ISSN 0857-6084

THAI JOURNAL OF OBSTETRICS AND GYNAECOLOGY

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

VOL. 28 NO. 1 JANUARY - MARCH 2020

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ISSN : 0857-6084. The Official Journal of the Royal Thai College of Obstetricians and Gynaecologists

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Published by: PIMDEE Co., Ltd. Tel: 091-009-4011 Fax: 0-2874-4401,

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Thai Journal Obstetrics and Gynaecology (TJOG) is the official journal of The Royal Thai College of Obstetricians and Gynaecologists (RTCOG). This is a double-blind peer-reviewed journal aiming to promote academic knowledge and provide a forum for publication in Obstetrics and Gynecology. Manuscripts submitted to TJOG will be accepted on the understanding that the author must not have previously submitted the paper to another journal or have published the material elsewhere.

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ISSN: 0857-6084 (Since 1989)
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TJOG is the official journal of RTCOG. This is a double-blind peer-reviewed journal aiming to promote academic knowledge and provide a forum for publication in Obstetrics and Gynecology. First issue of TJOG (Volume 1) was published in June 1989.

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Thai Journal of Obstetrics and Gynaecology

ISSN 0857-6084 **The Official Journal of the Royal Thai College of Obstetricians and Gynaecologists**

Vol. 28 No. 1 **JANUARY - MARCH 2020**

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EDITORIAL

At the beginning of New Year 2020, it's time for beginning the good things. May this year bring happiness, new inspirations and new success to all members of Royal Thai College of Obstetricians and Gynaecologists (RTCOG).

This year we have a special event of our celebration for the **50th anniversary of the founding of RTCOG**. We also have the good news that Thai Journal of Obstetrics and Gynaecology (TJOG) has been accepted for inclusion in the SCOPUS database since July 4, 2019.

Editor in Chief and managing staff were invited from TCI center to attend "**The 8th TCI-TRF-Scopus Collaboration Project**" on Thursday 9th January 2020 at the Jupiter 4-5 Rooms, IMPACT Challenger, Muang Thong Thani, Popular 1 Road, Ban Mai Subdistrict, Nonthaburi 11120, Thailand

This first issue of TJOG 2020 contains many interesting articles. One special article is "**Overweight and Obesity in Pregnancy"**.

For the upcoming New Year 2020, we would like to extend our warmest wishes to RTCOG members, editorial board, reviewers, authors and families. We thank to all the authors, readers, reviewers, and editors for your contributions to TJOG this past year and look forward to receiving your valuable contributions and support in year 2020.

Happy New Year 2020

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

Thai Journal of Obstetrics and Gynaecology
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SPECIAL ARTICLE

Overweight and Obesity in Pregnancy

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ABSTRACT

The prevalence of overweight and obesity in pregnancy have been increasing worldwide for the last several decades. This has also led to an increase in the incidences of many adverse pregnancy outcomes known to be associated with overweight and obesity pregnancies. The aim of this article is to address the definition, prevalence, importance and how to manage overweight and obese pregnant women.

Keywords: overweight, obesity, pregnancy.

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Received: 28 November 2019, **Revised:** 3 December 2019, **Accepted:** 10 December 2019

Obesity is a disease that occurs because excessive body fat accumulation. The diagnosis is based on the body mass index (BMI), which is calculated by a person's weight in kilograms divided by the square of their height in meters (kg/m^2). Using the World Health Organization (WHO) definition, overweight and obesity are defined as having a BMI of 25-29.9 kg/m^2 and 30 kg/m^2 or greater, respectively[1].

Prevalence

Worldwide, the prevalence of overweight and obesity in reproductive and pregnant women has been increasing to epidemic proportions over the last two decades[1]. In Thailand, overweight and obesity are also considered as an important health problems. The prevalences of overweight and obesity of Thai adults in 2018 were reported to be 19.0% and 4.8%, respectively[2]. A report from Rajavithi Hospital in Bangkok in 2009 found that the prevalences of overweight and obese women attending antenatal care to be around 13% and 4%, respectively[3].

Importance

Overweight and obesity are associated with several reproductive problems. Overweight and obese women have reduced fertility and take longer time to conceive for various reasons including increasing anovulation cycle, irregular menstruation, and reducing the chance of conception. A previous study reported that successful pregnancy and implantation rates after assisted reproductive technology to treat infertility declined by 1% with each 5 kg/m^2 BMI increase[4]. Once pregnancy is achieved, the rates of adverse pregnancy outcomes are higher in overweight and obese pregnant

women when compare to pregnant women with a normal BMI[5]. Higher adverse pregnancy outcomes associated with overweight and obesity include gestational diabetes, preeclampsia, spontaneous and medically indicated preterm birth, risk of congenital fetal malformation, rate of labor induction, prelabor or elective cesarean delivery, cesarean delivery, shoulder dystocia, postpartum hemorrhage, pelvic infection, wound infection or complication, large for gestational age fetus and fetal macrosomia and stillbirth, etc[5-6]. Fetal birth defects associated with overweight and obese pregnant women are neural tube defects, congenital heart defects and orofacial cleft[7-9]. The malformations may be related to diabetes in overweight and obese pregnant women[10]. Although higher rate of birth defects have been documented, prenatal screening and diagnosis of fetal aneuploidy and fetal malformation are also limited in maternal overweight and obese pregnant women[11]. Both ultrasonographic and maternal serum screening for fetal trisomy 18 and 21 are more difficult in overweight and obese pregnant women. Increasing the frequency of inadequate ultrasonographic nuchal translucency and nasal bone measurement during first trimester screening of overweight and obese pregnant women have been reported[12]. Second trimester maternal serum levels of alpha-fetoprotein, unconjugated estriol, human chorionic gonadotropin and inhibin-A are diluted in overweight and obese pregnant women because of the larger blood volume when compare to normal weight pregnant women. Thus, adjustments for maternal weight are needed. However, studies have reported that the detection rate of trisomy 21 did not increase after weight adjustments and the adjustments also reduced the detection of neural tube defects and increased the false positive rates of trisomy 18[13-25]. In the noninvasive prenatal test (NIPT), a 3-4% fetal DNA fraction is generally required to ensure a reliable NIPT result. Obesity is associated with lower fetal fractions and higher rates of failed NIPT[16]. Moreover, non-obstetric procedures such as anesthesia for overweight and obese pregnant women are also challenging. Difficulty of epidural and spinal analgesia placement and also complications from failed or difficult endotracheal intubation have also been reported[5].

How to manage overweight and obese pregnant women

Preconception care

Proper management should be initiated for overweight and obesity reproductive women since negative pregnancy test (preconceptional care). Reducing weight before pregnancy is the best way to decrease the risk of adverse pregnancy outcome. Lifestyle modifications including regular exercise and a balanced diet with low glycemic are the main recommendations. Weight-loss medications and bariatric surgery may be options for very obese women or those who have medical health problems related to obesity. Evaluation of underlying diseases such as pregestational diabetes, chronic hypertension and dyslipidemia before getting pregnant is also important. Preconceptional folic acid supplements should be provided.

Reproductive outcomes

Prenatal care

During pregnancy, overweight and obese pregnant women should be closely monitored for early signs of pregnancy complications, including hypertension and diabetes. Ultrasonographic fetal screening for congenital malformation is recommended. Pregnant women undergoing ultrasonography and her family should be counselled that there are limitations in ultrasonographic accuracy due to the thickness of the abdominal wall in overweight and obese pregnant women. A previous study found that obesity decreased the capacity for detection of an anomalous fetus by standard or targeted ultrasonography by at least 20% when compared with normal BMI women[17]. Moreover, obese pregnant women complicated with pregestational diabetes was even less in detection[17]. Serial monitoring for fetal growth by ultrasonography and fetal-well being assessment by external fetal monitoring are usually indicated[5]. If there are no obstetric or medical contraindications, exercise is proper for overweight and obese pregnant women. Beginning with as little as 5 minutes of exercise a day and adding 5 minutes each

week is suggested. The target point is to stay active for 30 minutes every day. However, planning a safe exercise program should be individually discussed with obstetricians[18]. The institute of Medicine (IOM) has published maternal weight gain guidelines based on prepregnancy BMI. For overweight and obese pregnant women, the IOM recommends a range of total weight gain of 15-25 and 10-20 lb, respectively, and recommended rates of weight gain in the second and third trimesters should be around 0.6 and 0.5 lb/week, respectively[19]. Weight loss during pregnancy is discouraged.

Intrapartum and postpartum care

The risk of labor, intrapartum and postpartum complications increase in overweight and obesity pregnant women, such as the rate of labor induction, anesthesia risk, rate of cesarean sections, and surgical wound complications. In the aspect of labor induction, there is no evidence to support for elective labor induction to prevent fetal macrosomia. For cesarean section, low vertical or midline abdominal incision are individually desired depending on maternal body habitus. Risk of surgical wound infection is directly related to BMI. Higher BMI is associated with a higher risk of surgical wound infection[20]. Several methods are suggested for reducing the risk of surgical wound infection such as closure of subcutaneous tissue when at least 2 cm deep, higher doses of perioperative antibiotic prophylaxis and negative-pressure wound therapy[5]. Breastfeeding is recommended for overweight and obese women if there are no other breastfeeding contraindications. It also may help with postpartum weight loss[21].

Conclusion

Overweight and obesity are important obstetric health problems. Management for preventing adverse maternal and neonatal outcomes should be provided for all stages of the pregnancy, from preconceptional through the antenatal, intrapartum and postpartum periods.

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OBSTETRICS

Cesarean Section Rate in Siriraj Hospital According to the Robson Classification

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ABSTRACT

Objectives: To determine the cesarean section (CS) rate in Siriraj Hospital according to Robson classification.

Materials and Methods: In this cross-sectional study, all pregnant women who delivered in Siriraj Hospital during January to August, 2017 were included. Data were retrieved from medical records, including baseline, obstetric, and delivery information. Pregnant women were categorized into ten-group according to Robson classification. Overall and group-specific CS rate and contribution of CS were reported.

Results: A total of 4,998 pregnant women were included. Mean maternal age was 29.9 years, 50.7% were nulliparous, and 17.9% had previous CS. Of all women, 2,442 were delivered by CS (48.86%). Majority of cases were in group 1 (nulliparous with a single cephalic term pregnancy in spontaneous labor, 31.21%), followed by group 3 (multiparous with a single cephalic term pregnancy in spontaneous labor, 25.21%) and group 5 (multiparous with a previous uterine scar with a single cephalic term pregnancy, 14.17%), respectively. Major contribution of CS were from group 5 (28.91%), group 1 (23.71%), and group 2 (17.65%). Group-specific CS rates in group 1, 2, and 4 (multiparous with a single cephalic term pregnancy without spontaneous labor) were 37.12%, 84.02%, 58.53%, respectively. Further analysis showed that 68.4% of nulliparous and 55% of multiparous women without spontaneous labor (subgroup 2b and 4b) had pre-labor CS and most indications could be unnecessary. CS rate in nulliparous and multiparous women with labor induction (group 2a and 4a) were 49.38% and 7.41%, respectively, and labor was induced before 40 weeks in majority of the women, possibly without appropriate indications.

Conclusion: Overall CS rate in Siriraj Hospital was 48.86%. Group 1 and 2 contributed to one-third of the procedures that appropriate interventions should be developed to reduce CS rate.

Keywords: Robson Classification, cesarean section, delivery, Induction of labor.

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Received: 21 September 2018, **Revised:** 17 October 2018, **Accepted:** 4 December 2018

อัตราการผ่าคลอดในโรงพยาบาลศิริราช ตามแบบ Robson classification

สิริเชษฐ์ อเนกพรวัฒนา, จิตติยาพร ยางน้อย, นิดา จารีมิตร, ดิฐกานต์ บริบูรณ์หิรัญสาร

บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาและเก็บข้อมูลอัตราการผ่าตัดคลอดในโรงพยาบาลศิริราชตามแบบรอบสัน (Robson classification)*

วัสดุและวิธีการ: *ทำการศึกษาแบบตัดขวาง ในสตรีตั้งครรภ์ทุกรายที่คลอดในโรงพยาบาลศิริราช ตั้งแต่เดือนมกราคมถึงสิงหาคม 2560 ทำการสืบค้นข้อมูลจากระบบเวชระเบียน ประกอบด้วย ข้อมูลพื้นฐาน, ข้อมูลทางสูติศาสตร์, และข้อมูลการคลอด สตรีตั้งครรภ์จะถูกจำแนกเป็น 10 กลุ่ม ตามแบบรอบสัน (Robson classification) และรายงานผลเป็นอัตราการผ่าตัดคลอดทั้งหมด และอัตราการผ่าตัดคลอดตามกลุ่ม*

ผลการศึกษา: *การศึกษานี้ทำในสตรีตั้งครรภ์ทั้งหมด 4,998 ราย อายุเฉลี่ยเท่ากับ 29.9 ปี ร้อยละ 50.7 ของสตรีตั้งครรภ์ทั้งหมดเป็นการตั้งครรภ์แรกร้อยละ 17.9 เคยได้รับการผ่าตัดคลอดมาก่อนในครรภ์ก่อน จากสตรีตั้งครรภ์ทั้งหมด มีการผ่าตัดคลอด 2,442 ราย คิดเป็นร้อยละ 48.86 สตรีตั้งครรภ์ส่วนใหญ่จัดอยู่ในกลุ่ม 1 (ครรภ์แรก เป็นครรภ์เดี่ยว ท่าศีรษะ ครบกำหนด และเจ็บครรภ์เอง, ร้อยละ 31.21) กลุ่ม 3 (ครรภ์หลัง เป็นครรภ์เดี่ยว ท่าศีรษะ ครบกำหนด และเจ็บครรภ์เอง, ร้อยละ 25.21) และกลุ่ม 5 (ครรภ์หลัง เคยผ่าคลอด เป็นครรภ์เดี่ยว ท่าศีรษะ และครบกำหนด, ร้อยละ 14.17) ตามลำดับ การผ่าตัดคลอดส่วนใหญ่เกิดในสตรีตั้งครรภ์ในกลุ่ม 5 (ร้อยละ 28.91) กลุ่ม 1 (ร้อยละ 23.71) และกลุ่ม 2 (ร้อยละ 17.65) ตามลำดับ อัตราการผ่าตัดคลอดในสตรีตั้งครรภ์กลุ่ม 1, 2 และ 4 (ครรภ์หลัง เป็นครรภ์เดี่ยว ท่าศีรษะ ครบกำหนด และไม่เจ็บครรภ์เอง) เท่ากับร้อยละ 37.12, 84.02 และ 58.53 ตามลำดับ จากการวิเคราะห์ข้อมูลเพิ่มเติม พบว่าร้อยละ 68.4 ของสตรีครรภ์แรก และร้อยละ 55 ของสตรีครรภ์หลัง ที่ไม่เจ็บครรภ์เอง (กลุ่ม 2b และ 4b) ได้รับการผ่าตัดคลอดก่อนเจ็บครรภ์โดยไม่มีข้อบ่งชี้ที่เหมาะสมเป็นส่วนใหญ่ นอกจากนี้ยังพบว่า อัตราการผ่าตัดคลอดในสตรีครรภ์แรกและครรภ์หลังที่ได้รับการชักนำการคลอด (กลุ่ม 2a และ 4a) เท่ากับร้อยละ 49.38 และ 7.41 ตามลำดับ และส่วนใหญ่พบว่าได้รับการชักนำการคลอดก่อนอายุครรภ์ 40 สัปดาห์ ซึ่งข้อบ่งชี้ของการชักนำการคลอดส่วนใหญ่ไม่เหมาะสม*

สรุป: *อัตราการผ่าคลอดในโรงพยาบาลศิริราช เท่ากับร้อยละ 48.86 การผ่าตัดคลอดในสตรีตั้งครรภ์กลุ่ม 1 และ 2 คิดเป็นประมาณ 1 ใน 3 ของการผ่าคลอดทั้งหมด ซึ่งควรมีการพัฒนากลยุทธ์เพื่อลดการผ่าตัดคลอดที่ไม่จำเป็นต่อไปในอนาคต ซึ่งจะช่วยการลดอัตราการผ่าตัดคลอดโดยรวมได้*

คำสำคัญ: *การแบ่งแบบรอบสัน, อัตราการผ่าตัดคลอด, การคลอด, การชักนำการคลอด*

Introduction

WHO has recommended that appropriate cesarean section (CS) rate is in between 10-15%[1]. Cesarean sections in medically-indicated patients decrease both maternal and fetal mortality rate. However, the procedures are also associated with various complications which require additional resources consumption such as endometritis, blood components transfusion, ICU admission and risk of uterine rupture in further pregnancy, etc.[2, 3] Therefore, unnecessary operations should be avoided because of potential risks of short-term and long-term adverse outcomes in women and fetuses with no additional benefits[1, 4-6].

Cesarean section rate has increased dramatically worldwide in both developed and developing countries[7]. In 2014, CS rate was 32.2% in the United States[8] while it was 25%, 19.5%, and 7.3% in Europe, Asia, and Africa, respectively. In Asia, CS rate has been growing for more than 15% from only 4.4% percent in 1990[9]. Thailand is one of the countries where CS rate has been rising up particularly for private cases or women delivered in private hospital, similar to what have been reported from other countries[10, 11]. Possible factors influencing the increasing trend include increased in maternal obesity[12-14], elderly gravidarum[15-17], and maternal desires[18-21].

Previously, there were a number of classification systems developing in attempt to identify and analyze the cause of excessive CS[18, 22-24]. However, none has been accepted internationally. Eventually, in 2014, WHO proposed the Robson classification system[1] as a global standard to classify pregnant women into ten systematic groups using basic obstetric information[25]. WHO also recommended the routinely use of Robson classification to analyze, synthesize and develop the strategy on regular basis to downsize unnecessary CS. In addition, the classification system is functional to follow-up, and evaluates the effectiveness of such strategy[1]. To date, the Robson classification is extensively used in many countries worldwide due to its ease of use, repeatable and clinically relevant.

Siriraj Hospital is a large university-based tertiary care hospital with over 7,000 deliveries each year. CS rate has increased to almost 50% in the past years, which is much higher than what has been recommended. It is possible that unnecessary CS could contribute to such increase in CS to some degree. In 2017, Siriraj Hospital has adopted Robson classification to classify pregnant women and evaluates possible causes of unnecessary CS and identify possible intervention to reduce CS rate.

Therefore, the primary aim of this study was to determine the CS rate in Siriraj Hospital according to Robson classification. The secondary objectives were to identify specific group of women with high CS rate, identify possible reasons, and develop strategy to decrease unnecessary CS.

Materials and Methods

After study protocol was approved by Siriraj institutional review board, a cross-sectional study was conducted in 4,998 pregnant women who admitted for delivery in Siriraj Hospital from January to August 2017. Data were extracted from medical records to classify the women into 10 groups according to Robson classification, including parity, gestational age, number of fetuses, fetal lie and presentation, previous CS, and onset of labor. The Robson classification is demonstrated in Table 1. Other characteristics were also recorded, including maternal demographic data, labor induction, route of delivery, and indications for CS.

Data for Robson classification was collected in a specific form by trained nurses after delivery of each woman. These data were entered into a spreadsheet and double checked by research assistant before final analysis.

Continuous variables were reported as mean and S.D., while categorical variables were reported as percentage. The all-case percentage distribution according to Robson classification was determined, together with CS rate, percentage contribution and relative contribution of CS in each group. Women in

group 2 and Group 4 were classified into those with labor induction (2a and 4a) and those with pre-labor CS (2b and 4b) for further detailed analysis. Indications for CS were collected as appeared in medical records. The results were reported and interpreted as stated in WHO's implementation manual[26].

Results

The total number of pregnant women delivered at Siriraj Hospital during the study period was 4,998. Baseline characteristics of pregnant women are shown in Table 2. Mean maternal age was 29.9±6.3 years, and the mean body mass index (BMI) was 22.1±4.4 kg/m^2. In women with cesarean delivery, maternal age and BMI were significantly higher and they were significantly more likely to be overweight and obese. In addition, they were also significantly more likely to be nulliparous.

