of Hospital Anxiety and Depression Scale (Thai HADS) and 2) to identify the risk factors that lead the patients to have anxiety and depression.

Materials and Methods

This cross-sectional study enrolled infertile women attending the infertile clinic at Siriraj Hospital, from July 2016 to February 2017. Eligible females were aged 18 years or older, had a history of infertility, and were able to read and write in Thai. All participants had never been diagnosed with any psychiatric problems. Prior to conducting the study, the study proposal and protocol had been approved by the Ethics Committee of Siriraj Institutional Review Board (Protocal No.745/2558 (EC1)).

The sample size (n = 385) was calculated from pilot study which has been done in the infertile clinic at Siriraj Hospital. It was done in 40 cases, 3 of them were founded to have anxiety and one of them had depression. Because of higher risk for losing data, thirty percent was added to sample size. Thus, the overall sample size would be 500.

The patients who received the questionnaires were informed about the objectives of the study, the confidentiality of the data, and that acceptance or refusal to participate in the study would not affect their treatment procedures. Consents to participate in the study were inferred from the action of the participant submitting the questionnaires to provided box at the

clinic.

Participants completed two questionnaires, the first parts containing the demographic and the fertility information. These questionnaires included age, sex, height, weight, educational levels, duration of infertility, a history of spontaneous abortion, type of infertility, the number of previous infertility treatment failures, and the number of previous treatment of infertility before visiting Siriraj Hospital.

The second parts of questionnaires contained Thai HADS for evaluating the psychological status. Thai HADS consists of two subscales, 1) anxiety (HADS-A) and 2) depression (HADS-D). Each subscale composes of seven items which ranging from 0 to 3 scores. The total score of HADS-A and HADS-D each ranges from 0 to 21, with a score of 8 to 10 on either HADS subscale is suggestive of higher risk for psychiatric condition (doubtful diagnosis) but the cut point do make the diagnosis of anxiety or depression is 11 or greater. The affected case would be sent to the psychiatrist.

Statistical analysis

This study used numbers and percentages to describe categorical variables and mean to describe continuous variables. Potential risks were compared by Chi square and analysis of variance (ANOVA) test.

Results

Among 500 questionnaires distributed to the participants, 18 questionnaires were lost and 61 questionnaires were incomplete filled. A total of 421 female infertile patients returned the complete questionnaires and there were considered as the participants in the study. The baseline characteristics of the 421 participants are shown in Table 1. Mean age was 36.5 years old and most of them had normal body mass index (BMI) (75.8%). About 90% of participants had obtained Bachelor's degree or higher education degree. Almost all of participants were employed and more than half had family income of greater than 50,000 Baht (61.3%).

Table 1. Baseline characteristics of participants (N = 421).

Characteristics	N (%)
Age (years) *	36.5 ± 4.6
BMI (kg/m^2) *	22.2 ± 3.8
BMI category	
Underweight (< 18.5 kg/m^2)	24 (5.7)
Normal (18.5-24.9 kg/m^2)	319 (75.8)
Overweight (≥ 25 kg/m^2)	78 (18.5)
Education	
Less than bachelor degree	38 (9)
Bachelor degree	252 (59.9)
Higher than Bachelor degree	131 (31.1)
Employment status	
Unemployed	33 (7.8)
Employed	388 (92.2)
Family income	
< 50,000 Baht	163 (38.7)
≥ 50,000 Baht	258 (61.3)

BMI: body mass index, *reported as mean ± standard deviation

History about infertility in participants is presented in Table 2. Most participants (67.7%) had duration of infertility less than 5 years and 80.2% of the participants had primary infertility. For the treatment failure, 71.3% have ever failed infertility treatment and 59% of previously failed cases had treatment failures at least 3 times. Most of the previously failed cases were failed in vitro fertilization (IVF) (74.7%).

Table 2. History of infertility (N = 421).

