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7. encourage and being aware of research into peer review and publishing and reassessing the journal's processes in the light of new findings.

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EDITORIAL

This second issue of Thai Journal of Obstetrics and Gynaecology (TJOG) 2019 contains many interesting articles. One special article is "**HIV infection and the abnormal cervical cytology**".

Editor in Chief and managing staff already attended the Thai Journal Citation Index meeting: "**The 6th Editors' Workshop**" under the TCI-TRF-Scopus Collaboration Project on 26 March 2019 at Ambassador Hotel, Bangkok, Thailand. The 6th Editor's Workshop was jointly organized by the Thai-Journal Citation Index Centre (TCI), the Thailand Research Fund (TRF), Scopus and NECTEC. The workshop "**Success, Lessons Leaned and Challenges of Pilot Project on Thai and ASEAN Journals for Indexing in Scopus in Year 1-2**" aims to reflect on the success, challenges and lesson learned from the first year of running the pilot project under the TCI-TRF-Scopus Collaboration Project scheme to certain Thai Editors.

Editorial Board of TJOG prepare journal for the 4th round re-evaluation for TCI indexed journals (2020-2024). Thus, there are many changes of the journal during this time.

RTCOG Annual Meeting 2019 will be held during 15-18 October 2019 at Dusit Pattaya, Thailand. The theme of this meeting is "**OBG 62 Next Gen**". All RTCOG members are cordially invited to participate this scientific meeting. All RTCOG members who would like to present their researches please prepare the abstract and follow RTCOG website.

Residents who would like to publish their researches in TJOG should submit their works before September 30, 2019. Our editorial team and constructive reviewers will let them know the results before December 31, 2019.

Wish to see you at RTCOG Annual Meeting 2019 at Dusit Pattaya, Thailand

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

Thai Journal of Obstetrics and Gynaecology
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SPECIAL ARTICLE

HIV Infection and the Abnormal Cervical Cytology

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ABSTRACT

Human immunodeficiency virus (HIV) infection has been known as a chronic, immunocompromising condition, which accelerates the natural history of many diseases, including cervical cancer. As known, human papillomavirus (HPV) is the principal etiologic organism and its persistent infection can transform normal cervical cells to cancers. HPV and HIV possibly co-facilitate the transmission of each other. In addition, the co-existence of oncogenic and non-oncogenic HPV appears very common. In 2018, the recommendations provided by the Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents for screening cervical cancer in HIV-infected women were launched. In contrast to the previous guideline by the Center for Disease Control and Prevention (2009) which showed that the screening interval was one year once the first three Papanicolaou (Pap) tests were negative, that in the recent recommendations is three years. Moreover, new techniques such as co-testing are taken into account. The article aims to share our experience at the Siriraj Female Sexually transmitted Diseases Clinic, Siriraj Hospital, which has been taking care of this special group of population for nearly two decades.

Keywords: HIV, HPV, Pap test.

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Introduction

Human immunodeficiency virus (HIV) infection has been known as a chronic, immunocompromising condition, which accelerates the natural history of many diseases, including cervical cancer. It has been widely accepted that human papillomavirus (HPV) is the principal etiologic cause and its persistent infection can transform normal cervical cells to cancers.

Compared with non-infected women, those living with HIV are more likely to have precancerous and cancerous lesions of cervix[1]. Moreover, cervical cancer is one of the most common malignancies associated with acquired immune deficiency syndrome (AIDs) in Thailand[2].

At the moment, cervical cancer screening tools have a high yield in early detection of cervical cancer. Evaluation of the morphologically altered cervical cells, or Papanicolaou (Pap) test, and/ or identification of oncogenic/ high risk HPV (hrHPV) appear to be promising tools. Negative results of both tests provide a greater reassurance and allow for a longer follow-up interval[3]. The reporting system of the Pap rest is based on the Bethesda system[4], including squamous component (atypical squamous cell of undetermined significance, ASCUS; low grade squamous intraepithelial lesion, LSIL; high grade squamous intraepithelial lesion, HSIL; atypical squamous cell cannot exclude HSIL, ASC-H; and squamous cell carcinoma, SCC) and glandular component (atypical glandular cell, AGC; adenocarcinoma in situ, AIS; and adenocarcinoma).

This review aims to demonstrate trends of abnormal Pap tests in HIV-infected women at the Siriraj Female Sexually Transmitted Diseases (STD) Clinic which has been working in this field for nearly two decades. Moreover, recommendations for screening cervical cancer in this special group of population and its association with genital warts, a disease caused by non-oncogenic HPV, are also included.