Characteristics according to Robson classification are shown in Table 3. The majority of pregnant women were nulliparous (50.7%), delivered at > 37 weeks (89.6%), were singleton pregnancy (98.4%), had vertex presentation (95.3%), and had spontaneous labor (74.2%). Previous cesarean delivery was found in 17.9% of cases. Overall CS rate in this study were as high as 48.86%.

Pregnant women were categorized into 10 groups according to Robson classification and total number of CS and percentage distribution of CS in each group were reported as shown in Table 4. The majority of women were in group 1 (31.21%), followed by group 3 (25.21%) and group 5 (14.17%), respectively. The 3 leading group-specific CS rates were observed in group 1, 2, and 4 were 37.12%, 84.02%, 58.53%, respectively. Major contribution of CS were group 5 (28.91%), group 1 (23.71%), and group 2 (17.65%).

The detailed analyses were performed in group 2 and group 4. The results are shown in Table 5 and 6, respectively. Each of the 2 groups was classified into 2 subgroups, i.e., those with labor induction (2a and 4a) and those with pre-labor CS (2b and 4b).

Table 1. Robson classification.

Group	Characteristics
Group 1	Nulliparous with single cephalic pregnancy, ≥ 37 weeks gestation in spontaneous labor
Group 2	Nulliparous with single cephalic pregnancy, ≥ 37 weeks gestation who either had labor induced (2a) or were delivered by caesarean section before labor (2b)
Group 3	Multiparous without a previous uterine scar, with single cephalic pregnancy, ≥ 37 weeks gestation in spontaneous labor
Group 4	Multiparous without a previous uterine scar, with single cephalic pregnancy, ≥ 37 weeks gestation who either had labor induced (4a) or were delivered by caesarean section before labor (4b)
Group 5	All multiparous with at least one previous uterine scar, with single cephalic pregnancy, ≥ 37 weeks gestation
Group 6	All nulliparous women with a single breech pregnancy
Group 7	All multiparous women with a single breech pregnancy, including women with previous uterine scars
Group 8	All women with multiple pregnancies, including women with previous uterine scars
Group 9	All women with a single pregnancy with a transverse or oblique lie, including women with previous uterine scars
Group 10	All women with a single cephalic pregnancy < 37 weeks gestation, including women with previous scars

Table 2. Baseline characteristics of pregnant women.

Characteristics	All women N = 4998	Vaginal delivery N = 2556	Cesarean delivery N = 2442	p value
	Mean ± SD	Mean ± SD	Mean ± SD	
Mean age ± SD (years)	29.9 ± 6.3	28.4 ± 6.2	31.6 ± 5.9	< 0.001
Mean BMI ± SD (kg/m^2)	22.1 ± 4.4	21.6 ± 4.0	22.7 ± 4.7	< 0.001
	N (%)	N (%)	N (%)	
BMI category				< 0.001
Underweight	914 (18.3%)	548 (22.4%)	366 (15.4%)	
Normal	3113 (62.3%)	1516 (62%)	1416 (59.7%)	
Overweight	684 (13.7%)	286 (11.7%)	398 (16.8%)	
Obesity	287 (5.7%)	84 (3.8%)	193 (8.1%)	
Parity				< 0.001
0	2536 (50.7%)	1237 (48.4%)	1299 (53.2%)	
1	1884 (36.9%)	898 (35.1%)	946 (38.7%)	
2	491 (9.8%)	326 (12.8%)	165 (6.8%)	
≥ 3	127 (2.5%)	95 (3.7%)	32 (1.3%)	

Table 3. Characteristics of pregnant women used for Robson classification.

Characteristics	N (%)
Parity	
Nulliparous	2536 (50.7%)
Multiparous	2462 (49.3%)
Gestational age	
≥ 37 weeks	4480 (89.6%)
< 37 weeks	518 (10.4%)
Number of fetuses	
Singleton	4916 (98.4%)
Multiple	82 (1.6%)
Fetal presentation	
Vertex	4761(95.3%)
Breech	221 (4.4%)
Others	16 (0.3%)
Previous cesarean delivery	894 (17.9%)
Onset of labor	
Spontaneous	3709 (74.2%)
Induction of labor or pre-labor cesarean delivery	1289 (25.8%)
Route of delivery	
Vaginal delivery	2556 (51.1%)
Cesarean delivery	2442 (48.9%)

Table 4. Robson classification.

Group	Women in group	CS in group	Group size (%)	CS rate in group (%)	Contribution of CS (%)	Relative contribution of CS (%)
1	1560	579	31.21	37.12	11.58	23.71
2	513	431	10.26	84.02	8.08	17.65
2a	162	80	3.24	49.38	1.06	3.28
2b	351	351	7.02	100.00	7.02	14.37
3	1260	119	25.21	9.44	2.38	4.87
4	120	70	2.40	58.33	1.40	2.86
4a	54	4	1.08	7.41	0.08	0.16
4b	66	66	1.32	100.00	1.32	2.70
5	708	706	14.17	99.72	14.13	28.91
6	133	131	2.66	98.50	2.62	5.36
6	133	131	2.66	98.50	2.62	5.36
7	88	87	1.76	98.86	1.74	3.56
8	82	73	1.64	89.02	1.46	2.99
9	16	16	0.32	100.00	0.32	0.66
10	518	230	10.36	44.40	4.60	9.42
Total	**4998**	**2442**	**100.00**	**48.86**	**48.86**	**100.00**

Table 5. Detailed analysis of pregnant women in group 2.

Group	N (%)	CS
2a (N = 162)		
GA (weeks)		
< 40	114 (70.4%)	54 (47.4%)
40 - 41	48 (29.6%)	26 (54.2%)
Mean birth weight ± SD (g)	2980.1 ± 417.4	
Indication for CS (N = 80)		
Failed induction		41 (51.3%)
Abnormal FHR		39 (48.7%)
2b (N = 351)		
< 40	305 (86.9%)	
40 - 41	46 (13.1%)	
Mean birth weight ± SD (g)	3173.2 ± 404.3	
Indication for CS		
Placenta previa		14 (4%)
CPD		69 (19.7%)
AMA		44 (12.5%)
Unfavorable cervix		25 (7.1%)
Elective		89 (25.4%)
Others / not specified		110 (31.3%)

FHR = fetal heart rate, CPD = cephalo-pelvic disproportion, AMA = advanced maternal age

Table 6. Detailed analysis of pregnant women in group 4.

Group	N (%)	CS
4a (N=54)		
GA (weeks)		
< 40	40 (74.1%)	2 (5%)
40-41	14 (25.9%)	2 (14.3%)
Mean birth weight ± SD (g)	3232.4 ± 505.2	
Indication for CS (N=4)		
Failed induction		1 (25%)
Abnormal FHR		3 (75%)
4b (N=66)		
< 40	59 (89.4%)	
40-41	7 (10.6%)	
Mean birth weight ± SD (g)	3190 ± 428.1	
Indication for CS		
Placenta previa		4 (6.1%)
CPD		10 (15.2%)
AMA		11 (16.7%)
Unfavorable cervix		4 (6.1%)
Elective		4 (6.1%)
Others / not specified		33 (50%)

FHR = fetal heart rate, CPD = cephalo-pelvic disproportion, AMA = advanced maternal age

In women with labor induction, CS rates were 49.38% and 7.41% of nulliparous and multiparous women (subgroup 2a and 4a, respectively). Labor induction was offered at before 40 weeks in 70.4% and 74.1% of women in subgroup 2a and 4a, respectively. Failed induction was reported as indication for CS in 51.3% and 25% of CS in subgroup 2a and 4a, respectively.

Women who had pre-labor CS contributed mainly in both group 2 and 4, i.e., 68.4% in nulliparous (subgroup 2b) and 55% in multiparous women (subgroup 4b). Most common recorded indications for subgroup 2b were elective (25.4%), cephalo-pelvic disproportion (19.7%), and advanced maternal age (12.5%). Most common recorded indications for subgroup 4b were advanced maternal age (16.7%), cephalo-pelvic disproportion (15.2%), and elective and unfavorable cervix (6.1% each). Other unspecified indications were found in 31.3% of subgroup 2b and 50% of subgroup 4b. Placenta previa was reported as indication for CS in 4% and 6.1% of subgroup 2b and 4b, respectively.

Discussion

Of 4,998 women, 2,442 women were delivered by CS, corresponding to 48.86% CS rate, which is much higher than what WHO has recommended at 10-15%[1]. The major contributions to this high rate were from groups 1, 2, and 5 (23.71%, 17.65%, and 28.91%, respectively). This was similar to other previous reports in Thailand and other countries worldwide[4, 6, 7, 27].

The results showed that majority of women delivering at Siriraj Hospital were nulliparous, i.e. 41.48% for group 1 and 2, and 27.61% for group 3 and 4. The ratio of the sizes of group 1:2 is 3.0, which is within the expected ratio of > 2:1 and the ratio of group 3:4 is 10.5 which is also as expected (higher than ratio

of group1/2). This indicated that not too many labor inductions or pre-labor CS were performed in nulliparous women and multiparous women without previous CS[26]. The size of group 5 (previous CS) was relatively high (14.17%) reflecting that there was high CS rate in the past. The high contribution of group 5 also associated with high overall CS rate that this group contributed the most of CS (28.91% of all CS). The findings were in agreement with previous studies[10, 27-29] and multi-country surveys by WHO[7]. If the CS rate in this group needs to be reduced, trial of labor after cesarean (TOLAC) should be considered, particularly for women with one previous transverse low-segment scar. However, TOLAC is currently not recommended in our institution. However, decreasing the rate of primary CS could help reducing the number of women in this group in the future.

CS rates in group 1 and 3 were quite high (37.12%, and 9.44%, respectively) as compared with WHO recommendation[7, 26]. This raised the concern regarding the appropriateness of indications for CS among these groups of women. The most common indications for CS in both groups were cephalo-pelvic disproportion and abnormal fetal heart rate pattern. There are still variations among obstetricians in the decision of CS from these indications, including criteria of diagnosis, management guidelines, and decisions for CS. In addition, concerns about possible medical lawsuits could also play an important role in decision-making process among these cases. Development and implementation of appropriate management and decision guideline or setting up a second-opinion system for CS could help reducing the CS rate in these groups of women in the future.

For labor inductions (subgroup 2a and 4a), the results showed that CS rate was still high, especially among nulliparous women (subgroup 2a) which was 49.38%. The success rate of labor induction was still unsatisfactory and much less than what has previously reported[30]. Further analysis showed that labor inductions were offered before 40 weeks in 70.4% and 74.1% of nulliparous and multiparous women (subgroup 2a and 4a). Although definite indications were not being able to identified, these inductions might not be appropriate in every case. Again, this also could be the results of the lack of a uniform guideline and management scheme. A guideline for labor induction should be developed and strictly implemented, starting from indications, appropriate timing, technics of induction, and decision for CS. If majority of these women were allowed to have spontaneous labor later, the rate of CS could be reduced from lower risk of CS as in group 1 and 3.

Pre-labor CS was identified as another important problem of excessive CS rate, especially in nulliparous women (subgroup 2b), which contributed to 68.4% of group 2 and 14.37% of overall CS. As documented in medical records, majority of indications were not absolute indications and might not be justified, including elective CS, cephalo-pelvic disproportion, advanced maternal age, and unfavorable cervix. This could be from many reasons. Many women are scared about labor pain and decide to have a pre-labor CS without appropriate counseling. It also could be the matter of better time management that pre-labor CS is more convenient for both women and obstetricians. Additionally, it is possible that some obstetricians chose to recommend pre-labor CS to avoid unexpected complications during labor and delivery, which could lead to medical lawsuit. However, these possible reasons could not be evaluated in this study.

Although these problems are relatively hard to solve due to individual variations in attitudes and perceptions, at least the results have shown the importance of pre-labor CS in Thai population. It is possible that many women and some obstetricians are unaware of the immediate and long-term adverse consequences of CS and still prefer CS than vaginal delivery. Therefore, improving health literacy to adequate level regarding this issue for both the women and obstetricians could help in reducing the rate of CS by reducing pre-labor CS. If these women were to be waited for spontaneous labor or had labor inductions with appropriate indications, overall CS rate would be reduced to some degree.

The sizes of group 6 and 7 (term, breech presentation) were 4.42%, which is slightly higher that what is expected in general population of 3-4%. The

CS rate of both groups were almost 100% due to the acceptance of breech presentation as an indication for CS and external cephalic version is not recommended in our institution. The size of group 10 (preterm) was relatively high at 10.36% with CS rate of 44.4%. This can be explained by that Siriraj Hospital is a tertiary referral hospital for high-risk and complicated pregnancies that these women are commonly complicated by preterm deliveries. In addition, these complicated cases were commonly indicated for CS partly due to coexisting complications.

The CS rate in group 8 (multifetal pregnancy) was also higher (89.02%) than average level as stated by WHO[26]. In multi-country survey by WHO, the CS rate in group 8 was 57.7%[7], and it ranged from 61.8-98.5% in other studies[10, 27-29]. However, CS rate in this group depends on types of multifetal pregnancy, parity status and previous uterine scar.

The strength of this study was that inclusion of large samples in a tertiary care hospital. Data collection was planned, and recorded by trained personnel before the women were discharged from the hospital. The study also demonstrated the ease and feasibility of implementing Robson classification. However, there were also some limitations in this study. First, this study was conducted in a short period of time (8 months) that the trend of CS rate cannot be evaluated. There might be some incorrect data, especially data on onset of labor, which could lead to possible misclassification of women into groups (group 1-4). However, these data were collected by on-duty nurses that such misclassifications should be minimal and would not have significant changes in the results. The absence of some details in medical records, especially indications for CS, precludes the exact evaluation of appropriateness of CS indications. Finally, the data of maternal and fetal outcomes were not collected to evaluate its correlation within each group. Future, larger studies might be needed to determine such correlation and evaluate if any future changes could reduce CS rate and whether it affect pregnancy outcomes. In addition, the study was conducted in a university-based tertiary care hospital that incidence of complicated cases could be unusually higher than other settings. But this probably might not be the reasons for such high CS rate in this setting.

Conclusion

In conclusion, the CS rate in Siriraj Hospital was high at 48.86%. The major contributions were in group 1, 2, and 5 of Robson classification. Major contributing factors could be the inappropriate indications for CS, especially in nulliparous women both in group 1 and 2. Indications for CS in women with spontaneous labor (group 1 and 3) need to be validated for appropriateness. Many indications for CS in those with pre-labor CS (group 2a and 4a) were unjustified. Labor inductions resulted in unsatisfactory success rate. Interventions to reduce the incidence of CS specifically among women in these groups would help to reduce the overall CS rate. Regular follow-up of CS rate and audit of compliance to standard guideline, especially in terms of induction of labor and indications for CS should be conducted in order to maintain standards of care in obstetric patients. The use of Robson classification should be continued to evaluate trend in CS rate, for internal and external audit of CS, and evaluate the success of future interventions.

Potential conflicts of interest

The authors declare no conflict of interest.

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Thai Journal of Obstetrics and Gynaecology
January 2020, Vol. 28, No. 1, pp. 16-23

GYNECOLOGY

Colposcopy Waiting Time for First-diagnosed Abnormal Cervical Cytology Patients: Experiences at Hatyai Hospital

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ABSTRACT

Objectives: To audit colposcopy waiting time for first-diagnosed abnormal cervical cytology patients at Hatyai Hospital following the standard requirements of the National Health Service Cervical Screening Program (NHSCSP) 2016.

Materials and Methods: A retrospective study was carried out for 123 first-diagnosed abnormal cervical cytology patients who attended the colposcopy clinic at Hatyai Hospital, Thailand between October 2017 and May 2018. Statistical analyses were performed.

Results: Median colposcopy waiting time at Hatyai Hospital was 11.87 days (interquartile range: 0, 14 days) which achieved the minimum requirements of NHSCSP 2016. However, 94.59% of patients with low grade lesion obtained colposcopy within 6 weeks (minimum requirement ≥ 99%) and 77.55% with high grade lesion obtained colposcopy within 2 weeks (minimum requirement ≥ 93%). The significant factor associated with below standard requirements of waiting time for colposcopy was the default rate.

Conclusion: Median colposcopy waiting time at Hatyai Hospital met the standard requirements of NHSCSP 2016 but the proportion of patients who obtained colposcopy within time failed to meet the standard requirements. Improvement in the colposcopy appointment system is essential to rectify this defect.

Keywords: appointments, schedules, cervical intraepithelial neoplasia, colposcopy.

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Received: 7 September 2018, **Revised:** 30 October 2018, **Accepted:** 12 December 2018

ระยะเวลารอคอยการตรวจด้วยกล้องขยายทางช่องคลอด ในผู้ป่วยที่ได้รับการวินิจฉัยว่ามีความผิดปกติทางเซลล์วิทยาของปากมดลูกเป็นครั้งแรก: ประสบการณ์ของโรงพยาบาลหาดใหญ่

ภรทิพย์ ทัศนานุตริยกุล, ศิชฌุพงศ์ หนูทอง

บทคัดย่อ

วัตถุประสงค์: *เพื่อทบทวนระยะเวลารอคอยการตรวจด้วยกล้องขยายทางช่องคลอด ในผู้ป่วยที่ได้รับการวินิจฉัยว่ามีความผิดปกติทางเซลล์วิทยาของปากมดลูกเป็นครั้งแรกในโรงพยาบาลหาดใหญ่ โดยอาศัยข้อกำหนดมาตรฐานของ the National Health Service Cervical Screening Program (NHSCSP) 2016.*

วัสดุและวิธีการ: *ดำเนินการวิจัยแบบเก็บข้อมูลย้อนหลังของผู้ป่วยที่ได้รับการวินิจฉัยว่ามีความผิดปกติทางเซลล์วิทยาของปากมดลูกเป็นครั้งแรก จำนวน 123 คน ที่มารับการตรวจด้วยกล้องขยายทางช่องคลอดที่โรงพยาบาลหาดใหญ่ ประเทศไทย ระหว่างเดือนตุลาคม พ.ศ.2560 ถึงเดือนพฤษภาคม พ.ศ.2561 นำข้อมูลดังกล่าวมาทำการวิเคราะห์ทางสถิติ*

ผลการวิจัย: *ค่ามัธยฐานของระยะเวลารอคอยการตรวจด้วยกล้องขยายทางช่องคลอดของผู้ป่วยที่ได้รับการวินิจฉัยว่ามีความผิดปกติทางเซลล์วิทยาของปากมดลูกเป็นครั้งแรกของโรงพยาบาลหาดใหญ่เท่ากับ 11.87 วัน (พิสัยระหว่างควอร์ไทล์: 0, 14 วัน) ซึ่งเป็นไปตามข้อกำหนดขั้นต่ำของ NHSCSP 2016 อย่างไรก็ตาม มีเพียงร้อยละ 94.59 ของผู้ป่วยที่มีความผิดปกติทางเซลล์วิทยาของปากมดลูกขั้นต่ำที่ได้รับการตรวจด้วยกล้องขยายทางช่องคลอดภายใน 6 สัปดาห์ (ข้อกำหนดขั้นต่ำอย่างน้อยร้อยละ 99) และร้อยละ 77.55 ของผู้ป่วยที่มีความผิดปกติทางเซลล์วิทยาของปากมดลูกขั้นสูงที่ได้รับการตรวจด้วยกล้องขยายทางช่องคลอดภายใน 2 สัปดาห์ (ข้อกำหนดขั้นต่ำอย่างน้อยร้อยละ 93) ปัจจัยที่มีความเกี่ยวข้องอย่างมีนัยสำคัญต่อการมีระยะเวลารอคอยการตรวจด้วยกล้องขยายทางช่องคลอดที่นานกว่าข้อกำหนด คือ อัตราการผิดนัดของผู้ป่วย*

สรุป: *ค่ามัธยฐานของระยะเวลารอคอยการตรวจด้วยกล้องขยายทางช่องคลอดของผู้ป่วยที่ได้รับการวินิจฉัยว่ามีความผิดปกติทางเซลล์วิทยาของปากมดลูกเป็นครั้งแรกของโรงพยาบาลหาดใหญ่ เป็นไปตามข้อกำหนดขั้นต่ำของ NHSCSP 2016 แต่สัดส่วนของผู้ป่วยที่ได้รับการตรวจด้วยกล้องขยายทางช่องคลอดภายในเวลาที่กำหนดไม่เป็นไปตามข้อกำหนดขั้นต่ำของ NHSCSP 2016 จึงมีความจำเป็นที่จะต้องพัฒนาระบบการนัดหมายการตรวจด้วยกล้องขยายทางช่องคลอดต่อไป*

คำสำคัญ: *การนัดหมาย, ตารางเวลา, รอยโรคก่อนมะเร็งของปากมดลูก, การตรวจด้วยกล้องขยายทางช่องคลอด*

Introduction

Cervical cancer is a serious public health's problem worldwide. It is the second most common female cancer in Thailand with 8,184 new cases recorded in 2012[1]. However, cervical cancer can be prevented by vaccination. Moreover, cervical cancer screening programs have been developed for early detection of precancerous lesions. Several methods are used to screen for cervical cancer including cervical cytology, co-testing, primary human papillomavirus (HPV) screening or visual inspection with acetic acid (VIA). Among these, cervical cytology is the most popular technique followed in Thailand.