Characteristics	N (%)
Duration of infertility (years)*	3.9 ± 2.8
Duration of infertility	
< 5 years	285 (67.7)
≥ 5 years	136 (32.3)
Infertility type	
Primary	340 (80.2)
Secondary	81 (19.8)
Previous abortion	87 (20.7)
Previous infertility treatment failure	300 (71.3)
Number of previous treatment failure (N=300)	
< 3 times	123 (41)
3-5 times	106 (35)
> 5 times	71 (24)
Number of previous treatment failure (N=300)	
Failed IUI	76 (25.3%)
Failed IVF	224 (74.7%)

* reported as mean ± standard deviation

Table 3. Diagnosis of anxiety and depression (N=421).

Diagnosis of anxiety and depression	N (%)
Anxiety score*	7 (4-9)
Depression score*	3 (1-5)
Diagnosis of anxiety	
No anxiety (score 0-7)	255 (61)
Doubtful (score 8-10)	111 (26)
Anxiety (score ≥ 11)	55 (13)
Diagnosis of depression	
No depression (score 0-7)	378 (90)
Doubtful (score 8-10)	31 (7)
Depression (score ≥ 11)	12 (3)

* reported as median (Interquartile range)

Table 3 demonstrates the diagnosis of anxiety and depression according to Thai-HADS questionnaires. Median anxiety and depression scores were 7 and 3, respectively. The prevalence of anxiety and depression was 13% and 3%, respectively. Doubtful diagnosis of anxiety and depression were found 26% and 7%, respectively.

Comparison of various characteristics between diagnosis of anxiety is shown in Table 4. Four risk factors significantly associated with anxiety were 1) duration of infertility 5 years or more, 2) previous infertility treatment failure, 3) previously failed IVF and 4) the number of treatment failure ≥3 times. The relative risks of anxiety were 1.88, 2.37, 1.72 and 2.61, respectively. No significant differences observed between groups in terms of age, income and previous abortion.

However, comparing risk factor associated with depression as shown in Table 5, there was no significant differences observed between groups in terms of age, income, duration of infertility, previous abortion, and failure of infertility treatment.

Table 4. Risk factor associated with anxiety disorder (N=421).

Characteristics	Anxiety (N)	No anxiety (N)	Relative risk (95%CI)
Age			
≥ 35 years	36	242	0.97 (0.58-1.64)
< 35 years	19	124	
Income			
≥ 50,000 Baht	36	222	1.2 (0.71-2.01)
< 50,000 Baht	19	144	
Duration of infertility			
≥ 5 yrs	26	110	1.88 (1.15-3.06)
< 5 yrs	29	256	
History of abortion			
Yes	13	74	1.19 (0.67-2.11)
No	42	292	
Previously failed infertility treatment			
Yes	47	253	2.37 (1.15-4.86)
No	8	113	
Previously failed IVF			
Yes	23	101	1.72 (1.05-2.82)
No	32	265	
Number of treatment failure			
≥ 3 times	36	141	2.61 (1.55-4.40)
< 3 times	19	225	

IVF: in vitro fertilization

Table 5. Risk factor associated with depression (N = 421).

Characteristics	Depression (N)	No depression (N)	Relative risk (95%CI)
Age			
≥ 35 years	9	269	1.54 (0.42-5.61)
< 35 years	3	140	
Income			
≥ 50,000 Baht	5	253	0.45 (0.15-1.40)
< 50,000 Baht	7	156	
Duration of infertility			
≥ 5 yrs	7	129	2.93 (0.95-9.08)
< 5 yrs	5	280	
History of abortion			
Yes	2	85	0.77 (0.17-3.44)
No	10	324	
Previously failed infertility treatment			
Yes	9	291	1.21 (0.33-4.39)
No	3	118	
Previously failed IVF			
Yes	6	118	2.40 (0.79-7.28)
No	6	291	
Number of treatment failure			
≥ 3 times	6	171	1.38 (0.45-4.20)
< 3 times	6	238	

IVF: in vitro fertilization

Discussion

The study aimed to identify the prevalence of anxiety and depression of infertile women at Siriraj Hospital using Thai Hospital Anxiety and Depression Scale (Thai HADS) and to identify the risk factors of anxiety and depression. Using the Thai HADs Questionnaires, this study revealed that the prevalence of anxiety and depression of infertile patients at Siriraj Hospital was 13% and 3%, respectively.

