ISSN 0857-6084

THAI JOURNAL OF OBSTETRICS AND GYNAECOLOGY

THE OFFICIAL JOURNAL OF
THE ROYAL THAI COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

VOL. 32 NO. 3 May - June 2024

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Thai Journal of Obstetrics and Gynaecology

The Official Journal of the Royal Thai College of Obstetricians and Gynaecologists

ISSN 0857-6084 E-ISSN 2673-0871

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Published by: PIMDEE Co., Ltd. Tel: 091-009-4011

Website: www.tci-thaijo.org, E-mail: vorapong.p@chula.ac.th

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Thai Journal of Obstetrics and Gynaecology

The Official Journal of the Royal Thai College of Obstetricians and Gynaecologists

ISSN 0857-6084 E-ISSN 2673-0871

Vol. 32 No. 3 May - June 2024

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Thai Journal of Obstetrics and Gynaecology
May 2024, Vol. 32, No. 3, pp. 171.

EDITORIAL

This third issue of Thai Journal of Obstetrics and Gynaecology 2024 contains many interesting articles. One special article is "Role of tranexamic acid in obstetrics and gynecology". The contents include action of tranexamic acid, pharmacokinetic, dosage, indication, contraindication and studies that were investigated the role of tranexamic acid in obstetrics and gynecology.

The Royal Thai College of Obstetricians and Gynaecologists (RTCOG) midyear meeting 2024 was already held during 23-26 April 2024 at Centara Grand at Central Plaza Ladprao Bangkok, Thailand. The theme of this meeting was "Smart Strong Sustainable OB&GYN". The meeting had successful outcomes with 800 participants. There also has many interesting scientific sessions.

The next RTCOG annual meeting will be held during 29 October – 1 November 2024 at Dusit Thani, Pattaya, Chonburi, Thailand. The theme of the meeting is "Optimizing OBGYN". Wish to see you at RTCOG Annual Meeting 2024 at Dusit Thani, Pattaya, Chonburi, Thailand

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

Thai Journal of Obstetrics and Gynaecology
May 2024, Vol. 32, No. 3, pp. 172-177.

SPECIAL ARTICLE

Role of Tranexamic Acid in Obstetrics and Gynecology

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ABSTRACT

Tranexamic acid is a synthetic lysine derivative that exerts an antifibrinolytic effect by reversibly blocking the lysine binding sites on plasminogen, thus preventing fibrin degradation. It has been approved by Food and Drug Administration for treatment of heavy menstrual bleeding and short-term prevention in patients with hemophilia. However, the role of tranexamic acid in obstetrics and gynecology is promising. This review aims to explore the role of tranexamic acid in obstetrics and gynecology.

Keywords: tranexamic acid, obstetrics, gynecology, postpartum hemorrhage, menorrhagia.

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Received: 17 April 2024, **Revised:** 29 April 2024, **Accepted:** 30 April 2024

Tranexamic acid

Tranexamic acid is a synthetic lysine derivative that exerts an antifibrinolytic effect by reversibly blocking the lysine binding sites on plasminogen, thus preventing plasmin (which is still formed by activation of plasminogen by a plasminogen activator) from interacting with lysine residues on the fibrin polymer and subsequent fibrin degradation[1].

The bioavailability of tranexamic acid was significantly higher after intravenous (IV) and intramuscular (IM) administration compared to oral administration. The bioavailability after IV, IM, and oral administration were 100%, 76.7%, and 36.4%, respectively. The time to peak concentration was also significantly shorter for IV administration compared to IM and oral administration[2].

The pharmacokinetics of tranexamic acid are not affected by the presence of food in the gastrointestinal tract; the oral bioavailability is approximately 34%. After oral administration of a single dose of 2 g to 10 fasting healthy male volunteers, the mean maximum plasma concentration of tranexamic acid was 14.4 mg/L and was achieved 2.8 hours postdose. The area under the concentration time curve from 0–6 hours was 59.5 mg*h/L. Tranexamic acid is minimally bound to plasma proteins (about 3%) at therapeutic plasma concentrations (5–10 mg/L), and this appears to be fully accounted

for by binding to plasminogen[1].

The main route of elimination of tranexamic acid is through the kidneys. After oral administration of 250 or 500 mg of tranexamic acid to healthy adults, 40 - 70% of the administered dose was excreted unchanged in the urine within 24 hours. The terminal elimination half-life is about 2 hours[1].

Dosage and administration

Tranexamic acid is approved for the treatment of menorrhagia (blood loss of > 80mL per cycle). The organic pathology as the cause of heavy menstrual bleeding should be excluded before initiating treatment. The drug is available for oral administration as 250 mg or 500 mg tablets and/or capsules and as a syrup containing 500 mg in 5 ml[1].

The recommended dosage of tranexamic acid differs from region to region. The recommended oral dose for the treatment of patients with menorrhagia is 1 to 1.5 g, 3-4 times daily for 3 to 4 days. The total daily oral dose should not exceed 4 g and treatment should be started once heavy menstrual bleeding has started[1].

Indication

Abnormal bleeding and its symptoms in hemorrhagic disease (purpura, aplastic anemia, cancer, leukemia, etc.), bloody sputum and hemoptysis in pulmonary tuberculosis, renal bleeding, genital bleeding, bleeding in prostatomegaly, abnormal bleeding during operation; menorrhagia[3].

The only Food and Drug Administration-approved usage of tranexamic acid is for heavy menstrual bleeding and short-term prevention in patients with hemophilia. This includes tooth extractions in patients with hemophilia, as well as menorrhagia in these patients[4, 5].

Contraindications and side effects

Tranexamic acid is generally well tolerated. It does not interfere with other coagulation factors; therefore, the risk of venous thromboembolism is not increased in those treated with the drug. The most common side effects are gastrointestinal complaints, such as nausea, vomiting, or diarrhea[6]. Another frequently experienced symptom is dysmenorrhea[6].

Tranexamic acid is contraindicated in women with active thromboembolic disease or a history or intrinsic risk of thrombosis or thromboembolism, including retinal vein or artery occlusion[7]. Casati et al reported that although the prevalence of postoperative complications in patients undergoing elective cardiac surgery did not increased in those receiving infusion of tranexamic acid infusion, an increased risk of procoagulant response due to antifibrinolytic treatment also was observed[8].

Due to the antifibrinolytic effect of tranexamic acid, its use can decrease bleeding. Therefore, it may play a role in obstetrics and gynecology. Here is an overview of its role in obstetrics and gynecology:

Role of tranexamic acid in obstetrics

1. Treatment of postpartum hemorrhage (PPH)

Tranexamic acid has been used as an additional treatment for PPH due to the related morbidity and mortality. More than 20,000 patients with PPH were arbitrarily grouped to receive tranexamic acid or a placebo in the WOMAN trial. Although there was no discernible change in thrombosis rates, the death rate from bleeding was much lower in the tranexamic acid group (1.5% vs 1.9%, p = 0.045), especially in women given treatment within 3 hours of giving birth (1.2% in the tranexamic acid group vs 1.7% in the placebo group, p = 0.008). However, hysterectomy was not reduced with tranexamic acid (3.6% of patients in the tranexamic acid group versus 3.5% in the placebo group, p = 0.84)[9].

The American College of Obstetricians and Gynecologists (ACOG) 2017 recommended that tranexamic acid should be considered in the setting of obstetric hemorrhage when initial medical therapy fails due to mortality reduction findings[10].

2. Prevention of PPH

Many studies have evaluated tranexamic acid

in prevention of PPH, either low-risk or high-risk patients. In low-risk patients, a study demonstrated that among women who underwent cesarean delivery and received prophylactic uterotonic agents, tranexamic acid treatment resulted in a significantly lower incidence of calculated estimated blood loss greater than 1000 ml or red blood cell transfusion on day 2 than placebo, but it did not result in a lower incidence of hemorrhage-related secondary clinical outcomes[11].

Ogunkua et al conducted a study to evaluate if prophylactic tranexamic acid treatment reduces calculated blood loss when compared to placebo in women undergoing an elective repeat cesarean delivery. They found that prophylactic treatment with tranexamic acid did not decrease the mean calculated blood loss. Significantly fewer participants had calculated blood loss > 2000 mL in the tranexamic acid group than in the placebo group and had lower D-dimer levels at 24 hours[12].

One meta-analysis suggested that prophylactic tranexamic acid administration is effective among women undergoing cesarean delivery in lowering postpartum blood loss and limiting hemoglobin drop[13].

For a high risk of PPH, Neumann et al conducted a study to assess the role of tranexamic acid in reducing blood loss during elective and unscheduled cesarean deliveries in women at high risk of postpartum hemorrhage. High risk factors for postpartum hemorrhage included obesity, hypertension, multiparity, previous cesarean delivery, multiple pregnancy, abnormally implanted placenta, placenta previa, abruption, uterine leiomyomas, polyhydramnios, and fetal macrosomia. Women at high risk of postpartum hemorrhage undergoing cesarean delivery were recruited and randomized to receive tranexamic acid (500 mg intravenously) or placebo (1:1) at least 10 minutes before the skin incision. A total of 212 women met the inclusion criteria and were randomized (tranexamic acid (n = 106) and placebo (n = 106)). They found that high risk women who received tranexamic acid had significantly less blood loss than women who received placebo. Mean blood loss estimates were 400.9 ml in the tranexamic acid group and 597.9 mL in the placebo group ($p < 0.001$). No woman was transfused in either group[14].

Ortuanya et al evaluated the effectiveness and safety of tranexamic acid in reducing intraoperative blood loss when administered prior to cesarean delivery in women at high risk of postpartum bleeding. Intravenous 1 g of tranexamic acid or placebo was used in a 1:1 ratio. They found that the tranexamic acid group compared to the placebo group showed significantly lower mean blood loss (442.94 ± 200.97 versus 801.28 ± 258.68 mL, $p = 0.001$), higher mean postoperative hemoglobin (10.39 ± 0.96 versus 9.67 ± 0.86 g/dL, $p = 0.001$), lower incidence of postpartum hemorrhage (1.0% versus 19.0%, $p = 0.001$) and lower need for use of additional uterotonic agents after routine management of the third stage of labor (39.0% versus 68.0%, $p = 0.001$), respectively[15].

Sentilhes et al compared the effect of tranexamic acid vs placebo to prevent blood loss after cesarean delivery among women with multiple pregnancies. Women with cesarean delivery before or during labor at 34 weeks of gestation were randomized to receive 1 g of tranexamic acid (n = 160) or placebo (n = 159), both with prophylactic uterotonics. They found that among women with multiple pregnancy and cesarean delivery, prophylactic tranexamic acid did not reduce the incidence of any blood loss-related outcomes[16].

From the evidence above, the ACOG states that current data are insufficient to recommend tranexamic acid prophylaxis for postpartum hemorrhage outside of the context of research[10, 12].

Role of tranexamic acid in gynecology

Tranexamic acid also plays a role in gynecology. Here is an overview of its role in gynecology.

1. Heavy menstrual bleeding

Tranexamic acid has been evaluated in the treatment of heavy menstrual bleeding. There has been a study that aimed to evaluate the effectiveness

of oral tranexamic acid treatment in patients with excessive dysfunctional perimenopausal menorrhagia. All patients (n = 132) took 500 mg of tranexamic acid (Transamine® 3 capsule 2 times per day) during their menstruations. They concluded that oral tranexamic acid is a reasonable treatment option for patients with excessive dysfunctional perimenopousal bleeding with a response rate[17].

2. Myoma uteri

- Myomectomy

A study aimed aim to compare the efficacy and safety profile versus tranexamic acid with ethamsylate to reduce bleeding during myomectomy. They found that oxytocin and tranexamic acid with ethamsylate had no significant value in lowering intraoperative blood loss compared to placebo for abdominal myomectomy which opens a new question about the role of hemostatic drug during myomectomy especially in centers with limited resources and had higher rates[18].

- Bleeding from myoma uteri

A pivotal randomized control trial investigating the effects of tranexamic acid on heavy menstrual bleeding found that tranexamic acid significantly reduced heavy menstrual bleeding; however, the study did not characterize leiomyomas[19]. The presence of leiomyomas was not considered an abnormal finding unless the leiomyomas were of sufficient number and size to warrant surgical management. In this multicenter, double-blind, parallel group study, women with heavy menstrual bleeding were randomized to receive tranexamic acid (1.3 g per dose) or placebo. The study found that women who received tranexamic acid (n=115) met all three primary efficacy end points: first, a significantly greater reduction in menstrual blood loss of -69.6 mL (40.4%) compared with -12.6 mL (8.2%) in the 72 women who received placebo (P<0.001); reduction of menstrual blood loss exceeding a prespecified 50 mL; and last, reduction of menstrual blood loss considered meaningful to women[19]. Tranexamic acid does not treat the fibroid directly, nor does there exist long-term treatment data[20].

3. Irregular uterine bleeding from contraception

There have been several studies to evaluate the treatment of tranexamic acid in irregular uterine bleeding from contraception. A randomized, double-blind study in women with irregular uterine bleeding from IM depot medroxyprogesterone acetate use found that a significantly higher proportion of women treated with tranexamic acid (250 mg 4 times daily for 5 days) (n = 50) compared to placebo (n = 49) stopped bleeding within 7 days after starting therapy (88% vs 8.2%, $p < 0.001$). At 4 weeks after treatment, a bleeding-free interval of > 20 days was found in 68% of subjects treated with tranexamic acid and 0% treated with placebo($p < 0.001$)[21].

Another study in women with irregular uterine bleeding secondary to levonorgestrel implants (Norplant®), found that bleeding stopped within 1 week in a significantly higher proportion of women treated with tranexamic acid (500 mg 4 times daily for 5 days) (n = 34) than with placebo (n = 34) (64.7% vs 35.3%, $p = 0.015$). However, 4 weeks after treatment, there were no significant difference between the tranexamic acid and placebo groups in the proportion of patients who had stopped bleeding (58.8 vs 76.5%) or in the mean duration of bleeding or spotting days (15.4 vs 12.7 days)[22].

From these studies, tranexamic acid may have a benefit in short-term treatment of irregular uterine bleeding from contraception.

4. Gynecological surgery

There have been a few studies to evaluate tranexamic acid for reducing blood loss in gynecological surgeries[23-26]. One study found that a single dose of intravenous tranexamic acid given 15 minutes before surgery could significantly reduce measurement blood loss in surgical staging for endometrial cancer[23]. Another study found that high-dose tranexamic acid was more effective in reducing

blood loss and blood transfusion without increasing the risk of postoperative complications. But the low dose was not effective[24]. Bahadori et al found that prophylactic administration of tranexamic acid resulted in a significant reduction in need for blood transfusion and the duration of hysterectomy[25]. Topsoee et al found that prophylactic treatment with tranexamic acid reduced the overall total blood loss in benign hysterectomy[26]. However, due to the limited number of studies, the clinical use of tranexamic acid for reducing blood loss in gynecological surgeries needs further investigations.

Conclusion

In conclusion, tranexamic acid plays a vital role in obstetrics and gynecology. It is effective in treating postpartum hemorrhage and heavy menstrual bleeding. For other indications, such as prevention of postpartum hemorrhage, heavy bleeding from myoma uteri, irregular bleeding from contraception, and reducing blood loss in gynecological surgeries, further research is still needed.

Potential conflicts of interest

The author declares no conflicts of interest.

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Thai Journal of Obstetrics and Gynaecology
May 2024, Vol. 32, No. 3, pp. 178-185.

GYNAECOLOGY

Clinical Characteristics and Risk Factors Associated with *Chlamydia Trachomatis* Infection in Women Presenting at "Da Nang Hospital for Women and Children"

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ABSTRACT

Objectives: To investigate clinical characteristics and risk factors associated with *Chlamydia trachomatis* infection in women examined at Da Nang Hospital for Women and Children.

Materials and Methods: This was a cross-sectional study of 600 women undergoing examinations at Da Nang Hospital for Women and Children from October 2018 to June 2019. All women were clinically examined and diagnosed with *C. trachomatis* infection by Enzyme-linked Immunosorbent Assay (ELISA) to determine the presence of serum immunoglobulin (Ig) M and IgG antibodies.

Results: *Chlamydia trachomatis (C. trachomatis)* infection rate was 26.0%, of which 70.5% had positive IgG antibodies and 41.6% had positive IgM antibodies, whereas 12.1% had both IgM and IgG antibodies. The majority of patients (49.3%) reported at least three clinical symptoms. The most prevalent clinical and testing manifestations were abnormal vaginal discharge (88.5%), vaginitis (75.0%), cervicitis (65.4%), and Candida co-infection (14.7%). Risk factors associated with *C. trachomatis* infection included manual laborer (odds ratio (OR) 2.1, 95% confidence interval (CI) 1.4 - 3.2, p = 0.0004), first sexual intercourse age < 18 years (OR 1.9, 95%CI 1.2 - 2.7, p = 0.0023), pelvic pain (OR 2.1, 95%CI 1.4 - 3.4, p = 0.0007), vaginitis (OR 2.0, 95%CI 1.2 - 3.2, p = 0.0076), and cervicitis (OR 2.2, 95% CI 1, 5 - 3.3, p = 0.0001).

Conclusion: *C. trachomatis* infection accounted for a high percentage of women aged 18 or older who had experienced sexual intercourse presenting at Da Nang Hospital for Women and Children. Following the investigation of the risk factors, clinicians should pay particular attention to high-risk patients (manual laborer, first sexual intercourse age < 18 years, pelvic pain, vaginitis, cervitis) to enhance sensitivity to disease screening and facilitate timely detection and diagnosis.

Keywords: *Chlamydia trachomatis*, ELISA, risk factors, characteristics, women

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Received: 13 February 2023, **Revised:** 10 October 2023, **Accepted:** 9 November 2023

Introduction

One of the most pressing social problems facing countries across the globe is the rise of sexually transmitted infections (STIs). Morbidity and mortality associated with STIs have a significant impact on quality of life as well as sexual, reproductive, and child health. According to the World Health Organization (WHO), there were an estimated 127.2 million incident *C. trachomatis* infections between 2012 and 2016 worldwide[1].

Untreated *C. trachomatis* infection leads to severe complications such as pelvic inflammatory disease, salpingitis, ectopic pregnancy, and infertility, affecting women and babies. However, it is often latent in nature, with 50.0 - 70.0% of infections reported to be asymptomatic[2]. In addition, this condition adversely affects many aspects of quality of life and increases the risk of cervical cancer and HIV infection by 2 to 3 times[3,4].

In Vietnam, the Central Highlands region occupies a large area and plays a crucial role in establishing trade links between the South and the North. However, there has not been a complete and systematic study of *C. trachomatis* infection in this region. Therefore, this study was conducted to investigate the clinical characteristics and identify risk factors related to *C. trachomatis* infection in patients examined at Da Nang Hospital for Women and Children.

Materials and Methods

This was a descriptive cross-sectional study of 600 women undergoing examinations at Da Nang Hospital for Women and Children from October 2018 to June 2019. The women were recruited using convenience sampling.

Sample size calculation

Formular

$$n = \frac{Z^2_{(1-\alpha/2)}p(1-p)}{d^2}$$

α: Type I error.

Z: standard normal distribution: $\alpha = 0,05 \rightarrow Z_{1-\alpha/2} = Z_{0,975} = 1,96$.

p: 0.51[5].

d: 0,04.

n: minimum sample size.

n = 600 women

Women aged 18 or older, who had experienced sexual intercourse were examined at Da Nang Hospital for Women and Children, were included. All women were informed about the study's purpose and signed a written consent form. Pregnant women, women with mental disorders, and those who refused to participate in the study were excluded.

Patients were examined in an outpatient clinic. The sociodemographic data, clinical and gynecological history were obtained from every eligible participant using a proforma. This was followed by a pelvic examination. Examining the clinical manifestations of abnormal discharge, assessing the condition of the vagina and cervix, mucopurulent endocervical discharge, abdominal and pelvic pain, cervical motion, and uterine or adnexal tenderness.

Laboratory tests performed on patients includes the Whiff test and wet mount microscopy of vaginal secretions for the detection of Trichomonas and Candida. Serology testing for the detection of anti - *Chlamydia trachomatis* IgM and IgG antibodies by ELISA technique, using SERION ELISA Kit.

The machine used to perform the test is Elisys Uno (HUMAN - Germany). The ELISA test was validated according to standard procedures of the Department of Biochemistry, Danang Hospital for Women and Children. The quality of the ELISA test was confirmed through the Internal Quality Control (IQC) of ELISA serology testing for anti - *C. trachomatis* antibodies at the Hospital.

Our study used the method of detecting *C. trachomatis* by ELISA to find specific antibodies against pathogens. The antigen used was major outer membrane protein (MOMP) (a species–specific antigen for *C. trachomatis*), attached to the surface of the bacterial envelope. The first immune response to Chlamydia infection is an IgM antibody, which appears after 2–3 weeks. In the following 6 to 8 weeks, IgG will be produced. Both IgM and IgG antibodies react to MOMP antigens.

Test results: levels of Anti - *Chlamydia trachomatis* IgM and IgG antibodies were as follows: + < 9 U/ml: Negative; 9 - 11 U/ml: Border line; 11 U/ml: Positive.

Table 1 reveals diagnostic criteria for *C. trachomatis* infection by serological tests[6]

Table 1. Result interpretation for C. trachomatis antibodies[6]

IgM	IgG	Meaning
-	-	- No evidence of C. trachomatis infection.
+	-	- Recent infection with C. trachomatis. A repeat test should be conducted to confirm the diagnosis.
-	+	- IgG antibodies persisted following C. trachomatis infection.
		- Presently infected with C. trachomatis.
		- Reinfection with C. trachomatis.
		- Chronic C. trachomatis infection. A repeat test confirms the diagnosis of chronic infection at one month and after three months (and/or the onset of clinical symptoms).
+	+	- Being infected with C. trachomatis

Ig: immunoglobulin

Data were coded and analyzed using Stata software. The chi-square test with a 95% significance level was used to determine the relationship between the variable of *C. trachomatis* infection and other variables including demographic and baseline characteristics, clinical symptoms, and testing results. The difference was considered statistically significant when $p < 0.05$ with a 95% confidence interval. A univariate and multivariate logistic regression analysis was used to identify risk factors and control for potential confounders of *C. trachomatis* infection.

The study had patient consent and was approved by the Ethical Review Committee of the Danang Hospital for Women and Children. Decision number of the Ethical Review Committee was 45/BVPSN-ĐN/HĐYD//2018.

Results

During the research period from October 2018 to June 2019 at Da Nang Hospital for Women and Children, 600 research samples were collected and analyzed. Patients' demographic and baseline characteristics and the gynecological history are illustrated in Table 2.

In our study, the prevalence of *C. trachomatis* infection was 156 cases, accounting for 26.0%. Among of these patients with positive *C. trachomatis* antibodies, IgG antibodies accounted for 70.5%, and 65 cases (41.6%) were positive for IgM antibodies. Only 19 cases (12.1%) were positive for both IgM and IgG antibodies.

The clinical symptoms were heterogeneities, including abnormal vaginal discharge, vulvar pruritus, dyspareunia, intermenstrual bleeding, dysuria,

abdominal and pelvic pain (Fig. 1). 49.3% of patients with at least three clinical symptoms. In wet mount testing, the more frequent coinfection manifestations were Candida (14.7%) (Table 3).

Table 2. Patients' baseline characteristics

Factors	n (%)
Demographic	
Age group	
18 – 25	101 (16.8)
26 – 35	401 (66.8)
36 – 45	94 (15.7)
> 45	4 (0.7)
Occupation	
Intellectual laborer	241 (40.2)
Manual laborer	232 (38.7)
Other	127 (21.1)
Marital status	
Single	20 (3.3)
Married	562 (93.7)
Divorced	11 (1.8)
Other	7 (1.2)
Gynecological history	
Age at first sexual intercourse	
< 18 years old	263 (43.8)
History of genital infections	
Yes	302 (50.3)
History of STIs	
Yes	216 (36.0)
History of contraceptive use	
No	564 (94.0)
Condom	22 (3.7)
Other	14 (2.3)

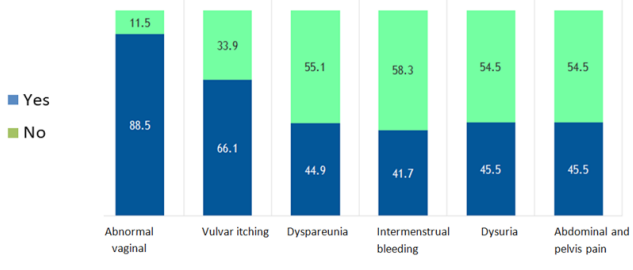

Fig. 1. Common symptoms in patients infected with C. trachomatis.

Table 3. Results of wet mount of abnormal vaginal discharge in patient' s C. trachomatis infection.

Co – infection factors	n (%)
Trichomonas	19 (12.2)
Candida	23 (14.7)
Other bacteria	19 (12.2)

A univariate analysis of factors affecting the rate of *C. trachomatis* infection found that patients with manual laborer, age at first sexual intercourse < 18 years, abnormal vaginal discharge, vulvar itching, lower abdominal and pelvic pain, vaginitis, and cervicitis were all associated with the risk of *C. trachomatis* infection. Particularly, it was found that patients with three or more clinical symptoms were at a 1.6 times greater risk of *C. trachomatis* infection (95%CI 1.1 – 2.3, p = 0.0154) (Table 4).

Table 4. Results of univariate logistic analysis of factors associated with C. trachomatis infection.

Factors	p value	OR value	95%CI
Patients' demographic	19 (12.2)		
Occupation	0.0009	1.9495	1.3 – 2.9
Age at first sexual intercourse	0.0139	1.6	1.1 – 2.3
Clinical symptoms			
Abnormal vaginal discharge	0.0031	2.3	1.3 – 3.9
Vulvar itching	0.0426	1.5	1.0 – 2.2
Lower abdominal and pelvic pain	0.0001	2.2	1.5 – 3.2
Three or more clinical symptoms	0.0154	1.6	1.1 – 2.3
Physical examinations			
Abnormal amount of vaginal discharge	0.0122	1.7	1.1 – 2.4
Vaginitis	0.0004	2.1	1.4 – 3.2
Cervicitis	< 0.0001	2.2	1.5 – 3.2
Vaginitis + Cervicitis	< 0.0001	3.0	2.1 – 4.4

CI: confidence interval, OR: odds ratio

Multivariate regression analysis revealed that there were five factors that influence *C. trachomatis* infection. Specifically, manual laborers had a 2.1 times higher risk of *C. trachomatis* infection than intellectual workers (p = 0.0004), being sexually active before the age of 18 increased the risk of *C. trachomatis* infection by 1.9 times (p = 0.0023), the group of patients with pelvic pain symptoms had a 2.1 times higher risk of *C. trachomatis* infection compared to the asymptomatic group (p = 0.0007). Similarly, the risk of *C. trachomatis* infection was 2.0 times higher in the group of patients with vaginitis (p = 0.0076) and 2.2 times higher in patients with cervicitis compared with the asymptomatic group (p = 0.0001) (Table 5).