HIV infection and the abnormal cervical cytology

HPV and HIV possibly facilitate the transmission of each other[5]. The enhanced HIV-infection susceptibility may be due to the decrease in production of antimicrobial molecules by HPV-infected keratinocytes[6] which results in easier entry of HIV through the epithelium[7, 8]. In addition, HIV-targeted T cells, including CD4 and CD8 cells, are the predominate cells surrounding high grade cervical intraepithelial neoplasia (CIN3)[9], which likely increase HIV entry and replication. Compared with non-infected women, HIV-infected women had higher HPV acquisition (RR 2.64, 95%CI 2.04-3.42) and lower HPV clearance (HR 0.72, 95% CI 0.62-0.84)[10]. During the state of immune depletion, HPV persists in the basal cells after lesion regression and can be reactivated[11]. This may lead to the progression from low-grade to high-grade cervical lesions and finally invasive cancer. Moreover, the HIV-1 Tat protein and gp120 disrupt epithelial tight junctions[12], causing the expression increment of HPV E6 oncoprotein which downregulates tumor suppressor genes like p53[13].

Women living with HIV have a greater prevalence of abnormal Pap test[14] and cervical cancer[15]. For example, the results of Women's Interagency HIV Study (WIHS), which the Pap tests were obtained every six months for up to eight years, in 1,931 HIV-infected women and 533 non-infected women, showed that the incidence of ASCUS or worse (ASCUS+) was doubled (179 vs 75 in 1,000 person-years) and the incidence of HSIL and SCC was tripled (4.4 versus 1.3 in 1,000 person-years)[14]. Additionally, based on an ecological study, compared to general population, HIV-infected women were about nine times more likely to suffer from cervical cancer[15].

Compatible with previous studies[16, 17], higher prevalence of abnormal cervical cytology was demonstrated in Thai HIV-infected women[18]. The prevalence of LSIL or worse (LSIL+) among HIV-infected women was 12.1% (77/636)[19], whereas the rate was 1.1% (261/23,676) in female patients attending the Siriraj Gynaecologic Clinic[20]. The following report in 2011 showed that, after seven 6-month Pap test, the cumulative incidence of ASCUS+, at which colposcopic examination is recommended[21], was much higher, at 37%, and CD4 <350 cells/mm3 was the predictive factor[22]. During 2007-2017, there were 1,433 new cases of HIV-infected women who attended the Siriraj Female STD Clinic. The worst results of three first Pap tests are shown in Table 1. The decline of new cases is demonstrated while their mean ages appear similar. Apparently, the prevalence of abnormal Pap tests remains being in the spotlight.

Table 1. The worst results of three first pap tests among new cases of HIV-infected women who attended the Siriraj Female STD Clinic during 2007-2017.

Year	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Number	143	189	183	166	142	147	142	94	88	70	69
Age (years)	30.2±6.8	32.0±8.8	33.6±9.4	34.1±9.0	34.7±8.9	35.0±9.6	35.1±10.7	36.4±10.5	36.2±11.3	37.3±14.2	37.9±12.0
ASCUS	12 (8.4)	18 (9.6)	17 (9.3)	10 (0.6)	16 (11.3)	13 (8.8)	13 (9.1)	6 (6.4)	8 (9.1)	2 (2.9)	3 (4.3)
LSIL	17 (11.9)	40 (21.3)	28 (15.3)	15 (9.0)	18 (12.7)	15 (10.2)	14 (9.9)	1 (1.1)	4 (4.5)	0	1 (1.4)
HSIL	7 (4.9)	10 (5.3)	7 (3.8)	12 (7.2)	12 (8.4)	8 (5.4)	5 (3.5)	15 (16.0)	14 (15.9)	9 (12.9)	7 (10.1)
ASC-H	1 (0.7)	1 (0.5)	1 (0.6)	3 (1.8)	4 (2.8)	4 (2.7)	1 (0.7)	0	0	0	0
AGC	0	1 (0.5)	0	2 (1.2)	0	1 (0.7)	1 (0.7)	0	2 (2.3)	0	0
Cancer	0	1 (0.5)	5 (2.7)	0	0	0	0	2 (2.0)	2 (2.3)	1 (1.3)	0

ASCUS= atypical squamous cell of undetermined significance, LSIL=low grade squamous intraepithelial lesion, HSIL=high grade squamous intraepithelial lesion, ASC-H=atypical squamous cell cannot exclude HSIL, AGC= glandular component