Similar findings were reported by the studies in Poland[11] and in Italy[12] where the prevalence of anxiety among infertile women was 15.53% and 14.7%, respectively. The study in Taiwan found that the prevalence of anxiety was 23.2%[2], relatively higher than what we found in this study. It may be from using different tools to diagnose anxiety. In the study from Taiwan, researcher used the MINI that conducted the interview by a board-certified psychiatrist, so that study in Taiwan had more chance to detect anxiety than self-questionnaires as in our study.

The Prevalence of depression in our study was 3%, lower than what reported by previous studies in other countries; for example 17% in Taiwan[2], 17.9% in Italy[12], 35.44% in Poland[11], 68.9% in Iraq[13]. The lower prevalence might be due to the different methods in detecting the psychiatric problems, and the baseline characteristics of the patients. In many studies, the participants were indicated for IVF or ICSI. Generally accept that patients undergoing IVF or ICSI typically tend to be under stress. This may explain the higher prevalence of depression reported in Poland and in Iraq[11,13].

The significant factors that lead to anxiety were duration of infertility ≥ 5 years, previously failed treatment, previously failed IVF and the failure of treatment ≥ 3 times. In other studies, the factor that associated with anxiety and depression were age and male infertility (Japan)[14], younger and longer history of infertility (Italy)[12], age, social concern, sexual concern (Hungary)[15], primary type of infertility, duration of infertility and treatment, and threat of husband's remarriage (Iraq)[13]. Therefore, inconclusive data to confirm what are the significant factors that affected anxiety in infertile couples.

Due to the low prevalence of the depression in this study, we could not detect the risk factors that lead to the depression.

The strengths of the study were 1) we used Thai version of questionnaires, which is simple and reliable, and 2) we compared the risk factors for anxiety and depression.

This study had some limitations. First, it was a cross sectional study. Thereby, the result could not evaluate the incidence of the anxiety and depression, because some cases may develop anxiety or depression after repeated treatment cycle. Also the method of the study, we had collected the data at one point of time and no further study after the participants underwent the treatment. So from time to time, the incidence might be increased. Second, the subjects were only females that may have higher stress. But in some cases, data from males may reveal some helpful hints to improve these psychiatric problems.

For the application of this research, due to the high prevalence of anxiety, infertile patients should be provided the psychological assessment and the affected cases need the intervention such as psychological support or psychiatric consultation to reduce the stress. Relieving stress in these patients might increase the success rate of infertility treatment. In this study, the affected cases were sent to the psychiatrist.

Further studies are required to evaluate the psychiatric problems in men or in couples to clarify the prevalence of anxiety and depression, the associated risk factors and the effect of anxiety and depression to the outcome of infertility treatment.

Conclusion

Prevalence of anxiety and depression in infertile women at Siriraj Hospital by using Thai HADS was 13% and 3% respectively. Duration of infertility ≥ 5 years, previous treatment failure, previously failed IVF and the number of treatment failure ≥ 3 times increased anxiety.

Potential conflicts of interest

The authors declare no conflict of interest.

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OBSTETRICS

Uterine Cooling during Cesarean Section to Reduce Intraoperative Blood Loss: A randomized controlled trial

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ABSTRACT

Objectives: The aim was to compare uterine cooling and routine cesarean section as a means of reducing intraoperative blood loss.

Materials and Methods: Pregnant women who underwent cesarean section at Khon Kaen Hospital between May and June, 2017 were randomly assigned to one of two groups: the uterine cooling (UC) group (n= 80) or the control group (n= 80). In the UC group, the uterus was wrapped using a sterile cooling swab while in the control group a routine cesarean section (CS) was performed.

Results: In UC group, there was a statistically significant reduction in intra-operative blood loss compared with routine CS (252.8 ± 133.8 vs 472.9 ± 201.8 ml), mean difference 220 ml (95%CI 166.6-273.5). Uterotonic drugs use was significantly less in the UC group (1.3% vs 10%, p = 0.02). Length of hospital stay was significantly less in the UC group (3.0 ± 0.5 vs 3.2 ± 0.7 day; p = 0.01). There was no significant difference between the two groups in postpartum hemorrhage. There was no intraoperative hypothermia found.