Table 5. Investigating independent factors of C. trachomatis infection using multivariable regression analysis.

Features	OR	95%CI	p value
Occupation	2.1	1.4 – 3.2	0.0004
Age at first sexual intercourse	1.9	1.2 – 2.7	0.0023
Lower abdominal pain and pelvic pain	2.1	1.4 – 3.4	0.0007
Vaginitis	2.0	1.2 – 3.2	0.0076
Cervicitis	2.2	1.5 – 3.3	0.0001

CI: confidence interval, OR: odds ratio

Discussion

Regarding the demographic and baseline characteristics of the study sample, age is one of the key features associated with STIs in general and *C. trachomatis* infection in particular. Different age groups have different biological and social risks. Many studies have shown that *C. trachomatis* infection is more prevalent in youths with strong sexual activity, which greatly affects reproductive health, fetus, and infants[1,2,5,7].

With regard to the infection rate of *C. trachomatis*, significant differences were found between the studies. The infection rate in our study was the same as that of Ahmadnia (2013)[7], but higher than that of Chandeying et al (2002)[8] and Francis et al (2017)[9]. This can be explained by different study methods, including the study subjects (women with/without clinical symptoms in population, women examined at general hosptals/specialized hospitals, or those who had complications due to *C. trachomatis* infection), methodology (sample size, tests used in diagnosis (culture, Polymerase chain reaction-enzyme linked immunosorbent assay (PCR-ELISA)), as well as changes in sexual habits, younger age at sexual intercourse, multiple sex partners and a sex partner with other concurrent sex partners.

PCR is recommended "gold standard" to defined diagnosis *C. trachomatis* by WHO, however, this is a complicated and expensive technique that requires a standard laboratory and highly trained technicians, as well as takes more time for results. So, it is difficult to apply frequently in developing countries like Vietnam. ELISA is an option for screening.

On the other hand, using ELISA for diagnosing *C. trachomatis* is valuable in epidemiological studies describing the spectrum of infections caused by *C. trachomatis*, supporting the diagnosis of acute complications due to *C. trachomatis* infection (Reiter-reactive arthritis), chronic and invasive infections (PID, infertility due to tubal factors, etc.)[10, 11]. Thanks to its many advantages, the ELISA technique is now widely used to screen and diagnose *C. trachomatis* at provincial levels of healthcare. Using this test is simple, cost-effective, and does not require extensive equipment. It provides faster results, assists with early detection, and contributes to the reduction of genital complications as well as the control of infection in the community[12]. However, the ELISA test has lower sensitivity and specificity than the polymerase chain reaction (PCR). Furthermore, the MOMP antigen used in ELISA is also present on the cell membrane of other pathogenic *C. trachomatis* serotypes (e.g., Trachoma, Lymphogranuloma venereum), so cross-reactivity with other *C. trachomatis* serotypes and some other bacterial strains can still occur[12]. Conversely, the antibody-forming reaction takes time, resulting in the possibility of missing patients at an early stage.

According to the WHO, the clinical manifestations of STIs, particularly *C. trachomatis* infection, are neither progressive nor specific. Approximately 50.0% - 75.0% of women infected with *C. trachomatis* are asymptomatic, but the pathogens are detectable when

tested. Therefore, this is a significant challenge in diagnosing and treating this disease in a timely manner in order to prevent its transmission to the spouse or partner. According to our findings, *C. trachomatis* infection causes a variety of symptoms that were similar to those described by many domestic and foreign researchers[2, 7, 13].

However, previous studies have shown that clinical symptoms are only predictive of *C. trachomatis* infection in men and of marginal value in women. According to Muvunyi (2011), common symptoms such as lower abdominal pain, dysuria, vaginal discharge, and vaginal itching are not related to the risk of *C. trachomatis* infection in women[14]. The studies of Gravningen (2012)[15], Torrone (2014)[16], Lallemand[17] (2016), and Pinto (2016)[18] also reported that multiple sexual partners and symptomatic sexual partners were significant predictors of *C. trachomatis* infection in women. Therefore, in our study, we examined the relationship between the number of reported symptoms and the prevalence of *C. trachomatis* infection. It was found that in patients with three or more clinical symptoms, the rate of *C. trachomatis* infection increased by 1.6 times. This finding also serves as a reminder for clinicians to consider the possibility of *C. trachomatis* infection in women with many clinical symptoms. However, the relationship between *C. trachomatis* infection and the number of clinical symptoms might not be statistically significant when using multivariate regression analysis. Therefore, further studies are needed to clarify this association.

After investigating related risk factors with multivariable regression analysis, there were five factors that are actually related to the prevalence of *C. trachomatis* infection, including manual laborer, lower abdominal and pelvic pain, vaginitis, and cervicitis. They doubled the odds of having chlamydial infection. Sexual intercourse at younger age was associated with a higher prevalence. These variables have been shown in many studies to be significantly related to *C. trachomatis* infection. According to a study conducted in Swaziland (2017), the risk of *C. trachomatis* infection in the unemployed group was 2.2 times higher than the stable employment group (OR 2.2, 95%CI 1.0 – 4.7, p = 0.045) and 2.8 times higher than in the other groups of labor (OR 2.8, 95%CI 1.5 – 5.5, p = 0.002)[19]. Similarly, regarding the age of sexual intercourse and the risk of STIs, Gravningen (2012) noted that younger sexual intercourse was associated with a higher prevalence of *C. trachomatis* infections ($p < 0.05$)[15]. Additionally, cervicitis is one of the common clinical symptoms of *C. trachomatis* infection. Research by Schoeman (2012) also found this association with OR 4.9[20].

Conclusion

C. trachomatis infection accounted for a high percentage of women aged 18 or older who had experienced sexual intercourse. Burden of *Chlamydia trachomatis* was high in this region. Manual laborers, women with coitarche before age of 18 years and women having genital symptoms had a doubled odds of having *Chlamydia trachomatis* infection. Following the investigation of the risk factors, clinicians should pay particular attention to high-risk patients to enhance sensitivity to disease screening and facilitate timely detection and diagnosis in order to prevent reproductive complications associated with *Chlamydia trachomatis* infection. This test helps detect infection early in patients with symptoms for timely treatment. Although this is not a PCR test - the gold standard, ELISA is low cost, takes short time to get results, and has simple techniques that are easy to perform, so it is meaningful in community screening.

Acknowledgments

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Potential conflicts of interest

The authors declare no conflicts of interest.

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Thai Journal of Obstetrics and Gynaecology
May 2024, Vol. 32, No. 3, pp. 186-195.

OBSTETRICS

Incidence, Risk factors, Maternal and Neonatal Outcomes of Second-stage Cesarean Section at Siriraj Hospital

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ABSTRACT

Objectives: To determine the incidence of cesarean section (CS) during second stage of labor, to evaluate maternal and neonatal outcomes, and to determine risk factors.

Materials and Methods: A retrospective cohort study was conducted in 636 women with term, singleton pregnancies with cephalic presentation who delivered during January to April 2021. Data were extracted from medical records, including baseline, antenatal care data, mode of deliveries and outcomes. The incidence of 2nd stage CS was estimated. Maternal and neonatal outcomes were compared between different modes of deliveries.

Results: Overall CS rate was 28.5% with 22.8% occurred during 1st stage and 5.7% had CS during 2nd stage of labor. CS during 2nd stage of labor contributed to 19.9% of all CS. Instrumental vaginal delivery was performed in only 5.5%. Those with 2nd stage CS were more likely to be overweight or obese, and to have gestational weight gain above recommendation. The most common indication for CS was cephalopelvic disproportion. Neonatal birth weight and rate of macrosomia were significantly higher among those with 2nd stage CS while birth asphyxia was more common among 1st stage CS. Other maternal and neonatal outcomes were comparable.

Conclusion: CS during second stage of labor occurred in 5.7% of all women, contribution to 19.9% of all CS. Those with 2nd stage CS were more likely to be overweight and obese, to have excessive gestational weight gain, and to have higher neonatal birth weight and rate of macrosomia. There was no increase in serious adverse outcomes in women with 2nd stage CS.

Keywords: cesarean section, second stage of labor, pregnancy outcomes, risk factors.

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Received: 22 July 2023, **Revised:** 12 October 2023, **Accepted:** 15 November 2023

อุบัติการณ์ ปัจจัยเสี่ยง และ ภาวะแทรกซ้อนของมารดาและทารก ของการผ่าตัดคลอดในระยะที่สองของการคลอดในโรงพยาบาลศิริราช

กนิษฐา ศรีกฤษณพล, ดิฐกานต์ บริบูรณ์หิรัญสาร

บทคัดย่อ

วัตถุประสงค์*: เพื่อศึกษาอุบัติการณ์ ผลการตั้งครรภ์ และประเมินปัจจัยเสี่ยงของการผ่าตัดคลอดในระยะที่สองของการคลอด*

วัสดุและวิธีการ*: ทำการศึกษาย้อนหลังโดยเก็บข้อมูลจากสตรีตั้งครรภ์ทั้งหมด 636 รายที่เป็นครรภ์เดี่ยว อายุครรภ์ครบกำหนดและทารกเป็นท่าศีรษะ ที่คลอดบุตรในช่วงเดือน มกราคม 2564 ถึง เมษายน 2564 รวบรวมข้อมูลจากเวชระเบียน ประกอบด้วย ข้อมูลทั่วไป ข้อมูลทางสูติศาสตร์และการฝากครรภ์ ข้อมูลการคลอด และภาวะแทรกซ้อนของสตรีและทารกแรกเกิด คำนวณอุบัติการณ์การผ่าตัดคลอดในระยะที่สองของการคลอด และเปรียบเทียบผลลัพธ์การคลอดของสตรีและทารกแรกเกิดในแต่ละวิธีการคลอด*

ผลการศึกษา*: พบอุบัติการณ์การผ่าตัดคลอดรวมทั้งหมดร้อยละ 28.5 ของสตรีตั้งครรภ์ทั้งหมด โดยเป็นการผ่าตัดคลอดในระยะที่หนึ่งของการคลอดร้อยละ 22.8 และการผ่าตัดคลอดในระยะที่สองของการคลอดร้อยละ 5.7 ซึ่งคิดเป็นร้อยละ 19.9 ของการผ่าตัดคลอดทั้งหมด พบว่ามีการใช้เครื่องมือช่วยคลอดทางช่องคลอดร้อยละ 5.5 สตรีที่ได้รับการผ่าตัดคลอดในระยะที่สองของการคลอด เป็นกลุ่มที่มีน้ำหนักเกินเกณฑ์หรือภาวะอ้วนและมีน้ำหนักตัวเพิ่มขึ้นเกินเกณฑ์สูงกว่า ข้อบ่งชี้การผ่าตัดที่พบมากที่สุดคือภาวะช่องเชิงกรานไม่ได้สัดส่วนกับขนาดของศีรษะทารก กลุ่มที่ผ่าตัดคลอดในระยะที่สองของการคลอดมีน้ำหนักทารกแรกเกิดและทารกที่มีน้ำหนักเกิน 4,000 กรัม สูงกว่าอย่างมีนัยสำคัญทางสถิติ ในขณะที่พบภาวะขาดออกซิเจนของทารกแรกเกิดสูงกว่าในกลุ่มการผ่าตัดคลอดในระยะที่หนึ่งของการคลอด ไม่พบความแตกต่างของผลการตั้งครรภ์ของสตรีและทารกแรกเกิดด้านอื่น ๆ ระหว่างการคลอดในแต่ละวิธี*

สรุป*: อุบัติการณ์การผ่าตัดคลอดในระยะที่สองของการคลอดเท่ากับร้อยละ 5.7 ของสตรีตั้งครรภ์ทั้งหมด โดยคิดเป็นร้อยละ 19.9 ของการผ่าตัดคลอดทั้งหมด ซึ่งพบเป็นกลุ่มสตรีมีน้ำหนักเกินเกณฑ์หรือภาวะอ้วนและมีน้ำหนักตัวเพิ่มขึ้นเกินเกณฑ์สูงกว่า และทารกมีน้ำหนักแรกเกิดและทารกที่มีน้ำหนักเกิน 4,000 กรัมสูงกว่า ไม่พบการเพิ่มขึ้นของผลการตั้งครรภ์ที่ไม่พึงประสงค์ชนิดร้ายแรงในการผ่าตัดคลอดในระยะที่สองของการคลอด*

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Introduction

The World Health Organization (WHO) suggests that appropriate cesarean section (CS) rate should be between 10% and 15% at population level[1]. However, data from 150 countries during 1990 to 2014 showed that the global average of CS rate has increased by 12.4% (from 6.7% to 19.1%) with an average annual rate of increase of 4.4% and Asia has the second largest absolute increase of 15.1% (from 4.4% to 19.5%)[2]. In concordance with the increase in overall CS rate, increased tendency of CS during second stage of labor has also been observed[3-5]. Studies in the United Kingdom showed that the rate of CS during second stage of labor increased from 0.5-0.9% to 2.1-2.2%[3, 4]. A study in Singapore reported that 4.4% of pregnant women had emergency second stage CS[6]. Another study in Australia reported that 5.6% of all cesarean section cases was done at full cervical dilatation, but there was no increasing trend over the last 5 years[7].

In association with the increasing incidence of CS during second stage of labor, increasing rates of failed operative vaginal delivery and reduced attempts at intraumental delivery have been documented[3, 5]. A previous study reported that the most common indication for CS during second stage of labor was failure to progress without an attempt at instrumental delivery[7]. Presence of a consultant at the time of delivery has been reported to be an important determinant for CS during second stage of labor that the chance of vaginal delivery was significantly increased from 30% to 70%[8, 9].

Cesarean section during second stage of labor has been associated with increased maternal and neonatal mortality and morbidity[4-6, 10-13]. Related complications include extension of uterine incision, maternal hemorrhage, intraoperative trauma to bladder or bowel, blood transfusion need, increase length of hospital stay, neonatal trauma, neonatal intensive care unit (NICU) admission, and perinatal asphyxia[13-15].

At Siriraj Hospital, there is also an increasing trend of CS over the past many years and overall CS rate is currently as high as 40-50%. However, there is still limited information on CS that was performed during the second stage of labor. In addition, the operation could also result in more serious complications than those performed during the first stage of labor. Therefore, the primary objective of this study was to determine the incidence of CS during the second stage of labor. In addition, possible risk factors as well as maternal and neonatal outcomes were evaluated. The information would provide additional information on CS rate and could lead to better decision-making process and care of pregnant women in the future.

Materials and Methods

A retrospective cohort study was conducted at the Department of Obstetrics and Gynecology, Faculty of Medicine Siriraj Hospital after approval of Siriraj Institutional Review Board (SIRB). Sample size was estimated from approximate incidence of CS during second stage of labor of 13% of all CS. At 95% significance level and 5% allowable error and estimated 35% CS rate form a pilot study, at least 550 delivering women were required. As data were collected from all women during January to April 2021, a total of 636 women were included.

Singleton, term with cephalic presentation women in spontaneous or induced labor were included in this study. Women who were indicated for CS (e.g., previous CS, placenta previa, etc.) were excluded. Medical records of 636 pregnant women who delivered during January to April 2021 who met inclusion and exclusion criteria were retrieved and data were extracted. The second stage of labor was defined as the stage of labor that cervical dilatation reaches 10 cm.

Routine antenatal care according to institutional guideline was provided either by attending residents or staff. Universal gestational diabetes mellitus (GDM) screening was offered to all pregnant women using 50-gram glucose challenge test and 100-gram oral glucose tolerance test. Any antenatal complications were managed as appropriate according to specific

management guidelines. Intrapartum care was managed by attending residents under staff supervision. Progress of labor monitoring and interventions during labor, including artificial rupture of the membranes, use of oxytocin and analgesics, and decision of CS were performed according to institutional guideline, customized to each woman. Intrapartum ultrasonography was not routinely performed.

Data collection included baseline characteristics, antenatal care data, complications during pregnancy, labor characteristics, intrapartum care, mode of delivery, indication for cesarean section, operative data, and maternal and neonatal outcomes. Regarding indication for CS, cephalopelvic disproportion (CPD) was diagnosed according to institutional guideline, i.e., when there was abnormal labor progression (including protracted cervical dilatation, arrest of cervical dilatation, prolonged deceleration phase or prolonged second stage) with adequate uterine contraction for at least 2 hours. Pre-pregnancy body mass index (BMI) was calculated from pre-pregnancy weight in kg divided by squared height in meter. According to the Institute of Medicine, BMI were classified into underweight (< 18.5 kg/m^2), normal (18.5-24.9 kg/m^2), overweight (25-29.9 kg/m^2), and obesity (≥ 30 kg/m^2) and corresponding recommended gestational weight gain were 12.5-18 kg, 11.5-16 kg, 7-11.5 kg, and 5-9 kg, respectively[16].

Data on perinatal outcomes included intraoperative complications, postpartum hemorrhage, uterine atony, neonatal birth weight birth asphyxia (Apgar score < 7), and neonatal intensive care unit (NICU) admission. Incidence of CS during second stage of labor was estimated. Various characteristics were compared between different modes of delivery to determine associated factors. In addition, maternal and neonatal outcomes were also evaluated and compared between different modes of delivery.

Descriptive statistics were used to describe various variables as appropriate, including mean, standard deviation, number, and percentage. Chi square test and analysis of variance (ANOVA) with Tukey post hoc test were used for comparison of characteristics between different modes of delivery. A p value of < 0.05 was considered statistically significant.

Results

During the study period, there were 636 deliveries that met the inclusion criteria and were included in the analysis. Baseline characteristics of the women are shown in Table 1. The mean age was 29.4 years, mean pre-pregnancy BMI was 22.5 kg/m^2, 53.3% were nulliparous, and 22.8% were overweight or obese. Mean gestational weight gain was 13.8 kg and 34.7% gained weight above recommendation. GDM and preeclampsia were diagnosed in 13.8% and 11.3% respectively.

Table 1. Baseline characteristics of pregnant women

Characteristics	n (%)
Mean age ± SD (years)	29.4 ± 5.9
Mean BMI ± SD (kg/m^2)	22.5 ± 4.9
GA at first ANC ± SD (weeks)	11.4 ± 5.9
Mean gestational weight gain ± SD (kg)	13.8 ± 5.8
Nulliparous	339 (53.3)
BMI category	
Underweight	126 (19.8)
Normal	365 (57.4)
Overweight	97 (15.3)
Obese	48 (7.5)
Gestational weight gain	
Below recommendation	176 (27.7)
Within recommendation	239 (37.6)
Above recommendation	221 (34.7)
GDM	88 (13.8)
Preeclampsia	72 (11.3)

SD: standard deviation, BMI: body mass index, GA: gestational age, ANC: antenatal care, GDM: gestational diabetes mellitus

Table 2 summarizes labor and delivery characteristics. Mean gestational age (GA) at delivery was 38.6 weeks of gestation. The majority (90.1%) of the women were in spontaneous labor 41.4% had cervical dilatation of ≥ 5 cm at admission. Artificial rupture of membranes, oxytocin infusion, and analgesic use were 53.8%, 54.4%, and 43.4%, respectively. Of the women included, 63 had induced labor (9.9%). Artificial rupture of membranes, oxytocin infusion, and analgesic use were 54%, 76.2%, and 45.2%, respectively. CS was performed in 181 women (28.5%) and CPD was the most common indication in 54.7%. CS during the second stage of labor occurred in 36 cases (5.7%). Of all CS, 80.1% occurred in 1st stage and 19.9% in 2nd stage of labor. In those with vaginal delivery, median duration of second stage of labor was 18 minutes and 35 (5.5%) were diagnosed with prolonged second stage and delivered by instrumental vaginal delivery (all were by vacuum extraction).

Table 2. Labor and delivery characteristics of the pregnant women (n = 636).

Characteristics	n (%)
Mean GA at delivery ± SD (weeks)	38.6 ± 1.1
Spontaneous of labor (n = 573)	
Cervical dilatation ≥ 5 cm on admission	237 (41.4)
Artificial rupture of membranes	308 (53.8)
Oxytocin infusion	312 (54.4)
Analgesic use	249 (43.4)
Induction of labor (n = 63)	
Artificial rupture of membranes	34 (54)
Oxytocin infusion	48 (76.2)
Analgesic use	28 (45.2)
Delivery mode	
Vaginal delivery	420 (66)
Instrumental vaginal delivery[b]	35 (5.5)
Cesarean section	181 (28.5)
Second stage duration (n = 420)	
Median duration (min) (IQR)	18 (11, 35)
Prolonged second stage	35 (5.5)
Indication for CS (n = 181)	
CPD	99 (54.7)
Non-reassuring fetal heart rate	42 (23.2)
Others[b]	40 (22.1)
Stage of labor at CS (n = 181)	
1st stage of labor	145 (80.1)
2nd stage of labor	36 (19.9)

[a] All are vacuum extraction. [b] Includes prolonged rupture of membranes, failed induction, fetal macrosomia.

GA: gestational age, SD: standard deviation, CPD: cephalopelvic disproportion, CS: cesarean section, IQR: interquartile range

Table 3 shows a comparison of various characteristics between different modes of delivery. BMI was significantly higher in those with all CS ($p < 0.001$), while gestational weight gain was comparable between groups. Those with CS were significantly more likely to be nulliparous and overweight or obese. Those with 2nd stage CS were more likely to be overweight or obese, and to have gestational weight gain above recommendation compared to those with 1st stage CS and vaginal delivery. GDM was also significantly more common among those with CS but rates of preeclampsia were comparable.

Table 3. Comparison of various characteristics between different modes of delivery.

Characteristics	Vaginal	1st stage CS	2nd stage CS	p value
	n = 455	n = 145	n = 36	
Mean age ± SD (years)	29.0 ± 5.9	30.1 ± 6.1	31.4 ± 4.7	0.018
Mean BMI ± SD (kg/m^2)	22.0 ± 4.6	23.6 ± 5.4[a]	24.2 ± 5[a]	< 0.001
Mean GA at delivery ± SD (weeks)	38.1 ± 1.0	38.8 ± 1.1[b]	38.8 ± 1.1	0.026
Mean gestational weight gain ± SD (kg)	13.8 ± 5.8	13.6 ± 5.9	15 ± 6.1	0.409
	n (%)	n (%)	n (%)	
Nulliparous	203 (44.6)	114 (78.6)	22 (61.1)	< 0.001
BMI category				0.002
Underweight	99 (21.8)	22 (15.1)	5 (13.9)	
Normal	270 (59.3)	81 (56)	14 (38.9)	
Overweight	59 (12.9)	27 (18.6)	11 (30.5)	
Obese	27 (6)	15 (10.3)	6 (16.7)	
Gestational weight gain				0.012
Below recommendation	133 (29.2)	39 (26.9)	4 (11.1)	
Within recommendation	178 (39.1)	50 (34.5)	11 (30.6)	
Above recommendation	144 (31.7)	56 (38.6)	21 (58.3)	
GDM	44 (9.7)	37 (25.5)	7 (19.4)	< 0.001
Preeclampsia	46 (10.1)	18 (12.4)	8 (22.2)	0.078

[a] significantly different from vaginal delivery ($p = 0.001$ and 0.019 for 1st and 2nd stage CS)
[b]: Significantly different from vaginal delivery ($p = 0.037$)
CS: cesarean section, SD: standard deviation, BMI: body mass index, GA: gestational age, GDM: gestational diabetes mellitus

A comparison of labor and delivery characteristics are shown in Table 4. Those with CS were more likely to occur in women with induction of labor. Among those with spontaneous labor, cervical dilatation ≥ 5 cm on admission was significantly less common in those with CS. Artificial rupture of membranes were more common in CS both in those with spontaneous labor and induction of labor. In terms of indications for CS, CPD was significantly more likely in those with 2nd stage compared to 1st stage CS (88.9% vs 46.2%, $p < 0.001$).

Comparisons of maternal and neonatal outcomes are shown in Table 5. Those with 2nd stage CS had significantly higher birth weight than those with vaginal delivery. Rate of macrosomia was highest among those with 2nd stage CS with a significant linear trend. Birth asphyxia was significantly more common among those with 1st stage CS. Other outcomes were comparable between the 3 groups.

Table 4. Comparison of labor and delivery characteristics between different modes of delivery.

Characteristics	Vaginal n = 455	1st stage CS n = 145	2nd stage CS n = 36	p value
	n (%)	n (%)	n (%)	
Onset of labor				< 0.001
Spontaneous	423 (93)	118 (81.4)	32 (88.9)	
Induction	32 (7)	27 (18.6)	4 (11.1)	
Spontaneous of labor (n = 573)				
Artificial rupture of membranes	253 (59.8)	39 (33.1)	16 (50)	< 0.001
Cervical dilatation ≥ 5 cm on admission	202 (47.8)	25 (21.2)	10 (31.3)	< 0.001
Oxytocin use	246 (54.2)	88 (62.4)	23 (63.9)	0.15
Analgesic use	197 (43.3)	60 (42.9)	18 (50)	0.723
Induction of labor (n = 63)				
Artificial rupture of membranes	23 (71.9)	8 (29.6)	3 (75)	0.004
Oxytocin use	27 (84.4)	17 (63)	4 (100)	0.081
Analgesic use	17 (53.1)	8 (30.8)	3 (75)	0.109
Indication for CS (N=181)				< 0.001
CPD	-	67 (46.2)	32 (88.9)	
Non-reassuring fetal heart rate	-	38 (26.2)	4 (11.1)	
Others	-	40 (27.6)	0 (0)	

CS: cesarean section, CPD: cephalopelvic disproportion

Table 5. Comparison maternal and neonatal outcomes between different mode of delivery.