Women with abnormal cervical cytology should undergo further investigation by colposcopy. Magnification of cervical epithelium, lower genital tract or anogenital area through colposcopy helps to detect precancerous lesions, malignancy or verify normality. In Thailand, colposcopy is usually performed by a gynecological oncologist or gynecologist who has undergone colposcopy training. Therefore, most patients with abnormal cervical cytology are referred to a tertiary care hospital for further investigations.

Lack of doctors is a serious public health problem in Thailand. Hatyai Hospital is a tertiary healthcare provider in lower-southern Thailand. Since 2013, the hospital has been the referral center from Songkhla and neighboring provinces, covering about 5 million people[2].

Waiting time for treatment may be affected by excessive patients, including waiting time for colposcopy. Periodically auditing of the colposcopy service is undertaken to improve clinical practice quality.

In Thailand, there are no standard guidelines for quality assurance in cervical cancer prevention. The National Health Service Cervical Screening Program (NHSCSP) has published guidelines regarding colposcopy and programmed management for assurance in cervical cancer prevention, including standard waiting time requirements for colposcopy[3]. To improve the referral system and colposcopy program of the study institute, the primary objective concerned investigation of colposcopy waiting time for first-diagnosed abnormal cervical cytology patients at Hatyai Hospital by using standard requirements of NHSCSP 2016. The secondary objective was to assess the factors associated with substandard requirements of NHSCSP 2016.

Materials and Methods

This study was approved by the Institutional Review Board of Hatyai Hospital. A retrospective study was performed at the colposcopy clinic of Hatyai Hospital between October 2017 and May 2018.

Sample size was calculated using the formula for descriptive studies: n = [DEFF*Np(1−p)]/ [(d2/Z21-α/2*(N−1)+p*(1−p)]. Base on study of Kietpeerakool et al[4], where DEFF=1, N=291, p=0.96, d=0.05, and Z1−α/2 = 1.96. Sample size plus 10% drop out was determined at 50.

At Hatyai Hospital, the colposcopy clinic is carried out once a week with examinations performed by a gynecological oncologist. On the first visit, patients with abnormal cervical cytology have their medical details recorded and undergo a gynecological examination by a general gynecologist before making an appointment to attend the colposcopy clinic. If patients default from their appointments, nurses at the colposcopy clinic make contact by telephone to arrange new appointments and record the reasons for default. If patients cannot be contacted or do not attend the second appointment, they are sent an advisory letter detailing the appointment process. Defaulters who fail to respond after receiving the advisory letter are classified as loss to follow-up.

Between October 2017 and May 2018, 152 women visited the colposcopy clinic. After exclusion of patients with prior diagnosis of abnormal cervical cytology, pregnancy, incomplete medical data or loss to follow-up, 123 women with first diagnosis of abnormal cervical cytology were included in the study. Demographic data and types of abnormal cervical cytology were collected from out-patient chart. Abnormal cervical cytology was categorized into 2 groups as low and high grade lesion. Low grade lesion consisted of atypical squamous cells - undetermined significance (ASC-US) and low grade squamous intraepithelial lesion (LSIL) and high grade lesion consisted of atypical squamous cells, cannot exclude high grade squamous intraepithelial lesions (ASC-H), high grade squamous intraepithelial

lesion (HSIL), invasive carcinoma, and glandular lesion (including atypical glandular cell, adenocarcinoma in situ and adenocarcinoma). Colposcopy waiting time was audited following the standard requirements of NHSCSP 2016[3]. Standard requirements for colposcopy were determined by the following criteria: (1) ≥ 99% of patients with low grade lesion should be seen within 6 weeks of referral and (2) ≥ 93% of patients with high grade lesion should be seen within 2 weeks of referral. A default rate should be less than 15%[3]. Date of receipt of referral was day 0 in all calculations.

Statistical analyses were performed using SPSS software version 17.0 (SPSS Inc., Chicago). Descriptive statistics were used to analyze demographic data. Continuous data were presented with mean ± standard deviation (SD) and median (interquartile quartile (IQR)) as appropriate. Discrete data were analyzed with Fisher's exact test. For all analyses, p value < 0.05 was considered statistically significant.

Results

Among the 123 first-diagnosed abnormal cervical cytology patients, mean age was 40.17±11.25 years, with HIV infected patients at 14.63%. Three-quarters of the patients lived in Songkhla Province and 57.72% were referred from other hospitals. More than 95% had universal health coverage or health insurance. The default rate was 17.89% (Table 1).

Table 1. Demographic data of first-diagnosed abnormal cervical cytology patients.

Characteristic	N (%)
Age (years)	40.17 ± 11.25
Residency	
Songkhla	96 (78.05)
Other provinces	27 (21.95)
Education	
Primary	35 (28.46)
Secondary or higher	88 (71.54)
Health insurance	
Yes	119 (96.75)
No	4 (3.25)
Religion	
Buddhism	103 (83.74)
Islam	20 (16.36)
Marital status	
Single	13 (10.57)
Married	110 (89.43)
Previous pregnancy	
Yes	99 (80.49)
No	24 (19.51)
HIV infection	
Yes	18 (14.63)
No	105 (85.37)
Referred case	
Yes	71(57.72%)
No	52 (42.28%)
Default	
Yes	22(17.89%)
No	101(82.11%)

Values are given as mean ± standard deviation and number (%).

All 123 patients were examined by conventional cervical cytology. Abnormal cervical cytology consisted of ASC-US 40 (32.52%), LSIL 34 (27.64 %), HSIL17 (13.82%), ASC-H 10 (8.13%), glandular lesion 14 (11.38%) and invasive carcinoma 8 (6.50%).

Median colposcopy waiting time of first-diagnosed abnormal cervical cytology patients at Hatyai Hospital was 11.87 days (IQR: 0, 14 days). Colposcopy waiting time for the low grade lesion group was 6 days (IQR: 0, 13.25 days) and 11 days (IQR: 4, 14 days) for the high grade lesion group. Colposcopy waiting time was further classified by the standard requirements of NHSCSP 2016. The results are shown in Table 2.

Table 2. Colposcopy waiting time for first-diagnosed abnormal cervical cytology patients classified by standard requirements of NHSCSP 2016.

Category	Results		Waiting time (days)		Standard requirement
	Standard	Substandard	Standard	Substandard	
Low grade lesion* (N=74)	70 (94.59)	4 (5.41)	6 (0, 11)	104 (66, 121.75)	≥ 99%
High grade lesion[ฮ] (N=49)	38 (77.55)	11 (22.45)	7 (0.75,11.25)	20 (17, 25)	≥ 93%

Values are given as number (%) and median (interquartile quartile),

NHSCSP: National Health Service Cervical Screening Program

* Standard requirement: woman with atypical squamous cells - undetermined significance (ASC-US) and low grade squamous intraepithelial lesion (LSIL) should be seen within 6 weeks of referral.

[†] Standard requirement: woman with atypical squamous cells, cannot exclude high grade squamous intraepithelial lesions (ASC-H), high grade squamous intraepithelial lesion (HSIL), glandular lesion and invasive carcinoma should be seen within 2 weeks of referral.

Table 3 shows the relationship between various factors and colposcopy waiting time for first-diagnosed abnormal cervical cytology patients. There was no statistical significance in the relationship between demographic factors and substandard requirements of NHSCSP 2016 except for the default rate ($p < 0.01$).

Reasons for not attending colposcopy appointments given by the 22 defaulting patients (17.89%) included appointment date met the menstrual cycle in 9 patients (40.91%), lack of health insurance in 3 patients (13.64%) and unknown causes (45.45%).

Discussion

Achieving appropriate times for colposcopy appointments is important for early diagnosis and treatment of precancerous cervical lesions. In Thailand, there are no standard guidelines for quality assurance in cervical cancer prevention. Here, standard requirements of NHSCSP 2016 were used to evaluate the quality of colposcopy treatment at Hatyai Hospital.

Standard requirements of NSHCSP 2016 state that at least 93% of patients with high grade lesion should be seen at a colposcopy clinic within 2 weeks. For low grade lesion, at least 99% of patients should be seen at a colposcopy clinic within 6 weeks[(3)]. Median colposcopy waiting time for first-diagnosed abnormal cervical cytology patients at Hatyai Hospital was 11.87 days (IQR: 0, 14 days). An overview of colposcopy waiting time recorded here concurred with NSHCSP 2016 requirements. However, the proportion of patients with abnormal cervical cytology failed to meet NSHCSP 2016 requirements. Only 77.55% and 94.59% of patients with high and low grade lesion were offered colposcopy appointments within 2 and 6 weeks, respectively.

Table 3. Factors associated with substandard requirements of the NHSCSP 2016.

Demographic	Low grade			High grade		
	N (%)			N (%)		
	Standard (N=70)	Substandard (N=4)	p value	Standard (N=38)	Substandard (N=11)	p value
Residency	56 (80.00)	3 (75.00)	1.00	27 (71.05)	10 (90.91)	0.25
Songkhla	14 (20.00)	1 (25.00)		11 (28.95)	1 (9.09)	
Other provinces						
Education						
Primary school	19 (27.14)	2 (50.00)	0.32	13 (34.21)	1 (9.09)	0.14
Secondary school	51 (72.86)	2 (50.00)		25 (65.79)	10 (90.91)	
Health insurance						
Yes	67 (95.71)	4 (100.00)	1.00	37 (97.37)	11 (100.00)	1.00
No	3 (4.29)	0 (0.0)		1 (2.63)	0 (0.00)	
Religion						
Buddhism	62 (88.57)	3 (75.00)	0.41	29 (76.32)	9 (81.82)	1.00
Islam	8 (11.43)	1 (25.00)		9 (23.68)	2 (18.18)	
Marital status						
Single	6 (8.57)	0 (0.00)	1.00	4 (10.53)	3 (27.27)	0.18
Married	64 (91.43)	4 (100.00)		34 (89.47)	8 (72.73)	
Previous pregnancy						
Yes	57 (81.43)	4 (100.00)	1.00	31 (81.58)	7 (63.64)	0.24
No	13 (18.57)	0 (0.00)		7 (18.42)	4 (36.36)	
HIV infection						
Positive	14 (20.00)	0 (0.00)	1.00	2 (5.26)	2 (18.18)	0.21
Negative	56 (80.00)	4 (100.00)		36 (94.74)	9 (81.82)	
Referral case						
Yes	37 (52.86)	3 (75.00)	0.62	24 (63.16)	7 (63.64)	1.00
No	33 (47.14)	1 (25.00)		14 (36.84)	4 (36.36)	
Default						
Yes	9 (12.86)	2 (50.00)	0.10	3 (7.89)	8 (72.72)	< 0.001
No	61 (87.14)	2 (50.00)		35 (92.11)	3 (27.27)	

Values are given as mean ± standard deviation and number (%).
NHSCSP: National Health Service Cervical Screening Program

Results showed that default rate at 17.89% was a significant factor associated with substandard requirements of NSHCSP 2016, higher than the minimal requirements of less than 15%[3]. Regarding other literature concerning Thailand, Kietpeerakool et al reported 15.8%[4] which concurred with our findings. Many reasons may be affiliated with default from colposcopy appointments. An appointment date that meets the menstrual cycle was determined as a major problem, followed by lack of health insurance. Other factors previously reported include human immunodeficiency virus infection, long waiting time

for colposcopy, younger age, not in paid employment, smoking, lack of post-school education, and not worried about having cervical cancer[4, 5].

Non-attendance of patients at colposcopy clinic is a complex problem[6]. Many background differences and various reported factors influence default of colposcopy appointments[7-9]. Here, several factors were identified as associated with default of colposcopy clinic appointments. Recent research has suggested strategies to reduce non-attendance of patients at colposcopy clinic including direct booking (short circuit to colposcopy by allowing patients direct appointments)[10], precolposcopy information with discussions to improve knowledge concerning colposcopy[11], and telephone reminders for appointment dates[12]. Interestingly, Balasubramani et al reported that intention of patients was a predictive factor for colposcopy attendance[13]. Improvement of knowledge regarding the importance of colposcopy is the key to successful management of colposcopy clinic. Moreover, changing conventional methods to liquid-based cervical cytology may help to decrease colposcopy waiting time. Physicians can use reflex HPV deoxyribonucleic acid (DNA) testing to triage negative-HPV DNA from positive-HPV patients. Only positive-HPV DNA patients require further investigation with colposcopy. This strategy may reduce unnecessary colposcopy and waiting time.

This research presented the first investigation at a regional hospital operated by the Ministry of Public Health, Thailand. One limitation was the single center study with small sample size. A multicenter study will provide a more detailed perspective of the situation throughout the country. Factors associated with default of colposcopy clinic appointments were not specifically investigated. Further research is required for a more comprehensive understanding of colposcopy treatment processes.

Conclusion

Median colposcopy waiting time at Hatyai Hospital met the standard requirements of NHSCSP 2016 but the proportion of patients who underwent colposcopy within specified time periods failed to meet the standard requirements. Improvements in the colposcopy appointment system are urgently required.

Potential conflicts of interest

The authors declare no conflict of interest.

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Thai Journal of Obstetrics and Gynaecology
January 2020, Vol. 28, No. 1, pp. 24-33

OBSTETRICS

Efficacy of a Single Dose Administration of Ibuprofen and Acetaminophen in Comparison with Acetaminophen for the Relief of Perineal Pain after Childbirth: A randomized controlled trial

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ABSTRACT

Objectives: To determine the efficacy of a single dose of ibuprofen plus acetaminophen versus acetaminophen alone for relief from acute perineal pain after childbirth.

Materials and Methods: A randomized, double-blind placebo-controlled trial was conducted on 404 women who gave birth by spontaneous vaginal delivery with mediolateral episiotomy at Queen Savang Vadhana Memorial Hospital between June 2017 and October 2017. Patients were randomized by block computer into 2 groups before delivery: one group received ibuprofen plus acetaminophen and another group received acetaminophen plus placebo. The medication was given immediately after complete perineal suturing. Perineal pain scores of both groups were assessed pre- and post-medication by visual analog scale (VAS). The adverse drug reactions were evaluated at 24 hours after medication.

Results: No difference of pre-medication perineal pain score was recorded for both groups. Median of perineal pain scores were 5 vs 5 ($p = 0.067$), respectively. Both groups were relieved their perineal pain within 24 hours. The median different pain relief scores were 5 vs. 3 ($p = 0.006$), respectively. There was dramatic pain relief in the short-term in the ibuprofen plus acetaminophen group, more than for the patients in the acetaminophen alone group (at 2-hours after taken medication). There was no adverse drug reaction.

Conclusion: A regimen of single dose ibuprofen plus acetaminophen has higher efficacy for relief from acute perineal pain than a conventional regimen with acetaminophen alone, and is safe to use for pregnant women after childbirth.

Keywords: episiotomy, perineal pain, ibuprofen, acetaminophen.

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Received: 11 March 2018, **Revised:** 29 November 2018, **Accepted:** 12 December 2018

การศึกษาประสิทธิภาพการใช้ยา ibuprofen ร่วมกับยา acetaminophen เปรียบเทียบกับการใช้ยา acetaminophen ในการลดความเจ็บปวดของแผลฝีเย็บภายหลังการคลอดบุตร

ปรียาภรณ์ หาระสาย, นุชนารถ พัฒนาปัญญาสัตย์

บทคัดย่อ

วัตถุประสงค์: *เพื่อหาประสิทธิภาพของยา ibuprofen ร่วมกับ acetaminophen เปรียบเทียบกับacetaminophen อย่างเดียวเพียงหนึ่งครั้งเพื่อลดอาการปวดเฉียบพลันของแผลฝีเย็บหลังการคลอดทางช่องคลอด*

วัสดุและวิธีการ: *รูปแบบการศึกษาเป็นการสุ่มตัวอย่างแบบปิดบังสองทางในกลุ่มหญิงตั้งครรภ์ที่คลอดโดยวิธีคลอดทางช่องคลอดและตัดฝีเย็บ ในโรงพยาบาลสมเด็จพระบรมราชเทวี ณ ศรีราชา ระหว่างเดือนมิถุนายน พ.ศ. 2560 ถึงตุลาคม พ.ศ. 2560 จำนวน 404 ราย ผู้ป่วยได้รับการสุ่มตัวอย่างแบบบล็อกด้วยคอมพิวเตอร์ก่อนคลอด เป็น 2 กลุ่ม: กลุ่มหนึ่งได้รับ ibuprofen ร่วมกับ acetaminophen อีกกลุ่มได้รับ acetaminophen เพียงอย่างเดียว โดยได้รับยาทันทีหลังจากการเย็บแผลฝีเย็บเรียบร้อย คะแนนความเจ็บปวดของฝีเย็บหลังคลอดทั้งสองกลุ่มจะได้รับการประเมินก่อนและหลังการให้ยาด้วย "10-cm visual analogue scale" และอาการไม่พึงประสงค์จากยาทั้งสองกลุ่มจะได้รับการประเมินที่ 24 ชั่วโมงหลังการใช้ยา*

ผลการศึกษา: *ไม่พบความแตกต่างในคะแนนความเจ็บปวดของแผลฝีเย็บก่อนการรักษาทั้งสองกลุ่ม (ค่ามัธยฐานคือ 5, p = 0.067) การได้รับยาทั้งสองกลุ่มสามารถลดความเจ็บปวดของแผลฝีเย็บภายใน 24 ชั่วโมง ได้แตกต่างกันอย่างมีนัยสำคัญ (ค่ามัธยฐานคือ 5 เทียบกับ 3 ตามลำดับ, p = 0.006) และสังเกตได้ว่ามีการบรรเทาอาการปวดในระยะสั้นอย่างรวดเร็วกว่าในกลุ่มที่ได้รับการยา ibuprofen ร่วมกับ acetaminophen เมื่อเทียบกับกลุ่มที่ได้รับยา acetaminophen เพียงอย่างเดียว (2 ชั่วโมง หลังการใช้ยา) ไม่พบอาการไม่พึงประสงค์จากยาทั้งสองกลุ่ม*

สรุป: *การใช้ยา ibuprofen ร่วมกับ acetaminophen เพียงครั้งเดียวมีประสิทธิผลมากขึ้นในการลดอาการปวดเฉียบพลันของแผลฝีเย็บในหญิงตั้งครรภ์หลังคลอดมากกว่าการได้รับ acetaminophen เพียงอย่างเดียว*

คำสำคัญ: *แผลฝีเย็บ, ความเจ็บปวดแผลฝีเย็บ, ไอบูโปรเฟน, อาเซทตามิโนเฟน*

Introduction

Episiotomy is the surgical enlargement of the vaginal orifice by an incision of the perineum during the last part of the second stage of labor to increase the diameter of the vaginal outlet during childbirth. The benefits of episiotomy with mother include reduced third-degree tear; preservation of the muscle relaxation of the pelvic floor and perineum, leading to improved sexual function; reduced risk of fecal and or urinary incontinence; and due to the straight, clean incision, easier repair and healing of an episiotomy than a laceration. Moreover, the neonatal benefits of episiotomy are that a shortened second stage of labor could prevent fatal asphyxia, cranial trauma, cerebral hemorrhage, and mental retardation. Hence, episiotomy has become one of the most commonly performed surgical procedures in the world[1].