Co-incident anogenital warts in HIV infection and the abnormal cervical cytology

Anogenital warts (AGWs) are caused by non-oncogenic HPV, mostly type 6 and 11. Our previous report demonstrated that AGWs dramatically increased the incidence of LSIL+, at 16 times higher than that in general gynaecologic patient population[23]. This could be explained by 2 theories, including the co-infection and the similar risk factors of non-oncogenic and oncogenic HPV. The impact scale of HIV on cervical cytology of women with AGWs remains obscured. In our clinic, 53 HIV-infected women presenting with genital warts during 2004-2011 were assessed every six months using a Pap test. Their mean age was 29.4±8.1 years. The median follow-up frequency was three (min-max = 1-21 times and interquartile range = 1-13 times). None of the patients had cervical cancer. The results of the Pap test are shown in Fig. 1.

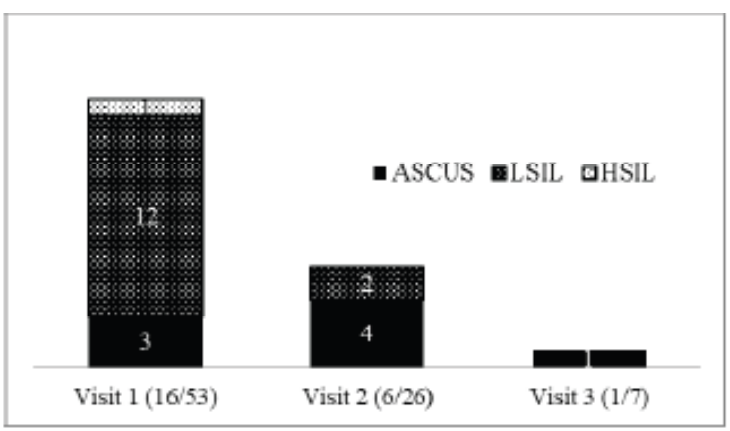

Fig. 1. Incidence of ASCUS+ in the first three visits of 6-month interval in HIV-infected women with anogenital warts
ASCUS = atypical squamous cells of undetermined significance, LSIL = low grade squamous intra-epithelial lesions, HSIL = high grade squamous intra-epithelial lesions, HSIL = high grade squamous intra-epithelial lesions

The prevalence of LSIL+ was 24.5% (13/53) at the first visit. This figure is much higher than that among non-infected cases with AGWs (24.5% vs 16.3%)[23]. Colposcopic examination was done for all HIV-infected

women with ASCUS+ and nine cases received biopsy and/or loop electrosurgical excision procedure (LEEP). Of these, high grade cervical intraepithelial neoplasia (CIN III) was reported in five patients. Patient No.1 had HSIL in the first Pap test. Patient No.2 had LSIL in the first Pap test and HSIL in the fifth visit. Patient No.3 had LSIL in the first three visits. Patient No.4 had a negative first Pap test, followed by persistent LSIL. In her 13th visit, patient No.4 had ASC-H before LEEP was done. Patient No.5 had negative Pap test for 10 times and ASCUS at the 11th visit. Based on our experience, many unnecessary colposcopic examinations were performed if considering ASCUS+ as the triage point for the procedure. Therefore, our current guideline is to perform annual Pap test for all patients with AGWs regardless of HIV serostatus and colposcopic examination is recommended only when Pap test is 'LSIL+'.

The screening of cervical cytology in HIV-infected women

For HIV-uninfected women, cervical cancer screening should begin at the age of 21 years regardless of the age of sex debut. Women aged 21-29 years should be screened with cervical cytology alone every 3 years. For women aged 30-65 years, co-testing every 5 years is preferred; however, screening with cytology alone every 3 years is acceptable. Screening should be discontinued up to the age of 65 years[3, 24]. On the contrary, the infected ones should continue the screening program throughout their lives.

A previous study demonstrated the sensitivity and the specificity for detecting CIN II+; at 75.8% and 83.4% for Pap test, and 92% and 51.4% for HPV DNA testing[10]. In HIV-infected women with normal Pap test but positive for oncogenic HPV, a 5-year cumulative risk of CIN II+ was as high as 16%. The subgroup analysis showed that HPV 16 played an important role as the cumulative risk of CIN III was 10% whereas that of HIV-infected women with other hrHPV types was 4%. Therefore, no matter what the Pap test is, those with positive HPV 16 should immediately undergo colposcopic examination[11]. Recently, co-testing (Pap test plus hrHPV DNA testing) has shown impressive detection rate of high grade CIN.