Outcomes	Vaginal n = 455	1st stage CS n = 145	2nd stage CS n = 36	p value
Mean birth weight ± SD (g)	3051.2 ± 361.5	3131.7 ± 438.4	3244.2 ± 403.3a	0.003
	n (%)	n (%)	n (%)	
Extension of uterine incision				< 0.001
Postpartum hemorrhage	423 (93)	118 (81.4)	32 (88.9)	
Uterine atony	32 (7)	27 (18.6)	4 (11.1)	
Birth weight for GA				
AGA	253 (59.8)	39 (33.1)	16 (50)	< 0.001
SGA	202 (47.8)	25 (21.2)	10 (31.3)	< 0.001
LGA	246 (54.2)	88 (62.4)	23 (63.9)	0.15
Macrosomia	197 (43.3)	60 (42.9)	18 (50)	0.723
Birth asphyxia				
NICU admission	23 (71.9)	8 (29.6)	3 (75)	0.004

[a] Significant difference compared to vaginal delivery (p = 0.01)

[b] Significant linear trend (p = 0.003)

CS: cesarean section, SD: standard deviation, GA: gestational age, AGA: average for gestational age, SGA: small for gestational age, LGA: large for gestational age, NICU: neonatal intensive care unit

Discussion

In this study, the overall CS rate was 28.5%. CS during second stage of labor occurred in 5.7% of all women, which contributed to 19.9% of all CS. The rate was higher compared with previous reports of 1.8-2.65% of all women[7, 10, 12, 13] and 4.8-5.6% of all CS[7, 10]. This might partly be due to differences in population characteristics and intrapartum care process between settings. Another important factor might be from the differences in the attempts of instrumental delivery.

A study in the United Kingdom observed a significant increasing trend of second-stage CS over a 30-year period that the rate increased from 0.5% in 1976 to 2.1% in 2006[4]. Similarly, a study in Ireland also reported that the rate of second-stage CS increased from 0.9% in 2006 to 1.8% in 2008[10]. More recent study also reported that the rate significantly increased by over a third in the ten-year period from 0.8% to 1.24%[11]. However, there was no observed trend over the 5 years from the other study in Australia[7].

Previous studies reported that approximately 40% of women had CS during second stage of labor without a trial of instrumental delivery[7, 10]. However, in this study, all the women underwent second stage CS did not have instrumental delivery attempts and the majority were diagnosed with cephalopelvic disproportion. This might be from lack of competency in performing the operation due to inadequate training and experience as a decline in instrumental deliveries is observed over the past decade in our institution. The results also showed that instrumental deliveries occurred in only 5.5% of all women in this study. However, the use of instrumental delivery might not always be successful and might not reduce the rate of CS during second stage of labor as a previous study. The proportion of second stage CS because of failed instrumental delivery also increased from 59.1% in 1976 to 71.0% in 2006[4]. Whether the use of instrumental deliveries will decrease the rate of second stage CS could not be determined from this study and needs to be explored in future studies.

The results of this study showed that women with second stage CS were more likely to be overweight or obese and to have excessive gestational weight gain than those with vaginal delivery and CS during first stage of labor. Nulliparity was common among those with CS at any stage and more common in women delivered by CS during second stage of labor[7, 10, 11, 13]. Overweight and obesity as well as excessive gestational weight gain have been consistently reported to increase the risk of CS[17]. Both conditions could lead to abnormal labor progression, difficult delivery and increase the risk of CS. On the other hand, risk of CS was lowered among obese women who gained weight below the recommendation, without increased adverse neonatal outcomes[17, 18]. Therefore, appropriate weight gain during pregnancy could help reduce CS rate, both overall and during second stage of labor.

In terms of adverse maternal and neonatal outcomes, no serious complication was observed in this study. This was similar to a previous study in Singapore[6]. However, other previous studies reported increased adverse outcomes among those with CS during second stage of labor, including postpartum hemorrhage, need for blood transfusion, NICU admission[4, 10, 13]. Macrosomia was more common among those with second stage CS which was consistent with higher diagnosis of cephalopelvic disproportion. These women could have normal labor progression until they reached second stage of labor. On the other hand, birth asphyxia was more common in those with first stage CS. This could be related to the higher rate of non-reassuring fetal heart rate in this group. A previous study reported higher rate of macrosomia in second stage CS[15] and others reported increased in low cord blood arterial pH value and neonatal birth asphyxia[4, 13]. Moreover, some studies reported intraoperative complications, such as uterine trauma and uterine incision extension[6, 13], such complications were not observed in this study. Some studies also reported that maternal and neonatal morbidities were comparable between those with second stage CS and instrumental

deliveries[11, 19].

The limitations of this study included the retrospective nature of data that some information was missing. There was relatively small number of women delivered by CS during second stage of labor which could result in less valid and reliable comparisons of some variables between groups. Generalization of the results are also limited due to the study was conducted in a single tertiary care center. However, the strengths of this study might include that this was probably among a few studies in Thailand concerning CS rate during second stage of labor in relatively low risk pregnant women. In addition, diagnosis and decision to perform a CS were verified by consultation staff and based on intrapartum management guideline.

The results of this study could help in more understanding of the rate of second stage CS and related outcomes. Associated risk factors that were identified could help caring physicians raise their awareness or better forecast of the condition that might lead to better and timely decision to minimize risk of adverse outcomes.

Further evaluation of second stage CS is still needed in various aspects and in different contexts of care, including incidence, risk factors, and related adverse maternal and neonatal outcomes. Larger prospective studies could provide more details regarding these interesting aspects. The results would be helpful in raising awareness of care providers and planning better intrapartum care.

Conclusion

In conclusion, the overall CS rate was 28.5%. CS during second stage of labor occurred in 5.7% of all women, which contributed to 19.9% of all CS. Most common indication was cephalopelvic disproportion. Those with second stage CS were more likely to be overweight and obese and to have excessive gestational weight gain. There were no significant serious adverse outcomes in women with second stage CS.

Potential conflicts of interest

The authors declare no conflicts of interest.

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Thai Journal of Obstetrics and Gynaecology
May 2024, Vol. 32, No. 3, pp. 196-204.

GYNAECOLOGY

Intravenous Dexamethasone for Preventing Postoperative Nausea and/or Vomiting in Total Abdominal Hysterectomy: A randomized double-blinded, placebo-controlled trial

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ABSTRACT

Objectives: To assess the efficacy of postoperative dexamethasone compared to placebo in reducing the incidence of postoperative nausea and/or vomiting (PONV) in women undergoing benign total abdominal hysterectomy (TAH).

Materials and Methods: Participants who were scheduled for TAH with or without adnexal surgery between August 2022 and April 2023 were included. The participants were randomly divided into two groups: the dexamethasone group (n = 43), who received 2 ml (8 mg) of intravenous dexamethasone injection, and the control group (n = 43) received 2 ml of normal saline at 2 hours after surgery.

Results: There was no significant difference in the incidence of PONV within 24 hours between the dexamethasone group and control group (32.6% vs 48.8%, relative risk 0.67(95% confidence interval 0.39 to 1.13), p = 0.09). The need for antiemetic drugs was not statistically different between groups (0% vs 9.3%, p = 0.05), and without serious adverse events in both groups. The dexamethasone group experienced a lesser pain score than the control group at 24 hours (4.7 ± 1.5 vs 5.8 ± 2.2, p = 0.01) after surgery. There was no difference in additional analgesic requirements.

Conclusion: The administration of 8 mg of intravenous dexamethasone postoperatively did not result in a significant reduction in PONV within the first 24 hours following benign TAH.

Keywords: postoperative nausea and vomiting, PONV, dexamethasone, hysterectomy.

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Received: 29 September 2023, **Revised:** 6 December 2023, **Accepted:** 20 December 2023

ผลของการการฉีดยาเดกซ่าเมทาโซนในการป้องกันภาวะคลื่นไส้ และหรือ อาเจียนหลังผ่าตัดมดลูก: การศึกษาแบบสุ่ม

กันยาวีร์ สุหงษา, เจษฎา วุฒิธรรมสุข, ทุมวดี ตั้งศิริวัฒนา

บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาผลของการฉีดยาเดกซ่าเมทาโซนในการลดภาวะคลื่นไส้และหรืออาเจียนหลังผ่าตัดมดลูกทางหน้าท้องที่ไม่ใช่มะเร็ง*

วัสดุและวิธีการ: *ผู้เข้าร่วมวิจัยที่ได้รับกำหนดการผ่าตัดมดลูกทางหน้าท้องและหรือปีกมดลูกและรังไข่ ระหว่างเดือนสิงหาคม พ.ศ.2565 ถึงเมษายน พ.ศ.2566 ได้รับการสุ่มแบ่งอาสาสมัครเป็นสองกลุ่ม กลุ่มละ 43 คน กลุ่มได้รับยาเดกซ่าเมทาโซนฉีดทางเส้นเลือดดำ ปริมาณ 2 มิลลิลิตร (ขนาด 8 มิลลิกรัม) และกลุ่มควบคุม ได้รับนอร์มอลซาไลน์ปริมาณ 2 มิลลิลิตร แบบฉีดทางเส้นเลือดดำ ที่สองชั่วโมงหลังผ่าตัด*

ผลการศึกษา: *ไม่พบความแตกต่างอย่างมีนัยสำคัญของอุบัติการณ์การเกิดคลื่นไส้อาเจียนภายใน 24 ชั่วโมงหลังผ่าตัดของกลุ่มที่ได้ยาเดกซ่าเมทาโซนและกลุ่มควบคุม (32.6% vs 48.8%, relative risk 0.67(95% confidence interval 0.39 to 1.13), p = 0.09) ไม่มีความแตกต่างอย่างมีนัยสำคัญทางสถิติในการขอยาต้านอาเจียนเพิ่ม (0% vs 9.3%, p = 0.05) ไม่มีผลข้างเคียงที่รุนแรงเกิดขึ้นในผู้ร่วมวิจัยทั้งสองกลุ่ม กลุ่มเดกซ่าเมทาโซนมีคะแนนความปวดหลังผ่าตัด 24 ชั่วโมง (4.7 ± 1.5 vs 5.8 ± 2.2, p = 0.01) ไม่พบว่ามีความแตกต่างในการขอรับยาแก้ปวดเพิ่มเติมในทั้งสองกลุ่ม*

สรุป: *การได้รับยาเดกซ่าเมทาโซน 8 มิลลิกรัมแบบฉีดทางเส้นเลือดดำหลังผ่าตัดไม่ช่วยลดภาวะคลื่นไส้อาเจียนอย่างมีนัยสำคัญทางสถิติในช่วง 24 ชั่วโมงหลังการผ่าตัดมดลูกทางนรีเวชที่ไม่ใช่มะเร็ง*

คำสำคัญ: *ยาเดกซ่าเมทาโซน, ภาวะคลื่นไส้อาเจียนหลังการผ่าตัด, ผ่าตัดมดลูก*

Introduction

postoperative nausea and/or vomiting (PONV) is a common symptom complained in early postoperative patients. PONV can be uncomfortable owing to substantial medical complications such as aspiration of stomach contents and wound dehiscence. Participants with severe PONV symptoms may be unable to walk, necessitating an extended hospital stay[1].

The Apfel simplified risk score is used to assess the risk of PONV for participants undergoing surgery under general inhaled anesthesia considering a) female sex, b) nonsmoking status, c) history of nausea and or vomiting, motion sickness, and d) postoperative intravenous opioids that each parameter was worth 1 point, for a total of 4 points. The respective risk of PONV was around 10%, 20%, 40%, 60%, and 80% when the total scores were 0, 1, 2, 3, and 4[1]. Our gynecologic participants got at least 2 points on the Apfel simplified risk assessment.

PONV has been demonstrably reduced by dexamethasone when used as a premedication for preventing chemotherapy-induced vomiting[2]. Notwithstanding, dexamethasone is not widely used to prevent PONV among participants undergoing benign total abdominal hysterectomy (TAH)[1].

The intravenous route of dexamethasone is an effective antiemetic mechanism explained by the central suppression of the brainstem[3]. Dexamethasone also inhibits multiple inflammatory cytokines, suppressing inflammation and decreasing pain[4].

Eight milligrams of intravenous dexamethasone significantly reduced PONV with no adverse events, including hypersensitivity, pruritus, dyspepsia, infected wound, and increased blood sugar level. The safety of a single dosage of dexamethasone has been established[5].

TAH is the most frequent procedure in benign uterine tumor[6]. Although the meta-analysis showed dexamethasone could reduce PONV incidence in participants who underwent abdominal surgery, their study included various operations and populations but the study included only a few participants who underwent TAH[7]. The benefit of dexamethasone to reduce PONV in gynecologic surgery especially TAH had limited data[7].

The difference in time administering intravenous dexamethasone before and after induction reported a significant reduction in PONV compared with placebo especially in 24 hours[8]. However, there is no evidence of dexamethasone used in the postoperative period to prevent PONV. The advantages of using 8 mg of intravenous dexamethasone included a reduction in the incidence of PONV; early ambulation, especially within the first 24 hours after surgery; reduced postoperative pain, increased satisfaction, and improved postoperative care[9]. Therefore, the authors conducted the randomized controlled trial (RCT) to assess the efficacy of postoperative dexamethasone compared to placebo in reducing the incidence of PONV in women undergoing benign TAH.

Materials and Methods

This was a randomized, double-blinded, placebo-controlled trial approved by the Khon Kaen Hospital Institute Review Board in Human Research. Recruited participants were diagnosed with benign gynecologic conditions and scheduled for TAH with or without adnexal surgery. Participants were excluded if they (a) had a known hypersensitivity to dexamethasone; (b) had conditions that might influence gastrointestinal motility (including previous bowel surgery, previous abdominal irradiation, chronic constipation, pancreatitis, peritonitis, hypothyroidism, and chronic use of drugs that impact intestinal peristalsis; (c) had underlying diabetes mellitus who got poor glycemic control; (d) were immunocompromised (tuberculosis, human immunodeficiency virus Infection); and/or, (e) experienced an intraoperative blood loss of more than 1,000 ml or blood loss that required blood transfusion. The participants were informed about the study at the gynecology ward before the surgery. The participants were required to sign the letter of consent before enrollment. Postoperative hysterectomy and/or adnexal surgery who met the eligibility criteria were randomly assigned into two groups using a computer-generated

block of four and allocation concealment using sequentially opaque envelopes.

Baseline characteristics were recorded, including age, body mass index (BMI), comorbid diseases, indications for surgery, previous abdominal surgery, operation, operative time, anesthetic time, anesthetic gas inhaler, intraoperative antiemetic drug, intraoperative dexamethasone, intraoperative opioids, total doses of morphine injection, and estimated blood loss. Before the operation, all participants received the same standard preoperative care, anesthetic protocol, and intravenous antibiotic prophylaxis after induction of anesthesia. The surgical procedures were performed by staff.

Two hours after the operation refers to the time participants transferred from the post-anesthesia care unit (PACU) to inpatient department (IPD), and the ward nurse opened the randomization list, which contained 2 ml of dexamethasone or normal saline, identical in appearance. The dexamethasone group received 2 ml (8 mg) of intravenous dexamethasone, while the control group received 2 ml of intravenous normal saline two hours after surgery. The surgeon and research assistant were blinded to the investigation. The research assistant asked the participants to assess the pain level using a 10-cm visual analog scale (VAS) after arriving at the IPD and gaining full consciousness before receiving intravenous drugs. After that, the participants were informed about various outcomes that might be observed (feelings of nausea and/or vomiting). While participants were asleep, research assistants observed the PONV symptoms every four hours until 24 hours after surgery. A digital clock was set up as the standard time for recording the outcomes. If they had any symptoms of PONV described as just nausea with or without vomiting, they could request the antiemetic drug metoclopramide 10 mg intravenously every 6 hours. Dipstick blood sugar was checked every 6 hours. If hyperglycemia (250 mg/dl or more) was detected, insulin was administered per standard protocol. At 24 hours postoperatively, the participants were asked to assess the pain scores by VAS. The postoperative care protocol was intravenous administration of an opioid agent (2 mg of morphine for weight < 50 kg or 3 mg for weight ≥ 50 kg) every 4 hours for 24 hours. Participants who complained of severe pain over 8 on the VAS score could request additional morphine injections to relieve the breakthrough pain. Prophylactic antibiotics (2 g of cefazolin) were given before surgery and continued for 24 hours after surgery. Ambulation was promoted the day after surgery. The postoperative feeding step was standardized as a liquid and soft diet on the first postoperative day and a regular diet for the next 24 hours.

Additional analgesics were provided according to the level of pain. Standard pain relief was based on the World Health Organization (WHO) analgesic ladder. For example, oral paracetamol 500 mg or ibuprofen 400 mg were given when the pain score was 4-7 out of 10, while intravenous morphine was provided when the pain was ≥ 8 out of 10.

Primary and secondary outcomes were assessed. The primary outcome was the incidence of PONV after a benign TAH within 24 hours. The secondary outcomes were additional antiemetic requirements, additional analgesic requirements, side effects of dexamethasone, pain score measured by VAS (0-10), and the duration of hospital stay.

Participants could be discharged when they could tolerate a regular diet, had no postoperative complications, including abnormal bleeding per vagina, fever, and wound complications, and could ambulate without assistance. Before discharge, the length of hospital stays, satisfaction, and adverse events were recorded.

The sample size was calculated by using the incidence of PONV from the pilot study (Pintervention = 0.4, Pcontrol = 0.73) with a power of 80%, an α level of 0.05, and a dropout rate of 5%. Eighty-six participants (43 per group) were required. Data were statistically analyzed based on an intention-to-treat analysis using STATA version 14. The student's t-test was used to analyze continuous data. Chi-squared and Fisher's exact test were used to analyze continuous and categorical data. A p value < 0.05 was considered statistically significant.

Results

Between August 2022 and April 2023, 89 eligible participants scheduled for benign TAH, with or without adnexal surgery, were enrolled in the study. One was excluded due to intraoperative estimated blood loss of more than 1,000 ml and received blood transfusion; two were excluded due to incidental intraoperative findings of malignancy. Eighty-six participants were randomly assigned to the dexamethasone and control groups (Fig. 1).

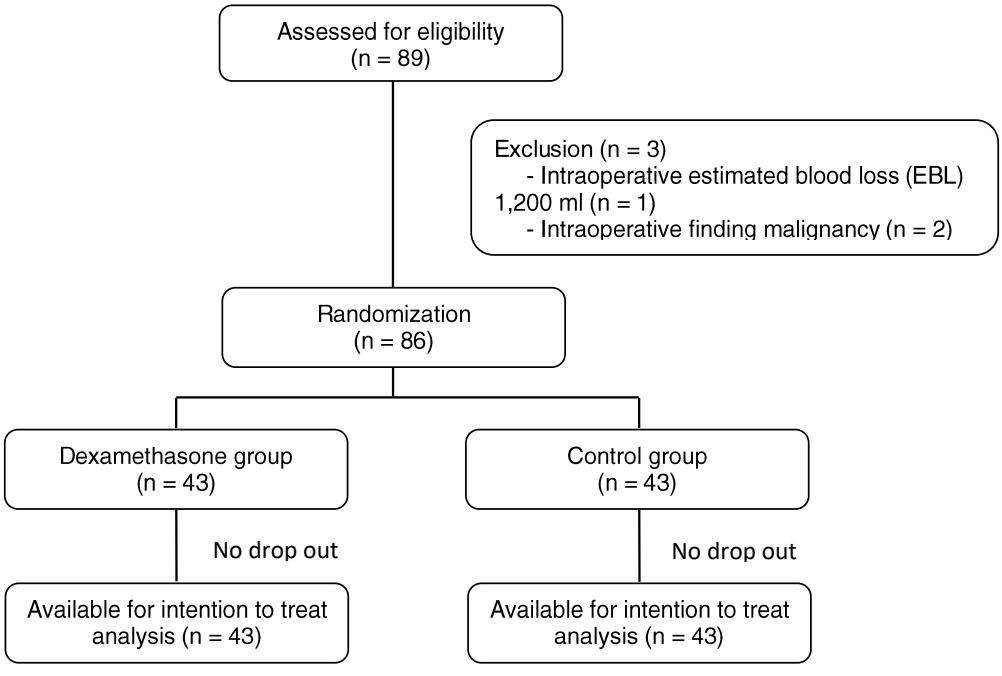

Fig. 1. Research study flow

Baseline characteristics were similar between groups, except hypertension in co-morbid diseases was found in the intervention group more than in the control group (Table 1).

The incidence of PONV within 24 hours of the dexamethasone group was 14 (32.6%), and the control group was 21 (48.8%), relative risk (RR) 0.67 (95% confidence interval (CI) 0.39-1.13), p = 0.09. After subgroup analysis, the incidence of PONV at 4, 8, 12, 16, 20, and 24 hours after surgery was not statistically significant (Table 2).

The additional antiemetic drugs were not significantly different among groups (0% vs 9.3%, p = 0.05) as well as additional analgesic drugs.

There were no serious adverse events found in this study. The incidence of dyspepsia and dizziness in the dexamethasone group was not statistically significant compared to the control group (14% vs 9.3%, p = 0.39 and 4.7% vs 0%, p = 0.24). Neither hyperglycemia nor insulin treatment were found (Table 3).

Pain scores measured by VAS (0-10) at 24 hours after surgery were lower in the dexamethasone group than in the control group. At 2 hours postoperatively, the scores were 7.7 ± 2.3 vs 8.6 ± 1.8 (mean difference 0.93 (95%CI 0.03-1.83), p = 0.04) and at 24 hours postoperatively, they were 4.7 ± 1.5 vs 5.8 ± 2.2 (mean difference 1.09 (95%CI 0.26-1.92), p = 0.01). The length of hospital stay was not different among groups (mean difference = 0.09 (95%CI 0.09-0.28), p = 0.32) (Table 3).

Table 1. Baseline characteristics.

	Dexamethasone group (n = 43)	Control group (n = 43)	p value
Age (yrs), mean ± SD	48.0 ± 8.1	49.4 ± 8.2	0.44 [a]
BMI (kg/m^2), mean ± SD	23.9 ± 3.4	25.7 ± 4.8	0.05 [a]
Co-morbid diseases, n (%)	11 (25.6)	18 (41.9)	0.11 [c]
Diabetes mellitus	1 (2.3)	5 (11.6)	0.20 [b]
Hypertension	4 (9.3)	15 (34.9)	< 0.001 [c]
Dyslipidemia	0 (0.0)	5 (11.6)	0.05 [b]
Thyroid	3 (7.0)	0 (0.0)	0.24 [b]
others	4 (9.3)	6 (14.0)	0.50 [c]
Indication for surgery, n (%)			
Leiomyoma	32 (74.4)	31 (72.1)	0.80 [c]
Adenomyosis	8 (18.6)	5 (11.6)	0.36 [c]
Adnexal disease	2 (4.7)	6 (14.0)	0.26 [b]
HSIL	1 (2.3)	1 (2.3)	1.00 [b]
Previous abdominal surgery, n (%)	23 (53.5)	27 (62.8)	0.38 [c]
Major abdominal surgery	12 (27.9)	12 (27.9)	1.00 [c]
Minor abdominal surgery	11 (25.6)	15 (34.9)	0.34 [c]
Operation, n (%)			
TAH c BS	30 (69.7)	29 (67.4)	0.82 [c]
TAH c unilateral SO	6 (14.0)	8 (18.6)	0.55 [c]
TAH c BSO	7 (16.3)	6 (14.0)	0.76 [c]
Operative time (min), mean ± SD	99.8 ± 29.0	101.8 ± 26.5	0.73 [a]
Anesthetic time (min), mean ± SD	132.9 ± 31.8	139.4 ± 30.5	0.33 [a]
Anesthetic substance for induction, n (%)			
Nitrous oxide	22 (51.2)	15 (34.9)	0.12 [c]
Propofol	43 (100.0)	43 (100.0)	1.00 [c]
Intraoperative drug, n (%)			
Ondansetron	22 (51.2)	27 (62.8)	0.26 [c]
Dexamethasone	19 (44.2)	23 (53.5)	0.38 [c]
Intraoperative opioid, n (%)			
Morphine	40 (93.0)	38 (88.4)	0.46 [c]
Fentanyl	3 (7.0)	5 (11.6)	0.43 [c]
Total dose of Morphine injection ± SD	22.7 ± 2.1	23.3 ± 2.7	0.22 [a]
Estimated blood loss (ml), mean ± SD	216.2 ± 28.0	168.3 ± 16.5	0.14 [a]

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

BMI: body mass index, SD: standard deviation, HSIL: high grade squamous intraepithelial lesion, TAH: total abdominal hysterectomy, BS: bilateral salpingectomy, SO: salpingo-oophorectomy, BSO: bilateral salpingo-oophorectomy

Table 2. Incidence of PONV within 24 hours.

Primary Outcome	Dexamethasone group (n = 43)	Control group (n = 43)	RR (95%CI)	p value
Incidence of PONV, n (%)				
within 24 hours	14 (32.6)	21 (48.8)	0.67 (0.39-1.13)	0.09 [a]
4 hours	5 (11.6)	6 (14.0)	0.83 (0.27-2.53)	0.50 [c]
8 hours	2 (4.7)	4 (9.3)	0.50 (0.10-2.59)	0.40 [b]
12 hours	1 (2.3)	3 (7.0)	0.33 (0.04-3.08)	0.30 [b]
16 hours	0 (0.0)	4 (9.3)	0	0.58 [b]
20 hours	3 (7.0)	4 (9.3)	0.75 (0.18-3.15)	0.50 [c]
24 hours	3 (7.0)	4 (9.3)	0.75 (0.18-3.15)	0.50 [c]

[b] Fisher's exact test, [c] chi-square test, significant $p < 0.05$*
CI: confidence interval, PONV: postoperative nausea and/or vomiting, RR: relative risk

Table 3. Secondary outcomes: additional drug requirements, side effects, pain score, and length of hospital stay.

	Dexamethasone group (n = 43)	Control group (n = 43)	RR (95%CI)	p value
Additional drug requirements, n (%)				
Metoclopramide	0 (0.0)	4 (9.3)	0	0.50 [b]
Morphine	0 (0.0)	0 (0.0)	-	-
Side effects of dexamethasone, n (%)				
Dyspepsia	6 (14.0)	4 (9.3)	1.50 (0.46-4.94)	0.39 [c]
Dizziness	2 (4.7)	0 (0.0)	0	0.24 [b]
Postoperative pain score, mean ± SD				
24 hours	7.7 ± 2.3	8.6 ± 1.8	0.93 (0.03-1.83)	0.04 [a*]
24 hours	4.7 ± 1.5	5.8 ± 2.2	1.09 (0.26-1.92)	0.01 [a*]
Length of hospital stay (days), mean ± SD	3.0 ± 0.6	3.0 ± 0.0	0.09 (0.09-0.28)	0.32 [a]

[a] student t-test, significant $p<0.05$*, [b] Fisher's exact test, c chi-square test, significant $p < 0.05$*
CI: confidence interval, SD: standard deviation

Discussion

The incidence of PONV was about 32% in participants who underwent benign TAH who received 8 mg of dexamethasone postoperatively, which was lower than the study by Selzer et al[9] who used 8 mg of dexamethasone intravenously for women who underwent cesarean delivery with intrathecal morphine and reported an incidence of PONV of more than 80%. Their results might be explained by intrathecal morphine-induced PONV symptoms, which are typically more common than the intravenous route[1]. However, when compared with placebo, our study also showed no statistically significant difference, which was similar to the study by Selzer[9].