Conclusion: Uterine cooling was associated with a reduction in intraoperative blood loss among pregnant women undergoing cesarean section.

Keywords: uterine cooling, cesarean section, postpartum hemorrhage.

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การศึกษาเปรียบเทียบการให้ความเย็นแก่มดลูกเพื่อลดการเสียเลือดระหว่างผ่าตัดคลอด

น้ำผึ้ง นวศิโรดม, อุษณีย์ สังคมกำแหง, ธนนิตย์ สังคมกำแหง

บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาเปรียบเทียบการให้ความเย็นแก่มดลูกเพื่อลดการเสียเลือดระหว่างผ่าตัดคลอดเปรียบเทียบกับการผ่าตัดคลอดแบบมาตรฐาน*

วัสดุและวิธีการ: *สตรีตั้งครรภ์ที่เข้ารับการผ่าตัดคลอดที่โรงพยาบาลขอนแก่นระหว่างเดือนพฤษภาคมถึงเดือนมิถุนายน พ.ศ.2560 แบ่งอาสาสมัครออกเป็นสองกลุ่ม กลุ่มแรกจำนวน 80 ราย ห่อมดลูกด้วยผ้าชุบน้ำเกลือเย็นระหว่างการเย็บมดลูกเป็นเวลาอย่างน้อย 5 นาที กลุ่มที่สองจำนวน 80 ราย รับการผ่าตัดคลอดแบบมาตรฐาน*

ผลการศึกษา: *การให้ความเย็นแก่มดลูกระหว่างผ่าตัดคลอดสามารถลดการเสียเลือดระหว่างผ่าตัดคลอดได้อย่างมีนัยสำคัญทางสถิติ เมื่อเทียบกับการผ่าตัดคลอดแบบมาตรฐาน ลดการเสียเลือดเฉลี่ย 220 มิลลิลิตร (252.8 ± 133.8 กับ 472.9 ± 201.8 มิลลิลิตร, $p < 0.001$) ลดการใช้ยากระตุ้นการหดตัวของมดลูกอย่างมีนัยสำคัญทางสถิติ (ร้อยละ 1.3 กับร้อยละ 10, $p = 0.02$) ลดระยะเวลาการนอนโรงพยาบาลได้อย่างมีนัยสำคัญทางสถิติ (3.0 ± 0.5 กับ 3.2 ± 0.7 วัน, $p = 0.01$) ส่วนอุบัติการณ์การตกเลือดหลังคลอดไม่มีความแตกต่างอย่างมีนัยสำคัญทางสถิติ และไม่พบว่าเกิดภาวะอุณหภูมิกายต่ำขณะผ่าตัด*

สรุป: *การให้ความเย็นแก่มดลูกช่วยลดการเสียเลือดระหว่างผ่าตัดคลอด*

คำสำคัญ: *การให้ความเย็นแก่มดลูก, การผ่าตัดคลอด, ภาวะตกเลือดหลังคลอด*

Introduction

Cesarean section (CS) rates have increased to as high as 25 to 30% in many parts of the world[1]. The most common complication during CS is postpartum hemorrhage, which leads to increased maternal mortality and morbidity[2]. The most frequent cause of hemorrhage is uterine atony, failure of the uterus (a) to contract sufficiently after delivery, and (b) to arrest bleeding from vessels at the placental implantation[3-6]. The uterus is a smooth muscle whose contraction is modulated most directly by intrinsic or extrinsic oxytocin. During pregnancy the spiral arteries within the uterus and beneath the placenta become enlarged in order to perfuse sufficient oxygen to the placenta. After separation of the placenta, the uterine smooth muscle cells contract in a pincer-like action to pinch the spiral arteries closed[7]. Many trials combined results from atony prophylaxis and treatment; for example, fundal massage, uterotonic drugs (i.e., oxytocin, methylergonovine, misoprostal, dinoprostone, tranexamic acid)[8-14], surgical method (i.e., uterine compression suture, internal iliac artery ligation, pelvic umbrella pack or peripartum hysterectomy)[15-17].