The WIHS study showed that HIV-infected women with three negative consecutive Pap tests were less likely to have precancerous or cancerous cervical lesions[16]. Thus, the Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents launched the recommendations that support early frequent screenings followed by extended intervals[25]. The initial interval can be 6-monthly or 12-monthly. After three negative results, regular 3-yearly interval is recommended. The age of the patients is one of the most important factors in determining screening practice due to the capacity of self-eradicating an HPV infection.

For those younger than 30 years, a Pap test is the sole screening tool. The recommendations are as in Table 2. HIV-infected women with 'ASCUS' are asked to repeat their Pap tests in the following 6-12 months. Colposcopy is recommended when 'ASCUS+' is reported on the repeat Pap test. In contrast, colposcopy is recommended immediately in case of a 'LSIL+' result. However, if hrHPV DNA testing is done for any reasons and shows positive result concomitantly with ASCUS in the first Pap test, colposcopocic examination can be directed to.

Table 2. Recommendations of cervical cancer screening in HIV-infected women aged < 30 years[25].

	Recommendations
Age < 21 years, including congenital HIV infection	First Pap test at < 1 year following sex debut or no later than the age of 21 years
Age 21-29 years	First Pap test at the time of HIV diagnosis and every year for the following 2 years. If all Pap tests are negative, the 3-year interval Pap test is recommended thereafter.

For the 'age ≥30 years' group, either Pap test or co-testing (Pap test plus hrHPV DNA testing) can be applied. Like the 'age <30 years' group, Pap test should be done immediately after the diagnosis and should be repeated at the 6-12 month interval. After three first consecutive negative Pap tests, either Pap test or co-testing at the 3-year interval is recommended. Results and management of cervical cancer screening for HIV-infected women aged ≥30 years is shown in Table 3. This is contrasting to the recommendations for the non-infected women in that if the co-testing is negative[3], the screening interval will be 5 years.

Table 3. Results and management of cervical cancer screening in HIV-infected women aged ≥30 years[25].

Pap test	hrHPV test	Management
Negative	Positive for non- HPV 16/18	Repeat co-testing at the following one year. Of the repeated test, if positive for either HPV 16 or HPV 16/18 or 'ASCUS+', colposcopy is recommended.
Negative	Positive for HPV 16 or HPV16/18	Colposcopy
ASCUS	Negative	Repeat Pap test at the following 6-12 months or co-testing at the following 12 months. Of the repeated test, if positive for either HPV 16 or HPV 16/18 or 'ASCUS+', colposcopy is recommended.
ASCUS	Positive for any HPV	Colposcopy
LSIL^{+}	Any	Colposcopy

ASCUS = atypical squamous cells of undetermined significance, LSIL = low grade squamous intra-epithelial lesions, hrHPV = high risk human papillomavirus

The prevalence of cervical cancer and its morbidities are greater in low-middle income countries. Globocan 2012 showed that the incidence of cervical cancer is highest in Asia and the Pacific region[26]. The age-standardised rate in Thailand vs the United States was 11.3 vs 5.2 per 100,000[27]. Thus, 6-month intervals of Pap test has been applied for all HIV-infected women in our clinic since 2004. In 2011, we reported that, in 821 HIV-infected women who received 6-month Pap tests during 2004-2009 (2,852 Pap results in total), 'ASCUS+' could be detected in 10% despite the first three negative Pap tests, especially among those with CD4 count ≤ 350 cells/mm^3. Of 95 HIV-infected women with ASCUS+, 76 underwent colposcopic examination. LEEP was done in 19 cases and showed 12 high grade CIN and one squamous cell carcinoma[22].

Prevention of HPV infection in HIV-infected women

Similar HPV prevention strategies can be applied for both HIV-infected women and general population. The basic one is proper condom use. Although HPV can exist in other regions aside from the penis such as scrotal area as well as other parts of external genitalia, a systemic review of longitudinal studies showed that consistent condom use offers effective protection from HPV infection and related cervical neoplasia. Thus, using condoms is a good complementary HPV-preventive instrument[28].