According to the difference of time administering intravenous dexamethasone before and after induction

reported the same effect, the intervention groups had lesser PONV incidence, especially in 24 hours[8]. However, dexamethasone was not given in all patients at induction period. Our study administered dexamethasone two hours after the operation refers to the time participants transferred from PACU to IPD, gained full consciousness, and complained suffering from PONV symptoms due to anesthetics gas inhaler or intraoperative opioids. Dexamethasone might have benefit in PONV and postoperative pain within 24 hours[9]. Weibo S et al reviewed 43 clinical trials that used 8 mg of intravenous dexamethasone to prevent vomiting in participants who underwent operation under general anesthesia. They recommended that a high dose of intravenous dexamethasone be used to prevent vomiting in participants who underwent an operation under general anesthesia[7], which contradicted our findings. The different results may be explained by the participants in this study who received standard treatment by an anesthesiologist using a gas inhaler, which affects PONV, which might explain the differences in findings. They assessed each participant individually using the Apfel simplified risk score and rating participants as at high or low risk of PONV. Anesthesiologists delivered intraoperative dexamethasone and antiemetic drugs to more than half of the participants, which could have contributed to the low incidence of PONV in both groups of this study.

The inflammatory process of surgery can cause pain. The dexamethasone group had considerably lower postoperative pain scores than the control group. This finding supported the concept that dexamethasone has anti-inflammatory properties and can minimize postoperative discomfort. According to Parthasarathy[10], intravenous dexamethasone 8 mg considerably reduced postoperative pain compared to placebo in surgical patients.

Our study participants reported dyspepsia and dizziness, and dizziness was reported in both groups without significant differences. None of the participants reported other complications, such as pruritus, high blood sugar levels that required insulin treatment, wound infections, and wound dehiscence.

The strengths of the study included a power of 80%, its prospective, double-blind, placebo-controlled design, adequate sample size, and absence of dropouts. Limitations of this study included the prophylactic PONV therapy during intra-operative administration of dexamethasone and antiemetic drugs would impact the incidence of PONV within 24 hours.

Conclusion

Postoperative administration of 8 mg of intravenous dexamethasone did not significantly reduce the incidence PONV in women undergoing benign TAH.

Acknowledgments

We thank (a) the Obstetric-Gynecologists, residents, and the ward nursing staff for their support throughout the research, and (b) Mr. Bryan Roderick Hamman for assistance with the English-language presentation of the manuscript under the aegis of the Publication Clinic, Research Affairs, Khon Kaen University.

Potential conflicts of interest

The authors declare no conflicts of interest.

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Thai Journal of Obstetrics and Gynaecology
May 2024, Vol. 32, No. 3, pp. 205-213.

OBSTETRICS

Prediction of Successful Normal Vaginal Delivery by Intrapartum Transperineal Ultrasonographic Measurement of the Angle of Progression

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ABSTRACT

Objectives: This study aimed to evaluate the angle of progression's predictive ability for successful normal vaginal delivery, establishing its cutoff value and clinical application.

Materials and Methods: In this prospective, diagnostic accuracy study, we enrolled pregnant women admitted to the labor room with term singleton cephalic presentation pregnancies, excluding those at risk of undergoing cesarean delivery with indications other than cephalopelvic disproportion. The angle of progression was measured using transperineal ultrasound during the active phase of labor.

Results: A total of 114 pregnant women were included in the study. Among these participants, 102 underwent vaginal delivery (89.5%), while 12 underwent cesarean delivery (10.5%). No significant differences were observed in age, body mass index, gestational age, cervical dilatation, amniotic membrane status, or fetal birth weight among the participants. However, multiparous women displayed a tendency towards higher vaginal delivery rates than nulliparous ones. The angle of progression's cut-off value, assessed by the area under the receiver operating characteristic curve, was 0.703. The optimal threshold on the curve, maximizing the area under the curve, was identified at 96.9 degrees, with a sensitivity of 82.4%, specificity of 58.3%, positive predictive value of 94.4%, and negative predictive value of 28% for predicting successful of normal vaginal delivery.

Conclusion: Transperineal ultrasound measurement of the angle of progression greater than 96.9 degrees showed good potential for predicting the success of normal vaginal delivery in pregnant women during the active phase of labor.

Keywords: angle of progression, intrapartum ultrasound, transperineal ultrasound, vaginal delivery.

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Received: 28 September 2023, **Revised:** 20 December 2023, **Accepted:** 3 January 2024

การทำนายความสำเร็จของการคลอดปกติทางช่องคลอดโดยใช้คลื่นเสียงความถี่สูงวัด angle of progression ผ่านภายนอกช่องคลอดในระยะการคลอด

เมธากวิน ตรีตรง, สุดถวิล ไกรนรา

บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาความสามารถและค่ามุมที่เหมาะสมของ angle of progression ในการทำนายการคลอดปกติทางช่องคลอดและความสำคัญต่อการประยุกต์ใช้ในทางคลินิก*

วัสดุและวิธีการ: *บทความนี้เป็นการศึกษาในรูปแบบการศึกษาเชิงสังเกตไปข้างหน้าเพื่อหาความแม่นยำในเครื่องมือการตรวจวินิจฉัยโดยทำการวัดค่า angle of progression ในกลุ่มหญิงตั้งครรภ์เดี่ยวและมีส่วนนำของทารกเป็นศีรษะที่เข้าสู่ระยะเร่งคลอดในห้องคลอดโรงพยาบาลหาดใหญ่โดยแยกหญิงตั้งครรภ์ที่มีความเสี่ยงต่อการผ่าตัดคลอดด้วยข้อบ่งชี้อื่นนอกเหนือจากการผิดสัดส่วนของขนาดทารกและอุ้งเชิงกราน*

ผลการศึกษา: *หญิงตั้งครรภ์จำนวน 114 คนได้เข้าร่วมในการศึกษานี้ พบว่า 102 คน (ร้อยละ 89.5) สามารถคลอดบุตรทางช่องคลอดได้และ 12 คน (ร้อยละ 10.5) คลอดบุตรด้วยวิธีการผ่าตัดคลอด โดยไม่พบความแตกต่างในด้านของ อายุ, ดัชนีมวลกาย, อายุครรภ์, การเปิดของปากมดลูก, สถานะของถุงน้ำคร่ำ และน้ำหนักแรกคลอดของทารกระหว่างสองกลุ่มนี้ อย่างไรก็ตามพบว่าอัตราการคลอดบุตรปกติทางช่องคลอดพบในหญิงตั้งครรภ์หลายครั้งมากกว่า ค่า angle of progression ที่ 96.9 องศา มีพื้นที่ใต้เส้นโค้ง receiver operating characteristic (ROC) มากที่สุดที่ 0.703 ในการทำนายความสำเร็จในการคลอดปกติทางช่องคลอด โดยมีความไว้อยู่ที่ร้อยละ 82.4, ความจำเพาะร้อยละ 58.3, ค่าการทำนายเป็นบวกร้อยละ 94.4 และค่าการทำนายเป็นลบร้อยละ 28*

สรุป: *การวัด angle of progression ด้วยคลื่นเสียงความถี่สูงผ่านภายนอกช่องคลอดในระยะคลอดที่ค่ามุมมากกว่า 96.9 องศา มีความสามารถในการทำนายความสำเร็จของการคลอดปกติทางช่องคลอดในระยะเร่งคลอด*

คำสำคัญ: *angle of progression, การตรวจคลื่นเสียงความถี่สูงในระยะคลอด, การตรวจคลื่นเสียงความถี่สูงผ่านภายนอกช่องคลอด, การคลอดปกติทางช่องคลอด*

Introduction

Traditionally, the assessment of labor progression heavily relies on digital pelvic examinations, primarily considering cervical dilatation and fetal head station as crucial clinical indicators for diagnosing protraction and arrest of labor. However, evidence suggests that pelvic examinations can be prone to inaccuracy and subjectivity, particularly in cases involving the presence of caput succedaneum, which can obscure the determination of fetal head station and position[1]. These unreliable clinical findings may lead to misjudgments in the management of pregnancies experiencing a lack of labor progression, delays in transferring patients to higher-level healthcare facilities, an increased incidence of unnecessary cesarean deliveries, and potential maternal and fetal morbidity.

As a result, there is a growing demand for more accurate and objective tools to complement the assessment of fetal head descent. In recent years, the use of intrapartum ultrasound has gained prominence due to its capacity to provide quantitative measurements and its widespread availability in most labor rooms. Several intrapartum ultrasound parameters have been reported to correlate with fetal head descent, including head-perineum distance, head-symphysis distance, angle of progression, and progression distance[2]. Among these, the angle of progression has demonstrated the highest potential to represent fetal head descent[3-5]. First described in 2009(5), it is defined as the angle between the long axis of the maternal pubic symphysis and a line drawn tangentially from the most descended part of the fetal skull.

Since then, studies have reported that the angle of progression can also serve as a predictive indicator for the mode of delivery[6-11]. However, the cut-off values have shown variability across these studies. Currently, there is no consensus or established clinical practice guidelines regarding the utilization of the angle of progression in general medical practice.

In this study, our primary objective is to determine the diagnostic performance of the angle of progression measured during the active phase of labor in predicting the likelihood of a successful normal vaginal delivery. Additionally, we aim to assess the cutoff and diagnostic value of the angle of progression in predicting normal vaginal delivery, beyond its role in representing fetal head station.

Materials and Methods

Following approval from the Ethics Committee of Hatyai Hospital, Songkhla, Thailand, this prospective diagnostic accuracy study took place at Hatyai Hospital, a tertiary referral center, from February to August 2023. The study included pregnant women aged 20 years or older with a viable singleton, cephalic presentation, admitted to the labor room between 37 completed weeks of gestation and 41 weeks and 6 days of gestation. These women were either undergoing spontaneous labor or induction of labor and were initially planned for vaginal delivery. Pregnant women with diagnosed uterine anomalies, estimated fetal weight exceeding 4,000 gm, and prenatal diagnosis of fetal anomalies were excluded. This exclusion was based on their probability of undergoing cesarean delivery with indications other than cephalopelvic disproportion. In our center's clinical practice, clinicians may choose to perform operative delivery without strictly adhering to the criteria for prolonged labor such as in cases of poor maternal effort, which can result in an inaccurate evaluation of the actual outcome. Therefore, the authors decided to exclude cases involving operative vaginal delivery from the analysis.

A sample size of 114 was calculated based on the area under the receiver operating characteristic (ROC) curve from the work of Perez et al[10] with alpha of 0.05 and power of 0.8.

The author randomly recruited 114 nonconsecutive series of pregnant women during various periods of the day. All pregnant women who met our specified criteria were included, as shown in Fig. 1. Information about the study was provided to the pregnant women, and their consent was obtained before performing the transperineal ultrasound. A workshop on the transperineal ultrasonographic measurement of the angle of progression was organized by a Maternal-Fetal Medicine (MFM)

specialist before commencing data collection and the researcher performed measurements under expert supervision.

The ultrasonographic measurement of the angle of progression was conducted upon the pregnant women entering the active phase of labor. In our study, we employed the traditional criteria for defining the active phase of labor, as outlined in the Friedman study, characterized by cervical dilatation exceeding 4 cm along with regular uterine contractions. Notably, we excluded the deceleration phase, where rapid descent of the fetal head has already occurred. Consequently, our study focused on laboring women with cervical dilatation ranging from 4 to 8 cm.

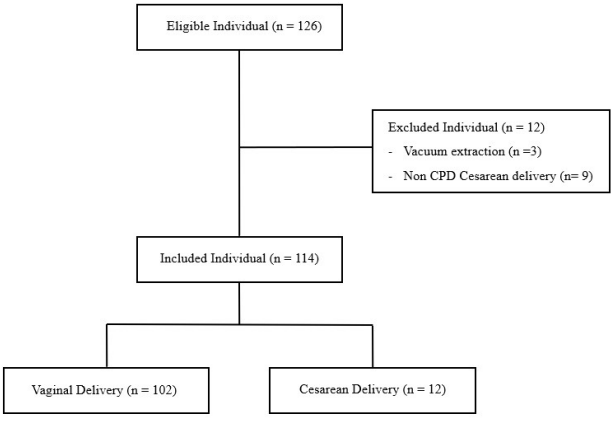

Fig. 1. A flow chart illustrating the process of inclusion and exclusion.

After bladder emptying, the pregnant women were positioned in a semi-recumbent posture[2]. Using a 5.5 MHz 4C-RS convex transducer from a 2D ultrasound device (GE LOGIQ V3), enclosed in a sterile glove, the transducer was gently placed vertically translabial. An image capturing the sagittal view of the long axis of the pubic bone and the lowest edge of the fetal skull was obtained in the same plane. Two caliper lines were drawn: one from the proximal edge of the pubic bone to the distal edge, and the other from the distal edge of the pubic bone to the lowest edge of the fetal skull, as shown in Fig. 2. The angle between these two calipers, automatically generated by the ultrasound machine and defined as the angle of progression, was recorded in the case record form.

Labor progression was monitored, and management decisions were made by the attending staff on duty at the time, who were unaware of the angle of progression data. In our center, there is no specific analgesia during labor except for intramuscular pethidine, and the management decision is based on the traditional criteria of secondary arrest of dilatation, as referenced from the Friedman study[12, 13]. Abnormal progression of labor is diagnosed when there is an absence of cervical progression for more than two hours, despite adequate uterine contractions. Pregnant women who underwent cesarean delivery for reasons other than cephalopelvic disproportion or those who delivered through operative vaginal methods, such as vacuum-assisted or forceps deliveries, were excluded from the study.

The data were analyzed using R-4.3.1 software. Demographic data were assessed, with continuous variables presented as mean, median and interquartile range while categorical data were shown as percentages. The cut-off value for the angle of progression was determined by calculating the maximum area under the receiver operating characteristics (ROC) curve, and sensitivity, specificity, positive predictive value, negative predictive value, and likelihood ratio were calculated.

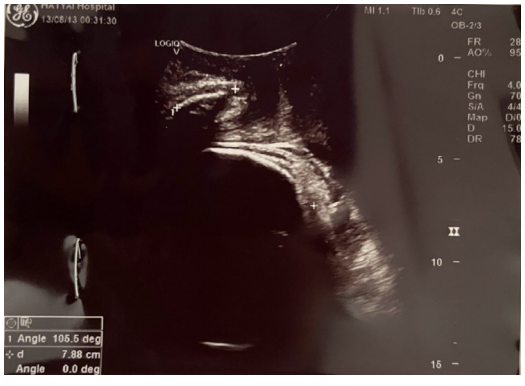

Fig. 2. Angle of progression

Results

A total of 114 nonconsecutive pregnant women were enrolled in the study. Among this group, 102 cases underwent vaginal delivery (89.5%), while 12 cases underwent cesarean delivery (10.5%). The demographic characteristics of the study group are detailed in Table 1. No significant differences were observed between the vaginal delivery and cesarean delivery groups regarding age, body mass index, gestational age, cervical dilatation, amniotic membrane status at the time of measurement, and fetal birth weight. However, multiparous patients showed a tendency toward a higher rate of vaginal deliveries when compared to nulliparous patients.

Table 1. Demographic data and obstetric outcomes.

Demographic	Total (n = 114)	Vaginal delivery (n = 102)	Cesarean delivery (n = 12)	p value
Age (median (IQR)), years	28 (24, 31)	28 (24.2, 31.8)	25.5 (22.2, 28)	0.098[a]
BMI at LR (median (IQR)), kg/m^2	27.7 (25.1, 30.9)	27.6 (24.9, 30.5)	30.2 (26.9, 32.8)	0.084[a]
Parity (%)				
Nulliparity	42 (36.8)	32 (31.4)	10 (83.3)	< 0.001[b]
Multiparity	72 (63.2)	70 (68.6)	2 (16.7)	
GA (median (IQR)), weeks	39 (38, 40)	39 (38, 40)	39 (39, 40)	0.045[a]
Cervical dilatation (median (IQR)), cm	5 (4, 6)	5 (4, 6)	4 (4, 5)	0.151[a]
Fetal head station (%)				0.256[b]
-3	1 (0.9)	1 (1)	0 (0)	
-2	42 (36.8)	34 (33.3)	8 (66.7)	
-1	43 (37.7)	41 (40.2)	2 (16.7)	
0	27 (23.7)	25 (24.5)	2 (16.7)	
+1	1 (0.9)	1 (1)	0 (0)	
Membranes status (%)				
Membranes intact	60 (52.6)	56 (54.9)	4 (33.3)	0.267[c]
Membranes ruptured	54 (47.4)	46 (45.1)	8 (66.7)	
Fetal birth weight (median (SD)), grams	3132 (373.5)	3110.7 (377.3)	3312.9 (293.4)	0.076[d]
APGAR (%)				0.105[b]
1 min				
8	1 (0.9)	0 (0)	1 (8.3)	
9	113 (99.1)	102 (100)	11 (91.7)	
5 min				
8	1 (0.9)	0 (0)	1 (8.3)	
9	113 (99.1)	102 (100)	11 (91.7)	

[a] = Ranksum test, [b] = Fisher's exact test, [c] = chi-square test, [d] = t-test
IQR: interquartile range, BMI: body mass index, LR: labor room, GA: gestational age, SD: standard deviation

The mean angle of progression in the study group was 106.3° (standard deviation (SD) 13.1). Specifically in the vaginal delivery group, the mean was 107.4°, while in the cesarean delivery group, it was 96.4°. Comparing vaginal and cesarean delivery group the angle of progression was significantly difference (Fig. 3).

The receiver operating characteristics (ROC) curve for the angle of progression (Fig. 4) demonstrated an area under the curve (AUC) of 0.751 (95% confidence interval (CI) 0.603-0.899). The optimized cut-off value for the angle of progression, which maximized the AUC, was determined to be 96.9°. This cut-off value for predicting successful normal vaginal delivery resulted in the sensitivity of 82.4% and specificity of 58.3%. The positive predictive value (PPV) was 94.4%, while the negative predictive value (NPV) was 28% (Table 2).

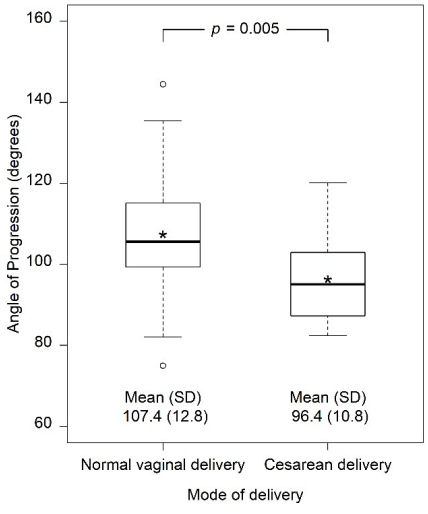

Fig. 3. Box plot of median and mean angle of progression in vaginal and cesarean delivery. (t-test).

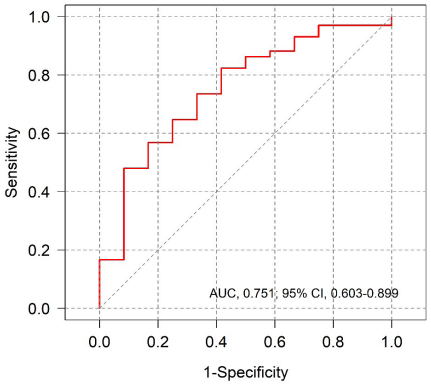

Fig. 4. The receiver operating characteristics (ROC) curve for the angle of progression.

Table 2. A two-by-two table presenting the optimized cut-off values along with their corresponding diagnostic values.

Primary Outcome	Vaginal delivery	Cesarean delivery	Predictive value	Total
AOP ≥ 96.9	84	5	0.94	89
AOP < 96.9	18	7	0.28	25
Sensitivity & specificity	0.82	0.58		
Total	102	12		114

AOP: angle of progression

Discussion

Based on the previous studies[14], our study affirms the reliability and reproducibility of intrapartum transperineal ultrasound measurements of the angle of progression in assessing fetal head descent during labor in pregnant women. Moreover, our findings supported the notion that the angle of progression serves as a valuable adjunctive tool to digital pelvic

examination, as it demonstrated predictive ability in determining the mode of delivery, with a validated cut-off point of 96.9°.

Our cut-off value aligned with findings from prospective study conducted in India by Vinutha et al[11], involving 185 laboring pregnant women in the early active phase of labor, it was determined that an intrapartum trans-labial ultrasound measurement of the angle of progression at 89° had the highest predictive value for predicting vaginal delivery. This measurement demonstrated an AUC of 0.789, a sensitivity of 79.3%, specificity of 65.6%, a PPV of 81.3%, and a NPV of 62.7%.

In contrast to the study by Perez et al[10] in Spain, which included 101 pregnant women and measured the angle of progression at the beginning of the active phase, it was found that the optimized cut-off value for the ROC curve was 125°, resulting in an AUC of 0.85, a sensitivity of 67.1%, and a specificity of 100%.

Eggebø[8] in the UK conducted a prospective study in two centers during 2013, which involved term singleton pregnant women experiencing prolonged labor according to the WHO and National Institute for Health and Care Excellence (NICE) guideline. The angle of progression was measured, with the finding that an angle of progression exceeding 110 degrees was a good predictor for vaginal delivery in the prolonged first stage of labor. However, it exhibited lower sensitivity and specificity compared to our study, with a sensitivity of 68%, specificity of 28%, a PPV of 88%, and a NPV of 43%.

The variation in cut-off values observed across studies can be attributed to numerous factors affecting the angle of progression, including fetal head station, fetal head position, and cervical dilatation at the time of measurement. As the angle of progression cannot be solely relied upon as the exclusive tool for predicting the success of vaginal delivery, fetal head position emerges as a crucial factor, as indicated by numerous prior studies[8, 9, 11, 15, 16]. Specifically, the occiput anterior position exhibits the higher probability of vaginal delivery, whereas the occiput posterior position is associated with the lower probability.

In our study, among the 12 cases that underwent cesarean delivery, a closer examination of the data revealed that five of these cases had an angle of progression exceeding the cut-off of 96.9°. Notably, among these cases, two were characterized by a fetal occiput posterior position, with angle of progression measurements of 120.1° and 103.7°, respectively.

Additionally, the fetal head station at the time the angle of progression is measured also influences the outcome. According to studies by Barbera et al[5], the angle of progression reflects the fetal head station, suggesting that a more positive or descending fetal head station theoretically increases the chances of a successful vaginal delivery.

In many of the previous studies, including our own, there is a lack of subgroup analysis for each of the factors mentioned above. This is because relying solely on a single value of the angle of progression may not be sufficient to accurately represent labor progression. As labor progresses over time, this dynamic process can introduce variability among the cut-off values observed in different studies.

Furthermore, the diagnostic criteria among the studies are also different. In our study, we employed the traditional criteria from the Friedman study, where the diagnosis of cephalopelvic disproportion was established after observing no cervical progression for two hours. In contrast, Eggebø et al[8] in the UK used diagnostic criteria from WHO and NICE, with a diagnosis threshold of 4 hours, potentially leading to differences in cut-off values. Perez et al[10] and Vinutha et al[11] did not specify the reference criteria for diagnosing prolonged labor in their respective studies. This variation in diagnostic criteria adds to the complexity of interpreting and comparing findings across different research studies.

The authors propose that the angle of progression can serve as an adjunctive tool to digital pelvic examination, enhancing the precision of labor progression assessment. Intrapartum ultrasound measurements of the angle of progression are not recommended as a standalone diagnostic tool for

cephalopelvic disproportion. Rather, they should be employed as a supplementary predictive tool for identifying cases with an elevated likelihood of experiencing challenges in achieving normal vaginal delivery. This approach aids practitioners in early detection, facilitating prompt management decision-making and minimizing delays in transfer of care.

The strength of our study lay in the absence of operator dependence. All measurements were exclusively conducted by the first author under expert supervision. Furthermore, there were no instances of missing data throughout the entire study period, enhancing the completeness and robustness of our findings. A limitation of our study was the lack of control for factors influencing the variation in the angle of progression, including fetal head station, fetal head position, cervical dilatation at the time of measurement, and parity of pregnant women, as mentioned earlier. A recommendation for future research is to improve the comprehensiveness and accuracy of objective parameter assessment in labor progression by incorporating serial measurements of the angle of progression or a combination of multiple intrapartum ultrasound parameters. Additionally, conducting subgroup analyses on factors that may impact the outcome could further enhance the depth of understanding.

Conclusion

Intrapartum transperineal ultrasound measurements of the angle of progression can serve as an adjunctive tool to digital pelvic examination, enhancing the precision of labor progression assessment. Due to its simplicity and reproducibility, intrapartum transperineal ultrasound measurements of the angle of progression can be widely used in primary health care centers after a simple training. Its implementation could be beneficial in management of cases with slow labor progression whether to reduce delayed decision to refer to a higher-level center or to reduce a hasty diagnosis of cephalopelvic disproportion leading to minimized unnecessary cesarean delivery.

Acknowledgments

The authors would like to express their gratitude to all the participants and acknowledge the support provided by the Department of Obstetrics and Gynecology at Hatyai Hospital in Songkhla, Thailand.

Potential conflicts of interest

The authors declare no conflicts of interest.

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Thai Journal of Obstetrics and Gynaecology
May 2024, Vol. 32, No. 3, pp. 214-224.

GYNAECOLOGY

Prevalence and Associated Factors of Perioperative Blood Transfusion in Patients Undergoing Laparoscopic Hysterectomy for Benign Gynecologic Conditions

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ABSTRACT

Objectives: To determine the prevalence and the associated factors of perioperative blood transfusion and to evaluate the efficiency of blood ordering and utilization in patients undergoing laparoscopic hysterectomy for benign gynecologic conditions.