Nowadays, there is a new technique to reduce blood loss during hysterotomy repair; viz., uterine cooling immediately following delivery of the fetus and placenta so as to promote better uterine contraction and involution resulting in less blood loss[7]. Calcium ions play an important role in muscle contraction. Release of calcium ions from the sarcoplasmic reticulum stores is the immediate initiator of contraction, and calcium's diffusion from the muscle filaments and re-uptake by the sarcroplasmic reticulum results in relaxation of contraction. In some smooth muscles, cold enhances contraction, perhaps by slowing the reuptake of calcium[18-20]. When the usual pharmacologic agents fail to induce adequate contraction of the uterine smooth muscle, the investigators suspect that application of cold may be essential[7]. This study was conducted to assess the efficacy of uterine cooling in cesarean section for reducing intraoperative blood loss.

Materials and Methods

This randomized controlled trial was conducted at the Department of Obstetrics and Gynecology, Khon Kaen Hospital, Thailand between May and June, 2017. The study was approved by the Khon Kaen Hospital Institutional Review Board for Human Research. Before enrollment, the study design was explained to the participants who signed the informed consent form. We included pregnant women who underwent cesarean section for indications of previous uterine scaring, cephalopelvic disproportion, abnormal fetal presentation, and/or non-reassuring fetal heart rate pattern. We excluded pregnant women who refused to participate in the study, unable to understand the nature of the study due to mental illness or mental challenge, underlying blood dyscrasia with coagulopathy or on anticoagulant therapy, inability to exteriorize the uterus during cesarean section, placenta previa, abruptio placenta and chorioamnionitis.

Eligible participants were randomized by computer generated block of four into two groups; the uterine cooling group and the routine cesarean section group. The random numbers were put into sequentially sealed opaque envelopes.

The uterine cooling was done immediately following delivery of the fetus and placenta. The uterus was externalized and the body of the uterus cephalad to the hysterotomy incision wrapped in sterile surgical swabs saturated in sterile iced normal saline. These swabs were refrigerated between -2 and 2°C. The uterus wrapping was performed for at least 5 min until the hysterotomy was repaired. The uterus was then replaced into the pelvic cavity. The control group underwent a routine cesarean procedure. Ten to 20 units of oxytocin prophylaxis was administered in the intravenous fluid running at 100-120 ml/h in both groups. The participants of both groups received the same pre- and post-operative care. All surgical procedures were performed by staff or residents under supervision. The types of surgical incision and procedures were decided by the respective surgeon. Intraoperative blood loss was measured by summing the blood volume in the suction bottles and swabs.

Baseline characteristics were recorded, including:

age, gravidity, parity, body mass index (BMI), indication for surgery, type of incision, surgeon, and pre-, intra- and post-operative temperature. The pre-, intra- and post-operative body core temperature by oral route were routinely recorded at the ward and operating room by regular and anesthesia nurses. The intraoperative body core temperature was recorded during repair of the uterus.

The primary outcome was intraoperative measurement of blood loss. The secondary outcomes were use of additional uterotonic drugs (i.e., oxytocin, methylergometrine, misoprostal, and sulprostone), additional surgical interventions (i.e., uterine compression suture, uterine artery ligation, and internal iliac artery ligation), requirement of blood transfusion, total blood loss > 1,000 ml, and cesarean hysterectomy.

We used a formula to test the difference between the two independent means of measuring blood loss as set out by Mitchell et al.[7] ; uterine cooling group 536 ml and control group 756 ml. The sample size of each group was 80 cases.

Statistical analyses were performed using STATA 13 software. Analyses of the effect of uterine cooling were based on an intention to treat basis. Continuous variables were analyzed using the Student t-test or Mann-Whitney U-test. Categorical variables were analyzed using the Chi-square test. The 95% confidence interval (CI) was calculated. A p value < 0.05 was required to confirm statistical significance.

Results

One hundred and sixty pregnant women were assessed for eligibility. A total of 160 patients were included; 80 were randomly assigned to the uterine cooling group and 80 to the control group. There were no patient withdrawals from the study. A total of 80 patients from each group were analyzed (Fig. 1).