Although the HPV vaccination is another propitious strategy, routine screening of cervical cytology remains the priority. Despites the lower immunogenicity among HIV-infected population, vaccination is included in the recommendations[25]. Currently, a 9-valent vaccine is recommended in some countries such as the United States[25] but is still not available in Thailand. The 2-valent or 4-valent HPV vaccines also showed good immunogenic response. However, in a recent phase 3, double-blinded

randomized controlled trial, being conducted in 575 HIV-infected women (aged ≥ 27 years) participants, that evaluated the efficacy of the 4-valent vaccine in protecting against persistent anal infection with HPV 6/11/16/18, anal HSIL after 52 weeks, or persistent oral HPV infection. The study did not support any of the mentioned benefits[29].

Conclusion

Abnormal cervical cytology in HIV-infected women has remained highly prevalent during the past decade. As most of them are precancerous lesions, there is a window of opportunity to prevent its progression to cervical cancer. Both the US recommendations and those of the Siriraj Female STD Clinic aim to follow all patients for the rest of their lives. However, the practice in our Clinic suggests the higher screening frequency for Thai HIV-infected women.

Potential conflicts of interest

The authors declare no conflict of interest.

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GYNECOLOGY

A Comparative Study of Quality of Life of Patients Who Underwent Total Laparoscopic Hysterectomy and Total Abdominal Hysterectomy

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ABSTRACT

Objectives: To evaluate the effect of total laparoscopic hysterectomy (TLH) on the quality of life compares to total abdominal hysterectomy (TAH) method in Thailand.

Materials and Methods: After approval from ethical committee was achieved, the study was conducted. Euro-quality of life five dimensions (EQ-5D) questionnaire was used to evaluate quality of life. The questionnaire was given to the patients before surgery, day 1, 7 and 28 after operation. The patients were already assigned to perform TAH or TLH by their voluntariness. General characteristics and operative procedure including complications were also recorded. Data analysis was performed by using SPSS version 22.

Results: Hundred cases of TAH and 102 cases of TLH were collected. Baseline characteristics, diagnosis, operative time and complication rate were not difference. Educational level and income were slightly higher in TLH group. TLH had less blood loss and shorter hospital stay and had tendency to mobilize better than TAH group. The other aspects of quality of life such as pain, self-care and doing usual activity were similar. Anxiety score in both groups were improved after the operation.

Conclusion: TLH can reduce blood loss, hospital stay without increasing the complications. There were slightly differences in quality of life between group and the differences were found in only short term after the operation. TLH still had the benefit on faster recovery, shorter hospital stay and less blood loss.

Keywords: total laparoscopic hysterectomy, quality of life, complication, EQ-5D.

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การศึกษาเปรียบเทียบคุณภาพชีวิตของผู้ป่วยที่เข้าผ่าตัดมดลูกแบบส่องกล้องและแบบเปิดหน้าท้อง

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บทคัดย่อ

วัตถุประสงค์: *เพื่อเปรียบเทียบผลของการผ่าตัดมดลูกแบบส่องกล้องเปรียบเทียบกับการผ่าตัดแบบเปิดหน้าท้องต่อคุณภาพชีวิตของผู้ป่วย*

วัสดุและวิธีการ: *การศึกษานี้เริ่มทำหลังจากได้รับอนุญาตจากกรรมการวิจัย โดยใช้แบบสอบถาม EQ-5D เพื่อประเมินคุณภาพชีวิตของผู้ป่วย โดยจะแจกแบบสอบถามให้กับผู้ป่วยเพื่อประเมินคุณภาพชีวิต ตั้งแต่ก่อนผ่าตัด หลังผ่าตัด 1, 7 และ 28 วัน ในผู้ป่วยที่เข้ารับการตัดมดลูกทั้งแบบส่องกล้อง และแบบเปิดหน้าท้องซึ่งผู้ป่วยจะเป็นผู้ตัดสินใจเลือกวิธีการผ่าตัดเอง นอกจากนั้นการศึกษานี้ยังเก็บข้อมูลเกี่ยวกับการผ่าตัดและภาวะแทรกซ้อนหลังผ่าตัดอีกด้วย โดยผลการศึกษานั้นจะถูกวิเคราะห์โดยใช้โปรแกรม SPSS รุ่น 22*