Materials and Methods: A cross-sectional retrospective study was conducted. The medical records of 974 patients who underwent laparoscopic hysterectomy for benign gynecologic conditions from July 2016 through October 2022 were reviewed. The possible associated factors for blood transfusion including demographic data, clinical diagnosis, preoperative and intraoperative data were retrieved and evaluated. Blood utilization indicators such as crossmatch-to-transfusion ratio (C/T ratio), transfusion index (TI), and transfusion probability (%T) were also calculated.

Results: The overall perioperative transfusion rate was 19.4% (189/974). In multivariable regression analysis, patients who had preoperative anemia (adjusted odds ratio (aOR) 6.89; 95% confidence interval (CI) 4.56-10.43), estimated blood loss ≥ 300 milliliters (aOR 8.64; 95%CI 5.46-13.69), uterine size ≥ 500 grams (aOR 1.99; 95%CI 1.23-3.20) and presence of pelvic adhesion (aOR 2.01; 95%CI 1.31-3.09) were independently associated with perioperative blood transfusion. Moreover, natural orifice trans-luminal endoscopic surgery trended towards a lower blood transfusion rate than total laparoscopic hysterectomy (aOR 0.43; 95%CI 0.21-0.89). For blood utilization indicators: C/T ratio was 6.15, TI was 0.35, and %T was 19.4%.

Conclusion: Preoperative anemia, higher blood loss, large uterine size, and pelvic adhesion were transfusion risk factors in patients undergoing laparoscopic hysterectomy. Blood utilization indicators were low, indicating that routine blood crossmatching might be unnecessary for all patients.

Keywords: packed red cell transfusion, transfusion rate, blood utilization, minimally invasive surgery.

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Received: 30 September 2023, **Revised:** 27 November 2023, **Accepted:** 6 December 2023

ความชุกและปัจจัยที่มีความสัมพันธ์กับการให้เลือดช่วงระยะการผ่าตัดในผู้ป่วยที่เข้ารับการผ่าตัดมดลูกผ่านกล้องเนื่องจากภาวะทางนรีเวชที่ไม่ใช่มะเร็ง

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บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาความชุกและปัจจัยที่มีความสัมพันธ์กับการให้เลือดช่วงระยะการผ่าตัด และประเมินความเหมาะสมในการจองเลือดและความคุ้มค่าในการใช้เลือด ในผู้ป่วยที่เข้ารับการผ่าตัดมดลูกผ่านกล้องเนื่องจากภาวะทางนรีเวชที่ไม่ใช่มะเร็ง*

วัสดุและวิธีการ: *การศึกษาข้อมูลจุดเวลาใดเวลาหนึ่งแบบย้อนหลัง แบบบันทึกข้อมูลทางการแพทย์ของผู้ป่วยจำนวน 974 คนที่เข้ารับการผ่าตัดมดลูกผ่านกล้องเนื่องจากภาวะทางนรีเวชที่ไม่ใช่มะเร็ง ตั้งแต่เดือนกรกฎาคม พ.ศ.2559 จนถึงเดือนตุลาคม พ.ศ.2565 ได้รับการทบทวน โดยปัจจัยที่เป็นไปได้ที่จะมีความสัมพันธ์กับการให้เลือดช่วงระยะการผ่าตัด รวมถึงข้อมูลทั่วไป การวินิจฉัยทางคลินิก ข้อมูลก่อนการผ่าตัด และข้อมูลการผ่าตัดได้รับการเก็บข้อมูลและประเมิน ตัวบ่งชี้ความคุ้มค่าในการใช้เลือด เช่น crossmatch-to-transfusion ratio (C/T ratio), transfusion index (TI), และ transfusion probability (%T) ได้รับการคำนวณร่วมด้วย*

ผลการศึกษา: *ความชุกของการให้เลือดทั้งหมดเท่ากับร้อยละ 19.4 (189/974) การวิเคราะห์แบบถดถอยพหุตัวแปร (multivariable regression) พบว่าผู้ป่วยที่มีภาวะซีดก่อนผ่าตัด (aOR 6.89; 95%CI 4.56-10.43) ปริมาณการเสียเลือดมากกว่าหรือเท่ากับ 300 มิลลิลิตร (aOR 8.64; 95%CI 5.46-13.69) มดลูกขนาดใหญ่มากกว่าหรือเท่ากับ 500 กรัม (aOR 1.99; 95%CI 1.23-3.20) และการมีพังผืดในอุ้งเชิงกราน (aOR 2.01; 95%CI 1.31-3.09) เป็นปัจจัยที่มีความสัมพันธ์กับการให้เลือดช่วงระยะการผ่าตัด นอกจากนี้การผ่าตัดมดลูกผ่านทางช่องธรรมชาติใช้การส่องกล้องแบบไร้แผล (Natural Orifice Transluminal Endoscopic Surgery; NOTES) มีแนวโน้มให้เลือดต่ำเมื่อเทียบกับการผ่าตัดมดลูกใช้การส่องกล้องทั้งหมด (Total Laparoscopic Hysterectomy; TLH) (aOR 0.43; 95%CI 0.21-0.89) สำหรับตัวบ่งชี้ความคุ้มค่าในการใช้เลือด C/T ratio เท่ากับ 6.15, TI เท่ากับ 0.35, และ %T เท่ากับร้อยละ 19.4*

สรุป: *ภาวะซีดก่อนผ่าตัด ปริมาณการเสียเลือดมาก มดลูกขนาดใหญ่ และการมีพังผืดในอุ้งเชิงกราน เป็นปัจจัยที่มีความสัมพันธ์กับการให้เลือดในผู้ป่วยที่เข้ารับการผ่าตัดมดลูกผ่านกล้อง ตัวบ่งชี้ความคุ้มค่าในการใช้เลือดต่ำ บ่งชี้ถึงการเตรียมเลือดแบบ crossmatch อาจจะไม่จำเป็นสำหรับผู้ป่วยทุกราย*

คำสำคัญ: *การให้ส่วนประกอบเม็ดเลือดแดง, อัตราการให้เลือด, ความคุ้มค่าในการใช้เลือด, การผ่าตัดมดลูกผ่านกล้อง*

Introduction

Hysterectomy is the most common gynecological operation, which has an incidence of 180-351 cases per 100,000 person-years[1, 2]. Laparoscopic hysterectomy (LH), the less invasive alternative method to laparotomy, is now widely used, and the rate is increasing[2-4]. This is due to several reasons, including a smaller surgical wound, less postoperative pain, faster return to regular activities[5], lower blood loss and reducing perioperative complications when compared to laparotomy[6]. While laparoscopic hysterectomy was safe, it still carried the risk of bleeding that a blood transfusion was required, similar to other surgical procedures. According to previous studies, the incidence of blood transfusion in laparoscopic hysterectomy was 1.2-5.2%[7, 8], which was lower than the incidence of blood transfusion in all hysterectomy surgeries (2.7-11.2%)[7-10]. Although the incidence of perioperative blood transfusion was quite low, it was important to be aware of several adverse sequelae associated with blood transfusions, such as adverse reactions, bloodborne infection, thromboembolic events, and sepsis[9].

A number of retrospective studies had addressed the several factors associated with blood transfusion in patients undergoing total hysterectomy, such as low preoperative hemoglobin/hematocrit levels, higher mean estimated blood loss, large uterine weight, obesity, prolonged operative time and patients with uterine fibroids[7, 8, 10, 11]. Moreover, one retrospective study found a significant association between pelvic adhesion and perioperative blood transfusion in patients who underwent total laparoscopic hysterectomy[7]. Most of previous research reported the incidence and relevant risk factors of blood transfusion in all patients undergoing hysterectomy, regardless of any route. However, there is a paucity of studies on transfusion rate and risk factors of blood transfusion in patients undergoing laparoscopic hysterectomy.

Generally, there are two standard methods for blood preparation, the first one is type and screen and the second one is crossmatching. In our institution, only crossmatching method is currently used for blood preparation and transfusion in gynecologic surgery. However, several studies found that blood ordering and utilization are still inefficient and need to be improved[12-14]. Furthermore, a previous study had shown that the type and screen method, which determined the blood type using the ABO and Rh group systems, was not only safe but also more cost-effective compared to crossmatching[15].

The primary objective of this study was to determine the prevalence of perioperative blood transfusion in patients undergoing laparoscopic hysterectomy of benign conditions. The second objectives were to identify the associated factors for perioperative blood transfusion and to evaluate the efficiency of blood ordering and utilization. The blood utilization indicators were crossmatch-to-transfusion ratio (C/T ratio), transfusion index (TI), and transfusion probability (%T).

Materials and Methods

After obtaining Bangkok Metropolitan Administration (BMA) Human Research Ethics Committee (BMAHREC) approval, a cross-sectional retrospective chart review was conducted at Charoenkrung Pracharak Hospital. The patients who had undergone elective laparoscopic hysterectomy for benign gynecological indication between July 1, 2016 and October 31, 2022 were included. The patients who had a bleeding disorder or were converted to laparotomy were excluded. The patients whose

pathology reports provided the definitive cancer diagnosis were also excluded.

A total of 974 patients elective laparoscopic hysterectomy for benign gynecological indication were enrolled and reviewed. Of these patients, those who required perioperative blood transfusions were considered case or transfusion group. On the other hand, those who did not require any transfusion were considered control group or non-transfusion group.

The medical records were reviewed to determine the prevalence of blood transfusion. Patient demographic data, preoperative comorbidities, and perioperative data were retrieved. Variables included age, parity, body mass index (BMI), past medical history (history of diabetes mellitus and hypertension), smoking status, preoperative hemoglobin/hematocrit level, preoperative platelet count, anticoagulant/ antiplatelet use, history of previous abdominal surgery, and American society of anesthesiologists classification (ASA class) were obtained. The types of hysterectomy procedure were classified into total laparoscopic hysterectomy (TLH), laparoscopic assisted vaginal hysterectomy (LAVH), and natural orifice transluminal endoscopic surgery (NOTES). Perioperative variables included surgeon experience, surgical indication, concomitant adnexal surgery, uterine size, pelvic adhesion, endometriosis, estimated blood loss (EBL), operative time, major complications (include bowel injury, ureteric/bladder injury and vascular injury), and length of hospital stay were evaluated.

In our institution, the decision of perioperative blood transfusion depended on the transfusion trigger of the patients' hematocrit levels less than 30%[16]. The decision to give blood transfusion relied on many factors such as preoperative hemoglobin and hematocrit levels, the amount of estimated intraoperative blood loss (EBL), intraoperative hemodynamic changes, and signs of organ ischemia. These determinations are made based on the clinical judgment and expertise of the attending surgeon.

To determine the efficiency of blood ordering and utilization, blood utilization indicators such as crossmatch-to-transfusion ratio (C/T ratio), transfusion index (TI), and transfusion probability (%T) were also calculated. The C/T ratio represented the ratio of blood crossmatching units to the number of transfused blood units. The C/T ratio greater than 2.5 suggests that less than 40% of the crossmatched units were used. The TI represented the number of transfused blood units per number of patients crossmatched, a value of 0.5 or more of TI indicated a substantial blood utilization during surgery. Lastly, the %T signified the percentage of patients who received transfusions among those who underwent crossmatching. The %T of more than 30 indicated a significant need for blood during surgery[16] while a %T below 30 was associated with a reduced transfusion risk and was recommended for type and screen method.

Statistical analysis

The data analysis was performed using IBM SPSS version 26 software. Continuous variables were computed and presented as means with standard deviations or medians with an interquartile range where appropriate. Categorical variables were presented as numbers with percentages. Patient demographic data, preoperative comorbidities, and perioperative data were compared across an incidence of packed red blood cell transfusion using chi-square, independent t-tests, Fisher's exact test and Mann-Whitney U tests where appropriate. A p value of < 0.05 was considered statistically significant. Multivariable logistic regression modeling identified independent variables associated with perioperative transfusion and presented as adjusted odds ratio (aOR) with 95% confidence intervals (CI). A two-tailed p value < 0.05 was considered statistically significant.

Results

A total of 974 hysterectomies were recruited during the study period. Among these, 516 (53%) were TLH, 325 (33.4%) LAVH, and 133 (13.6%) NOTES hysterectomy. The overall perioperative transfusion rate was 19.4% (189/974). The transfusion group consists of 189 patients who had a blood transfusion. The non-transfusion group consists of 785 patients

who did not receive a blood transfusion.

Patient demographic and preoperative data between transfusion group and non-transfusion group were compared and shown in Table 1. Baseline characteristic of age, body mass index, parity, past medical history, smoking status, anticoagulant and antiplatelet use, thrombocytopenia, ASA class and previous abdominal surgery were not different between the two groups. Patients in transfusion group were more likely to have lower hemoglobin (10.45 vs 12.16 g/dl, p < 0.001), lower hematocrit level (32.69 vs 37.01%, p < 0.001) and had anemia (75.1 vs 37.2%, p < 0.001) when compared to non-transfusion group.

Table 1. Comparison of demographic and preoperative data between transfusion and non-transfusion groups.

Variables	Non-transfusion n = 785	Transfusion n = 189	p value
Age (years), mean ± SD	45.07 ± 9.05	45.02 ± 6.76	0.925
BMI (kg/m^2), mean ± SD	24.91 ± 4.73	24.08 ± 4.42	0.028
BMI, n (%)			0.212
Underweight	34 (4.3)	13 (6.9)	
Normal	281 (35.8)	67 (35.4)	
Overweight	141 (18.0)	41 (21.7)	
Obesity	329 (41.9)	68 (36.0)	
Parity, n (%)			0.113
Nulliparous	315 (40.1)	64 (33.9)	
Multiparity	470 (59.9)	125 (66.1)	
Past medical history, n (%)			
Diabetes	76 (9.7)	19 (10.1)	0.877
Hypertension	165 (21)	30 (15.9)	0.112
Smoker, n (%)	14 (1.8)	4 (2.1)	0.764
Anticoagulant/Antiplatelet use, n (%)	22 (2.8)	1 (0.5)	0.065
Previous abdominal surgery*, n (%)	323 (41.1)	92 (48.7)	0.060
Hemoglobin (g/dl), mean ± SD	12.16 ± 1.17	10.45 ± 1.72	< 0.001
Hematocrit (%), mean ± SD	37.01 ± 3.07	32.69 ± 4.43	< 0.001
Anemia, n (%)	292 (37.2)	142 (75.1)	< 0.001
Thrombocytopenia, n (%)	5 (0.6)	1 (0.5)	0.999
ASA classification, n (%)			0.615
1	423 (53.9)	98 (51.9)	
≥ 2	362 (46.1)	91 (48.1)	

SD: standard deviation, BMI: body mass index, ASA: American society of anesthesiologists
Anemia: hematocrit < 36%, Thrombocytopenia: platelet count < 150 x10^3/uL,
* Previous abdominal surgery included cesarean section, tubal sterilization, laparotomy, laparoscopy (uterine or adnexal surgery) and non-gynecologic surgery

Surgical and intraoperative data between two groups were compared and shown in Table 2. Uterine fibroid was the most common indication for hysterectomy (55.9%) and TLH was the most common route of surgery (53%). In the bivariable analysis, the factors such as surgical indication (p = 0.009), route of surgery (p = 0.006) were significantly different between the two groups. Moreover, the transfusion group were likely to have larger uterine size (370 vs 230 gm, p < 0.001), longer operative time (205 vs 162 min, p < 0.001), more

EBL (600 vs 150 ml, p < 0.001), presence of pelvic adhesion (52.4 vs 32%, p < 0.001) and presence of endometriosis (24.3 vs 15.5%, p = 0.004) than the non-transfusion group. However, there was no significant difference in surgeon experience and concomitant adnexal surgery between two groups. In this study, the three most common complications in our study were bowel injury (1.03%), followed by ureteric/bladder injury (0.72%) and vascular injury (0.31%).

Table 2. Comparison of surgical and intraoperative data between transfusion and non-transfusion groups.

Variables	Non-transfusion n = 785	Transfusion n = 189	p value
Experience, n (%)			0.765
Fellow	147 (18.7)	30 (15.9)	
Staff < 3 years	98 (12.5)	26 (13.8)	
Staff 3-5 years	108 (13.8)	29 (15.3)	
Staff > 5 years	432 (55.0)	104 (55.0)	
Indication, n (%)			0.009
Uterine fibroids	425 (54.1)	119 (63.0)	
Endometriosis/Adenomyosis	204 (26.0)	50 (26.5)	
Other	156 (19.9)	20 (10.6)	
Route, n (%)			0.006
TLH	414 (52.7)	102 (54.0)	
LAVH	251 (32.0)	74 (39.2)	
NOTES	120 (15.3)	13 (6.9)	
Size (gm), median (range)	230 (15-2800)	370 (10-5300)	< 0.001
Size (gm)			< 0.001
< 500	655 (83.4)	122 (64.6)	
≥ 500	130 (16.6)	67 (35.4)	
Time (min), mean ± SD	162.19 ± 62.68	205.95 ± 65.44	< 0.001
Time (min), n (%)			< 0.001
< 180	513 (65.4)	70 (37.0)	
≥ 180	272 (34.6)	119 (63.0)	
EBL (ml), median (range)	150 (10-1400)	600 (10-3000)	< 0.001
EBL (ml), n (%)			< 0.001
< 300	547 (69.7)	38 (20.1)	
≥ 300	238 (30.3)	151 (79.9)	
Pelvic adhesion, n (%)	251 (32.0)	99 (52.4)	< 0.001
Endometriosis, n (%)	122 (15.5)	46 (24.3)	0.004
Concomitant adnexal surgery, n (%)	732 (93.2)	179 (94.7)	0.464
Admission day (days), median (range)	3 (2-15)	4 (2-34)	< 0.001
Major complication*, n (%)	12 (1.5)	8 (4.2)	0.024

TLH: total laparoscopic hysterectomy, LAVH: laparoscopic assisted vaginal hysterectomy, NOTES: natural orifice translumenal endoscopic surgery, EBL: estimated blood loss, SD: standard deviation
*Major complication included bladder injury, ureteric injury, bowel injury and vascular injury

Multivariable logistic regression analysis identified the independent factors associated with blood cell transfusion, as demonstrated in Table 3. According to EBL, the patients who had EBL ≥ 300 milliliters were strongest associated with increased perioperative blood transfusion (aOR 8.64; 95%CI 5.46-13.69). As for preoperative variables, it was observed that only preoperative anemia, defined as a hematocrit level below 36%, was significantly associated with an increased transfusion rate (aOR 6.89; 95%CI 4.56-10.43). There was a trend towards a decreased risk of blood transfusion associated with NOTES hysterectomy when compared to TLH (aOR 0.43; 95%CI 0.21-0.89). Additionally, patients with pelvic adhesion (aOR 2.01; 95%CI 1.31-3.09) and uterine size ≥ 500 grams (aOR 1.99; 95%CI 1.23-3.20) were associated with increased risk for perioperative blood transfusion. In contrast, surgical indication, operative time, endometriosis, and major complications therefore were not significantly associated with perioperative blood transfusion.

A total of 974 patients had 2,105 crossmatched units requested, but only 342 units were used. The indicator to evaluate efficacy of blood product utilization was calculated, crossmatch-to-transfusion ratio (C/T ratio) was 6.15 (the appropriate value is ≤ 2.5), transfusion index (TI) was 0.35 (the appropriate value is ≥ 0.5), and transfusion probability (%T) was 19.4% (the appropriate value is ≥ 30%). These results indicated excessive blood ordering for elective laparoscopic hysterectomy in our institution.

Table 3. Regression analysis for factor associated with perioperative blood transfusion in patients undergoing laparoscopic hysterectomy for benign gynecologic conditions.

Variables	Adjusted odds ratio (95%CI)[t]	p value
Anemia	6.89 (4.56-10.43)	< 0.001
Indication		
Uterine fibroids	Ref	
Endometriosis/Adenomyosis	0.88 (0.45-1.69)	0.875
Other	0.97 (0.48-1.93)	0.966
Route		
TLH	Ref	
LAVH	0.85 (0.55-1.29)	0.435
NOTES	0.43 (0.21-0.89)	0.023
Size ≥ 500 gm	1.99 (1.23-3.20)	0.005
Time ≥ 180 min	1.31 (0.86-2.01)	0.211
EBL ≥ 300 ml	8.64 (5.46-13.69)	< 0.001
Pelvic adhesion	2.01 (1.31-3.09)	0.001
Endometriosis	0.94 (0.57-1.57)	0.825
Major complication	2.45 (0.77-7.85)	0.131

TLH: total laparoscopic hysterectomy, LAVH: laparoscopic assisted vaginal hysterectomy, NOTES: natural orifice translumenal endoscopic surgery, EBL: estimated blood loss, CI: confidence interval

*Complications include bladder injury, ureteric injury, bowel injury and vascular injury

t Adjusted for anemia, indication for surgery, operative route, uterus size ≥ 500 gm, operative time ≥ 180 min, EBL ≥ 300 ml, pelvic adhesion, endometriosis, and major complication

Discussion

Among the 974 patients included in our study, the prevalence of blood transfusion in women who underwent laparoscopic hysterectomy was estimated

to be as high as 19.4%. Our findings revealed a higher transfusion rate compared to previous studies. This difference could be attributed to our hospital's status as a laparoscopic center, where we routinely handle complex laparoscopic cases. The percentage of women with pelvic adhesions in our study was higher (35.9%) than previous studies, which ranged from 18% to 25%[7, 17]. Furthermore, a contributing factor was the high prevalence of enlarged uterus, with 20.2% of patients presenting uterine weighing in excess of 500 grams. These factors reflected the surgical complexity and might potentially increase the risk of bleeding and transfusion during surgery. In addition, our hospital has not been implemented a restricted blood transfusion protocol. The decision relied on the judgment and expertise of attending surgeons and anesthesiologists. These factors can result in variability in transfusion practices among different surgeons and potentially lead to an increase in unnecessary transfusions.

In our study, we also classified EBL in two groups: the first group is EBL < 300 milliliters and the second group is EBL ≥ 300 milliliters. The requirement for perioperative blood transfusion was higher in the group of EBL ≥ 300 milliliters which increased by approximately 8.6-fold compared to the group with EBL < 300 milliliters. In agreement with previous retrospective studies, a higher incidence of perioperative bleeding was significantly correlated with a higher transfusion rate[10, 11].

Obviously, patients who required a transfusion were more likely to have preoperative anemia than those who did not. This finding correlated with previous reports[10, 18], which indicated a significantly higher risk of transfusion in anemic patients. Preoperative anemia is a reversible factor that can be identified prior to surgery. Elfazari et al[8] also reported a significant reduction in the requirement of blood transfusion in patients with higher preoperative hematocrit levels during hysterectomy. To provide the best patient care, surgeons should consider preoperative preparation alternative strategies, including oral iron administration, preoperative intravenous iron infusion, erythropoietin, and gonadotropin-releasing hormone analog therapy which can increase the hemoglobin level before the day of surgery.

The patients with pelvic adhesions were more likely to receive a blood transfusion than those without adhesions. Saad-Naguib et al[7] identified one of the risk factors for blood transfusion in patients who underwent hysterectomy, the presence of pelvic adhesions during intraoperative TLH increased the risk of transfusion. Maclaran et al[19] reported a significant trend toward increasing blood loss in patients with adhesions. Preexisting intra-abdominal adhesion can complicate hysterectomy due to limitations in manipulating the uterus, distortion of normal pelvic anatomy and obscuring visualization of the operative field. All of these reasons could induce accidental vascular injury and bleeding complications.

This study also observed that patients with uterus ≥ 500 grams had a higher overall transfusion rate compared to those with uterine weight < 500 grams. In consistent with Huang et al[20], in single-port laparoscopic hysterectomy, patients with a uterine weight 500 grams or more experienced higher blood loss and a greater likelihood of blood transfusion compared to those with uterine weight less than 500 grams. Another retrospective study on laparoscopic supracervical hysterectomy also indicated that large uterus, particularly it weighed more than 500 grams, were associated with an increased risk of blood loss and prolonged intraoperative time[21]. In general, a large uterus had more vascular supply and distortion of uterine anatomy due to uterine pathology, such as uterine fibroids. These factors might make it more challenging to visualize structures and achieve effective hemostasis.

Interestingly, our study demonstrated that the rate of blood transfusion following NOTES hysterectomy was lower than TLH. This discrepancy can be attributed to several factors. Firstly, NOTES hysterectomy used a vaginal incision without abdominal incision, which reduced the amount of bleeding. Secondly, it provided the advantage of earlier access to and blockage of the uterine vessels,

resulting in reduced intraoperative blood loss[22]. Lastly, patients with high-complexity factors, such as preexisting endometriosis and a history of pelvic adhesion were not considered candidates for NOTES hysterectomy. A meta-analysis that included 6 studies comparing vaginal NOTES and laparoscopic hysterectomy revealed that blood loss was lower in patients who underwent vaginal NOTES[23]. In another aspect, Puisungnoen et al[24] reported that there was no significant difference in the requirement for blood transfusion between the NOTES hysterectomy and TLH groups. These findings suggested that NOTES hysterectomy was safe and might be a potential alternative to TLH.

There are two methods of preoperative blood preparation. One is crossmatching, which involved fully typing the blood. The other is type and screen, which involved matching only essential processes, including the ABO and Rh group systems, as well as an antibody screening test. In our hospital, for elective laparoscopic hysterectomy procedures, it is our standard practice to crossmatch a minimum of two units of packed red cell. For the evaluation of blood utilization, the result showed a high C/T ratio of 6.15, which correlated with previous literatures[13, 14, 25]. Furthermore, the low %T of 19.4 and TI of 0.35 in our study indicated a low probability of a patient requiring a blood transfusion during surgery. These indicators underscored the importance of improving an effective blood request model to reduce unnecessary blood ordering and transfusion. It is essential to develop the maximum surgical blood ordering system (MSBOS). This provides guidelines for preoperative blood preparation for each surgical procedure and implies the type and screen (T&S) protocol[26]. Previous study reported after adapting MSBOS could achieve a substantial reduction in the number of crossmatching[27]. Similarly, a recent study conducted in a tertiary care center in India also observed a trend of overordering blood for most laparoscopic surgeries. After adapting MSBOS, they achieved a substantial reduction in the number of crossmatching, approximately 2,152 units, and saved 75,320 man-hours in their laboratory[28].