Hence, perineal trauma is a determinant factor for postpartum perineal pain especially on the first day after delivery. In the puerperal period, the presence of pain entails difficulties to practice motherhood and perform daily activities, such as self-care and newborn care. It also interferes with the women's sleep, rest, movements, urination, evacuation, and appetite. These difficulties can cause important physical, psychological, and emotional problems that contribute towards a negative delivery experience. Pain management is important for pregnant women who give birth by spontaneous vaginal delivery[2].

Pharmacological and non-pharmacological treatments have been investigated for perineal pain control after vaginal delivery. Traditionally, oral analgesics (acetaminophen, nonsteroidal anti-inflammatory agents), local anesthetics, and cold and warm sitz baths are used in postpartum care to treat perineal lesions. Music therapy is an alternative medicine which has been found to be effective in reducing the perceived perineal pain[3]. Acetaminophen is the most common analgesic used for perineal pain. Other analgesia is also used such as opioid, non-opioid, and the combination of both. For example, in Thailand, the combination of acetaminophen/tramadol tablet is used as a rectal suppository for reducing perineal pain[4]. Nonsteroidal anti-inflammatory drugs (NSAIDs) are widely used for relief pain in clinical practice. Ibuprofen has a similar efficacy and fewer adverse effects. The NSAIDs are used commonly with minimal secretion in breast milk[5, 6].

The management of perineal pain was reviewed by the Cochrane Database of systematic reviews in 2013. The result of ten studies included states that more women experienced pain relief with paracetamol compared with placebo. In addition, there were significantly fewer women having additional pain relief with paracetamol compared with placebo[7]. In 2016, the result from twenty-eight studies of a single dose of NSAIDs for the perineal pain during the postpartum period revealed that a single dose of NSAIDs achieved adequate pain relief at four hours and at six hours. And NSAIDs versus paracetamol were also more effective for adequate pain relief at four hours but not at six hours post-administration[8].

Kamondetdecha R., studied about ibuprofen versus acetaminophen for the relief of perineal pain after childbirth, in Thailand. In the randomized controlled trial, two hundred and ten pregnant women were randomly allocated to receive either ibuprofen or acetaminophen. Pain in the ibuprofen group was considerably more reduced than the acetaminophen group at one hour of treatment (mean pain rating 2.18 vs. 2.88, respectively; $p < 0.003$). After two hours, both groups had similar analgesic properties[9].

These two compounds differ in their mode of action. Ibuprofen is an NSAID that inhibits cyclooxygenase (COX) enzymes: COX-1 and COX-2 and subsequent synthesis of prostaglandins and related compounds at peripheral sites within injured tissue. The mode of action of acetaminophen is not completely understood but appears to be related to the inhibition of a sub-class of COX enzyme isoforms in the central nervous system[10]. Cochrane Databases of systematic review in 2013 reviewed the single oral dose of ibuprofen plus paracetamol for acute postoperative pain. The results achieved at least 50% maximum pain relief over six hours in combination drugs more than ibuprofen alone or placebo and resulted in longer times to remediation than placebo[11].

However, studies of the single dose of combining two or more drugs with different mechanisms of action, such as NSAIDs and acetaminophen, for perineal pain relief after delivery have been limited. The hypothesis is that in pregnant women who give birth by spontaneous vaginal delivery with episiotomy, this combination of ibuprofen and acetaminophen provides superior analgesia than acetaminophen alone.

The main purpose of the present study was to evaluate the efficacy of ibuprofen and acetaminophen versus acetaminophen and placebo for relief from perineal pain after childbirth in 1, 2, 4, 6, and 24 hours after taking medication, using 10-cm visual analog scale for evaluation median of different pain relief scores. The secondary objectives were to evaluate side effects between both groups within 24 hours.

Materials and Methods

The study collected data from June 2017 to September 2017 at Queen Savang Vadhana Memorial Hospital, Chonburi, Thailand. The study was conducted on the pregnancy women who chose vaginal delivery in this presenting time. The inclusion criteria were performed in the latent phase of first stage of labor. They consisted of single fetus pregnancy, vertex presentation, term pregnancy, history of antenatal care more than 4 times, no history of allergy to ibuprofen or acetaminophen, no history of medical condition known to be potentially exacerbated by acetaminophen or NSAIDs, include a history of asthma, significant renal or liver impairment, gastrointestinal ulcer. Pregnant women who met the criteria was given information of the research and were asked to consent before admission. The study was approved by the Research and Ethical Committee of the Queen Savang Vadhana Memorial Hospital, No. 3/2560.

The sample size was calculated based on previous study of Kamondetdecha R., the study about ibuprofen versus acetaminophen for the relief of perineal pain after childbirth in Thailand, that analysis standard deviation difference of pain rating score at 4 hour, showed 80% power of study, the target sample size was 338 women (169 per group)[9]. As potential loss to follow-up in each group was estimated at 20%, total sample size was set at 404 women. Finally, 404 pregnant women were enrolled in this study. All participants were randomly picked to receive either ibuprofen plus acetaminophen or placebo plus acetaminophen orally by computer block randomization technique. The placebo pills were physically similar to the real drug of ibuprofen. Intrapartum management was the same for both, using the standard protocol in hospital. Mediolateral episiotomies and repairs were performed by staff, residents, nurses, and medical students that were covered by staff or resident in all case using the standard procedures under local anesthesia. All participants received the drug immediately after complete perineal suturing by the first investigator in labor room. After that all participants were asked, by the second investigator, to give pain score by visual analog scale after perineal repair, before taking the drug and at 1, 2, 4, 6 and 24 hours after treatment. Patients were allowed to use a supplemental analgesic, that is acetaminophen. The patient, first and second investigator were blinded to the medication.

Women with mediolateral episiotomy with a third or fourth-degree tear after normal vaginal delivery, who had complications of delivery such as postpartum hemorrhage, delivery by cesarean section route, delivery by operative vaginal delivery were excluded. Moreover, the patients who were allowed to use of any intravenous analgesic drug within 24 hours or left the research were identified as drop-outs. Excluded and drop-out patients were not included in the trial.

The primary outcome of the present study was to evaluate the efficacy of ibuprofen and acetaminophen versus acetaminophen and placebo for relief from perineal pain after childbirth in 1, 2, 4, 6, and 24 hours after taking medication, using 10-cm visual analog scale from 0 (“no pain”) to 10 (“worst pain ever”) for evaluation median of different pain relief scores. The perineal pain score was recorded before the subject took the first dose of analgesia and at 1, 2, 4, 6, and 24 hours after treatment.

The secondary outcomes evaluated were for side effects, including nausea, vomiting, stomach pain and dizziness after 24 hours of treatment. All the data were

collected by two investigators (first investigator in labor room and second investigator in the postpartum room) who were blinded to group assignment.

The data analyses by intention to treat were performed using SPSS Statistics version 20 (SPSS Inc., Chicago, IL). Demographic and clinical characteristic data were history of vaginal delivery, degree of perineal tear, type of vaginal technique suture, type of skin technique suture, operator, that were presented as number and percentage (%) for categorical variables and were compared between the groups using the chi-square test. The other demographic and clinical characteristic data were maternal age, maternal weight, gestational age, birth weight, length of 2nd stage of labor, length of suturing, and volume of blood loss, that were presented as mean ± standard deviation for continuous variables, and were compared between the groups using independent samples t-test. The outcome of continuous variables, such as sequential measures on the visual analog pain scale and overall satisfaction measures on visual analog scales were compared between the groups using Mann-Whitney U test. And the outcome of categorical variables, such as the presence of side effects were compared between the groups using the chi-square test. Adjusted 95% confidence interval (CI) were estimated. A p value of < 0.05 was considered to be statistically significant.

Results

During the study period four hundred and four women were screened for inclusion criteria in the present trial, and signed consent form (Fig. 1).

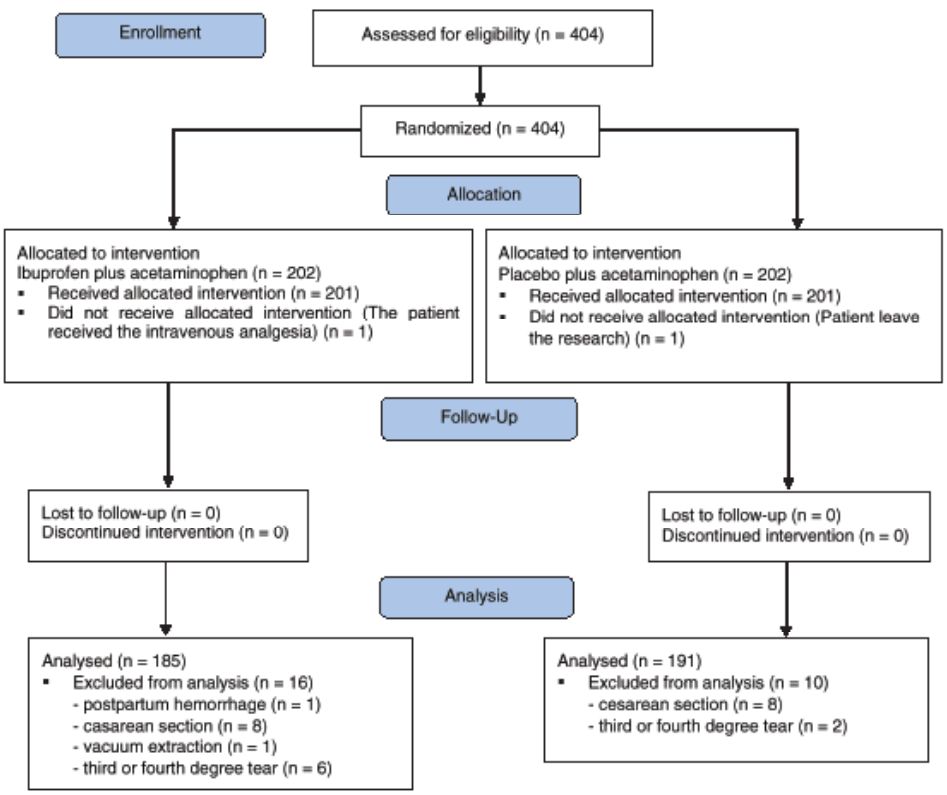

Fig. 1. Study flow diagram.

Then the 202 pregnant women were randomly assigned to receive ibuprofen 400 milligrams and acetaminophen 1,000 milligrams (treatment group), and 202 to receive placebo and acetaminophen 1,000 milligrams (control group). The treatment group excluded 16 pregnant women due to postpartum

hemorrhage[1], delivery by cesarean section route[8], operative vaginal delivery[1] and third-or fourth-degree tear after normal vaginal delivery[6]. The control group excluded 10 pregnant women due to delivery by cesarean section route[8] and third-or fourth- degree tear after normal vaginal delivery[2]. The total number pregnant women to receive drugs for both groups were 378 with 186 randomly assigned to receive ibuprofen 400 milligrams and acetaminophen 1,000 milligrams, and 192 to receive placebo and acetaminophen 1,000 milligrams. One pregnant woman of the treatment group received the intravenous analgesia drug and one pregnant woman of the control group left the study. The results of these groups were analyzed 185 in the treatment group with 191 in the control group. The two groups were similar in demographic data, clinical features, and the median onset of pain score (Table 1).

Table 1. Material demographics and clinical features.

Variables	Treatment groups		
	Ibuprofen plus Acetaminophen (n = 185)	**Acetaminophen (n = 191)**	**p value**
Maternal age (year)	27.08 ± 5.75	26.44 ± 5.88	0.286
Maternal weight (kilograms)	67.42 ± 9.91	66.95 ± 9.99	0.648
History of vaginal delivery (times)			0.122
Yes	115 (62.2%)	96 (56.2%)	
1	84 (45.4%)	68 (35.6%)	
2	26 (14.1%)	22 (11.5%)	
3	5 (2.7%)	6 (3.1%)	
Gestational age (weeks)	38.39 ± 1.08	38.54 ± 1.87	0.344
Birth weight (kilograms)	3055.59 ± 375.16	3089.63 ± 370.64	0.377
Degree of perineal tear			0.056
- First degree tear	14 (7.6%)	6 (3.1%)	
- Second degree tear	171 (92.4%)	185 (96.9%)	
Type of vaginal technique suture			0.717
- interrupted	21 (11.4%)	24 (12.6%)	
- continuous unlock closure	164 (88.6%)	167 (87.4%)	
Type of skin technique suture			0.688
- Interrupted	18 (9.7%)	21 (11%)	
- Continuous subcuticular closure	167 (90.3%)	170 (89.0%)	
Operators			0.532
- Medical student	5 (2.7%)	12 (6.3%)	
- Nurse	162 (87.6%)	161 (84.3%)	
- Resident	15 (8.1%)	15 (7.9%)	
- Staff	3 (1.6%)	3 (1.6%)	
Length of 2nd stage of labor (minutes)	20.04 ± 20.80	20.10 ± 18.48	0.976
Length of suturing (minutes)	24.6 ± 11.64	26.97 ± 12.37	0.56
Volume of blood loss (milliliters)	203.51 ± 42.04	202.47 ± 35.39	0.795
Median onset of pain score	5 (5,7)*	5 (3,6)*	0.067+

* Median (Q1,Q3), + Mann-Whitney U test

There was no difference in the median onset of perineal pain scores which were 5 vs 5 (p = 0.067), respectively. The ibuprofen plus acetaminophen group was consistently better for perineal pain relief than the acetaminophen alone group at short-acting in 2 hours after treatment, the median of perineal relief pain scores was 3 vs 2 (p = 0.001), respectively. And at the long effect at 24 hours after treatment, the median of perineal relief pain scores was 5 vs 3 (p = 0.006), respectively (Table 2). The median severity of perineal pain at first and second hour after treatment of the treatment group (ibuprofen plus acetaminophen) dropped sharply compared with that of the control group (acetaminophen plus placebo) (Fig. 2).

There was one pregnant woman of the treatment group and three pregnant women of the control group who required for additional analgesia due to the increasing pain score within 24 hours.

Table 2. Median pain score and median different pain relief score.

Variables	Ibuprofen plus Acetaminophen (n = 185)		Acetaminophen (n = 191)		p value
	Pain score	median different pain relief score	Pain score	median different pain relief score	
Onset of pain score	5		5		0.067
at first hour	3	2 (0.5,3)	4	1 (0,2)	0.002
at 2rd hour	2	3 (1,5)	3	2 (1,3)	0.001
at 4th hour	1	4 (2,6)	1	3 (2,5)	0.004
at 6th hour	0	5 (3,6)	0	4 (2,5)	0.025
at 24th hour	0	5 (3,7)	0	4 (3,6)	0.006

Median (Q1, Q3)

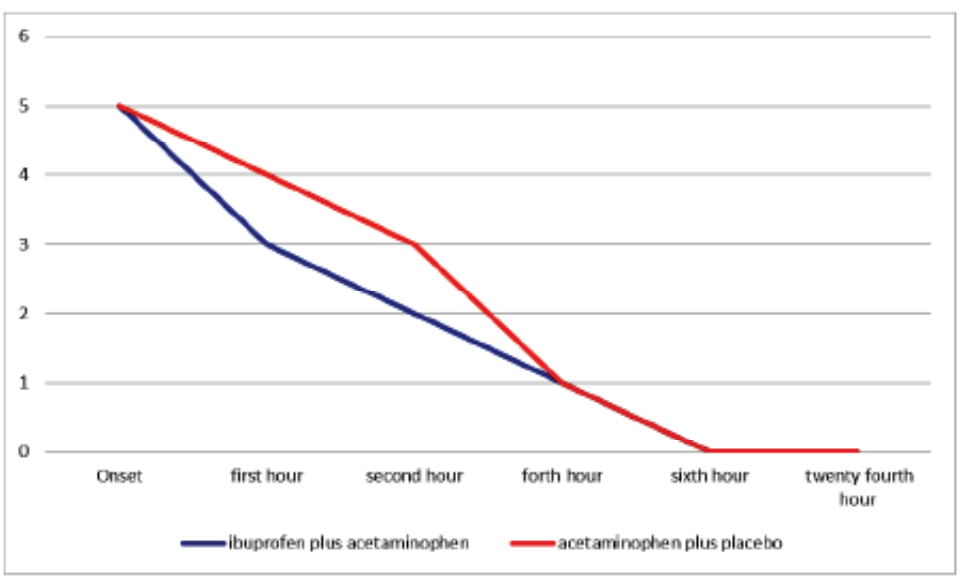

Fig. 2. Median pain intensity assessed using the visual analog scale.

Only one pregnant woman in the treatment group had a complication which was postpartum hemorrhage due to uterine atony. No adverse drug reaction was reported in both groups.

Discussion

This study was designed to test the hypothesis that concurrent administration of ibuprofen and acetaminophen results in greater analgesic efficacy than acetaminophen alone in the management of perineal pain.

The single dose combination of ibuprofen 400 mg and acetaminophen 1,000 mg provided significantly better analgesic efficacy than acetaminophen alone in short time. Significant perineal pain relief was faster in the first and second hour after treatment (Fig. 2). Both groups could control perineal pain in 24 hours, with only one pregnant woman in first group and three pregnant women of second group requiring additional analgesia. So, this difference was manifested by a more rapid onset of action and more prolonged duration of effect (Table 2). Additive or synergistic effects of combined therapy with ibuprofen and paracetamol have been shown by other authors in different diseases and conditions. Combination of ibuprofen and paracetamol provides better analgesia than paracetamol alone after postoperative pain[11, 12] or oral surgery[13, 14].

A recently published review indicated that ibuprofen plus paracetamol combinations provide better analgesia than either drug alone (at the same dose) in the treatment of postoperative pain, with a smaller chance of needing additional analgesia over about eight hours, and with a smaller chance of experiencing an adverse event[11]. The combination of acetaminophen and ibuprofen is superior to acetaminophen alone at 6 hours or acetaminophen and codeine at 4 hours in controlling postoperative pain after Mohs surgery and cutaneous reconstruction[12]. The study confirmed that the treatment group had more pain relief than the control group. But the pain-reduction effect of 6 and 8 hours was different from our research because of differentiation of evaluated pain in the study.

In 2010, randomized, double-blind, placebo-controlled, parallel-group, single-dose, 2-center modified factorial United States study about postoperative dental pain management resulted in concurrent ibuprofen and paracetamol appearing to provide significantly better analgesic efficacy compared with ibuprofen or paracetamol alone at all time intervals, and for the sum of pain relief and pain intensity differences from 4 to 6 hours (all, $p < 0.001$)[13]. In another study, the systematic review in participants after surgical removal of lower wisdom teeth, ibuprofen 400 mg was shown to be superior to 1,000 mg paracetamol with a risk ratio for at least 50% pain relief at 6 hours of 1.47 (95% confidence interval [CI] 1.28 to 1.69). For the combined drug, the risk ratio for at least 50% maximum pain relief over 6 hours was 1.77 (95% CI 1.32 to 2.39) based on total pain relief data[14].

It can be seen that the study of pain reduction in surgical patients results in the same. Although these studies were used in patients with moderate to severe pain, the difference was that these studies were not for a single dose of medication. Therefore, this study could not measure the long term effect of the study.

This study was not consistent with previous studies of pain in patients with soft tissue injury. For example, Hung KKC, et al's study of patients with mild to moderate pain after soft tissue injuries. After visiting the emergency department, there were no difference in analgesic effects or side effects observed after using oral paracetamol, ibuprofen, or a combination of both[15]. In addition, the study by Bondarsky EE, et al., showed that the combination of ibuprofen and acetaminophen did not reduce pain scores or the need for rescue analgesics compared with either agent alone, in emergency department patients with pain secondary to acute musculoskeletal injuries[16]. The differences in this study might be due to different populations. As a result, the mechanism of pain varies.

The strengths of the present study included the use of randomized, double-blind control trial; minimal number of patients who were excluded or dropped out of the study; several measures of pain intensity; and measurement of a variety of side effects. The available data on efficacy of combinations of ibuprofen and

acetaminophen in perineal pain is limited. The result of this study can be widely used because of the use and availability of an ordinary drug. Even though the study has shown that median difference of pain relief score of both groups is truly different by statistics, we can see that a slight difference in pain score would result in the same treatment which is reducing the pain within 24 hours. Therefore, there is no clinical difference significantly.

Limitations of the present study included the evaluation of side effect of neonatal breast feeding. Lidocaine is known to have an onset < 2 min and a duration of 1 to 2 hours[17]. The present study cannot control its dosage in this protocol, so this may affect perineal pain relief score at first and second hour.