Baseline characteristics were similar between the uterine cooling and control groups (Table 1, 2). Cephalopelvic disproportion was the most common indication for cesarean section.

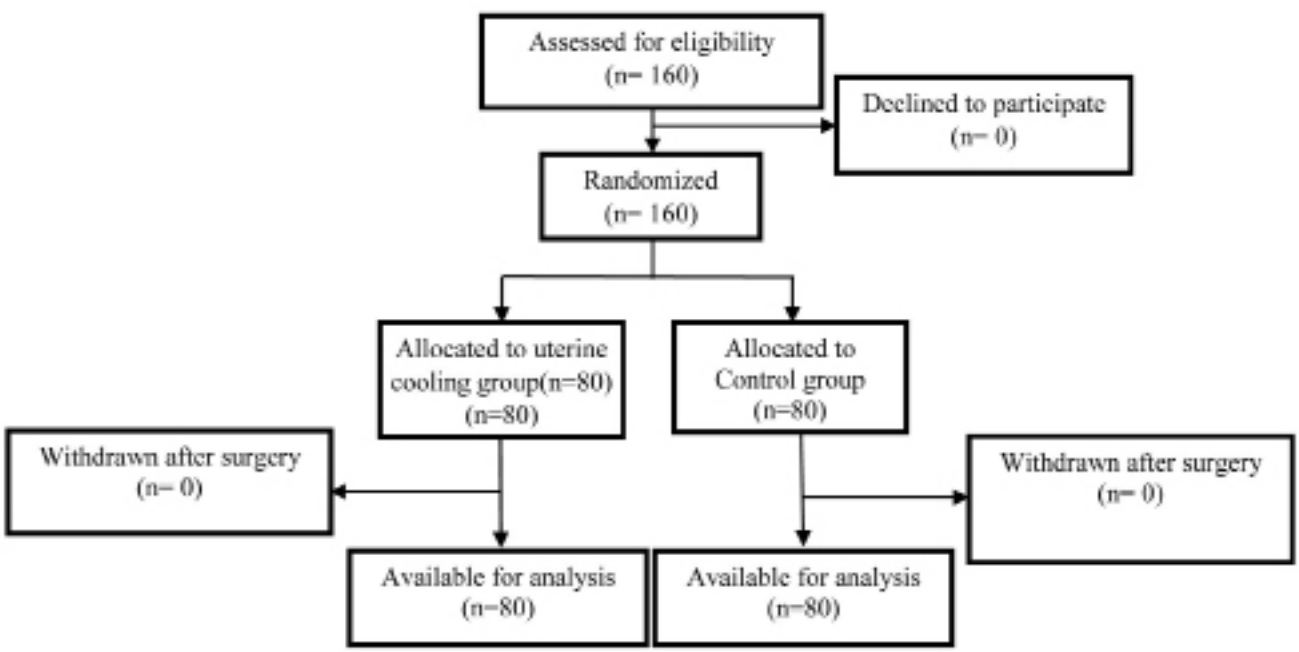

Fig. 1. Flow diagram.

Table 1. Demographic characteristics.

	Uterine cooling (n = 80) Mean ± SD or n (%)	Control (n = 80) Mean ± SD or n (%)	p value
Age (years)	28.5 ± 5.9	29.2 ± 6.1	0.45
BMI (kg/m^2)	29.1 ± 4.9	28.5 ± 4.3	0.43
Gravidity	1.9 ± 1.1	2 ± 0.9	0.57
Parity	0.7 ± 0.7	0.7 ± 0.6	0.90
History of postpartum hemorrhage	1 (1.3)	0	NA
Oxytocin used before cesarean section	5 (6.3)	4 (5.0)	0.73
Indication			0.83
Previous uterine scar	31 (38.8)	32 (40)	
Cephalopelvic disproportion	34 (42.6)	34 (42.5)	
Abnormal fetal presentation	5 (6.2)	7 (8.8)	
Non-reassuring fetal heart rate pattern	10 (12.5)	7 (8.8)	

SD: standard deviation.

Table 2. Surgical characteristics.