The strengths of our study included being the first to evaluate the prevalence and associated factors of blood transfusion that scope in only laparoscopic hysterectomy and including various types of laparoscopy. However, there were some limitations. Firstly, its single-center design and retrospective nature introduced biases during the medical record review. Secondly, there were gaps in data for some participants, and key information like preoperative preparation, which could influence surgical outcomes, reasons for transfusions, and individual transfusion thresholds were missing. Another limitation was the variation in skills and expertise among the surgeons involved in the study. Lastly, the study's primary focused on determining prevalence led to the calculation of the sample size using a prevalence formula, potentially affecting the accuracy of associations between the factors.

Understanding the prevalence of perioperative blood transfusion and associated factors relating to transfusion requirement is valuable for preoperative blood preparation, surgical planning, and patient counseling. Patients at a higher risk of requiring a transfusion should receive more preoperative treatments to mitigate the risk of transfusion. In our opinion, based on our hospital data and our finding of ineffective blood ordering, we recommend introducing the MSBOS policy in transfusion practice. For low-risk patients, complete cross-matching should be replaced by preoperative type and screen to avoid unnecessary investigations, save hospital costs, and reserve blood units for emergency patients.

Conclusion

The overall prevalence of blood transfusion was as high as 19.4%. Preoperative anemia, intraoperative blood loss ≥ 300 milliliters, larger uterine size ≥ 500 grams, and pelvic adhesions were significantly associated with an increased risk of perioperative blood transfusion in patients undergoing laparoscopic hysterectomy for benign gynecologic conditions. Data of impulsive over-ordering of blood in our study might be useful in developing a new transfusion strategy in

our setting. Moreover, we recommend the type and screen method for preoperative blood preparation in low-risk patients undergoing elective laparoscopic hysterectomy for benign gynecologic conditions.

Potential conflicts of interest

The authors declare no conflicts of interest.

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Thai Journal of Obstetrics and Gynaecology
May 2024, Vol. 32, No. 3, pp. 225-233.

OBSTETRICS

Prevalence and Factors Associated with High Postpartum Depression Score Using Thai Edinburgh Postnatal Depression Scale in Charoenkrung Pracharak Hospital

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ABSTRACT

Objectives: This study aimed to estimate the prevalence of high postpartum depression score at 6-week postpartum using Thai Edinburgh postnatal depression scale (EPDS).

Materials and Methods: This cross-sectional study was conducted in December 2022 - May 2023. Two hundred and ninety-four participants were included. Personal data and obstetrics outcome of participants were collected on the 2nd day and 6-week of the postpartum period. Thai version of EPDS was recorded at 6 weeks postpartum. EPDS score at least 11 were considered as high postpartum depression score. Personal data and obstetrics outcome were analyzed by using t-test and regression analysis to identify associating factors.

Results: Of all 264 participants who were followed-up at 6-week postpartum period, it was found that 46 participants had high postpartum depression scores with the prevalence of 17.42%. After multivariate analysis, unintended pregnancy adjusted odds ratio (aOR 2.27, 95% confidence interval (CI) 1.06-4.76), maternity leave (aOR 0.47, 95%CI 0.23-0.99), postpartum stressful event (aOR 4.55, 95%CI 2.13-9.74) and inadequate social support (aOR 5.26, 95%CI 2.33-12.5, p <0.001) were statistically significantly associated with high postpartum depression scores.

Conclusion: The prevalence of high postpartum depression scores at 6 weeks was 17.42%. Healthcare professionals should be aware of postpartum depression and pay extra attention to patients with unintended pregnancy, postpartum stressful event, and inadequate social support. Taking maternity leave may be advocated.

Keywords: postpartum depression, Edinburgh postnatal depression scale.

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Received: 30 September 2023, **Revised:** 29 December 2023, **Accepted:** 5 January 2024

ความชุกและปัจจัยที่เกี่ยวข้องกับการมีคะแนนภาวะซึมเศร้าหลังคลอดสูงโดยใช้แบบคัดกรองภาวะซึมเศร้าหลังคลอดเอดินบะระที่โรงพยาบาลเจริญกรุงประชารักษ์

เรียงกานท์ ศรมยุรา, อัจจิมา ตันกุล, จิรพร เหลืองเมตตากุล

บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาความชุกและปัจจัยที่เกี่ยวข้องกับการมีคะแนนภาวะซึมเศร้าหลังคลอดสูง โดยใช้แบบคัดกรองภาวะซึมเศร้าหลังคลอดเอดินบะระ*

วัสดุและวิธีการ: *การศึกษาแบบตัดขวางนี้เริ่มศึกษาตั้งแต่เดือนธันวาคม พ.ศ.2565 ถึงเดือนพฤษภาคม พ.ศ.2566 อาสาสมัคร 294 คนได้เข้าร่วมในงานวิจัย ข้อมูลส่วนตัวของอาสาสมัคร และข้อมูลเกี่ยวกับการคลอดได้ถูกรวบรวมที่วันที่ 2 และที่ 6 สัปดาห์หลังคลอดบุตร อาสาสมัครได้ทำแบบคัดกรองภาวะซึมเศร้าหลังคลอดเอดินบะระที่ 6 สัปดาห์หลังคลอดบุตร โดยคะแนนรวมที่มากกว่าเท่ากับ 11 จะถือว่าเป็นคะแนนภาวะซึมเศร้าหลังคลอดที่สูง ข้อมูลส่วนตัว และข้อมูลการคลอดจะถูกวิเคราะห์เพื่อหาปัจจัยที่เกี่ยวข้องกับการมีคะแนนภาวะซึมเศร้าหลังคลอดสูง*

ผลการศึกษา: *พบอาสามัคร 46 คน จากอาสาสมัคร 264 คนที่มาติดตามที่ 6 สัปดาห์หลังคลอดมีคะแนนภาวะซึมเศร้าหลังคลอดสูงที่ 6 สัปดาห์ คิดเป็นร้อยละ 17.42 โดยพบปัจจัยที่เกี่ยวข้องอย่างมีนัยสำคัญทางสถิติได้แก่ การตั้งครรภ์ที่ไม่ได้เกิดจากความตั้งใจ (aOR 2.27, 95%CI 1.06-4.76) การได้ลาคลอดบุตร (aOR 0.47, 95%CI 0.23-0.99) การมีเหตุการณ์อื่นที่ทำให้ความเครียดหลังคลอด (aOR 4.55, 95%CI 2.13-9.74) และการมีความช่วยเหลือทางสังคมที่ไม่เพียงพอ (aOR 5.26, 95%CI 2.33-12.5, P<0.001)*

สรุป: *ความชุกของการมีคะแนนภาวะซึมเศร้าหลังคลอดสูงที่ 6 สัปดาห์หลังคลอดเท่ากับร้อยละ 17.42 บุคลากรทางสาธารณสุขควรคำนึงถึงภาวะซึมเศร้าหลังคลอด โดยเฉพาะอย่างยิ่งในผู้ป่วยที่การตั้งครรภ์ไม่ได้เกิดจากความตั้งใจ มีเหตุการณ์อื่นที่ทำให้เกิดความเครียดหลังคลอด และได้รับความช่วยเหลือทางสังคมไม่เพียงพอ อีกทั้งยังอาจสนับสนุนการลาคลอดบุตรอีกด้วย*

คำสำคัญ: *ภาวะซึมเศร้าหลังคลอด, แบบคัดกรองภาวะซึมเศร้าหลังคลอดเอดินบะระ*

Introduction

Postpartum depression is defined as major and minor depressive episodes that occur in the postpartum period[1]. Postpartum depression is caused by both environmental and genetic factors[2]. Postpartum depression is often unrecognized because changes in appetite, sleep and libido may be attributed to postpartum changes, and new mothers may be reluctant to report their mood changes[3, 4]. Mothers with postpartum depression show low mood, diminish capacity to experience pleasure and may feel a sense of detachment from their infants[5]. Suicide and infanticide also remained significant concern[1, 6].

In the present, diagnosis of peripartum depression uses DSM-5 criteria of major depressive episode with onset of mood symptoms occurs during pregnancy or in the 4 weeks following pregnancy[6]. However, recommendations from obstetricians often extend the postpartum period until 12 months after delivery[3, 5]. In general, screening for postpartum depression was made before referring to psychiatrist for diagnosis and treatment. Several screening instruments for peripartum depression were developed to be used during pregnancy and the postpartum period. The Edinburgh postnatal depression scale (EPDS) developed by Cox et al[7] most frequently used in the research setting and clinical practice. EPDS consisted of 10 self-reported questions and took less than 5 minutes to complete. Each question had four choices with the score of 0, 1, 2 and 3. Hence, the total scores were 30. Thai version of the EPDS was translated and validated by Vacharaporn et al[8] and threshold score at least 11 was proposed with sensitivity 100%, specificity 88% and degree of agreement 0.38.

Systematic review of 565 studies from 80 countries worldwide in 2021 found prevalence of postpartum depression 17.22% with the prevalence in southeast Asia 13.53% and associated factors for postpartum depression were marital status, educational levels, social support, violence, gestational age, breast feeding, infant death, planned pregnancy, financial problems, partnership, life stress, smoking, alcohol use and living conditions[9]. In Thailand, a cross-sectional study in 2011 at General hospital[10] found prevalence of postpartum depression at 6 weeks postpartum was 10.4% using EPDS with marital status, partner relationship, plan of this pregnancy, maternal anxiety and newborn complication identified as associated factors. In 2017, a study at Taksin Hospital[11] found prevalence of postpartum depression at 6 weeks postpartum was 18.8% using EPDS with maternal anxiety and social support identified as associated factors. Trend of postpartum depression seems to rise over time.

Previous studies in Thailand were done many years ago and there were drastically changed in culture and lifestyle after the outbreak of COVID-19 infection. These alongside with economy regression might increase postpartum depression. Therefore, we would like to study the associating factors with postpartum depression in this era; patients at risk can be effectively identified, diagnosed, and treated postpartum depression.

This research aimed to study the prevalence and factors associated with high postpartum depression score at 6-week postpartum in Charoenkrung Pracharak hospital using Thai EPDS.

Materials and Methods

This cross-sectional study was conducted in Charoenkrung Pracharak Hospital, Bangkok, Thailand in December 2022 – May 2023. The protocol was approved by the Bangkok Metropolitan Administration Human Research Ethics Committee (R004h/65_EXP). The sample size was calculated based on Nuanchawee's study[11] in 2017 which identified 18.8% of prevalence of postpartum depression at 6 weeks. Then total sample size in this study was 294 with estimated 20% data loss. The inclusion criteria were participants who were at least 18 years old, delivered at Charoenkrung Pracharak Hospital, and could read and write Thai. Participants were enrolled and their consent forms were obtained during the 3rd trimester or immediate postpartum period. Participants who had psychotic disorders that could not communicate

or had depressive disorder before delivery was excluded. For participants with psychotic disorders that could not communicate, we excluded them by reviewing their medical records. For the participants with depressive disorder, we exclude them by reviewing medical record in Charoenkrung Pracharak Hospital, and by asking whether they have depressive disorder before delivery that had to be treated by a psychiatrist.

On the 2nd day of postpartum period, a questionnaire was given to each participant to be answered in an isolated room with no distraction. Participants had to write their answers in the questionnaire. The questionnaire consisted of questions about age, educational levels, family income, adequacy of income, family type (nuclear or extended family), marital status, tobacco use (during this pregnancy), alcohol drinking (during this pregnancy), substance use (during this pregnancy), parity, underlying disease, antepartum complication (i.e. gestational hypertension, preeclampsia, gestational diabetes mellitus, and placenta previa), intention of pregnancy and newborn sex expectation. At 6-week postpartum visit, the Thai version of Edinburgh postnatal depression scale (EPDS)[7] and another questionnaire were given to the participants to be answer in an isolated room with no distraction. Participants had to write their answers in the EPDS and the questionnaires. This questionnaire consisted of questions about maternity leave (defined as 90 days maternity leave from work), breast feeding (breast milk only, formular milk only or combine), breast feeding complication, duration of sleep (estimated by the participants as accumulate time of sleep per night), postpartum stressful event (defined as any stressful event happened during the postpartum period apart from childbirth related event), adequacy of social support (defined as the support participants got from their partner, family, and friends in the postpartum period; the participant will be determining whether they were receiving adequate social support). Obstetrics outcomes were collected by chart review on the participant's and newborn's medical records. These outcomes consisted of gestational age, route of delivery, intrapartum complication (i.e. retained placenta, cervical tear, third- and fourth-degree perineal tear), postpartum complication (i.e. infected episiotomy wound, and metritis), postpartum hemorrhage, birth weight, congenital anomaly (i.e. esophageal atresia, and cardiac malformations), newborn complication (i.e. pneumonia, sepsis, severe birth asphyxia, transient tachypnea of newborn, and jaundice that need phototherapy), birth injury (i.e. cephalhematoma, and clavicle fracture), neonatal intensive care unit (NICU) admission. Participants who had EPDS score at least 11 would be referred to the psychiatrist. Unfortunately, psychiatric diagnosis and treatment would not be accounted in our study.

Primary outcome was prevalence of high postpartum depression score at 6-week postpartum (define as Thai version of EPDS score at least 11). The secondary outcomes were factors (personal data and obstetrics outcome) associated with high postpartum depression score by comparing between normal and high postpartum depression score groups. All data were analyzed with SPSS software (version 26). The data were summarized by using descriptive statistics and were shown with numbers, percentage, mean and standard deviation. Regression analysis was used to analyze the associating factors. After univariate analysis, all factors that were statistically significant were included in multivariate analysis. Adjusted odds ratio (aOR) along with 95% confidence interval (CI) were presented. A p value < 0.05 was considered statistically significant.

Results

In December 2022 – May 2023, 336 participants met the inclusion criteria. There were 29 participants who denied enrollment. Thirteen participants were fallen into the exclusion criteria. Two of them were excluded due to having psychotic disorder that cannot communicate and eleven of them were excluded due to having depressive disordered before delivery. Apart from participants who denied enrollment or had fallen into the exclusion criteria, the total number of participants in our study was 294. Thirty participants did not follow-up at the 6-week postpartum period. Of 264 participants, 46 of them had a high postpartum

depression score. Therefore, the prevalence of high postpartum depression score was 17.42%. There are 2 participants that have other ethnicities with 262 Thai participants. The demographic data are shown in Table 1. The rate of unintentional pregnancy, postpartum stressful event, and inadequate social support was significantly higher in high postpartum depression score group than normal postpartum depression score group. The rate of maternity leave was significantly lower in high postpartum depression score group than normal postpartum depression score group.

Table 1. Comparison of demographic and preoperative data between transfusion and non-transfusion groups.

Variables	Normal depression score, n = 218 (%)	High depression score, n = 46 (%)	Crude odds ratio (95% confidence interval)	p value
Age (years) mean ± SD	29.4 ± 6.1	27.2 ± 6.4	-	0.029[t]
< 20	9 (4.1)	5 (10.9)	Reference	
20-34	162 (74.3)	34 (73.9)	0.38 (0.12-1.20)	0.098
≥ 35	47 (21.6)	7 (15.2)	0.27 (0.07-1.04)	0.056
Education level				
Secondary school and below	58 (26.6)	16 (34.8)	Reference	
High school	57 (26.1)	7 (15.2)	0.45 (0.17-1.16)	0.099
Vocational education	37 (17.0)	11 (23.9)	1.08 (0.45-2.58)	0.866
Bachelor's degree and above	66 (30.3)	12 (26.1)	0.66 (0.29-1.51)	0.323
Family income (baht/month) mean ± SD	32,473.5 ± 20,821.5	29,865.9 ± 15,544.7	-	0.449[t]
< 15,000	27 (13.6)	5 (12.2)	Reference	
15,000 - 30,000	92 (46.5)	19 (46.3)	1.12 (0.38-3.27)	0.842
> 30,000	79 (39.9)	17 (41.5)	1.16 (0.39-3.45)	0.787
Inadequate income	28 (13.0)	7 (15.6)	1.23 (0.5-3.03)	0.651
Nuclear family	105 (48.2)	24 (52.2)	1.18 (0.62-2.22)	0.621
Unmarried	93 (42.7)	24 (52.2)	1.47 (0.78-2.77)	0.238
Tobacco use	5 (2.3)	-	-	0.591[F]
Alcohol drinking	15 (6.9)	2 (4.3)	0.62(0.14-2.79)	0.529
Substance use	3 (1.4)	-	-	> 0.999[F]
Nulliparous	98 (45.0)	24 (52.2)	1.33 (0.70-2.50)	0.373
Underlying disease	22 (10.1)	3 (6.5)	0.62 (0.18-2.17)	0.456
Antepartum complication	74 (33.9)	21 (45.7)	1.64 (0.86-3.11)	0.135
Unintended pregnancy	51 (23.4)	22 (47.8)	3.03 (1.56-5.88)	0.001
Match sex expectation	196 (90.3)	41 (89.1)	0.88 (0.31-2.47)	0.806
Six weeks postpartum				
Maternity leave	155 (71.1)	23 (50.0)	0.41 (0.21-0.78)	0.006
Breast feeding				
Breast milk only	119 (54.6)	20 (43.5)	Reference	
Formula milk only	5 (2.3)	3 (6.5)	1.46 (0.75-2.81)	0.263
Combine	94 (43.1)	23 (50.0)	3.57 (0.79-16.12)	0.098
Breast feeding complication	84 (38.5)	22 (74.8)	1.46 (0.77-2.77)	0.244
Duration of sleep ≥ 6 hours	96 (44.2)	16 (34.8)	0.67 (0.35-1.30)	0.241
Postpartum stressful event	58 (26.6)	33 (71.7)	7.00 (3.45-14.22)	< 0.001
Inadequate social support	21 (9.6)	21 (45.7)	0.13 (0.06-0.26)	< 0.001

[t] = independent t-test, [F] = fisher's exact test, SD: standard deviation

Table 2 shows obstetrics outcomes of both high and normal postpartum depression score groups which were not statistically different.

Table 3 demonstrates the associations between high postpartum depression score and several variables using logistic regression. After regression analysis, unintentional pregnancy (aOR 2.27, 95%CI 1.06-4.76, p = 0.035), present of postpartum stressful event (aOR 4.55, 95%CI 2.13-9.74, p < 0.001) and inadequate social support (aOR 5.26, 95%CI 2.33-12.5, p < 0.001) were statistically significant factors associated with high postpartum depression score. In the contrary, receiving maternity leave (aOR 0.47, 95%CI 0.23-0.99) reduced the prevalence of high postpartum depression score. Other factors were assessed but failed to show statistically significant association with high postpartum depression score.

Table 2. Obstetrics outcome.

Variables	Normal depression score, n = 218 (%)	High depression score, n = 46 (%)	Crude odds ratio (95% confidence interval)	p value
Gestational age (weeks) mean ± SD	38.0 ± 1.8	37.4 ± 2.2	-	0.062[t]
< 37	28 (12.8)	7 (15.2)	Reference	
37-42	190 (87.2)	39 (84.8)	0.82 (0.34-2.01)	0.667
Vaginal delivery	133 (61.0)	25 (54.3)	Reference	
Cesarean delivery	85 (39.0)	21 (45.7)	1.31 (0.69-2.50)	0.403
Primary cesarean delivery	61 (71.8)	13 (61.9)		
Repeated cesarean delivery	24 (28.2)	8 (38.1)		
Intrapartum complication	14 (6.4)	2 (4.3)	0.66 (0.15-3.02)	0.595
Postpartum complication	9 (4.1)	2 (4.3)	1.06 (0.22-5.06)	0.964
Postpartum hemorrhage	18 (8.3)	2 (4.3)	0.51 (0.11-2.26)	0.371
Birth weight (g) mean ± SD	3,084.4 ± 531.8	2,962.9 ± 493.7	-	0.156[t]
< 2,500	23 (10.6)	8 (17.4)	1.68 (0.70-4.03)	0.249
2,500-4,000	183 (83.9)	38 (82.6)	Reference	
> 4,000	12 (5.5)	-	-	
Congenital anomaly	8 (3.7)	1 (2.2)	0.58 (0.07-4.78)	0.616
Newborn complication	95 (43.6)	18 (40.0)	0.86 (0.45-1.66)	0.659
Birth injury	15 (6.9)	3 (6.5)	0.94 (0.26-3.40)	0.930
NICU admission	9 (4.1)	2 (4.3)	1.06 (0.22-5.06)	0.946

[t] = independent t-test, NICU: neonatal intensive care unit, SD: standard deviation

Table 3. Regression analysis.

Variables	Univariate analysis		Multivariate analysis	
	Crude odds ratio (95% confidence interval)	p value	Adjusted odds ratio (95% confidence interval)	p value
Unintended pregnancy	3.03 (1.56-5.88)	< 0.001	2.27 (1.06-4.76)	0.035
Maternity leave	0.41 (0.21-0.78)	0.006	0.47 (0.23-0.99)	0.049
Postpartum stressful event	7.00 (3.45-14.22)	< 0.001	4.55 (2.13-9.74)	< 0.001
Inadequate social support	0.13 (0.06-0.26)	< 0.001	5.26 (2.33-12.5)	< 0.001

[t] = independent t-test, NICU: neonatal intensive care unit, SD: standard deviation

Discussion

The prevalence of high postpartum depression score in our study was 17.42% which was approximated to the worldwide prevalence of postpartum depression of 17.22%[9]. A systematic review of global prevalence of depression in general population[12] found more increasing prevalence of depression after the COVID-19 pandemic in women than men. With the same trend, increasing prevalence of postpartum depression after the COVID-19 pandemic could also be expected with postpartum women. Our study showed approximate rate of postpartum depression with the study by Nuanchawee in 2017 at Taksin Hospital[11]. They used the same cut point of Thai version of EPDS (score of at least 11) to define high postpartum depression score as our study and reported the prevalence of postpartum depression of 18.8%. The higher prevalence of high postpartum depression score than the one in the previous study at Taksin Hospital, which was conducted before the era of COVID-19, was not found in our study. This might result from the fact that our study was undertaken in December 2022 – May 2023 when the COVID-19 pandemic eased up. Also, there was not any participant being infected with COVID-19 during the time when the questionnaire was given. In contrast to the study at Taksin Hospital, the study at General Hospital[10] reported the prevalence of postpartum of 10.4%, which showed lower prevalence of postpartum depression score than the one in our study. This might stem from differences of cut point of EPDS. The study in General hospital used a score of at least 13 to define high postpartum depression score. Although the EDPS was originally developed with the threshold score at least 13 suggested by the developer, the study by Vacharaporn[8] found using cut point of 11 of Thai version of EDPS showed better sensitivity and specificity (sensitivity 100% and specificity 88% for cut point of 11, sensitivity 66.6% and specificity 93.75% for cut point of 13).

Inadequate social support was pointed out to be associated with high postpartum depression scores in our study. A study of association between social support and postpartum depression by Hahyeon et al[13] also showed the same trend. They reported that women with moderate or low social support were more likely to have postpartum depression (moderate social support (OR 1.78, 95%CI 1.26–2.53), low social support (OR 2.76, 95%CI 1.56-4.89)). Our study focused on perceived social support which might not be equal to the actual support. Previous studies found perceived social support to have more effects on maternal mental health and wellbeing than actual support[14, 15].

Postpartum stressful event is another relating factor with high postpartum depression score. A study of effect of stressful life event in the year before delivery on the likelihood of postpartum depression by Mina et al[16] revealed the likelihood of postpartum depression was higher among women who had high relational stress. This showed the importance of postpartum visit in identifying not only physical but also mental and psychological problems of the new mothers.

Our study also found that unintended pregnancy was associated with high postpartum depression score. A prospective cohort study by Mercier et al[17] found unintentional pregnancy to be associated with depression at 3 and 12 months postpartum (3 months (relative risk (RR) 2.1, 95%CI 1.2-3.6, and 12 months (RR 3.6, 95%CI 1.8-7.1)). In our study, we found 27.7% of all pregnancies to be unintentional. Unintended pregnancy could result from lack of family planning and poor knowledge on contraception[19]. After birth, some mothers would deny their child to ever be resulted from unintentional pregnancy[18]. Since our study collected this information at the immediate postpartum period, the actual rate of unintended pregnancy may be higher than the one in our study. Unintended pregnancy could lead to suboptimal antenatal care, and adverse pregnancy outcome. Patient education and family planning should be promoted to lower rate of unintended pregnancy.

We found that taking maternity leave was associated with lower rate of high postpartum

depression score. A cross-sectional study by Kornfeind and Sipsma found that every additional week of maternity leave was associated with the lower rate of postpartum depressive symptoms (OR, 0.58, 95% CI 0.40–0.84)[20]. Taking maternity leave allowed new mothers to adjust to mother life, bond with the newborn, have time for wound healing, and breast feeding.

Previous studies found breastfeeding reduce the rate of postpartum depression[21, 22]. In our study, however not statistically significant, we also found higher number of participants using formula milk and lower number of breastfeeding in high postpartum depression score group compared to normal score group.

Strengths

We collected some of the personal data on the 2nd day of postpartum period while participants were in the hospital to avoid recall bias. The data was collected completely so the result was reliable. Moreover, our study used Thai version of Edinburgh postnatal depression scale instead of the Edinburgh postnatal depression scale instead of the 2 questions and 9 questions (2Q9Q) questionnaire to identify participants with high postpartum depression score. The 2Q9Q questionnaire was a screening tool for depression. Apart from being wildly used in clinical and research setting, the 2Q9Q questionnaire might not be suitable to be used in postpartum patients since the questionnaire of 2Q9Q included changes in sleep pattern which would be the common situation among breastfeeding mothers.

Limitations

The limitations of our study were firstly, our study did not follow-up participants with high postpartum depression score on the psychiatric diagnosis and treatment so, the actual rate of postpartum depression could not be calculated. Secondly, participants who were unable read and write Thai were exclude from our study. These participants could be uneducated Thai people, or they could have other ethnicities. Therefore, the rate of high postpartum depression score in our study might be different from the actual rate. Thirdly, because our study lacked antepartum depression testing, participants who did not recognize or deny themselves of having depressive disorder before delivery would be included in our study.

Clinical Application

From our study, patients with risk factors of high postpartum depression score should be identified early and health care personnel should pay extra attention. All women in the postpartum period should be educated about symptoms of postpartum depression and reassured not to hesitate in reporting any feelings of anxiety to health care provider when having those symptoms. Patients with risk factors must have more frequent and early postpartum visits which should contain both physical and mental cares. Moreover, new mothers should be recommended to take maternity leave as it resulted in lower chance of having high postpartum depression score.