Past studies, the results confirmed the same way with this study in combination of ibuprofen and paracetamol provided better analgesia than paracetamol alone after postoperative pain[11,12] or oral surgery[13,14] . And some results were different, that showed the combination of drug did not reduce pain scores after soft tissue injury[15] and patients with pain secondary to acute musculoskeletal injuries[16]. No comparative studies have been conducted with the same drug, included the same population with this study. If further studies are needed to confirm the efficacy of the drug, only moderate to severe pain, the combination of new NSAIDs or opioid for perineal pain relief, do not use local anesthesia to reduce the confounder that evaluation abount pain.

Conclusion

A regimen of single dose ibuprofen plus acetaminophen has higher efficacy for relief from acute perineal pain rather than a conventional regimen with acetaminophen alone, and is safe to use for pregnant women after childbirth.

Acknowledgment

The authors would like to thank Alisara Wongsuttilert, M.D., Faculty of Medicine, Burapha University, Thailand and Wanlop Jaidee, Ph.D., Faculty of Public Health, Burapha University, Thailand

Potential conflicts of interest

The authors declare no conflict of interest.

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Thai Journal of Obstetrics and Gynaecology
January 2020, Vol. 28, No. 1, pp. 34-43

OBSTETRICS

Prevalence of False Positive 50-g Glucose Challenge Test in Risk-based Screening Before 20 Weeks of Gestation and Relationship with Adverse Pregnancy Outcomes

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ABSTRACT

Objectives: To determine the prevalence of false positive results of 50-g glucose challenge test (GCT) in risk-based screening before 20 weeks of gestation and relationship with pregnancy outcomes.

Materials and Methods: A total of 500 singleton pregnancy who were at risk for gestational diabetes mellitus (GDM) and received 50-g GCT for GDM screening before 20 weeks of gestation were included. Women with abnormal 50-g GCT received 100-g OGTT for GDM diagnosis. Prevalence of false positive results of 50-g GCT and GDM were estimated. Various baseline characteristics and pregnancy outcomes were compared between groups.

Results: Mean age was 33.4 ± 4.9 years, mean Body mass index (BMI) was 22.9 ± 4.4 kg/m^2, and 45.6% were nulliparous. Common GDM risks were age ≥ 30 years (81.6%), family history of diabetes mellitus (DM) (30.4%), and overweight/obesity (24.6%). Mean gestational age at GDM screening was 9.8 ± 3.9 weeks. Normal 50-g GCT was found in 243 women (48.6%), 187 women (37.4%) had false positive GCT, and 70 women (14%) had GDM. Women with GDM had significantly higher age, BMI, and more likely to be overweight or obese than others ($p < 0.05$). Gestational weight gain was comparable between normal and false positive GCT but it was significantly greater than GDM ($p < 0.001$). A significant trend of increasing in the rate of large for gestational age (LGA) was observed in normal GCT, false positive GCT, and GDM group (14.4%, 21.9%, and 25.7%, respectively, $p = 0.013$). Logistic regression analysis showed that false-positive GCT and GDM independently increased the risk of LGA (adjusted odds ratio 1.76, 95% confidence interval 1.05-2.94, and 2.15, 95% confidence interval 1.1-4.23).

Conclusion: Prevalence of false positive GCT was 37.4%. False-positive GCT and GDM independently increased risk of LGA.

Keywords: false positive, gestational diabetes, glucose challenge test, large for gestational age.

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Received: 20 July 2018, **Revised:** 3 December 2018, **Accepted:** 6 December 2018

ความชุกของการเกิดผลบวกลวงจากการตรวจคัดกรองเบาหวานระหว่างตั้งครรภ์และความสัมพันธ์กับผลลัพธ์ที่ไม่ดีของการตั้งครรภ์

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บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาความชุกของผลบวกลวงจากการตรวจคัดกรองภาวะเบาหวานระหว่างตั้งครรภ์ในสตรีที่มีความเสี่ยง ด้วยวิธี 50-g glucose challenge test (GCT) ก่อนอายุครรภ์ 20 สัปดาห์ และความสัมพันธ์กับผลลัพธ์ที่ไม่ดีของการตั้งครรภ์*

วัสดุและวิธีการ: *ทำการศึกษาในสตรีตั้งครรภ์เดี่ยว จำนวน 500 คน ที่มีความเสี่ยงในการเกิดภาวะเบาหวานระหว่างตั้งครรภ์ และได้รับการตรวจคัดกรองด้วยวิธี 50-g GCT ก่อนอายุครรภ์ 20 สัปดาห์ หากผลการตรวจคัดกรองผิดปกติจะได้รับการตรวจวินิจฉัยภาวะเบาหวานด้วยวิธี 100-g oral glucose tolerance test (OGTT) ทำการวิเคราะห์หาความชุกของผลบวกลวงจากการตรวจคัดกรองภาวะเบาหวาน และความชุกของภาวะเบาหวานระหว่างตั้งครรภ์ ทำการเปรียบเทียบข้อมูลต่างๆ และผลลัพธ์ของการตั้งครรภ์ระหว่างกลุ่มที่ผลการตรวจคัดกรองปกติ กลุ่มที่เกิดผลบวกลวงจากการตรวจคัดกรอง และกลุ่มที่ได้รับการวินิจฉัยภาวะเบาหวานระหว่างตั้งครรภ์*

ผลการศึกษา: *อายุเฉลี่ยของสตรีตั้งครรภ์เท่ากับ 33.4 ± 4.9 ปี ค่าเฉลี่ยดัชนีมวลกายเท่ากับ 22.9 ± 4.4 กิโลกรัม/ตารางเมตร ร้อยละ 45.6 เป็นการตั้งครรภ์แรก ปัจจัยเสี่ยงต่อภาวะเบาหวานระหว่างตั้งครรภ์ที่พบบ่อยได้แก่ อายุ 30 ปีขึ้นไป (ร้อยละ 81.6), มีประวัติโรคเบาหวานในครอบครัว (ร้อยละ 30.4), น้ำหนักเกินหรือมีภาวะอ้วน (ร้อยละ 24.6) อายุครรภ์เฉลี่ยที่ได้รับการตรวจคัดกรองคือ 9.8 ± 3.9 สัปดาห์ พบว่าการตรวจคัดกรองได้ผลปกติ 243 ราย (ร้อยละ 48.6) ผลบวกลวง 187 ราย (ร้อยละ 37.4) และ 70 ราย (ร้อยละ 14) ได้รับการวินิจฉัยว่ามีภาวะเบาหวานระหว่างตั้งครรภ์ พบว่าหญิงตั้งครรภ์ที่มีภาวะเบาหวานระหว่างตั้งครรภ์จะมีอายุ ดัชนีมวลกาย และมีภาวะน้ำหนักเกินหรืออ้วน สูงกว่ากลุ่มอื่นอย่างมีนัยสำคัญ ($p < 0.05$) กลุ่มที่ผลการตรวจคัดกรองปกติและกลุ่มที่ตรวจพบผลบวกลวงมีน้ำหนักที่เพิ่มขึ้นระหว่างตั้งครรภ์สูงกว่ากลุ่มที่มีภาวะเบาหวานระหว่างตั้งครรภ์อย่างมีนัยสำคัญ ($p < 0.001$) พบอัตราการเกิดทารกน้ำหนักเกินเกณฑ์ มีแนวโน้มสูงขึ้นอย่างมีนัยสำคัญ ในกลุ่มที่ผลการตรวจคัดกรองปกติ กลุ่มผลบวกลวง และกลุ่มที่มีภาวะเบาหวานระหว่างตั้งครรภ์ (ร้อยละ 14.4, 21.9, 25.7, ตามลำดับ, $p = 0.013$) จากการวิเคราะห์แบบ logistic regression analysis พบว่ากลุ่มผลบวกลวงและกลุ่มที่มีภาวะเบาหวาน เพิ่มความเสี่ยงต่อการเกิดทารกน้ำหนักเกินเกณฑ์อย่างมีนัยสำคัญ (adjusted odds ratio 1.76, 95% confidence interval 1.05-2.94, และ 2.15, 95% confidence interval 1.1-4.23 ตามลำดับ)*

สรุป: *ความชุกของผลบวกลวงจากการตรวจคัดกรองภาวะเบาหวานระหว่างตั้งครรภ์เท่ากับร้อยละ 37.4 โดยกลุ่มผลบวกลวงและกลุ่มที่มีภาวะเบาหวานระหว่างตั้งครรภ์ เพิ่มความเสี่ยงต่อการเกิดทารกน้ำหนักเกินเกณฑ์อย่างมีนัยสำคัญ*

คำสำคัญ: *ผลบวกลวง, ภาวะเบาหวานระหว่างตั้งครรภ์, 50-g glucose challenge test, ทารกน้ำหนักเกินเกณฑ์*

Introduction

Gestational diabetes mellitus (GDM), defined as carbohydrate intolerance that is first recognized during pregnancy, is one of the most common medical complications of pregnancy. GDM increases the risk of various maternal and neonatal complications, including preeclampsia, macrosomia, operative delivery, shoulder dystocia, and birth trauma, and also increases the risk of the baby developing diabetes later in life[1, 2].

Although there is still no global consensus regarding GDM screening and diagnostic strategy, a 2-step approach is currently recommended[1, 2]. A 50-g glucose challenge test (GCT) is used as a screening test, and individuals meeting or exceeding the screening threshold then undergo a 100-g oral glucose tolerance test (OGTT) for GDM diagnosis. Screening is generally performed at 24-28 weeks of gestation, but early screening is suggested in high-risk women. Repeat screening is recommended at 24-28 weeks of gestation if the result of early testing is negative.

Women with abnormal GCT but normal OGTT (false-positive GCT) can be considered as an early form of glucose intolerance that similar adverse outcomes to GDM could develop. Current standard of care is to treat only those who are diagnosed with GDM. However, there is growing evidence to suggest that mild maternal hyperglycemia in the absence of GDM is associated with adverse perinatal outcome. Previous studies have reported that women with false positive GCT were at increased risk of various adverse pregnancy outcomes, including large for gestational age (LGA), macrosomia, shoulder dystocia, cesarean delivery[3-7], but conflicting results have also been reported[8-10].

Although a clinical practice guideline for GDM has been developed and implemented in our institution since 2000, the information on pregnant women with false positive GCT are limited. Therefore, the primary objective of this study was to determine the prevalence of false positive GCT results in risk-based screening before 20 weeks of gestation. The secondary objectives were to evaluate associations between different 50-g GCT results and various characteristics and adverse pregnancy outcomes. Understanding the characteristics of this specific group of women and its association with adverse pregnancy outcomes will help in care improvement as well as developing appropriate strategies to prevent possible associated adverse outcomes.

Materials and Methods

After approval from Siriraj Institutional Review Board, this cross-sectional study was conducted at the Department of Obstetrics and Gynaecology, Siriraj Hospital, which is Thailand's largest tertiary care university hospital. According to the institutional clinical practice guideline[11], GDM screening and diagnosis is offered to all at-risk women. Risk factors for GDM include age ≥ 30 years, pre-pregnancy body mass index (BMI) ≥ 25 kg/m^2, family history of diabetes, presence of hypertension, previous GDM, and history of fetal macrosomia, stillbirth, or fetal anomaly. A 50-g GCT with a cut-off value of ≥ 140mg/dL is used for GDM screening. For patients who meet or exceed the cut-off, a 100-g OGTT is used to diagnose the GDM using the criteria of Carpenter and Coustan. These procedures are offered during the patient's first visit, and they are then repeated at 24-28 weeks of gestation if the first screening result was normal. Sample size was estimated from an estimated prevalence of false positive GCT of 20%. At 95% significance level and 4% allowable error, at least 462 cases were required including 20% loss.

This was a cross-sectional study to

determine the prevalence of false positive GCT results in risk-based screening before 20 weeks of gestation. Data were collected retrospectively from medical record review of 500 at-risk women who started antenatal care before 20 weeks of gestation according to the described screening and diagnostic procedures were included by simple random sampling of women attended antenatal care clinic during January to June 2017. Women with pre-gestational diabetes, multifetal pregnancy, fetal anomaly, intrauterine fetal death, or did not received GDM screening according to institutional guideline were excluded. Women who were diagnosed with GDM from repeat testing were also not included. Data were obtained from medical records, including baseline clinical characteristics, obstetrics data, GDM risk factors, results of 50-g GCT and 100-g OGTT, delivery data, and pregnancy outcomes. Pre-pregnancy BMI status and gestational weight gain (GWG) were categorized according to Institute of Medicine (IOM) recommendation[12]. As part of routine services, all at-risk women received counseling regarding dietary and lifestyle modification during their antenatal care by attending nurses. Further intensive counseling was provided if the women were diagnosed with GDM.

Data on pregnancy outcomes related to GDM included gestational age at delivery, route of delivery, complications during pregnancy, birth weight, and birth asphyxia. Infant birth weight was categorized according to gestational age to LGA and small for gestational age (SGA) if birth weight was ≥ 90^{th} or < 10^{th} percentile for normal newborns, according to standard reference data. Macrosomia was defined as infant birth weight ≥ 4,000 g.

Pregnant women were categorized according to 50-g GCT and 100-g OGTT results in to normal GCT, false positive GCT, and GDM groups. Prevalence of false positive GCT and GDM were estimated. Characteristics and pregnancy outcomes were compared among the 3 groups to evaluate their relationship with different 50-g GCT results.

All data analyses were performed using SPSS Statistics version 21 (SPSS, Inc., Chicago, IL, USA). Data were presented as number and percentage for categorical variables, and mean and standard deviation for continuous variables. Analysis of variance (ANOVA) with Bonferroni post hoc test and chi square test were used to compare variables between groups as appropriate. Logistic regression analysis was used to evaluate independent association between GCT results and adverse outcomes. A p value of < 0.05 was considered to be statistically significant.

Results

A total of 500 women who underwent 50-g GCT for GDM screening before 20 weeks of pregnancy were included. All received GDM screening according to institutional guideline. Table 1 shows baseline characteristics of the women. Mean age was 32.4 years and 45.6% were nulliparous. While majority of the women have BMI in normal range (62.8%), 17.4% and 7.2% were overweight and obese, respectively. Common GDM risks were age > 30 years (81.6%), family history of DM (30.4%), and BMI ≥ 25 kg/m^2 (24.6%). Majority of the women had only 1 risk (64.6%) while 6.6% had at least 3 risks.

GDM screening characteristics and results are shown in Table 2. Mean gestational age (GA) at screening was 9.8 weeks and mean 50-g GCT was 144.2 mg/dL. Of 500 women screened, 48.6% had normal 50-g GCT and GDM was diagnosed by 100-g OGTT in 14%. False positive 50-g GCT, i.e., positive 50-g GCT with normal 100-g OGTT, was found in 37.4%. Among 70 GDM cases, insulin was required in 8 women (11.4%).

Table 1. Baseline characteristics of pregnant women (N = 500).

Characteristics	Mean ± SD
Mean age ± SD (years)	32.4 ± 4.9
Mean pre-pregnancy BMI ± SD (kg/m^2)	22.9 ± 4.4
	N (%)
Nulliparous	228 (45.6%)
Pre-pregnancy BMI category	
Underweight	63 (12.6%)
Normal weight	314 (62.8%)
Overweight	87 (17.4%)
Obesity	36 (7.2%)
GDM risks	
Age ≥ 30 years	408 (81.6%)
Family history of diabetes	152 (30.4%)
Pre-pregnancy BMI ≥ 25 kg/m^2	123 (24.6%)
Previous GDM	11 (2.2%)
Previous macrosomia	2 (0.4%)
Previous stillbirth	8 (1.6%)
Previous fetal anomaly	4 (0.8%)
Hypertension	8 (1.6%)
Number of GDM risks	
1 risk	323 (64.6%)
2 risks	144 (28.8%)
≥ 3 risks	33 (6.6%)

SD: standard deviation, BMI: body mass index, GDM: gestational diabetes mellitus

Table 2. GDM screening characteristics and results (N = 500).

Characteristics	Mean ± SD
Mean GA at GDM screening ± SD (weeks)	9.8 ± 3.9
Mean 50-g GCT ± SD (mg/dL)	144.2 ± 35.3
	N (%)
GDM screening results	
Normal 50-g GCT	243 (48.6%)
False positive (normal 100-g OGTT)	187 (37.4%)
GDM	70 (14%)
Insulin requirement (N = 70)	8 (11.4%)

GDM: gestational diabetes mellitus, GA: gestational age, SD: standard deviation, GCT: glucose challenge test, OGTT: oral glucose tolerance test

Table 3 shows comparison of maternal characteristics between different 50-g GCT results. Women in false positive GCT and GDM groups were significantly older than normal GCT group. GDM women were significantly more likely to have ≥ 3 GDM risks compared to the other 2 groups (p = 0.002). Women with GDM had significantly higher BMI than the other 2 groups and they were significantly more likely to be overweight and obese. However, compared to those with normal GCT, false positive GCT and GDM groups had significantly lower gestational weight gain (14.5 vs. 13.3 vs. 11.6 kg, respectively, p < 0.001). GDM women were significantly more likely to gain weight less than recommendation (34.3%) while women with normal GCT were significantly more likely to gain weight greater than recommendation (39.1%) (p = 0.03).

Table 3. Comparison of maternal characteristics between different GDM screening results.

Characteristics	Normal GCT N = 243	False positive GCT N = 187	GDM N = 70	p value[a]
Mean age ± SD (years)	31.6 ± 5.1[c]	33.4 ± 4.5	32.6 ± 5.3	0.001[b]
Mean pre-pregnancy BMI ± SD (kg/m^2)	22.5 ± 4.5	22.8 ± 4.3	24.7 ± 4.4[d]	0.001[b]
Nulliparous (%)	124 (51.0%)	74 (39.6%)	30 (42.9%)	0.05
GDM risks				
Age ≥ 30 years	193 (79.4%)	163 (87.2%)	52 (74.3%)	0.02
Family history of diabetes	68 (28.0%)	60 (32.1%)	24 (34.3%)	0.49
Previous GDM	2 (0.8%)	3 (1.6%)	6 (8.6%)	< 0.001
Number of GDM risks				0.002
1 risk	173 (71.2%)	113 (60.4%)	37 (52.8%)	
2 risks	60 (24.7%)	62 (33.2%)	22 (31.4%)	
≥ 3 risks	10 (4.1%)	12 (6.4%	11 (15.7%)	
Pre-pregnancy BMI category				
Underweight	36 (14.8%)	24 (12.8%)	3 (4.3%)	
Normal weight	153 (63.0%)	121 (64.7%)	40 (57.1%)	
Overweight	40 (16.5%)	31 (16.6%)	16 (22.9%)	
Obesity	14 (5.8%)	11 (5.9%)	11 (15.7%)	
Mean GWG ± SD (kg)	14.5 ± 4.6	13.3 ± 4.7	11.6 ± 4.8	< 0.001[e]
GWG category				0.03
Less than recommendation	48 (19.8%)	52 (27.8%)	24 (34.3%)	
Adequate	100 (41.2%)	82 (43.9%)	27 (38.6%)	
Greater than recommendation	95 (39.1%)	53 (28.3%)	19 (27.1%)	

[a] Chi square test, b ANOVA, [c] Significantly lower than the other 2 groups, p = 0.001,
[d] Significantly higher than normal (p = 0.001) and false positive groups (p = 0.006).
[e] All groups were significantly different: normal vs. false positive, p = 0.034; normal vs. GDM, p < 0.001; false positive vs. GDM, p = 0.028, GDM: gestational diabetes mellitus, GCT: glucose challenge test, SD: standard deviation, BMI: body mass index, GWG: gestational weight gain

Table 4 shows comparison of pregnancy outcomes between different groups of 50-g GCT results. GA at delivery, route of delivery, birth weight, rate of pregnancy induced hypertension (PIH), SGA, birth asphyxia, and neonatal intensive care unit (NICU) admission were comparable between the 3 groups. A significant increasing trend was observed in the rate of LGA: 14.4% in normal GCT, 21.9% in false positive GCT, and 25.7% in GDM groups (p = 0.013). Significant increase in macrosomia in GDM women was also observed (p = 0.03). Neonatal hypoglycemia occurred in only among women with GDM in 32.8%.