	Uterine cooling (n=80) Mean ± SD or n (%)	Control (n=80) Mean ± SD or n (%)	p value
Cesarean section			0.75
Emergency	46 (57.5)	28.5 ± 4.3	
Elective	34 (42.5)	2 ± 0.9	
Incision			0.61
Low midline	54 (67.5)	51 (63.8)	
Pfannenstiel	26 (32.5)	29 (36.2)	
Surgeon			0.61
Staff	25 (31.2)	28 (35.0)	
Residents	55 (68.7)	52 (65.0)	
Preoperative body temperature	37.0 ± 0.3	36.9 ± 0.3	0.34
Intraoperative body temperature	37.1 ± 0.2	37.0 ± 0.2	0.46
Postoperative body temperature	37.1 ± 0.3	37.1 ± 0.3	0.86

SD: standard deviation.

There was a statistically significant difference in intraoperative blood loss between the uterine cooling and routine cesarean section groups (252.8 ± 133.8 vs 472.9 ± 201.8 ml). The mean difference

was 220 ml (95%CI 166.6-273.5). Uterotonic drugs use was significantly less in the uterine cooling group (1.3% vs 10%, p = 0.02). Length of hospital stay was significantly less in the uterine cooling group (3.0 ± 0.5 vs 3.2 ± 0.7 day, p = 0.01). The surgical time was slightly less in the uterine cooling group (35.8 ± 11.4 vs 40.8 ± 14.7 min, p = 0.02). There was no significant difference between groups in postpartum hemorrhage. There was no intraoperative hypothermia found (Table 3).

Table 3. Outcomes.

	Uterine cooling (n=80) Mean ± SD or n (%)	Control (n=80) Mean ± SD or n (%)	p value
Intraoperative measurement blood loss (ml)	252.8 ± 133.8	472.9 ± 201.8	< 0.001
Surgical time (min)	35.8 ± 11.4	40.8 ± 14.7	0.02
Length of hospital stay (days)	3.0 ± 0.5	3.2 ± 0.7	0.01
Use of uterotonic drug	1 (1.3)	8 (10)	0.02
Use of additional surgical intervention	0	1 (1.3)	0.15
Postpartum hemorrhage	1 (1.3)	4 (5)	0.17

SD: standard deviation.

Discussion

The current study demonstrated that uterine cooling could reduce intraoperative blood loss, use of additional uterotonic drugs, and length of hospital stay among pregnant women undergoing cesarean section. The mean difference in intraoperative blood loss in the uterine cooling group was 220 ml. This finding is higher than the 198 ml reported by Mitchell et al. in a similar study[7].

The in-room swab preparation technique used in our study seemed more convenient than the one used by Mitchell et al[7]. In the current study, the icy swabs were prepared using mixed icy sterile normal saline solution with sterile dry swabs in the operative room, while Mitchell et al. prepared the icy swabs using a sterile slush machine. The advantage of the technique used in this study was that the icy swabs would available for every operative room.

The results for the uterine cooling group in the current study differed from those of Mitchell et al[7]. We observed a significantly lower use of additional uterotonic drugs by the uterine cooling group (1.3% vs 10%, p = 0.02); possibly because of good uterine contraction. Length of hospital stay was also shorter (3.0 vs 3.2 days, p = 0.01) albeit not representing a significant clinical difference. The surgical time was shorter in the uterine cooling group (35.8 ± 11.4 vs 40.8 ± 14.7 min, p = 0.02); suggesting that cooling promoted uterine contraction, reducing bleeding and the need for repair procedures; making the operation faster.

There is inconclusive evidence regarding the most appropriate temperature for uterine cooling, thus further study is needed to determine this parameter.

The strengths of the current study were adequate sample size, measurement of blood loss, and use of locally available material. The limitation of our study was that we included only low risk pregnant women.

In summary, the current study demonstrated that uterine cooling effectively reduced intra-operative blood loss compared with routine cesarean section.

Conclusion

Ten percent lidocaine spray was an effective option for pain management during office-based EB.

Gynecologists should, therefore, consider using this spray in routine practice.

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Potential conflicts of interest

The authors declare no conflict of interest.

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