Conclusion

The prevalence of high postpartum depression score at 6 weeks in our study was 17.42%. Unintentional pregnancy, present of postpartum stressful event and inadequate social support were associated with high postpartum depression score. Taking maternity leave may be advocated because of lower rate of high postpartum depression score.

Potential conflicts of interest

The authors declare no conflicts of interest.

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Thai Journal of Obstetrics and Gynaecology
May 2024, Vol. 32, No. 3, pp. 234-244

GYNAECOLOGY

Prevalence of Metabolic Syndrome in Thai Women with Polycystic Ovary Syndrome

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ABSTRACT

Objectives: To assess the prevalence and associated risk of metabolic syndrome (MS) among Thai women with polycystic ovary syndrome (PCOS).

Materials and Methods: A retrospective study was conducted in 337 women visiting Khon Kaen University Hospital between January 2014 and December 2021. The data on weight, height, waist circumference (WC), waist to hip ratio (WHR), and laboratory results were reviewed. The diagnosis of MS was made by International Diabetes Federation (IDF) and National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria. Multiple logistic regression was applied to calculate adjusted odds ratio (aORs) and 95% confidence intervals (CIs)

Results: Three hundred and thirty-seven patients were reviewed. Median (interquartile range) of age, body mass index (BMI), WC, and WHR were 24 (21–29) years, 25 (21-31) kg/m^2, 80 (70-90) cm, and 0.85 (0.79-0.89), respectively. The prevalence of MS was 27.3% and 20.8% according to the criteria of IDF and NCEP ATP III, respectively. Age 30 years or older (aOR 1.89, 95%CI 1.06-3.40), positive family history of MS and/or diabetes mellitus (aOR 2.77, 95% CI 1.66-4.65), and having exercise behavior (aOR 0.45, 95% CI 0.23-0.86) were found to be independently associated with MS in PCOS women.

Conclusion: MS was highly prevalent among PCOS women residing in the Northeast Thailand. Factors associated with MS odds included age, family history of MS and/or diabetic mellitus, and exercise behavior.

Keywords: metabolic syndrome, abnormal glucose metabolism, obesity, PCOS.

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Received: 30 August 2023, **Revised:** 25 October 2023, **Accepted:** 30 November 2023

ความชุกของกลุ่มอาการเมทาบอลิกในสตรีไทยที่ได้รับการวินิจฉัยกลุ่มอาการถุงน้ำในรังไข่หลายใบ

บราลี สังเกต, นันทสิริ เอี่ยมอุดมกาล, น้ำเพชร จำปาทอง

บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาความชุกและปัจจัยที่เกี่ยวข้องของกลุ่มอาการเมทาบอลิก ในสตรีที่ได้รับการวินิจฉัยกลุ่มอาการถุงน้ำในรังไข่หลายใบ (Polycystic Ovary Syndrome; PCOS)*

วัสดุและวิธีการ: *การศึกษานี้เป็นการศึกษาย้อนหลัง (Retrospective study) โดยเก็บรวบรวมข้อมูลในสตรี 337 รายที่ได้รับการวินิจฉัย PCOS ซึ่งมารับบริการที่โรงพยาบาลศรีนครินทร์ในช่วง พ.ศ. 2557-2564 ข้อมูลทั่วไปได้แก่ น้ำหนัก, ส่วนสูง, ดัชนีมวลกาย, เส้นรอบเอว, เส้นรอบเอวต่อสะโพก, และความดันโลหิต ข้อมูลทางห้องปฏิบัติการได้แก่ การเผาผลาญน้ำตาลกลูโคส (glucose metabolism) ประเมินโดนการตรวจ 75-g Oral Glucose Tolerance Test (OGTT) และระดับไขมันในเลือดเมื่อมารักษาครั้งแรก กลุ่มอาการเมทาบอลิกวินิจฉัยโดยใช้เกณฑ์ของ International Diabetes Federation (IDF) และ National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) ปัจจัยที่เกี่ยวข้องของกลุ่มอาการเมทาบอลิกวิเคราะห์โดยวิธี logistic regression*

ผลการศึกษา: *ในสตรีที่ได้รับการวินิจฉัย PCOS จำนวน 337 ราย มีค่า median (interquartile range) ของอายุ, ดัชนีมวลกาย, เส้นรอบเอว และเส้นรอบเอวต่อสะโพก เท่ากับ 24 (21-29) ปี, 25 (21-31) กิโลกรัม/ม^2, 80 (70-90) ซม. และ 0.85 (0.79-0.89) ตามลำดับ พบความชุกของกลุ่มอาการเมทาบอลิก ร้อยละ 27.3 และ 20.8 เมื่อใช้เกณฑ์วินิจฉัยของ IDF และ NCEP ATP III ตามลำดับ ปัจจัยเสี่ยงของการเกิดกลุ่มอาการเมทาบอลิก ได้แก่ อายุมากกว่า 30 ปี (aOR 1.89,95%CI 1.06-3.40), มีประวัติคนในครอบครัวเป็นโรคเบาหวานหรือกลุ่มอาการเมทาบอลิก (aOR 2.77,95%CI 1.66-4.65) และพฤติกรรมการออกกำลังกาย (aOR 0.45,95%CI 0.23-0.86)*

สรุป: *ความชุกของกลุ่มอาการเมทาบอลิกพบได้สูงในสตรีที่ได้รับการวินิจฉัย PCOS ในภาคตะวันออกเฉียงเหนือของไทย โดยพบความชุกร้อยละ 27.3 และ 20.8 เมื่อใช้เกณฑ์วินิจฉัยของ IDF และ NCEP ATP III ตามลำดับ ปัจจัยเสี่ยงของการเกิดกลุ่มอาการเมทาบอลิกได้แก่ อายุ, ประวัติคนในครอบครัวเป็นโรคเบาหวานหรือกลุ่มอาการเมทาบอลิก และพฤติกรรมการออกกำลังกาย*

คำสำคัญ: *กลุ่มอาการเมทาบอลิก, ภาวะการเผาผลาญน้ำตาลผิดปกติ , ภาวะอ้วน, กลุ่มอาการถุงน้ำในรังไข่หลายใบ*

Introduction

Polycystic Ovary Syndrome (PCOS) is the most prevalent endocrinopathy affecting 8 to 13% of women of reproductive age[1]. This complex disorder is characterized by hyperandrogenism, ovulatory dysfunction and polycystic ovarian morphology[2]. In addition to reproductive disturbance, women with PCOS are at an elevated risk of various metabolic disturbances, including diabetes mellitus, dyslipidemia, and cardiovascular disease[3, 4].

The etiology of PCOS remains uncertain, but existing evidence indicates that its pathophysiology is complex and multifactorial, involving endocrine, metabolic, genetic, epigenetic, and environmental factors[5]. Insulin resistance and central obesity are commonly observed features and believed to play a central role in the development of the syndrome[6, 7]. These factors increase the risk of metabolic syndrome (MS) in women with PCOS. MS is a cluster of endocrinopathy and metabolic disturbances including central obesity, abnormal lipid profiles, insulin resistance, and hypertension[8, 9]. This syndrome is associated with long-term consequences and brings PCOS women to an increased risk of cardiovascular disease (CVD). As a result, international societies recommend CVD screening among these women[3].

The overall prevalence of MS in women with PCOS was reported to be 30%, and regardless of age, the risk of having MS among these women was 2.5 times higher when compared to healthy controls[10, 11]. The reported prevalence differed according to ethnicity of study population[12]. Up to the present, four studies in Thailand have reported the prevalence of MS in PCOS women[13-16]. Three studies conducted in Bangkok found the prevalence of 18-33.3%[13-15], while another one study in Chiang Mai reported the prevalence of 24.3%[16]. No prior studies have investigated this issue among PCOS women residing in the Northeastern region of Thailand. Consequently, the present study aimed to assess the prevalence of MS among PCOS patients attending the gynecological endocrinology clinic at Srinagarind Hospital, the Northeastern region of Thailand.

Materials and Methods

Study setting and participants

This study was a retrospective study conducted at the gynecological endocrinology clinic at Srinagarind Hospital, Khon Kaen University, Thailand, which is a tertiary hospital in the Northeastern sector. The study was approved by the Khon Kaen University Ethics Committee for Human Research (HE651219). The data from reproductive-aged PCOS patients visiting the clinic between 2014-2021 were collected. A diagnosis of PCOS was based on the revised Rotterdam 2003 criteria[17]. Women who had been previously diagnosed with diabetes mellitus, dyslipidemia, or other endocrinologic abnormalities or had history of steroid or other hormonal usage or had incomplete medical records were excluded. The objectives of the present study were to investigate the prevalence and associated factors of metabolic syndrome in PCOS women.

Data collection and variables of interest

The demographic and laboratory data were extracted from the computer-based medical records system and added to a data collection form created by one of the authors. Afterward, the data were transferred to the Microsoft Excel program and double-checked for accuracy by another author before analysis. The clinical variables of interest included age, age at menarche, parity, presence of clinical hyperandrogenism, exercise behavior, family history of DM and/or MS, and anthropometrics indices (body weight, height, waist circumference (WC), waist-to-hip ratio (WHR)). Early menarche was defined as menarche before the age of 12 years. Clinical hyperandrogenism included hirsutism, acne and androgenic alopecia. Additionally, the laboratory results of plasma glucose levels and lipid profiles obtained from the initial visit were collected.

The diagnosis of MS was made based on two international standards criteria: The International Diabetes Federation (IDF)[8] and The National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III)[18]. According to the IDF criteria, women with central obesity (WC ≥ 80 cm) plus two out of the following conditions were diagnosed to have MS: Systolic blood pressure (SBP) ≥ 130 mmHg or diastolic blood pressure (DBP) ≥ 85 mmHg, triglyceride (TG) level ≥ 150 mg/dl, high density lipoprotein (HDL) level < 50 mg/dl, and fasting plasma glucose (FPG) level ≥ 100 mg/dl. On the other hand, the NCEP ATP III criteria requires the presence of three out of the following five criteria: WC ≥ 88 cm, SBP ≥ 130 mmHg or DBP ≥ 85 mmHg, TG level ≥ 150 mg/dl, HDL level < 50 mg/dl, and FPG level ≥ 100 mg/dl.

Glucose metabolism was determined by a 75-gm oral glucose tolerance test (OGTT). Abnormal plasma OGTT was classified according to the American Diabetes Association (ADA) 2021 criteria (19) which comprises of as follows: impaired fasting glucose (IFG) which is defined as fasting plasma glucose (FPG) levels from 100 to 125 mg/dl, impaired glucose tolerance (IGT) which is 2-hour plasma glucose (2-h PG) levels from 140 to 199 mg/dl, and type 2 diabetes mellitus (T2DM) which is FPG ≥ 126 mg/dl or 2-h PG ≥ 200 mg/dl.

The definition of obesity was defined as body mass index (BMI) ≥ 25 kg/m^2 according to WHO recommendation for Asian populations[20]. Women with WC ≥ 80 cm or WHR ≥ 0.8 were considered to have central obesity.

Statistical analysis

Statistical analysis was performed using Stata program version 10. Descriptive statistics including mean with standard deviation (SD), median with interquartile range (IQR), and number with percentage were used to report the characteristics of the patients. To compare patient characteristics between the groups (MS and Non-MS), categorical variables were assessed using the chi-squared test or the Fisher's exact test, while continuous variables were evaluated using student's t-test or Mann-Whitney U test as appropriate.

We used simple logistic regression to explore the association between individual risk factors and MS. The multiple logistic regression model was used to analyze independent risk factors for MS, and the results were presented using adjusted odds ratios (aOR) with their corresponding 95% confidence intervals (CIs). We computed variance inflation factor (VIF) to determine multicollinearity between the covariates in the regression model. Multicollinearity is considered when the VIF is higher than 5. A p value of < 0.05 was considered to be statistically significant.

Results

During the study period, medical records of 337 PCOS women were reviewed. The prevalence and abnormal components of MS are presented in Table 1. The prevalences of MS were 27.3% (95% CI 22.6%-32.4) and 20.8% (95% CI 16.6%-25.5%) according to the IDF and NCEP ATP III, respectively. All PCOS women who met IDF criteria for MS had elevated waist circumference compared to a rate of 77.1% of women diagnosed by NCEP ATP III criteria. PCOS women with MS based on IDF criteria trended to have lower prevalence of abnormal glucose metabolism and lipid profile compared to those with MS according to NCER ATP III criteria. Approximately half of the women with MS met three criteria, while the remaining half had four or five criteria (Table 1).

Table 2 demonstrates the clinical and laboratory characteristics of PCOS women. Of 337 women, the median (interquartile range) of age, body weight, BMI, waist circumference, and waist to hip ratio (WHR) were 24 years (21-29), 66 kg (53-81), 25 kg/m^2 (21-31), 80 cm (70-90), and 0.85 (0.79-0.89), respectively. In comparison to women who did not meet criteria for MS, those with MS had a significantly higher body weight, BMI, waist circumference, WHR, and blood pressure.

Additionally, PCOS women with MS had significantly elevated levels of abnormal glucose and lipid parameters compared to those without MS, including higher fasting plasma glucose (FPG), 2-hour glucose, triglyceride (TG) levels, and lower high-density lipoprotein (HDL) levels.

Table 1. Prevalence and abnormal components of metabolic syndrome criteria.

Components for diagnosis	Prevalence of MS			
	IDF criteria		NCEP-ATPIII criteria	
	MS (n= 92) 27.3% , 95% CI 22.6% - 32.4%)	Non- MS (n= 245) 72.7%, 95% CI 67.6% - 77.4%	MS (n= 70) 20.8%, 95% CI 16.6% - 25.5%	Non- MS (n= 267) 79.2%, 95% CI 74.5% - 83.4%
Elevated Waist circumference	92 (100%) (95% CI 96.1% - 100%	77 (31.1%) 95% CI 25.6% - 37.3%	54 (77.1%) 95% CI 67.1% - 87.2%	33 (12.4%) 95% CI 8.4% - 16.3%
Blood pressure ≥ 130/85 mmHg	73 (79.3%) 95% CI 70.9% - 87.8%	(18.8%) 95% CI 13.9% - 23.7%	56 (80.0%) 95% CI 70.4% - 89.6%	63 (23.6%) 95% CI 18.5% - 28.7%
Triglyceride level ≥ 150 mg/dl	54 (58.7%) 95% CI 48.4% -68.9%	(13.5%) 95% CI 9.2% - 17.8%	46 (65.7%) 95% CI 54.3% - 77.1%	41 (15.4%) 95% CI 11.0%-19.7%
HDL level < 50 mg/dl	66 (71.7%) 95% CI 62.4% - 81.1%	(18.0%) 95% CI 13.1% - 22.8%	54 (77.1%) 95% CI 67.1% - 87.2%	56 (21.0%) 95% CI 16.1% -25.9%
FPG ≥ 100 mg/dl	41 (44.6%) 95% CI 34.2% - 54.9%	(6.5%) 95% CI 3.4% - 9.6%	37 (52.9%) 95% CI 40.9% - 64.8%	20 (7.5%) 95% CI 4.3% - 10.7%
Number of MS criteria				
0	NA	96 (39.2%) 95% CI 33.0% - 45.6%	NA	114 (42.7%) 95% CI 36.7% - 48.9%
1	NA	85 (34.7%) 95% CI 28.7% - 41.0%	NA	93 (34.8%) 95% CI 29.1% - 40.9%
2	NA	61 (24.9%) 95% CI 19.6% - 30.8%	NA	60 (22.5%) 95% CI 17.6% - 28.0%
3	50 (54.3%) 95% CI 43.6% - 64.8%	3 (1.2%) 95% CI 0.3% - 3.5%	40 (57.1%) 95% CI 44.7% - 68.9%	NA
4	34 (37.0%) 95% CI 27.1% - 47.7%	NA	23 (32.9%) 95% CI 22.1% - 45.1%	NA
5	8 (8.7%) 95% CI 3.8% - 16.4%	NA	7 (10.0%) 95% CI 4.1% - 19.5%	NA

MS: metabolic syndrome, IDF: International Diabetes Federation, NCEP-ATPIII: National Cholesterol Education Program Adult Treatment Panel III, CI: confidence interval, HDL: high-density lipoprotein, FPG: fasting plasma glucose, NA: not applicable

Abnormal glucose metabolism (AGM) determined by a 75-gm oral glucose tolerance test (OGTT) was found in 116 (34.4%) women. Out of these, 18 women (5.3%) had DM, 50 women (14.8%) had IFG, and 72 women (21.4%) had IGT. A significantly higher number of women with AGM were

observed in the MS group (59/92 women, 64.1%) compared to those without MS (57/245 women, 23.3%). Impaired glucose tolerance (IGT) was detected in 30 (32.6%) women with MS which was also significantly higher than those without MS (42/245 women, 17.1%) (Table 2).

Table 2. Clinical and metabolic characteristics of PCOS women stratified by the presence of MS based on IDF criteria.

Characteristics	Total (n = 337)	MS (n = 92)	Non-MS (n = 245)	p value
Age (years)	24 (21 – 29)	25 (21.5 – 30)	24 (21 – 28)	0.189
Age at menarche (years)	13 (12 – 14)	12.5 (12 – 13)	13 (12 – 14)	0.031
Nulliparity	310 (92.0%)	84 (91.3%)	226 (92.2%)	0.777
Exercise behavior[1]	87 (25.8%)	15 (16.3%)	72 (29.4%)	0.014
Family history of DM	94 (27.9%)	39 (42.4%)	55 (22.5%)	< 0.001
Family history of MS	52 (15.4%)	26 (28.3%)	26 (10.6%)	< 0.001
Body weight (kilograms)	66 (53 – 81)	85 (75 – 95)	59 (50 – 71)	< 0.001
BMI	25 (21 – 31)	31 (28 – 35)	23 (19 – 27)	< 0.001
Waist circumference (cm)	80 (70 – 90)	90 (84 – 100)	73 (68 – 81)	< 0.001
Waist to hip ratio	0.85 (0.79 – 0.89)	0.89 (0.85 – 0.96)	0.83 (0.77 – 0.88)	< 0.001
Newborn complication	95 (43.6)	18 (40.0)	0.86 (0.45-1.66)	0.659
Birth injury	15 (6.9)	3 (6.5)	0.94 (0.26-3.40)	0.930
NICU admission	9 (4.1)	2 (4.3)	1.06 (0.22-5.06)	0.946
Clinical hyperandrogenism[2]	243 (72.1%)	63 (68.5%)	180 (73.5%)	0.363
Systolic blood pressure	121 (110 – 132)	135.5 (128.5 – 141)	117 (107 – 126)	< 0.001
Diastolic blood pressure	73.1 (11.5)	79.7 (12.5)	70.6 (10.0)	< 0.001
Lipid profiles				
Total cholesterol	194 (172 – 221)	188 (169.5 -222.5)	197 (172 – 220)	0.337
HDL	57 (46 – 71)	42.5 (39 – 50.5)	62 (52 – 77)	< 0.001
LDL	129 (107 – 152)	130 (109.5 – 156.5)	129 (106 – 151)	0.194
Triglyceride	112 (78 – 151)	157.5 (125 – 197.5)	98 (71 – 127)	< 0.001
Abnormal glucose metabolism	116 (34.4%)	59 (64.1%)	57 (23.3%)	< 0.001
DM	18 (5.3%)	15 (16.3%)	3 (1.2%)	< 0.001
Impaired fasting glucose	50 (14.8%)	35 (38.0%)	15 (6.1%)	< 0.001
Impaired glucose tolerance	72 (21.4%)	30 (32.6%)	42 (17.1%)	0.002

Data are presented as number (percentage), median (interquartile range) or mean (standard deviation)
PCOS: polycystic ovarian syndrome, MS: metabolic syndrome, IDF: International Diabetes Federation, BMI: body mass index, DM: diabetes mellitus, HDL: high-density lipoprotein, LDL: low-density lipoprotein
[1] Planned and repetitive form of physical activity
[2] Including hirsutism, acne, and androgenic alopecia

Table 3 shows the characteristics associated with the odds of being affected by MS among PCOS women. Three variables were independently associated with MS including patients' age, family history of DM and/or MS, and self-reported exercise behavior. PCOS women who had family history of DM/

MS were at the highest odds of developing MS (aOR 2.77, 95% CI 1.66-4.65). Older women (age 30 years or older) had almost twice the odds of being affected by MS as compared with younger women (aOR 1.89, 95% CI 1.06-3.40). Reporting to have exercise behavior (an intended and repetitive form of physical activity) was associated with a 55% decreased overall odds of MS (aOR 0.45, 95% CI 0.23-0.86).

Table 3. Characteristics of PCOS women and risk of MS according to IDF criteria.

Variables	MS prevalence n (%)	OR (95%CI)[1]	Adjusted OR (95% CI)[2]
Age			
< 30 Years (n=266)	64 (24.1)	reference	reference
≥ 30 years (n=71)	28 (39.4)	2.06 (1.18 – 3.57)	1.89 (1.06 – 3.40)
Age at menarche			
Early menarche[3] (n=62)	21 (33.9)	reference	Reference
Later menarche (n=275)	71 (25.8)	0.68 (0.38 – 1.23)	0.76 (0.41 – 1.42)
Parity status			
Nulliparity (n=310)	84 (27.1)	reference	reference
Multiparity (n=27)	8 (29.6)	1.13 (0.48 – 2.69)	1.07 (0.54 – 2.11)
Clinical hyperandrogenism[4]			
Absent (n=94)	29 (30.9)	reference	reference
Present (n=243)	63 (25.9)	0.78 (0.46 – 1.32)	0.71 (0.40 – 1.24)
Exercise behavior[5]			
Absent (n=250)	77 (30.8)	reference	reference
Present (n=87)	15 (17.2)	0.47 (0.25 – 0.87)	0.45 (0.23 – 0.86)
FH of DM and/or MS			
Absent (n=218)	42 (19.3)	reference	reference
Present (n=119)	50 (42.0)	3.04 (1.85 – 4.99)	2.77 (1.66 – 4.65)

The variance inflation factor of the regression model was 1.03, indicating no significant correlation among the variables.
PCOS: polycystic ovarian syndrome, MS: metabolic syndrome, IDF: International Diabetes Federation, OR: odds ratio, CI: confidence interval, FH: family history, DM: diabetes mellitus
[1] Simple logistic regression analyses
[2] Multiple logistic regression analyses adjusted with all factors presented in this table
[3] Menarche before the age of 12 years
[4] Including hirsutism, acne, and androgenic alopecia
[5] Planned and repetitive form of physical activity

Discussion

The prevalence of MS in PCOS women in our study was 27.3 % and 20.8% according to the definition of the IDF criteria and NCEP III ATP criteria, respectively. Significant independent variables correlated with the odds of being affected by MS among Thai women with PCOS were patient's age, family history of DM and/or MS, and exercise behavior. The present findings highlight a group of PCOS women who requires comprehensive care to prevent long-term consequences of MS.

The finding of this study was consistent with a previous study by Indhavivadhana et al(14), which also reported a higher prevalence of MS in PCOS women when using the IDF criteria (21.2%) compared to the NCEP ATP III criteria (18%). The discrepancy

in this prevalence rates could be attributed to the utilization of a lower waist circumference cut-off in the IDF criteria, which is ethnic specific for Asian women[9].

Prevalence of MS among women varied across the settings. The US national survey estimated that MS affected approximately 11% of US females[21]. Insulin resistance, a core endocrinopathy of PCOS, is central to the pathogenesis of metabolically unhealthy, placing women with PCOS at an increased risk of being affected by MS. In a previous study analyzing the US hospitalization database, 0.64% of hospitalized women had a PCOS diagnosis. Of these, 12.2% were found to have concomitant MS[22]. PCOS was associated with an increased risk of cardiovascular disease. The risks of different types of cardiovascular disease among PCOS women were affected by anthropometric measures and MS status[22]. In a previous study conducted among Korean women with PCOS, the prevalence of MS varied from 11.9% to 19.7% depending on the characteristics of study cohorts[23].

When compared to general Thai female population, the prevalence of MS among PCOS women from our study was two times higher. Previous studies conducted among healthy women in Bangkok[24,25] and Khon Kaen[26] of Thailand reported the prevalence of MS based on the NCEP III ATP criteria to be 8.2% to 10.3% and 14.6%, respectively. This data reaffirmed that PCOS women had higher risk of developing metabolic abnormalities compared to the general population. Thus, screening for MS, which is considered as a cardiovascular risk factor, is recommended among these women[27].

To date, there are four previous studies assessing the prevalence of MS among Thai PCOS women. Among these, three were conducted in Bangkok[13-15] and one in ChiangMai[16]. All the prior studies enrolled reproductive-aged PCOS women based on the revised Rotterdam diagnostic criteria. Three studies[13, 15-16] used the IDF criteria, and one study[14] used both the IDF and NCEP ATP III criteria for MS diagnosis. Despite the same ethnicity and PCOS phenotype, the prevalence of MS varied among the studies. In comparison to studies which diagnosed MS using the IDF criteria, our study revealed a lower MS prevalence than that reported by Weerakiet et al[13] which was conducted in Bangkok and found 33.3% of MS in PCOS women. However, our MS prevalence was comparable to the findings of three other studies from Bangkok[14,15] and Chiang Mai[16] which reported the MS prevalence of 21.2-24.6% and 24.3%, respectively. This variation in prevalence could be attributed to differences in age and BMI across the studies. It is noteworthy that as age and BMI increase, the prevalence of MS tends to rise[28, 29]. While the age and BMI in our study aligned with the other three studies with similar prevalence, they were lower compared to the study reported by Weerakiet et al[13].

The prevalence of MS significantly increased with increasing age[28, 29]. Interestingly, MS risk that is age-related appears to be apparent in PCOS women[29]. In this study, the prevalence of MS among PCOS women also increased with increasing age. PCOS women aged 30 years or older were 2 times more likely to be affected by MS (aOR 1.89; 95% CI 1.06-3.40) than younger women.

Evidence has shown an association between a family history of DM or MS and risk of metabolic disturbances among PCOS women[30, 31]. In an epidemiologic study undertaken in Chinese females, PCOS women with a positive paternal history of both DM and HT were more likely to have an adverse metabolic profile than those without that history[30]. In study conducted among European females, the prevalence of MS was 16.4% of PCOS women with a family history of type 2 DM, whereas only 8.6% of those without a family history of DM[31]. In the present study, family history of DM and/or MS was a significant independent predictor of the odds of being affected by MS among Thai women with PCOS. Thai women with PCOS who had family history of DM and/or MS were approximately 2.8 times more likely to have MS than those without that history. The information regarding the history of DM and/or MS in the family

of PCOS women thus should be assessed.