Table 4. Comparison of pregnancy outcomes between different GDM screening results.

Characteristics	Normal GCT N = 243	False positive GCT N = 187	GDM N = 70	p value[a]
GA at delivery ± SD (weeks)	38.2 ± 1.4	38.3 ± 4.4	37.7 ± 1.8	0.33[b]
Birth weight ± SD (g)	3054.1 ± 445.5	3019.1 ± 498.2	3104.4 ± 526.8	0.42[b]
PIH	18 (7.4%)	10 (5.3%)	3 (4.3%)	0.52
Route of delivery				
Vaginal delivery	102 (42%)	83 (44.4%)	27 (38.6%)	0.59
Primary C/S	88 (36.2%)	65 (34.8%)	22 (31.4%)	
Repeat C/S	53 (21.8%)	39 (20.9%)	21 (30.0%)	
SGA	17 (7.0%)	23 (12.3%)	4 (5.7%)	0.09
LGA	35 (14.4%)	41 (21.9%)	18 (25.7%)	0.04[c]
Macrosomia	5 (2.1%)	0 (0.0%)	3 (4.3%)	0.03
Neonatal hypoglycemia	0 (0%)	0 (0%)	23 (32.8%)	< 0.001
Apgar < 7				
1 minute	12 (4.9%)	6 (3.2%)	5 (7.1%)	0.38
5 minute	1 (0.4%)	0 (0.0%)	1 (1.4%)	0.27
NICU admission	4 (1.6%)	4 (2.1%)	3 (4.3%)	0.41

[a] Chi square test, b ANOVA, [c] Chi square for trend = 6.22, p = 0.013

GDM: gestational diabetes mellitus, GCT: glucose challenge test, GA: gestational age, SD: standard deviation, PIH: pregnancy induced hypertension, C/S: cesarean section, SGA: small for gestational age, LGA large for gestational age, NICU: neonatal intensive care unit

Table 5 shows the results pf logistic regression analysis to determine independent associated factors for LGA. After adjusting for potential confounders, factors independently increased the risk of LGA were false positive GCT and GDM independently increased the risk of LGA (adjusted odds ratio (ORs) 1.76, 95% confidence interval (CI) 1.05-2.94, and 2.15, 95%CI 1.1-4.23). On the other hand, factors that significantly decreased the risk of LGA were pre-pregnancy underweight (adjusted ORs 0.35, 95%CI 0.13-0.92), and gestational weight gain less than recommendation (adjusted ORs 0.34, 95%CI 0.17-0.68).

Table 5. Logistic regression analysis to determine independent associated factors for LGA.

Characteristics	Adjusted OR	95% CI	p value
GDM screening results			
Normal GCT	1.0		
False-positive GCT	1.76	1.05-2.94	0.032
GDM	2.15	1.1-4.23	0.026
Pre-pregnancy BMI			
Normal	1.0		
Underweight	0.35	0.13-0.92	0.034
Overweight/obese	1.11	0.64-1.91	0.716
Gestational weight gain category			
Within recommendation	1.0		
Less than recommendation	0.34	0.17-0.68	0.002
Greater than recommendation	0.97	0.58-1.64	0.914

Adjusted for age, parity, and family history of DM.
LGA large for gestational age, ORs: odds ratio, GDM: gestational diabetes mellitus, GCT: glucose challenge test, BMI: body mass index, DM: diabetes mellitus.

Discussion

Some evidence suggested that mild maternal hyperglycemia in the absence of GDM could be associated with adverse perinatal outcomes, including LGA, macrosomia, shoulder dystocia, cesarean delivery[3-7]. A false positive GCT can be considered as an early form of glucose intolerance that adverse outcomes related to GDM could develop, as reported from previous studies, including LGA, macrosomia, shoulder dystocia, cesarean delivery[3-7].

The results of this study showed that prevalence of false positive GCT was 37.4%. This was relatively high compared to previous reported rate between 8.8% to 34.4%[4-7, 9, 10]. The differences might be from variations in screening and diagnostic protocols, including the cut off level of 50-g GCT[4, 5, 7, 10] and criteria for GDM diagnosis[5, 6, 10]. Similar to other studies, women with false positive GCT and GDM were more likely to be older and multiparous[3, 4, 6-8]. However, while some studies also reported higher pre-pregnancy BMI and GWG among women with false positive GCT[3, 4, 8], the results of this study showed that only women with GDM had significantly higher pre-pregnancy BMI than the other 2 groups.

Interestingly, in terms of GWG, significantly less weight gain was observed in both women with false positive GCT and GDM compared to those with normal GCT. Women with false positive GCT and GDM were more likely to gain weight less than recommendation. This is probably due to the effect of dietary counseling and weight gain monitoring among these groups of women. Currently, as a part of routine care, dietary counseling and weight gain control advice are given to women with false positive GCT in a more intensive fashion than those with normal GCT. In addition, these women might have some concerns and awareness regarding the abnormal results and the possibility of developing GDM and related pregnancy complications that they follow the dietary and weight gain control advice more strictly during their antenatal care.

Some previous studies demonstrated and increased in the risk of various adverse outcomes among women with false positive GCT, including LGA, macrosomia, shoulder dystocia, and cesarean delivery[4-7, 13]. On the other hand, indifferences in adverse pregnancy outcomes between normal and false positive GCT had also been reported from some studies[8-10]. Conflicting results were possibly partly

due to different in population characteristics, GDM risks, and thresholds used for the GCT and different diagnostic criteria for GDM[3-8, 10, 13].

In this study, while most of adverse pregnancy outcomes were comparable among the 3 groups, a significant increasing trend in LGA was observed with increasing degree of GCT abnormalities (14.4% in normal GCT, 21.9% in false positive GCT, and 25.7% in GDM group, p = 0.013). A previous study has reported an increase in adverse outcomes along with the greater degree of GCT abnormality, including preeclampsia, birth weight, LGA, cesarean delivery, and shoulder dystocia[6]. It should also be noted that the rate of LGA in women with normal GCT and false positive GCT were relatively higher than 10.5% reported among low-risk pregnant women from the same institution[14], which might reflects that this group of women are still at some risk for abnormal fetal growth. As there are different screening and diagnostic strategies for GDM, i.e., universal vs. selective screening and one-step vs. 2-step approach, there is still no consensus which is the most appropriate strategy. A recent Cochrane systematic review showed no clear evidence which strategy is best for diagnosing GDM[15]. Alternative to the current 2-step approach used in our institution, the use of The International Association of the Diabetes and Pregnancy Study Groups (IADPSG) strategy could possibly increase the diagnosis of GDM to some degree. Although there was a report that GDM diagnosed by IADPSG criteria might have more adverse pregnancy outcomes than women with normal glucose tolerance[16], the American College of Obstetricians and Gynecologists stated that the additional women in whom GDM would be diagnosed by IADPSG criteria may be at a lower risk of adverse outcomes than and may not derive similar benefits from diagnosis and treatment as women in whom GDM was diagnosed by traditional criteria[1]. However, the use of selective screening based on risk factors might miss some GDM women among those without any risk compared to universal screening strategy. Further studies are needed to verify if universal screening would provide additional benefits that is also cost-effective.

After adjusting for potential confounders, false positive GCT and GDM independently increased the risk of LGA (adjusted ORs 1.76, 95%CI 1.05-2.94, and 2.15, 95%CI 1.1-4.23). On the other hand, factors that significantly decreased the risk of LGA were pre-pregnancy underweight (adjusted ORs 0.35, 95%CI 0.13-0.92), and GWG less than recommendation (adjusted ORs 0.34, 95%CI 0.17-0.68). The results are in concordance with other studies that reported both pre-pregnancy BMI and GWG were important determinants of decreasing risk of LGA[14, 17-19].

Some limitations of this study need to be mentioned. As stated earlier, due to a wide variation in GDM screening, diagnostic protocol and criteria, in addition with possible differences in population characteristics related to GDM, generalization of the results of this study might be limited. Moreover, the actual effects of dietary counseling and advice about weight gain control during antenatal care that were routinely provided to all at-risk pregnant women could not be measured. There were also limited samples in subgroup analysis. Larger studies in specific subgroups is needed to validate the results.

In the application of the results into clinical practice, these at-risk women should be informed regarding the risk of GDM-related adverse outcomes, including LGA, even in the absence of GDM. Since GWG is modifiable, appropriate behavioral and dietary intervention for at-risk women, especially those with false positive GCT, could help in better weight gain control that could lower the risk of LGA. These women should be informed about this important issue and awareness of weight gain control should be raised. In addition, close monitoring of weight gain and fetal growth surveillance among these women should be encouraged among caring physicians.

Although no current recommendation for any intervention or treatment among women with false positive GCT, a previous study has demonstrated that the treatment of women with abnormal GCT results improved outcomes by reducing both birth weight and the cesarean deliveries[20]. Further studies with more widely generalizable are needed to elucidate the relationship between 50-g GCT and adverse outcomes

and also to investigate the benefits of specific intervention to prevent or minimize the risk of such adverse pregnancy outcomes.

Conclusion

In conclusion, prevalence of false positive GCT was 37.4% among women who were at-risk for GDM. A significant increasing trend in LGA was observed with increasing degree of GCT abnormalities. False positive GCT and GDM independently increased the risk of LGA, while pre-pregnancy underweight and GWG less than recommendation independently reduced the risk of LGA.

Acknowledgements

The authors gratefully acknowledge Miss Maria Asad-dehghan for assistance with data collection procedure.

Potential conflicts of interest

The authors declare no conflict of interest.

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Thai Journal of Obstetrics and Gynaecology
January 2020, Vol. 28, No. 1, pp. 44-51

OBSTETRICS

The Association between Anterior Uterocervical Angle and Pregnancy between 16-24 Weeks of Gestation

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ABSTRACT

Objectives: To determine the association between gestational age and anterior uterocervical angles measured between 16 and 24 weeks of pregnancy.

Materials and Methods: A descriptive cross-sectional study was conducted among pregnant women at gestational age between 16-24 weeks, specifically in those who had access to the antenatal care clinic at Rajavithi hospital, Bangkok, Thailand, between July 2017 and March 2018. The women underwent anterior uterocervical angle measurements by means of transvaginal ultrasonography, which was performed by a well-trained sonographer. A correlation and regression analysis between the anterior uterocervical angles and the gestational weeks were carried out, while a predictive nomogram of the anterior uterocervical angle was developed for potential cases of angle changes associated with advancing gestational age.

Results: A total of 249 pregnancies (at least 15 measurements per week of gestation) were included in the study. The anterior uterocervical angle was not significantly associated with gestational age at 16 0/7 – 24 6/7 weeks (Pearson's correlation, $r = 0.038$, $p = 0.553$). From the linear regression analysis, the parity was the significant factor associated with anterior uterocervical angle ($p < 0.001$). The mean ± standard deviation of anterior uterocervical angles were 96.1 ± 21.5 degrees and 108.9 + 20.0 degrees in the nulliparity and the multiparity groups, respectively.

Conclusion: The anterior uterocervical angle at 16-24 weeks was found to be independent of the gestational age. However, it was still significantly related to the parity.

Keywords: uterocervical angle, gestational age, preterm birth.

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Received: 19 September 2018, **Revised:** 22 November 2018, **Accepted:** 12 December 2018

ความสัมพันธ์ของมุมระหว่างปากมดลูกกับมดลูก กับอายุครรภ์ ในสตรีตั้งครรภ์ช่วงอายุครรภ์ 16-24 สัปดาห์

ตฤณญา ไชยวงศา, จิตติมา รุจิเวชพงศธร

บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาความสัมพันธ์ของมุมระหว่างปากมดลูกกับมดลูกในสตรีตั้งครรภ์ อายุครรภ์ระหว่าง 16 - 24 สัปดาห์*

วัสดุและวิธีการ: *เป็นการศึกษาวิจัยเชิงพรรณนา ภาคตัดขวาง ทำการศึกษาในสตรีตั้งครรภ์ อายุครรภ์ระหว่าง 16 -24 สัปดาห์ ที่มารับการตรวจที่คลินิกฝากครรภ์ โรงพยาบาลราชวิถี ระหว่างเดือนกรกฎาคม พ.ศ. 2560 ถึง มีนาคม พ.ศ. 2561 ทำการวัดมุมระหว่างปากมดลูกและมดลูกโดยผู้เชี่ยวชาญด้านคลื่นเสียงความถี่สูง โดยใช้เครื่องตรวจคลื่นเสียงความถี่สูงตรวจผ่านทางช่องคลอด และทำการวิเคราะห์ข้อมูลหาความสัมพันธ์ของมุมระหว่างปากมดลูกกับมดลูก และอายุครรภ์*

ผลการวิจัย: *สตรีตั้งครรภ์ที่เข้าร่วมงานวิจัยทั้งหมด 249 คน ซึ่งมีสตรีตั้งครรภ์แต่ละช่วงอายุครรภ์อย่างน้อย 15 คน ผลงานวิจัยพบว่ามุมระหว่างปากมดลูกกับมดลูก ไม่มีความสัมพันธ์กับอายุครรภ์ที่เพิ่มขึ้นในช่วงอายุครรภ์ 16 0/7-24 6/7 สัปดาห์ (Pearson's correlation, r = 0.038, p = 0.553) และจากการวิเคราะห์แบบ linear regression พบว่าปัจจัยเดียวที่มีผลต่อมุมระหว่างปากมดลูกกับมดลูก คือ จำนวนการตั้งครรภ์ โดยพบว่าสตรีตั้งครรภ์หลังมีมุมระหว่างปากมดลูกกับมดลูกกว้างกว่าสตรีตั้งครรภ์แรกอย่างมีนัยสำคัญทางสถิติ (p < 0.001) ค่าเฉลี่ยของมุมระหว่างปากมดลูกกับมดลูก ± ส่วนเบี่ยงเบนมาตรฐาน ในสตรีตั้งครรภ์แรก และสตรีตั้งครรภ์หลัง คือ 96.1 ± 21.5 องศา และ108.9 ± 20.0 องศา ตามลำดับ*

สรุป: *มุมระหว่างปากมดลูกและมดลูกไม่สัมพันธ์กับอายุครรภ์ที่เพิ่มขึ้นในช่วงอายุครรภ์ 16-24 สัปดาห์ แต่พบว่ามุมระหว่างปากมดลูกและมดลูกมีความแตกต่างกันในสตรีตั้งครรภ์แรกและครรภ์หลัง*

คำสำคัญ: *มุมระหว่างปากมดลูกกับมดลูก, อายุครรภ์, การคลอดก่อนกำหนด*

Introduction

Preterm birth, which is defined as any birth before the completion of the 37 weeks of gestation, is one of the leading causes of perinatal and neonatal morbidity and mortality worldwide[1]. Accordingly, several attempts have been made from healthcare professionals around the world to determine the effective methods for early prediction and prevention of preterm birth; for examples include, risk categorization based on previous history of preterm birth, and the use of biochemical markers such as fetal fibronectin and short cervical length as common screening tools[2, 3]. The pregnancies that are associated with high risk of preterm birth can receive great benefit from certain preventative methods such as progesterone administration (both intramuscular injection and vaginal progesterone)[4], cervical pessary[5, 6] and cervical cerclage[7].

During pregnancy, there are many detectable anatomical changes that occur such as the increase in uterine size, fetal growth, the descent of amniotic sac, and the changes in tissue intrinsic factors. These changes are also associated with cervical softening, cervical shortening, cervical volume, and the uterocervical angle[8, 9]. Some anatomical changes may be predictive of spontaneous preterm birth. For example, Arabin et al demonstrated that preterm births can be prevented in cases of cervical insufficiency through the use of Arabin pessary. They suggested that the use of the pessary changes the inclination of the cervical canal, which can lead to a more acute uterocervical angle, thus decreasing direct pressure on internal os[10]. Accordingly, the assessment of the uterocervical angle may be predictive of preterm birth.

Currently, the transvaginal ultrasound between 16-24 weeks of gestation, which has led to the assessment of short cervical length, has been demonstrated to be a good predictor of preterm birth[11]. Its detection rate of possible spontaneous preterm birth before the completion of 34 weeks was 20-60%, depending on the design of each study[2, 11, 12]. Analogous to cervical length, other anatomical parameters such as the uterocervical angle may also be useful as a potential determination factor in the development of new predictive tools for spontaneous preterm birth. Recently, the anterior uterocervical angle (AUCA) has been introduced as a new parameter in the prediction of preterm birth. Sochacki-Wójcicka et al conducted a retrospective study to evaluate AUCA in women who spontaneously delivered preterm, and demonstrated that the risk of preterm delivery before 34 weeks increased with more obtuse AUCA[13]. These results were the same as those from a study by Dziadosz et al[14]. However, for clinical or research use of AUCA in predicting preterm birth, normal reference ranges of AUCA for each gestational week must first be created. Therefore, we conducted this study with the aim of determining the association between AUCA and gestational age, and to construct reliable reference ranges of AUCA as a function of gestational age, for cases of gestational age dependency.

Materials and Methods

This prospective descriptive cross-sectional study was conducted on Asian singleton pregnancies at gestational age between 16 0/7 and 24 6/7 weeks. This study was approved by the Ethics Committee of Rajavithi Hospital, Bangkok, Thailand. Pregnant women with access to the antenatal care clinic at the Department of Obstetrics and Gynecology, Rajavithi Hospital, Bangkok, Thailand, between July 1, 2017 and March 31, 2018 were recruited into the study with informed consent. The inclusion criteria were: 1) singleton pregnancy between 16 0/7 and 24 6/7 weeks of gestation; 2) accurate gestational age based on a reliable last menstrual period, along with a fetal biometry in the first half of pregnancy; and 3) low-risk pregnancies without any serious medical problems.

Women with history of spontaneous preterm birth, progesterone use, fetal anomalies, maternal medical complications such as diabetes mellitus and hypertension, history of cervical cerclage or cervical surgery, history of cervical cancer, abnormal vaginal bleeding, uterine structure abnormalities, infection or inflammation of the vagina or cervix, preterm delivery in the current pregnancy and loss to follow-up were all excluded from the study.

The AUCA is the angle between the cervix and the anterior lower uterine segment, which can be measured by transvaginal ultrasound. All ultrasound examinations were performed by the same well-trained sonographer to avoid interobserver variability, using Voluson S8 (GE ultrasound medical system) with a transvaginal 4-10 MHz transducer. The patients needed to completely empty their bladder before examination. The transvaginal probe was gently inserted into the anterior vaginal fornix. The image of the cervix was obtained at a midsagittal plane. The three best images per patient were selected and measured for AUCA. The AUCA was defined by the intersection of two lines, where the first line was drawn from the internal os to the external os, and the second line was drawn parallel to the anterior of the lower uterine segment crossing the internal os. The mean AUCA of the three best images of each woman was calculated and used for analysis. All women were followed-up until delivery. The perinatal outcomes were assessed for birth weight and gestational age at delivery. All data were collected and computerized for storage.

The appropriate sample size was determined using a formula for estimating an infinite population mass. The two-tail alpha-value was 0.05 ($Z\alpha$ /2= 1.96), the standard deviation (SD) was 26, which was applied from a study by Dziadosz et al[14], while the margin of error (D) was 3.5. At least 208 participants were included in the study; however, a final of 250 participants were required based on the 20% unexpected drop out.

The statistical analysis was performed using IBM SPSS version 21.0 (IBM SPSS Statistics for Windows, Release 2011. Armonk, NY: IBM Corp). The maternal baseline characteristics were reported using statistical mean, standard deviation and various percentages as appropriate. A regression analysis with Pearson's correlation was performed to determine the correlation between AUCA and gestational age. From the measurements, a p value < 0.05 was considered as statistically significant. In case a significant correlation was found, normal reference ranges of AUCA for each gestational week would be constructed.

Results

A total of 271 pregnant women were eligible during the study period. Twenty-two cases were excluded from the study because of loss of follow-up. Therefore, 249 uncomplicated singleton pregnant women were finally available for analysis. All of them met the criteria and attended antenatal care clinic at Rajavithi Hospital, between July 1, 2017 and March 31, 2018.

Of these 249 pregnant women, the mean (±SD) maternal age was 28.2±6.8 years, and the mean (±SD) BMI was 22.6±4.2 kg/m^2. About half of the participants were nulliparous (51.0%). Most of the babies were born by vaginal delivery (71.1%). The mean (±SD) gestational age at delivery was 38.7±1.2 weeks and the mean birth weight (±SD) was 3,098.4±386.7 g (Table 1).

The AUCA was measured at gestational period between 16 0/7 through 24 6/7 weeks, with at least 15 measurements per week. The mean AUCA of all pregnant women (±SD) was 102.3±21.7, while the mean AUCA for each gestational age is shown in Table 2. The intraobserver reliability score was calculated, and the intraclass correlation co-efficiency was 0.9 (95% CI, 0.91-0.94; p < 0.001). The association between AUCA and gestational age, based on regression analysis and Pearson's correlation, showed no statistical significance (r = 0.038, p = 0.553).

Table 1. The maternal baseline characteristics and the perinatal outcome.

Baseline characteristics	n = 249 (100%)
Age (years), mean ± SD	28.2 ± 6.8
BMI (kg/m^2), mean ± SD	22.6 ± 4.2
Nationality n (%)	
Thai	187 (75.1%)
Myanmar	41 (16.5%)
Cambodian	12 (4.8%)
Laos	9 (3.6%)
Parity n (%)	
Nulliparity	127 (51.0%)
Multiparity	122 (49.0%)
Smoking n (%)	2 (0.8%)
Cervical length (cm), mean±SD	4.4 ± 1.0
Route of delivery n (%)	
Vaginal delivery	177 (71.1%)
Cesarean section	72 (28.9%)
Gestational age at delivery (weeks), mean±SD	38.7 ± 1.2
Birth weight (g), mean±SD	3,098.4 ± 386.7

BMI: body mass index, SD: standard deviation

Table 2. The mean and standard deviation of the anterior uterocervical angle for each gestational age between 16 0/7 - 24 6/7 weeks.

Gestational age (weeks)	n	Mean	SD
16 0/7 - 16 6/7	19	102.3	24.2
17 0/7 - 17 6/7	27	97.6	23.2
18 0/7 - 18 6/7	59	102.2	20.5
19 0/7 - 19 6/7	32	105.3	25.6
20 0/7 - 20 6/7	34	102.4	20.1
21 0/7 - 21 6/7	22	99.2	23.0
22 0/7 - 22 6/7	25	107.3	25.2
23 0/7 - 23 6/7	16	98.1	19.4
24 0/6 - 24 6/7	15	105.4	15.5

SD: standard deviation

The univariate and multivariate analysis demonstrated that the increase in gestational age was not related to changes in AUCA, and neither were advanced maternal age, BMI of more than 30 kg/m^2, smoking, changes in cervical length, gestational age at delivery, or birth weight. The only significant factor that was found to be associated with changes in AUCA was the parity. The multiparity group were found with more obtuse AUCA than the nulliparity group, with statistical significance (the mean difference was 12.8 degrees, 95%CI 7.6-18.0, p<0.001) (Table 3). The mean (±SD) angles were 96.1±21.5 degrees and 108.9±20.0 degrees in the nulliparity and multiparity groups, respectively. This study found that 44.9% of pregnant women who delivered at term had AUCA > 105 degrees.

Table 3. The univariate and multivariate analysis in associating the demographic data and the anterior uterocervical angle.

Variables	AUCA		Univariate analysis			Multivariate analysis		
	Mean	(SD)	Crude MD	95%CI	p value	Adjusted MD	95%CI	p value
Gestational age (weeks)	102.3	21.7	0.4	- 0.8, 1.6	0.545	0.2	- 0.9, 1.4	0.687
Age (years)								
< 35	100.9	21.7	Ref.					
≥ 35	106.6	21.4	2.9	- 0.3, 6.0	0.075			
BMI (kg/m^2)								
< 30	102.3	21.9	Ref.					
≥ 30	102.4	18.4	0.0	- 12.6,12.7	0.996			
Parity (%)								
Nulliparity	96.1	21.5	Ref.					
Multiparity	108.9	20.0	12.8	7.6,18.0	< 0.001	12.8	7.6,18.0	< 0.001
Smoking								
No	102.4	21.8	Ref.					
Yes	92.1	14.1	-10.3	- 40.7, 20.1	0.505			
Cervical length (cm)	102.3	21.7	3.0	0.3, 5.7	0.033	3.0	-0.8,1.6	0.480
Gestational age at delivery (weeks)	102.3	21.7	0.2	- 2.1, 2.6	0.846			
Birth weight (g)	102.3	21.7	0.0	- 0.0, 0.0	0.780			

AUCA: anterior uterocervical angle, SD: standard deviation, MD: mean difference, CI: confidence interval, BMI: body mass index

Discussion

The anterior uterocervical angle (AUCA) is now being used as a new predictor of spontaneous preterm birth with a good sensitivity[14], especially when used together with cervical length. However, for clinical use, we have aimed to develop normal reference ranges of AUCA for comparative purposes. We have hypothesized that AUCA may increase with advancing gestational age. Therefore, we conducted this study to answer the hypothesis and to construct normal reference ranges of AUCA for each gestational week, for cases where AUCA was gestational age dependent. However, in contrast to the hypothesis, this study demonstrated that AUCA was not significantly related to advancing

gestational age (16-24 weeks). Therefore, we could not establish the normal reference ranges for each gestational week. Interestingly however, the AUCA of the nulliparous women was significantly different from that of the multiparous women. Thus, based on the observations, we instead proposed the use of AUCA values specific to parity in clinical practices.

Based on a previous study reported by Dziadosz et al, the uterocervical angle ≥ 95 degrees and ≥ 105 degrees was a significant predictor of spontaneous preterm birth before the completion of 37 weeks and 34 weeks, respectively, with a sensitivity level of about 80%[14]. Likewise, a study by Farràs Llobet A et al showed that 33.7% of women who had anterior uterocervical angle > 105 degrees delivered at term[15]. However, our study found that 44.9% of pregnant women who delivered at term had AUCA > 105 degrees. This difference in results compared with our study may possibly be explained by the difference in population characteristics such as body or pelvic parameters[16]. Therefore, the cutoff point of the AUCA used for predicting preterm birth should be based on the normal values created for its own population. From this study, the mean (± SD) anterior uterocervical angle that could be used as a predictor for spontaneous preterm birth in Asian women of gestational age between 16 0/7-24 6/7 weeks should be 102.3 ± 21.7 degrees.

As mentioned above, the interesting insight gained from this study was that AUCA was significantly wider among multiparous women, when compared to that of nulliparous women. This might be explained by the fact that, during pregnancy, the uterus becomes enlarged, and the ligaments are stretched to support the growing uterus, which then becomes weakened. The prior delivery processes can cause permanent changes in pelvic floor or an incomplete recovery. As a result, the uterus often becomes retroverted after the delivery of the baby[17-19]. Because of the difference in AUCA in accordance with the parity, the clinical application of AUCA in predicting spontaneous preterm birth must take the parity into account, with the normal values for the parity being used separately. The mean (±SD) anterior uterocervical angles were 96.1 ± 21.5 degrees and 108.9 ± 20.0 degrees in nulliparous and in multiparous women, respectively.

The strengths of this study included: 1) prospective nature of the study, specifically designed to measure the uterocervical angle in pregnant women between 16 0/7 and 24 6/7 weeks of gestation, and 2) a single well-trained operator was used in order to avoid interobserver variability. The limitations of our study were as follows: 1) there had been no comparison of AUCA in the same woman between different gestational weeks, which could more clearly show the association between gestational age and uterocervical angle; and 2) a lack of information about the position of the uterus before pregnancy. Fundamentally, the changes in AUCA during pregnancy may depend on the AUCA angle before pregnancy. The normal position of a non-pregnant uterus could be anteverted, anteflexed, retroverted or retroflexed[20, 21]. In most women, the uterus lies anteverted and anteflexed. We hypothesized that the differences in the angle among pregnant women at the same gestational age may be caused by a neutral positioning of the uterus before pregnancy or a pathologic condition such as pelvic endometriosis. In order to prove this hypothesis, further studies would be needed.

Conclusion

In conclusion, the anterior uterocervical angle at 16-24 weeks was gestational-age independent; however, based on observation, it was significantly related to the parity. The normal values according to parity were provided, and they could potentially be used in determining the risk of preterm birth, but further confirmatory studies for the usefulness are required. Because of its gestational period independency, AUCA may be superior to other parameters such as cervical length in terms of simplicity in clinical use.

Acknowledgments

The authors would like to thank all participants from the Department of Obstetrics and Gynecology, Rajavithi Hospital.

Potential conflicts of interest

The authors declare no conflict of interest.

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Thai Journal of Obstetrics and Gynaecology
January 2020, Vol. 28, No. 1, pp. 52-59

OBSTETRICS

Using Abdominal Binder for Reducing Postoperative Wound Pain after Cesarean Delivery: A randomized controlled trial

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ABSTRACT

Objectives: To determine the effect of using abdominal binder after cesarean delivery on postoperative wound pain, physical function and analgesic drugs use.

Materials and Methods: A randomized controlled trial was conducted between January and April 2018 at KhonKaen Hospital. Fifty women who underwent elective cesarean delivery were randomly allocated to either the abdominal binder group or routine standard care. The primary outcome was postoperative wound pain as measured by a visual analog scale (VAS) scores at 6, 24, and 48 hours after using the binder. The secondary outcomes included physical function as measured by distance 6-minute walk test (6MWT), time to first ambulation, analgesic drugs use and adverse effects.

Results: Postoperative wound pain was indicated by a significantly lower VAS score in the binder group with the repeated measures ANOVA ($F= 30.78$, $p < 0.005$). The respective postoperative VAS score at 6, 24, and 48 hours was also significantly lower in the binder group (mean ± SD at 6, 24, and 48 hr. = 4.77 ± 1.97, 3.73 ± 1.48, and 2.51 ± 1.63 vs. standard care 6.85 ± 2.26, 5.49 ± 2.34, and 4.66 ± 2.21; $p < 0.05$). Postoperative opioid drugs use in the binder group was significantly less than in the standard care (5.22 ± 1.20 mg vs. 7.63 ± 2.43 mg; $p < 0.01$). There were no significant differences in the 6MWT and time to first ambulation between the two groups. No serious adverse effects were reported.

Conclusion: Using abdominal binder can reduced pain and analgesic drugs used in postoperative cesarean delivery.

Keywords: abdominal binder, postoperative cesarean delivery, pain, physical function, analgesic drugs.

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Received: 25 Septermber 2018, **Revised:** 9 November 2018, **Accepted:** 13 December 2018

การใช้ที่รัดหน้าท้องเพื่อลดการปวดแผลผ่าตัดหลังคลอดบุตร

ธัญญารัตน์ สิงห์แดง, อุษณีย์ สังคมกำแหง, ธนนิตย์ สังคมกำแหง

บทคัดย่อ

วัตถุประสงค์: *เพื่อเปรียบเทียบผลการใช้ที่รัดหน้าท้องต่อความปวดแผล ความสามารถในการเคลื่อนไหวและการใช้ยาลดปวดในสตรีตั้งครรภ์หลังผ่าตัดคลอด*

วัสดุและวิธีการ: *สตรีตั้งครรภ์ที่เข้ารับการผ่าตัดคลอดบุตรแบบไม่ฉุกเฉินที่โรงพยาบาลขอนแก่น ระหว่างเดือนมกราคม ถึงเดือนเมษายน พ.ศ.2561 จำนวน 50 ราย ได้รับการสุ่มเป็นกลุ่มที่ได้ใช้ที่รัดหน้าท้องหลังผ่าตัดคลอด และกลุ่มที่ได้รับการดูแลตามมาตรฐานตามปกติ โดยประเมินการปวดแผลผ่าตัดโดยใช้แถบเครื่องมือวัดความปวด (visual analog scale) ทดสอบความสามารถในการเคลื่อนไหวจากระยะทางการเดินโดยใช้แบบทดสอบการเดินใน 6 นาที (6 minutes walk test; 6MWT) เวลาครั้งแรกที่เริ่มขยับตัวหลังผ่าตัด(time to first ambulation) การใช้ยาลดปวดหลังการผ่าตัดคลอดและผลไม่พึงประสงค์จากการใช้ที่รัดหน้าท้อง*

ผลการวิจัย: *การใช้ที่รัดหน้าท้องมีการปวดแผลหลังผ่าตัดที่ 6, 24 และ 48 ชั่วโมง น้อยกว่ากลุ่มที่ได้รับการดูแลตามมาตรฐาน VAS ที่ 6, 24 และ 48 ชั่วโมง (mean ± SD; 4.77 ± 1.97, 3.73 ± 1.48, 2.51 ± 1.63 และ 6.85 ± 2.26, 5.49 ± 2.34, 4.66 ± 2.21; p< 0.05) การใช้ปริมาณยาลดปวดกลุ่มน้อยกว่าอย่างมีนัยสำคัญทางสถิติ ในกลุ่มใช้ที่รัดหน้าท้อง 5.22 ± 1.20 มิลลิกรัม และ 7.63 ± 2.43 มิลลิกรัม (p < 0.01) แต่ความสามารถในการเคลื่อนไหวแบบ 6MWT และเวลาครั้งแรกที่เริ่มเคลื่อนไหวไม่แตกต่างกัน และไม่พบภาวะแทรกซ้อนที่รุนแรงของการใช้ที่รัดหน้าท้อง*

สรุป: *การใช้ที่รัดหน้าท้องสามารถลดการปวดแผลผ่าตัด และลดปริมาณการใช้ยาลดปวดหลังผ่าตัดคลอดบุตรได้*

คำสำคัญ: *ที่รัดหน้าท้อง, หลังผ่าตัดคลอดบุตร, ความสามารถในเคลื่อนไหว, การปวดแผล, ยาลดปวด*

Introduction

One of most frequent major abdominal surgeries is cesarean delivery[1]. In Thailand, the prevalence of cesarean delivery has increased considerably during the past few decades[2]. Complications related to major abdominal surgery include atelectasis, pneumonitis, paralytic ileus, urinary infection and postoperative wound pain[3-4]. Acute pain after cesarean section can cause anxiety and distress to mother, reducing effective breastfeeding, and the time available for mother-infant contact[5]. It is not only pain but also fear of injury at the surgical site that makes patients reluctant to ambulate, raising the risk of thrombotic events and atelectasis[6].

Numerous pharmacological pain control studies have been conducted after cesarean delivery[7] but few investigators have assessed the benefits of nonpharmacological interventions. Even though some narcotics are safe to use during breastfeeding, some women would rather avoid using them because they are concerned that use of narcotics might hinder their ability to care for the newborn or have adverse effects on the neonate[8]. The use of an effective nonpharmacological alternative is thus of interest. Abdominal binders are being used increasingly as a form of alternative medicine[9]. Some studies suggest that the use of an abdominal binder might aid the management of pain following major abdominal surgery by limiting motion and supporting the abdominal wall during recovery[10]. Compression at the surgical site increases blood flow and reduces inflammation thereby aiding tissue repair[11]. The additional benefits of this device beyond pain control are prevention of herniation[11], wound seroma, and hematoma[12].

A systematic review reported that the effect of abdominal binder for pain control after cesarean delivery remains unclear[13], and there is insufficient evidence to support the use of abdominal binders for pain control after cesarean delivery[14]. Therefore, the aims of the present study were to assess whether using abdominal binders mitigate postoperative pain, improve physical activities and reduce analgesic use after cesarean delivery.

Materials and Methods

Following approval by the Khon Kaen Hospital Ethics Committee on Human Research, this randomized controlled trial enrolled women who had undergone elective cesarean delivery at Khon Kaen Hospital, Khon Kaen, Thailand, between 1 January and 30 April 2018. To be included in the study women (a) had to be 18 years of age or older, (b) had undergone elective low transverse cesarean delivery under spinal anesthesia combined with intrathecal morphine and (c) were able to understand and follow written and oral instructions in Thai. Women were excluded if they had a body mass index (BMI) > 35 kg/m^2, any postoperative drainage, walking disability, chronic cough, peri-operative organ injury, or post-cesarean hysterectomy.

Randomization was done by computer generated block of 4. Women were allocated to a group that used either abdominal binder or routine standard care. Group assignments were written down and placed into opaque envelopes. All women eligible to join the study were invited to participate and consent. Demographic data were collected. Since the women and data collectors were aware; they were wearing a binder or not, there was no blinding to the study. Randomization was done after finished the operation. In the intervention group, at 2 hours post operation, standardized postpartum nurse will apply elasticized, adjustable abdominal binder over the abdominal surgical incision at 5% smaller than the women'postoperative abdominal circumference measured at umbilicus. Women wore it for 2 days after operation and checked every 4 hours by standardized training nurse at postpartum ward and was took off between 10 PM. and 8 AM.

The primary outcome was postoperative wound pain measured by visual analogue scale (VAS) by standardized training nurse at postpartum ward at postoperative 6, 24, and 48 hours. Women were instructed to place a mark on a 10 cm line corresponding to the severity of pain (0 cm - no pain, 10 cm - worst pain experienced). Secondary outcomes were postoperative mobilization at day 1 and day 2 as measured by distance 6-minute walk test (6MWT) down a straight hospital corridor. Women were asked

to record the time of their first ambulation, the time of first analgesic drug requirement, side effects and adverse effects. The postpartum nurses recorded the amount of analgesic drugs used. Both groups received standard postoperative nursing care (at postoperative day 1 used tramadol 50 mg intravenous prn for VAS pain score 4 every 6 hr. After step diet acetaminophen 500 mg 1-2 tablets per oral was given prn for pain q 4-6 hr. Side effects and adverse effects were recorded.

Sample size calculation

The sample size was calculated from a pilot study included 30 women; 15 cases in each group. We used a formula to test the difference between the two independent proportions with a type I error of 5%, $Z\beta$ was set as 1.28 with a power of 90%. The sample size in each group was 25 cases.

Statistical analysis

The data were analyzed on an intention to treat, using repeated measure analysis of variance (ANOVA) for the primary outcome, and the data were presented using descriptive statistics. A $p < 0.05$ was considered statistically significant. Continuous variables were analyzed using the student's t-test and were presented as mean and standard deviation (SD. Categorical variables were assessed using a chi-square or Fisher's exact test and presented as percentages. The survival analysis for the secondary outcomes were time to first ambulation and time to first analgesic drug requirement.

Results

Of the 70 women initially enrolled in the study, 50 were included in the final analysis (25 in the abdominal binder group, and 25 in the routine standard care) (Fig. 1), The demographic characteristics were similar in both groups (Table 1). Among the 50 women, there were no differences in age, parity, previous cesarean delivery, blood loss, or operative time between groups. Eleven (44%) had a vertical skin incision in the binder group versus 6 (24%) in the routine standard care. 14 women (56%) had a pfannenstiel incision in the binder group versus 19 (76%) in the routine standard care group. There was no significant difference ($p = 0.135$).

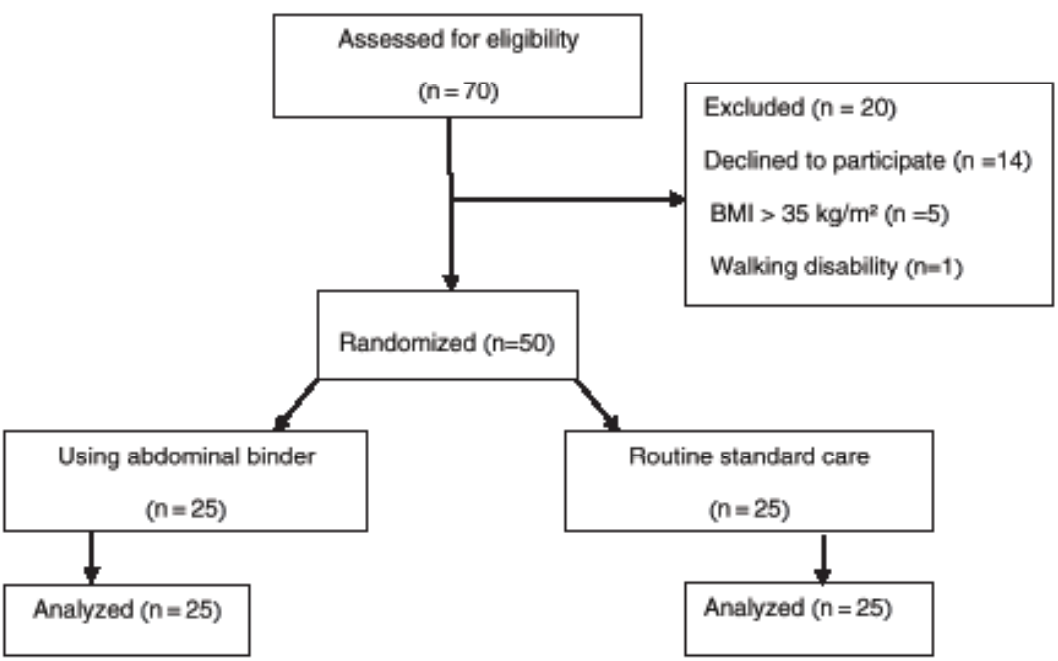


Fig. 1. Study flow diagram.