Exercise has been observed to result in improved cardiometabolic parameters among PCOS women. MS risk among PCOS women declined by approximately 20% (aOR 0.78; 95% CI 0.62-0.99) for every hour of vigorous exercise (i.e. aerobics, fast bicycling) per week[32]. In the present study, exercise behavior, defined as an intended and repetitive form of physical activity), was associated with a 55% decreased odds of MS (aOR 0.45; 95% CI 0.23-0.86). Future studies assessing intervention to effectively implement exercise training among PCOS women are needed.

Insulin resistance with compensatory hyperinsulinemia in PCOS induces oxidative stress, systemic inflammation, and hyperandrogenism which can lead to MS[22]. Various strategies have been proposed to alleviate symptoms of PCOS i.e. lifestyle modification and supplementation of vitamins, minerals, and probiotics[33]. These interventions also seem to be beneficial in decrease MS risk among PCOS women due to the protective effects against insulin resistance, oxidative stress and inflammation. Our study is the first study assessing the prevalence of MS among PCOS women in the Northeast Thailand. Standardized criteria were applied to diagnose PCOS and MS. However, there were some limitations in this study. Firstly, the retrospective data collection limited the availability of some clinically important information regarding behavioral (i.e. physical and drinking status) and sociodemographic factors (i.e. educational attainment, income, working status, marital status, living condition) which might influence to the development of MS. In addition, being a single-center hospital-based study, the findings might not be fully representative of all Thai PCOS women.

Conclusion

MS was highly prevalent among PCOS women residing in the Northeast Thailand with a rate of 27.3% and 20.8% according to the criteria of IDF and NCEP ATP III, respectively. Factors associated with MS odds included age, family history of MS and/or diabetic mellitus, and exercise behavior.

Acknowledgement

We would like to acknowledge Mr. Gurdeep Singh, for editing the manuscript via English Editing Publication Clinic, Khon Kaen University, Thailand.

Potential conflicts of interest

The authors declare no conflicts of interest.

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Thai Journal of Obstetrics and Gynaecology
May 2024, Vol. 32, No. 3, pp. 245-253.

OBSTETRICS

The Effect of Hyoscine Butylbromide for Shortening the Active Phase of the First Stage of Labor: A randomized, double-blind, placebo-controlled trial

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ABSTRACT

Objectives: To study the efficacy and safety of hyoscine butylbromide for shortening the active phase of the first stage of labor.

Materials and Methods: After receiving informed consent, singleton pregnant women who planned vaginal delivery at Khon Kaen Hospital between July 2022 and April 2023 were randomly allocated into two groups: the control group (n = 61) received 1 mL (20 mg) of intravascular hyoscine butylbromide, while the control group (n = 61) received 1 mL of intravascular normal saline at 5-6 cm cervical dilatation. The duration of the active phase of the first stage of labor and adverse events were analyzed.

Results: Baseline characteristics were not statistically different between groups. Hyoscine butylbromide significantly shortened the active phase of the first stage of labor compared to the control group (88.5 ± 66.7 min vs 188.5 ± 101.9 min, respectively, mean difference -100.02 min (95% confidence interval -130.72 to -69.31, p <0.001)). There were no significant maternal or neonatal adverse outcomes.

Conclusion: Hyoscine butylbromide effectively shortened the active phase of the first stage of labor.

Keywords: hyoscine butylbromide, first stage of labor, duration of labor.

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Received: 27 September 2023, **Revised:** 10 January 2024, **Accepted:** 15 January 2024

ผลของยาฮัยออสซีน-บิวทิลโบรไมด์เพื่อลดเวลาในระยะเร่งของ ระยะที่หนึ่งของการคลอด: การศึกษาแบบสุ่มและปกปิดสองทางเทียบกับยาหลอก

จงรักษ์ คำคง, มนสิชา พงษ์สมัครไทย, มาลีชาติ ศรีพิพัฒนะกุล, ทุมวดี ตั้งรัตนศิริวัฒนา

บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาประสิทธิภาพและความปลอดภัยของยาฮัยออสซีน-บิวทิลโบรไมด์ในการลดเวลาระยะเร่งในระยะที่หนึ่งของการคลอด*

วัสดุและวิธีการ: *สตรีตั้งครรภ์เดี่ยวที่วางแผนจะคลอดบุตรทางช่องคลอดที่โรงพยาบาลขอนแก่นระหว่างเดือน กรกฎาคม พ.ศ. 2565 ถึง เมษายน พ.ศ. 2566 ได้รับการเชื้อเชิญให้เข้าร่วมวิจัย หลังจากลงนามในหนังสือยินยอมแล้ว จะมีการสุ่มแบ่งเป็นสองกลุ่ม คือกลุ่มทดลองจำนวน 61 คนจะได้รับยาฮัยออสซีน-บิวทิลโบรไมด์ปริมาณ 1 มิลลิลิตร (ขนาด 20 มิลลิกรัม) แบบฉีดทางหลอดเลือดดำ ในขณะที่กลุ่มควบคุมจำนวน 61 คน ได้รับน้ำเกลือปริมาณ 1 มิลลิลิตร แบบฉีดทางหลอดเลือดดำ เมื่อปากมดลูกเปิด 5-6 เซนติเมตร หลังจากนั้นทำการประเมินระยะเร่งของระยะที่หนึ่งของการคลอดและภาวะแทรกซ้อน*

ผลการศึกษา: *ลักษณะพื้นฐานของประชากรในทั้งสองกลุ่มไม่แตกต่างกันอย่างมีนัยสำคัญทางสถิติ กลุ่มฮัยออสซีน - บิวทิลโบรไมด์มีระยะเร่งในระยะที่หนึ่งของการคลอดสั้นกว่ากลุ่มควบคุมอย่างมีนัยสำคัญทางสถิติ (88.5 ± 66.7 นาที และ 188.5 ± 101.9 นาที ตามลำดับ) โดยค่าเฉลี่ยแตกต่างกัน -100.02 นาที (95%CI: -130.72 to -69.31, p <0.001) ไม่พบผลกระทบหรือผลข้างเคียงจากยาต่อมารดาและทารกในครรภ์อย่างมีนัยสำคัญ*

สรุป: *การได้รับฮัยออสซีน-บิวทิลโบรไมด์ทางหลอดเลือดดำสามารถช่วยลดเวลาในระยะเร่งในระยะที่หนึ่งของการคลอดได้*

คำสำคัญ: *ยาฮัยออสซีน-บิวทิลโบรไมด์, ระยะที่หนึ่งของการคลอด, ระยะเวลาคลอด*

Introduction

Prolonged labor can increase maternal and neonatal morbidity and mortality, including postpartum hemorrhage, rupture of the uterus, maternal death, neonatal injury, and perinatal asphyxia[1]. Active labor management can shorten labor duration and reduce the cesarean delivery rate[2]. In 1968, O'Driscoll et al were the first to define the concept of active labor management, which proposed to reduce the duration of labor without increasing maternal or neonatal morbidity and mortality[2]. Cervical dilatation and effacement are essential determinants of the duration of labor and can be facilitated by medical and non-medical procedures[3]. Medical procedures such as oxytocin, analgesics, prostaglandins, muscle relaxants, and antispasmodic drugs can shorten the first stage of labor[3]. Hyoscine butylbromide (HBB) is an anticholinergic agent, also known as scopolamine, which inhibits cholinergic transmission in the pelvic parasympathetic ganglia, and alleviates spasms in the smooth muscles of female genitalia, particularly the cervico-uterine plexus. Thus, HBB acts as a spasmolytic agent at the cervix and promotes cervical dilatation without the effect on uterine contractions so that it can reduce the active phase of the first stage of labor[4-6]. Common adverse effects of HBB include dry mouth, flushing, nausea, blurred vision and dizziness. Mohaghegh et al reported some adverse effects, including maternal tachycardia and dry mouth but without other major maternal adverse effects[7]. Although it is unclear whether it crosses the placenta to the fetus, many studies have not found neonatal adverse effects as evidenced by no difference in Apgar scores[8-12].

Several studies[7-13] on HBB have reported that it can shorten labor time compared to control groups, whereas Duada et al reported the contrary effect[14]. While many studies[7-13] suggest a potential reduction in labor duration with the use of HBB, the underlying mechanism and robust evidence for its efficacy remain unclear. The current study aimed to elucidate the impact of HBB on labor duration by assessing its effectiveness in promoting cervical dilatation and shortening the active phase of the first stage of labor. Additionally, safety evaluations of HBB were conducted as secondary outcomes.

The primary outcome was duration in the active phase of the first stage of labor. The secondary outcomes were the duration of the second and third stages of labor, drug adverse effects, and maternal and neonatal outcomes.

Materials and Methods

Before the initiation of the research, the study protocols were reviewed and approved by the Khon Kaen Hospital Institute Review Board in Human Research. This randomized, double-blind, placebo-controlled trial was conducted at the labor room.

Recruited participants included term singleton pregnant women 18 or older with a cephalic presentation and planned vaginal delivery. Participants were excluded if they (a) received epidural anesthesia; (b) had unstable fetal status (e.g., placental abruption, meconium-stained amniotic fluid, fetal anomaly, non-reassuring fetal status); (c) had contraindications for HBB; and/or, (d) had medical complications during the pregnancy (e.g., maternal fever, thyroid diseases, cardiovascular diseases, autoimmune diseases, gestational diabetes mellitus, pregnancy-induced hypertension).

After giving written informed consent, the participants were assigned to one of two groups, either the HBB or the control group, using computer-generated block-of-four randomization. Allocation concealment was done using sealed opaque envelopes. Baseline characteristics were recorded: age, body mass index (BMI), parity, induction by misoprostol/ oxytocin/ ruptured amniotic membrane before the active phase, and meconium-stained amniotic fluid. Participants were informed about the outcomes that they were observed and recorded, including the duration of the active phase of the first, second, and third stages of labor, adverse effects, and maternal and neonatal outcomes.

All participants received intrapartum care by standardized physicians and labor room nurses with

the same protocol as follows. In the latent phase of the first stage of labor, participants underwent pelvic examinations every 4 hours and observed uterine contractions and fetal heart rate every hour. In the active phase of the first stage of labor, participants underwent pelvic examinations every hour to early detect the cervical progression and accurately accessed duration of the active phase of the first stage of labor. One participant underwent a pelvic examination from one physician who had to standardize using corrections from a cervical dilatation chart. Uterine contractions and fetal heart rate were observed every 30 minutes. The progression of labor was closely documented. Induction or augmentation was performed according to obstetric indications. When cervical dilatation reached 5-6 cm, the eligible participants were masked and randomly allocated into the HBB group or the control group for receiving the intervention. The HBB group was administered 1 mL (20 mg) of HBB intravenously, while the control group was administered 1 mL of normal saline solution (placebo) intravenously. The pharmacist prepared the HBB and placebo in an identical type of syringe using aseptic technique. Participants and healthcare providers were blinded to the treatment groups.

When the cervical dilatation reached 10 cm, the participants were transferred to the delivery room. The primary outcome was duration in the active phase of the first stage of labor, which was recorded using a standard digital clock. The secondary outcomes were recorded, including the duration of the second and third stages of labor, estimated blood loss, uterine atony, postpartum hemorrhage, adverse drug effects, neonatal birth weight, Apgar score at 1 and 5 minutes, and the rate of admission to neonatal intensive care unit (NICU).

The sample size was calculated based on a pilot study of 30 patients with a power of 90%, an α level of 0.05, we get different duration 69 min between two groups from this formula and a dropout rate of 15%. Thus, 122 participants (61 in each group) were required. Data were analyzed based on an intention-to-treat analysis using STATA version 14. The student's t-test and Mann-Whitney U test were used to analyze continuous data. Chi-squared and Fisher's exact test were used to analyze categorical data. A p value < 0.05 was considered statistically significant.

Results

Between July 2022 and April 2023, 122 participants were randomly assigned, 61 to the HBB group and 61 to the control group. Two participants were dropped out, 1 cesarean section in HBB group and 1 cesarean section in control group due to cephalopelvic disproportion. The dropout rate was 1.6% (2/122), and all 60 participants in each group were analyzed by intention-to-treat as shown in Fig. 1.

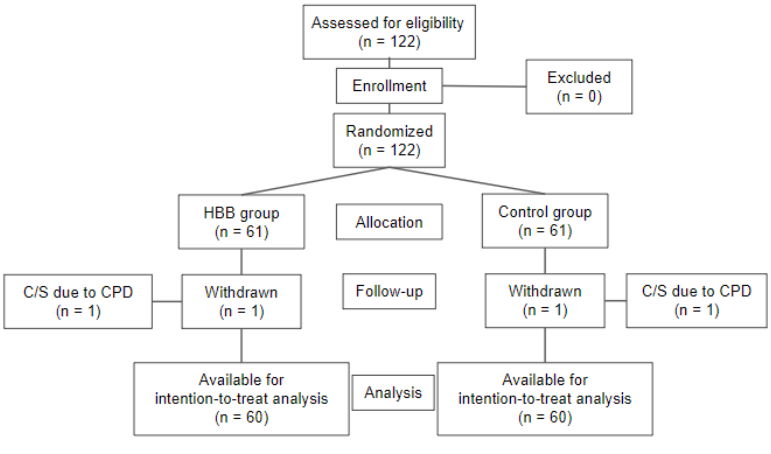


Fig. 1. Study flow.
C/S = cesarean section, CPD = cephalopelvic disproportion

Baseline characteristics including age, BMI, parity, induction by misoprostol or oxytocin or combined misoprostol with oxytocin, ruptured amniotic membrane before the active phase, and meconium-stained amniotic fluid were similar between groups as shown in Table1.

Table 1. Demographics and clinical characteristics of the participants.

Characteristics	HBB group	Control group	p value
Maternal age (years)	26.9 ± 5.9	27.5 ± 5.4	0.523[t]
Gestational age (weeks)	39.1 ± 1.1	39.2 ± 1.0	0.544[t]
Body mass index (kg/m^2)	28.5 ± 4.5	27.1 ± 4.1	0.088[t]
Multipara	34 (56.7)	35 (58.3)	0.853[c]
Amniotic membrane rupture before the active phase	34 (56.7)	37 (61.7)	0.577[c]
Meconium-stained amniotic fluid	1 (1.7)	3 (5)	0.619[f]
Induction of labor with misoprostol	10 (16.7)	9 (15)	0.803[c]
Augmentation of labor with oxytocin	16 (26.7)	19 (31.7)	0.547[c]
Combination of misoprostol and oxytocin used	5 (8.3)	3 (5)	0.717[f]

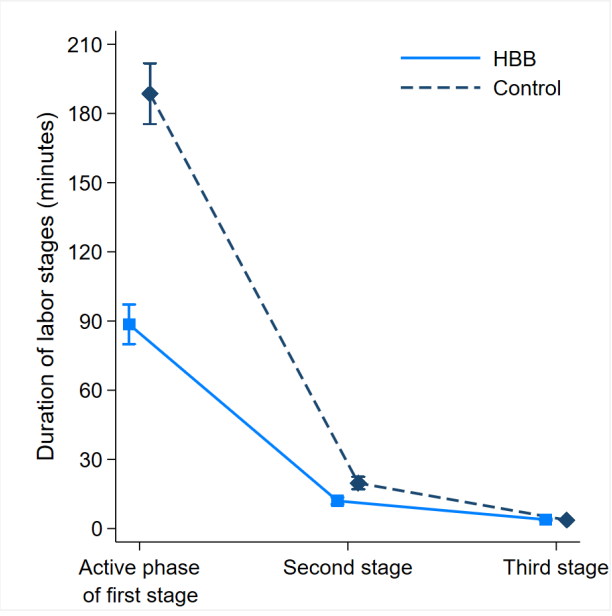
HBB: hyoscine butylbromide
Data are presented as number (%), mean ± standard deviation, or median (interquartile range).
p value corresponds to t = independent samples t-test, c = chi-square test, f = Fisher's exact test. * Significant at p value < 0.05

The HBB group had a significantly shorter time in the active phase of the first stage of labor than the control group (88.5 ± 66.7 min vs 188.5 ± 101.9 min, mean difference -100.02 min, 95%CI -130.72 to -69.31, p < 0.001). The HBB group also had a significantly shorter time in the second stage of labor than the control group (12.0 ± 11.7 min vs 19.7 ± 20.9 min, mean difference -7.73 min, 95%CI -13.8 to -1.67, p = 0.012). Notwithstanding, no significant differences were observed in the duration of the third stage of labor (3.8 ± 2.4 min vs 3.7 ± 2.7 min, mean difference 0.18 min, 95%CI -0.75 to -1.12, p = 0.7) (Table 2, Fig. 2).

Table 2. Duration of the active phase of the first stage, second stage and third stage of labor between the HBB group and the control group.

Duration of labor stage (min)	HBB group	Control group	Absolute difference (95%CI)	p value
All participants (n = 120)	(n = 60)	(n = 60)		
Active phase of first stage	88.5 ± 66.7	188.5 ± 101.9	-100.02 (-130.72 to -69.31)	< 0.001*
Second stage	12.0 ± 11.7	19.73 ± 20.9	-7.73 (-13.8 to -1.67)	0.012*
Third stage	3.8 ± 2.4	3.70 ± 2.7	0.18 (-0.75 to 1.12)	0.700
Nullipara (n = 51)	(n = 24)	(n = 27)		
Active phase of first stage	109.6 ± 70.9	201.8 ±83.0	-92.15 (-134.19 to -50.11)	< 0.001*
Second stage	17.6 ± 15.3	26.3 ± 28.5	-8.74 (-21.27 to 3.78)	0.171
Third stage	3.6 ± 1.9	3.0 ± 2.0	0.62 (-0.46 to 1.69)	0.260
Multipara (n = 69)	(n = 36)	(n = 33)		
Active phase of first stage	72.3 ± 59.3	179.0 ± 113.8	-106.70 (-149.05 to -64.36)	< 0.001*
Second stage	7.7 ± 5.0	15.0 ± 11.5	-7.29 (-11.44 to -3.15)	0.001*
Third stage	4.0 ± 2.8	4.2 ± 3.1	-0.11 (-1.55 to 1.28)	0.875

HBB: hyoscine butylbromide, CI: confident interval
[†] Absolute difference is the mean difference with 95%CIs estimated by generalized linear models with a robust error variance.



HBB: hyoscine butylbromide

Fig. 2. Mean duration of the active phase of the first stage, second stage and third stage of labor between the HBB group and control group.

For the subgroup analysis, in multipara women, the active phase of the first stage of labor was significantly shorter in the HBB group (72.3 ± 59.3 min) compared to the control group (179.0 ± 113.8 min), with a mean difference of -106.70 min ($p < 0.001$). For nullipara women, the HBB group also had a significantly shorter active phase of the first stage of labor (109.6 ± 70.9 min) compared to the control group (201.8 ± 83.0 min), with a mean difference of -92.15 min ($p < 0.001$). In multipara women, the second stage of labor was significantly shorter in the HBB group (7.7 ± 5.0 min) compared to the control group (15.0 ± 11.5 min), with a mean difference of -7.29 min ($p = 0.001$). However, in nullipara women, the duration of the second stage of labor did not show a significant difference between the HBB and control groups (17.6 ± 15.3 min vs 26.3 ± 28.5 min, mean difference -8.74 min, $p = 0.171$). The duration of the third stage of labor showed no significant difference between the HBB and control groups in both multipara women (4.0 ± 2.8 min vs 4.2 ± 3.1 min, mean difference -0.11 min, $p = 0.875$) and nullipara women (3.6 ± 1.9 min vs 3.0 ± 2.0 min, mean difference 0.62 min, $p = 0.260$) (Table 2).

Maternal outcomes, including uterine atony, estimated blood loss (mL), postpartum hemorrhage, and adverse drug effects, were not significantly different between the two groups. No abnormal neurologic ocular or urological manifestations were reported. Neonatal outcomes, including Apgar score at 1 and 5 minutes and neonatal birth weight, were not significantly different between groups, there were no admissions to the NICU in both groups (Table 3).

Table 3. Obstetric outcomes and adverse drug effects between the HBB group and the control group.

	HBB group (n = 60)	Control group (n = 60)	p value
Estimate blood loss (mL)	120 (100 - 150)	120 (100 - 175)	0.442[m]
Maternal complication			
Uterine atony	9 (15)	10 (16.7)	0.803[c]
Postpartum hemorrhage	1 (1.7)	1 (1.7)	1.000[f]
Adverse drug effects			
Dry mount	10 (16.7)	6 (10)	0.283[c]
Palpitation	3 (5)	2 (3.3)	1.000[f]
Flushing	3 (5)	2 (3.3)	1.000[f]
Nausea	4 (6.7)	4 (6.7)	1.000[f]
Vomiting	2 (3.3)	1 (1.7)	1.000[f]
Neonatal birth weight (g)	3,107.6 ± 376.4	3,126.5 ± 410.7	0.794[t]
Apgar score			
at 1 min	8 (8-9)	8 (8-9)	0.774[m]
at 5 min	9 (9-10)	9 (9-10)	0.935[m]

HBB: hyoscine butylbromide
Data are presented as number (%), mean ± standard deviation, or median (interquartile range).
p value corresponds to [m] = Mann-Whitney U test, [c] = chi-square test, [f] = Fisher's exact test, or [t] = independent samples t-test

Discussion

The current study showed that compared to the placebo, intravascular administration of HBB when cervix dilate 5-6 cm reduce the duration of the active phase of the first stage of labor with 100.02 min compared with the control group (88.5 ± 66.7 min vs 188.5 ± 101.9 min (95%CI -130.72 to -69.31, $p < 0.001$). The results of the current study were similar to the findings of Yousuf[8] and Samules et al[9] and others[10-12], HBB was clinically effective in both nullipara and multipara for shortening the first stage of labor. These results support that the mechanism of HBB action is by inhibiting cholinergic neurotransmission in the pelvic parasympathetic ganglia and alleviating spasms in the smooth muscles of the cervix and promoting cervical dilatation[4-6,15].

In contrast, Duada et al[14] reported that administering 20 mg via intramuscular injection in the active phase did not significantly shorten the first stage of labor, while the current study administered the same dose of HBB, but intravenously. The reason for these results might be due to the different routes of drug administration that consistent with Brand et al reported that the peak activity of HBB administered by intramuscular injection was 1-2 hours[16] whereas after intravenous administration, the peak effect was 20-60 minutes, the onset of action was about 10 minutes, and the action lasted 2 hours[4-6,15]. However, intramuscular administration of HBB 40 mg reported by Al Qahtan et al and Kandi et al showed significant shortening of the active phase of the first stage of labor[17-18]. In the current study, the mean time difference of the first stage of labor between the two groups was 100 min, while Samuels et al found the mean time difference was 72 min[9], the result might be due to the different times of drug administration. Our study administered the drug at 5-6 cm of cervical

dilatation, while Samuels et al administered the drug at 3-4 cm of cervical dilatation[9]. In the second stage of labor, the HBB group also had a significantly shorter time, similar to Yousuf[8], but in contrast to other studies[10-12]. Subgroup analysis among nullipara and multipara women revealed that the second stage of labor duration between the HBB and control groups was significantly shortened only in the multipara women. This might be supported by the studies reviewed that during labor, multiparous had less uterocervical resistance and increased uterine efficiency than nulliparity[19, 20], so, this might be the reason for the shorter time in second stage of labor among multipara women.

There was no difference in the duration of the third stage of labor between the HBB and control groups in this study. This was similar to the findings of Yousuf[8], Imaralu et al[10], and others[11-12], which supported that HBB did not affect uterine contractions[4-6, 15]. In the current study, HBB did not significantly affect the rate of cesarean section and the delivery route, similar to Samuels et al and other studies[10, 13]. The estimated blood loss, uterine atony, and postpartum hemorrhage were not significantly different in both groups. This observation suggested no adverse effect on uterine contraction during the postpartum period. This was similar to the findings of other authors[9,11]. However, it contrasted with the study by Imaralu et al, which showed that HBB was also associated with significantly less postpartum blood loss. This can be explained by shorter durations of labor causing less myometrial exhaustion that might reduce postpartum hemorrhage (PPH)[21].

The median Apgar score at one and five minutes was not different between the two groups. Moreover, both groups had no neonatal admission to the intensive care unit. This was similar to the findings of other studies, explaining that HBB did not cross the placenta and, therefore, did not cause respiratory depression in neonates[7-12, 14]. In the current study, maternal adverse effects were not statistically significant between the two groups. This observation was consistent with other reports. No significant major adverse effects were associated with intravascular HBB use[11, 12]. This study provides evidence that HBB significantly diminishes the duration of the active phase of the first stage of labor. In alignment with the 2018 World Health Organization recommendations[23], which revised the definition of the active phase of labor to commence at cervical dilation of 5 cm, the current study administered the drug when the cervix was dilated between 5-6 cm, while other studies[9-11] administered it at 3-5 cm. The observed mean time difference in this study, compared to other studies[9-11], suggests that administering the drug at an appropriately timed dilation can lead to a more substantial reduction in the duration of the active phase of the first stage of labor. Additionally, adverse effects from HBB were mild and manageable. Therefore, HBB emerges as a potential drug of choice for promoting cervical dilatation during the active phase of the first stage of labor.

Although, the current study showed no different effect to maternal and neonatal outcomes, but reducing 100 min in labor process could reduce not only the time that pregnant women suffered from labor pain which one of the most painful conditions that women typically experience in life but also stress during labor process that might have negative impact on the pregnancy mental health[22].

The main strengths of this study were that it was a randomized, double-blind, placebo-controlled trial with an adequate sample size. The study's limitations were that it lacked a cost-effectiveness analysis. Further studies are required to determine the effect of HBB in the difference of dosage, time to administration, and route of administration to reduce complications in prolonged labor.

Conclusion

In summary, compared to the placebo, intravascular hyoscine butylbromide significantly shortened the active phase of the first stage of labor without any adverse effect on maternal and neonatal outcomes.

Acknowledgments

We thank (a) the participants for their cooperation, (b) the labor room nursing staff and physicians for their assistance, (c) the staff from the Obstetrics and Gynecology Department at Khon Kaen Hospital for their support, (d) the pharmacist for preparing drug and placebo, and (e) Mr. Bryan Roderick Hamman for assistance with the English-language presentation of the manuscript under the aegis of the Publication Clinic, Research Affairs, Khon Kaen University.

Potential conflicts of interest

The authors declare no conflicts of interest.

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