Table 1. Demographic characteristics.

	Abdominal binder (n=25) mean ± SD or n (%)	Routine standard care (n=25) mean ± SD or n (%)
Age (years)	27.16 ± 4.92	28.68 ± 4.44
Parity		
Nulliparous	5 (20)	6 (24)
Multiparous	20 (80)	19 (76)
Previous cesarean delivery		
Yes	18 (72)	14 (56)
No	7 (28)	11 (44)
BMI (kg/m^2)	25.13 ± 3.87	22.06 ± 3.57
Skin incision		
Vertical	11 (44)	6 (24)
Pfannenstiel	14 (56)	19 (76)
Operative time (min)	44.04 ± 14.68	41.16 ±14.46
Blood loss (ml)	335.52 ± 170.87	310 ± 96.82

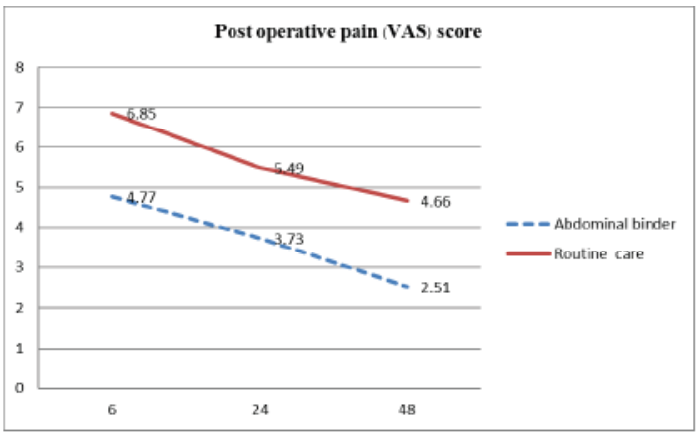
SD: standard deviation, BMI: body mass index

The main outcome was shown in Table 2. A repeated ANOVA was run to determine if there were any differences in VAS between groups at 6, 24, and 48 hours postoperatively. The results revealed that using an abdominal binder resulted in statistically significant differences in mean VAS over its time course ($F = 30.78$, $p < 0.01$). Among the 25 cases using the abdominal binder, the respective mean VAS at 6, 24, and 48 hours postoperatively were 4.77 ± 1.97, 3.73 ± 1.48, and 2.51 ± 1.63, which was significantly different from the routine standard care group (6.85 ± 2.26, 5.49 ± 2.34, and 4.66 ± 2.21; $p < 0.01$, $p < 0.01$, and $p < 0.01$) (Fig. 2).

Table 2. Postoperative pain (VAS) score.

Postoperative pain (VAS) score	Abdominal binder (n=25) mean ± SD	Routine standard care (n=25) mean ± SD	p value
6 hours	4.77 ± 1.97	6.85 ± 2.26	< 0.01
24 hours	3.73 ± 1.48	5.49 ± 2.34	< 0.01
48 hours	2.51 ± 1.63	4.66 ± 2.21	< 0.01

SD: standard deviation, VAS: visual analogue scale



X = postoperative time (hr.), Y = postoperative pain score by VAS (mean)

Fig. 2. Postoperative pain score by visual analogue scale (VAS) between abdominal binder group and routine standard care group.

The other results were shown in Table 3. No statistically significant differences between group were detected in (a) 6MWT at postoperative day 1 or 2 (p = 0.42, 0.48); (b) amount of acetaminophen used on postoperative day 1 or 2 (p= 0.21, 0.07); (c) time to first ambulation (p = 0.31); (d) time to first intravenous analgesic drug requirement (p = 0.35); or time to first oral analgesic drug requirement (p = 0.10). The amount of opioid used on postoperative day 1 in the binder group was, however, significantly less than in the routine standard care group (p < 0.01). Compliance wearing the binder and doing 6MWT was 100%. Itching was found in 3 women in the binder group. There was no serious adverse effect in the current study.

Table 3. Secondary outcomes.

	Abdominal binder (n=25) mean ± SD	**Routine standard care (n=25) mean ± SD**	**p value**
Postoperative 6MWT (m)			
Day 1	151 ± 57.48	136.30 ± 76.71	0.42
Day 2	159.20 ± 63.88	144.12 ± 82.87	0.48
Postoperative analgesic drugs used (mg)			
Tramadol day 1	5.22 ± 1.20	7.63 ± 2.43	< 0.01
Acetaminophen day 1	113.24 ± 248.27	107.54 ± 458.03	0.21
Acetaminophen day 2	145.83 ± 275.01	524 ± 600.19	0.07
First post op ambulation (hrs)	11.34 ± 6.99	13.33 ± 6.75	0.31
First analgesics requirement (hrs)			
Intravenous	2.49 ± 5.75	3.75 ± 3.27	0.35
Oral	11.45 ± 11.94	6.27 ± 10.00	0.10

SD: standard deviation, 6MWT: 6-minute walk test

Discussion

This randomized controlled trial investigated the effect of abdominal binders in women who had undergone elective cesarean delivery with respect to pain, physical function and analgesic drug requirement. We found that use of an abdominal binder reduced pain 6, 24, and 48 hours postoperatively and reduced the amount of opioid used on postoperative day 1. Physical function and the amount of analgesic drug used were unaffected by use of an abdominal binder.

The findings of the current study agreed with Ghana et al[5] who evaluated post- cesarean delivery pain scores when wearing a binder to reduce waist circumference 5% between 08:00 and 22:00. They reported that the binder group had significantly lower pain scores than the non binder group. By contrast, Giller et al[14] reported that the pain scores among women who wore an abdominal binder both day and night were not significantly different from the control group.

The mechanism of how an abdominal binder controls postoperative pain is multifactorial[15], the binder reduces shear forces at the incision interface resulting in less discomfort while ambulating and less pain as the binder disperses direct pressure away from incision.

It is known that early mobilization postoperatively prevents many surgical complications. The current study used 6MWT to evaluate the rate of mobilization and found that 6MWT on postoperative day 1 and 2 and time to first ambulation were not different in the binder versus the non binder group. Cheifetz et al[16] used an abdominal binder to reduce abdominal circumference by 10-20%. It was worn at the first mobilization and at all times when out of bed. The 6 MWT distance between postoperative day 1, 3, and 5 were compared. They found that 6MWT on day 5 in the binder group was better than the control group. Arici et al[17] similarly used an abdominal binder to reduce abdominal circumference by 10-20%; it was worn at first mobilization and at all times when out of bed. They compared 6 MWT distance at postoperative day 1, 4, and 7 and found that an abdominal binder increased patient mobility at day 4 and 7 after surgery because it (a) reduced postoperative pain, (b) made the patients feel safe and (c) encouraged ambulation. The abdominal binder may thus improve physical function from day 4 after surgery. Giller et al[14] found that the respective amount of analgesic drugs (ibuprofen, acetaminophen, morphine, ketorolac) used on postpartum day 1 and 2 was not different between groups. By contrast, in our study, the amount of intravenous analgesic drug used in the binder group at postoperative day 1 was less than the control group; evidenced by an overall lower pain score. Decreasing opioid use in the breastfeeding woman can reduce side effects to the neonate caused by opioid transmission through the breastmilk (e.g., sedation, constipation and respiratory depression).

The adverse effect found in the current study was itching (3 women in the binder group). Compliance wearing the binder and doing 6MWT was 100%. No serious adverse effect was found in this study.

We found that using an abdominal binder can reduce pain and the amount of analgesic drug used among women who have undergone a cesarean delivery. According to the current study, an abdominal binder can be used as an easy to use, nonpharmacological method for treating acute postoperative pain.

Strengths of the current study were all of the population had no loss to follow-up and used a simple intervention.

Limitation of the current study were the same type of operation and anesthesia in both groups. For further research, we suggest the effects of abdominal binder used should be tested on different type of operation and anesthesia.

Conclusion

This research indicated that abdominal binder usage after cesarean delivery decreased postoperative pain and amount of analgesic drug used albeit there was no clinical benefit on postoperative physical function. Abdominal binder usage was thus an easy to use, nonpharmacological method for reducing pain and opioid use after cesarean delivery.

Potential conflicts of interest

The authors declare no conflict of interest.

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Thai Journal of Obstetrics and Gynaecology
January 2020, Vol. 28, No. 1, pp. 60-64

CASE REPORT

Pulmonary Endometriosis: A case report

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ABSTRACT

A 49-year-old female had progressive diffused chest tightness for one week. Physical examination and chest film showed the right-side pneumothorax as over 40% pneumothorax. After the pneumothorax was drained by a pigtail catheter, an exploratory thoracotomy operation was conducted. The right upper lobe and pleural lesions were resected by a thoracic surgeon. The histopathology revealed emphysema of the lung, with pulmonary and pleural endometriosis. The gynecologist was consulted and laparoscopic surgery was performd for diagnosis. The endometriosis was shown at the diaphragmatic area without pelvic endometriosis. The lesions were resected. The histopathology showed endometriosis of diaphragmatic area. The five-year follow-up did not show evidence of recurrence, and hormonal treatment was not used.

Keywords: emphysema, pulmonary endometriosis, pneumothorax.

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Received: 7 January 2019, **Revised:** 1 November 2019, **Accepted:** 6 December 2019

Introduction

Endometriosis is the presence of endometrial tissue outside of the uterus. The most common sites are the ovaries, uterosacral ligaments, uterus, and the peritoneum. The extrapelvic- endometriosis is also known as the ectopic endometrium which has been found in the umbilicus, abdominal scars, breasts, extremities, pleural cavity, and lungs. The presence of endometrial tissue in the lung is called thoracic endometriosis syndrome (TES)[1-2]. Thoracic endometriosis affects the airway, pleura, and lung parenchyma. The clinical symptoms of lung endometriosis are associated with catamenial chest pain and hemoptysis. Imaging studies and histopathological examination play important roles in the diagnosis of TES. Surgery of lung endometriosis is able to provide radical relief[2]. Important recent advances in the understanding of lung endometriosis

could guide physicians to improve the diagnosis and treatment.

Case Report

In June of 2013, a 49-year-old woman, parity 0, who had no underlying disease had progressive diffused chest tightness for one week. She had regular menstruation with no dysmenorrhea. The symptoms she suffered included mild shortness of breath and intermittent headaches for which she had visited at the emergency room at Chang Gung Memorial Hospital, Linkou, Taiwan. The patient had no fever, palpitation, or diarrhea, nor abdominal or urinary discomfort. The physical examination and chest film showed the right-side pneumothorax as over 40% pneumothorax (Fig. 1). The patient had a history of spontaneous pneumothorax for the last three years. The first episode of spontaneous pneumothorax which had occurred three years previously was treated with intercostal drainage (ICD). The second episode of pneumothorax required drainage of the pneumothorax by a pigtail catheter, by which a pigtail catheter had been used in draining air from the pleural spaces internally. The thoracic surgeon provided treatment for wedge resection at the upper lobe of the right lung, and the right pleural lesions. The histopathology revealed emphysema, endometriosis at the right lung, and the pleura of the right lung. After the exploratory thoracotomy, the histopathological confirmation of ectopic endometriosis was obtained. The thoracic surgeon had then transferred the patient to a gynecological department for the treatment of endometriosis. The pelvic examination had regularly pelvic organs and cul-de-sac. The ultrasonography showed normal uterus and both ovaries. The ectopic endometriosis was diagnosed preoperatively. The application of laparoscopy was a consideration for intra-abdominal diagnosis. There was no evidence for pelvic endometriosis. The endometriosis spots were seen in the diaphragmatic area and were resected (Fig. 2). The tissue biopsies showed the endometriosis from the histopathological report. On the basis of the clinical outcome, the patient did not undergo the hormonal treatment. The patient had then followed-up for five years without recurrence. The study was exempt from the requirement for approval by an institutional review board.

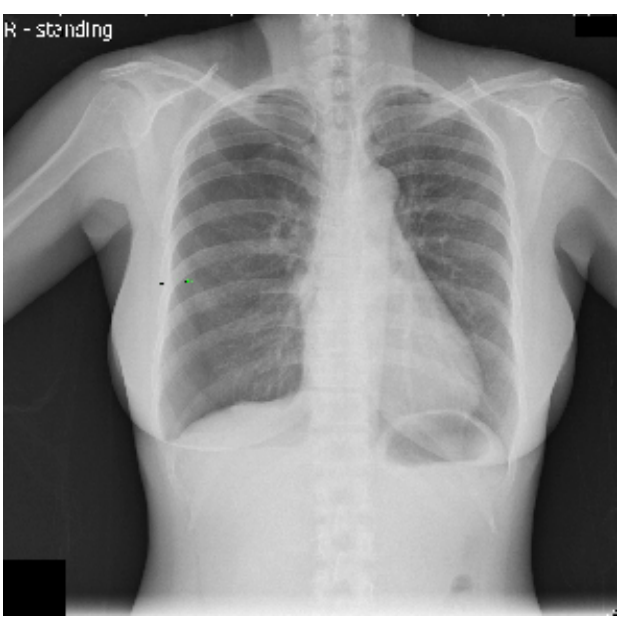

Fig. 1. Chest film showed the pneumothorax of the right lung (green line).

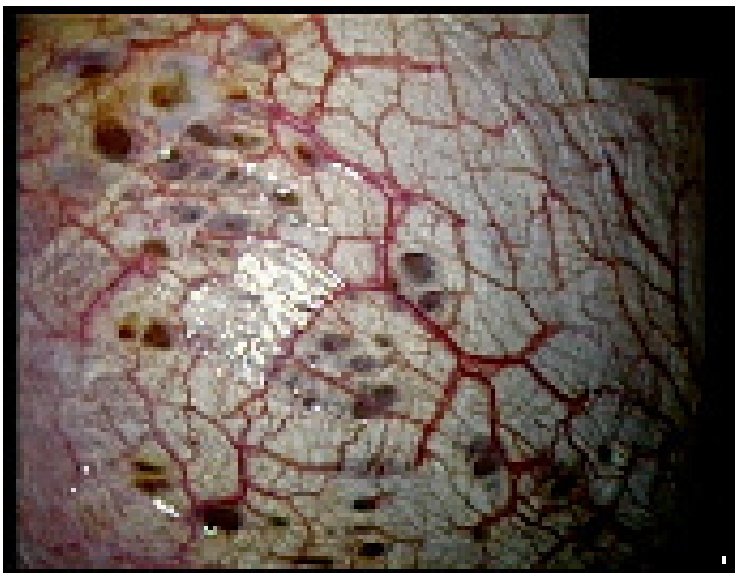

Fig. 2. The endometriotic spots located at the right diaphragmatic area.

Discussion

Endometriosis was first reported by Carl Von Rokitansky in 1860. The characteristic of endometriosis is the presence of endometrial glands outside the uterine cavity. The extrapelvic endometriosis can occur at the lung, which was called pulmonary endometriosis and thoracic endometriosis. Endometriosis of the lung is a clinically serious form of the disease. Bronchopulmonary endometriosis was first described by Hart in 1912, and the catamenial pneumothorax was described in 1956. The symptoms consist of catamenial pneumothorax, catamenial hemoptysis, catamenial haemothorax, and pulmonary nodule[1]. The spread of distant endometriosis rests on hypotheses of venous or lymphatic circulation[2]. The catamenial hemoptysis had been reported for 74 cases. Of these, 37 cases were in the right lung, 19 cases were in the left, and 6 cases were bilateral[1]. Thoracic endometriosis appears through various clinical presentations such as catamenial pneumothorax (73%), catamenial hemothorax (14%), catamenial hemoptysis (7%), and lung nodules (6%). The 61 patients with pulmonary endometriosis who underwent gynecological examination showed no evidence of pelvic endometriosis. The Computed-Tomography (CT) findings for pulmonary endometriosis included well-defined opacities, thin-wall cavities, and nodular lesions[3]. As in our case, the patient suffered from tightness of breath, and right side spontaneous pneumothorax without underlying disease, while she had a history of spontaneous pneumothorax for the last three years. The CT findings showed nodular lesions and well-defined opacities in both lungs and the right lung pneumothorax. The thoracic endometriosis had been reported with the recurrence rate of pneumothorax within four years. Surgical treatment is controversial while depending on the severity of the clinical symptoms and signs[1-8] as shown in Table 1. In our case, the first episode of spontaneous pneumothorax from three years previously was treated with ICD. The patient had undergone resection of the tissues at the upper lobe of the right lung and the right pleural nodule lesions to relieve dyspnea in the second episode of spontaneous pneumothorax. The patient had histopathological endometriosis of the lung. Laparoscopy was used to explore the pelvic endometriosis, and then the endometriosis spots

were seen in the diaphragmatic area and were resected. The histopathological examination confirmed endometriosis of the diaphragmatic area with no pelvic endometriosis. The pulmonary endometriosis was mostly diagnosed with thoracoscopy or thoracic surgery. The prognosis depended on the response of hormonal therapy during follow-up[7]. The patient had been followed up for 5 years without recurrence of pulmonary endometriosis or pelvic endometriosis, so hormonal treatment was not prescribed for the long-term treatment of this patient. After surgery, the recurrence rate during hormonal therapy was 0.05 times per year. The recurrences were detected during the period without hormonal therapy were 0.14 times per year[7]. The postoperative hormonal treatment could reduce the recurrence rate including gonadotropin-releasing hormone agonist (GnRH), dienogest, continuous oral contraceptives (OCs), and cyclic OCs[1-8]. The recurrence rates were 0%, 16.7%, 18%, 33% with GnRH agonists, dienogest, continuous OCs, cyclic OCs[7].

The pulmonary endometriosis is preoperatively difficult to diagnose from the symptom of catamenial pneumothorax. The multidisciplinary team consisting of a pulmonologist, thoracic surgeon, pathologist, gynecologist, and the radiologist is required to helping diagnose and provide treatment of pulmonary endometriosis as soon as possible to avoid delayed diagnoses.

Table 1. The review of pulmonary endometriosis.

Author	Year	Age	Symptoms	Investigation	Surgery
Huang H, et al.[1]	2013	29	Catamenial hemoptysis	Chest CT: opaque lesion in the left superior lobe	Explore thoracotomy
Pankratjevaite L, et al.[2]	2017	36	Chest pain, breathlessness	Severe bleeding through the chest probe	Right side minithoracotomy
Maniglio P, et al.[3]	2017	37	Chest pain, breathlessness	Chest film and CT chest: pneumothorax	Thoracoscopic resection
Ichiki Y, et al.[4]	2012	28-40	Right side spontaneous pneumpthorax	Chest film and CT chest: pneumothorax	VATS
Mukku V, et al.[5]	2019	40	Chest tightness	Chest CT: pneumothorax	VATS
Shikino K, et al.[6]	2016	46	Chest pain	Chest CT: pneumothorax	VATS
Fukuda S, et al.[7]	2018	18-47	Dyspnea	Chest film or Chest CT	Thoracoscopic surgery
Furuta C, et al.[8]	2018	26-42	Dyspnea	Chest film or Chest CT	Thoracosopic surgery

CT: Computed Tomography, VATS: Video assist thoracoscopic surgery

Acknowledgement

The authors appreciate the Asia-Pacific Association for Gynaecologic Endoscopy and Minimally Invasive Therapy (APAGE) for providing the International Fellowship Endoscopy Training Program at Chang Gung Memorial Hospital for Dr. Phornsawan Wasinghon

Potential conflicts of interest

The authors declare no conflict of interest.

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