ผลการศึกษา: *จากผู้ป่วยที่เข้ารับการผ่าตัดแบบเปิดหน้าท้อง 100 ราย และ แบบส่องกล้อง 102 ราย พบว่า ลักษณะโดยทั่วไปของผู้ป่วย โรคที่เป็นสาเหตุให้ตัดมดลูก ระยะเวลาการทำผ่าตัด และภาวะแทรกซ้อนนั้นไม่มีความแตกต่างกัน แต่ในกลุ่มผู้ป่วยที่เข้ารับผ่าตัดแบบส่องกล้องนั้นจะมีรายได้ และระดับการศึกษาที่สูงกว่าเล็กน้อย รวมทั้งมีการเสียเลือดที่น้อยกว่า และ ระยะเวลาในการนอนโรงพยาบาลสั้นกว่า ในส่วนของคุณภาพชีวิตนั้น ในกลุ่มที่ผ่าตัดแบบส่องกล้อง จะสามารถเคลื่อนไหวได้เร็วกว่า แต่ในแง่ความเจ็บปวด หรือการทำกิจวัตรประจำวันนั้นไม่ได้มีความแตกต่างกันอย่างมีนัยสำคัญ ในส่วนของความกังวลนั้นทั้งสองกลุ่มมีคะแนนหลังผ่าตัดดีขึ้นกว่าก่อนผ่าตัด*

สรุป: *การผ่าตัดมดลูกแบบส่องกล้องนั้นจะลดการเสียเลือด ลดระยะเวลาในการนอนโรงพยาบาล โดยที่ไม่ได้เพิ่มภาวะแทรกซ้อน ในส่วนความแตกต่างของคุณภาพชีวิตระหว่างกลุ่มนั้นพบเพียงเล็กน้อย และความแตกต่างนั้นเป็นเพียงระยะสั้นหลังผ่าตัด อย่างไรก็ตามการผ่าตัดผ่านกล้องยังมีประโยชน์ในแง่ของการฟื้นตัวที่เร็วกว่า การนอนโรงพยาบาลที่สั้นกว่า และเสียเลือดที่น้อยกว่า*

คำสำคัญ: *การผ่าตัดมดลูกแบบส่องกล้อง, คุณภาพชีวิต, EQ-5D*

Introduction

Hysterectomy is one of the common procedures performed by gynecologists. Hysterectomy can be performed by exploratory, laparoscopic and robotic assisted in manner. Exploratory is the most common manner to perform hysterectomy worldwide[1]. Laparoscopic hysterectomy usually refers to a hysterectomy which at least one part of the operation is undertaken laparoscopically[2]. In our study, we focused on total laparoscopic hysterectomy (TLH) which was defined as the entire operation including suturing of the vaginal vault is performed laparoscopically[2]. Nowadays, TLH is increasing its popularity. Minimally invasive surgery has various benefits such as faster recovery, shorter hospitals stay and earlier return to work. Therefore, the proportion of laparoscopic to exploratory hysterectomy is increasing[3, 4]. Most of the researches focused on complications, operative time and cost of treatment[3-5]. However, quality of life is an important aspect to be concerned. There are many methods to evaluate the quality of life. Each method can be used to evaluate quality of life in different aspect. Moreover, quality of life in each community depends on cultural, social and familial supporting system.

Assessment of health quality is an abstract, subjective and difficult to measure[6]. Several questionnaires are available to measure in different aspects of health quality. The Euro-quality of life five dimensions (EQ-5D) is a simple self-administered instrument used to measure health related quality of life (HRQOL)[6]. This questionnaire assesses five socially domains including mobility, self-care, usual activity, pain/discomfort and anxiety/ depression. Each domain was classified into 5 levels starting from 1 which means the best to 5 that means the worst. Moreover, EQ-5D also accompanies by a visual analogue scale (VAS) on which the subject is asked to provide a self-assessment their own health ranged from 0 to 100 which are the worst to the best imaginable health state respectively[6]. Therefore, EQ-5D is a generic instrument intended for use by different health professionals. EQ-5D is a holistic view of health, which includes the medical definition, as well as the fundamental importance of independent physical, emotional and social functioning. Each domain is classified in to 5 steps of health quality and easily to use, interpret and compare. Therefore, EQ-5D can be used to measure quality of life of the patient in several conditions such as postoperative evaluation for patients' health. EQ-5D is already translated into Thai language. Thai version EQ-5D has been proven for reliability and acceptability of the questionnaire[7]. Because of the simply and precise of the questionnaire, it does not disturb the patient too much. Therefore, the response rate to the questionnaire is very high.

There have been some studies compared the quality of life of the patients who underwent different type of hysterectomy such as TAH (total abdominal hysterectomy) vs TLH (total laparoscopic hysterectomy) vs VH (vaginal hysterectomy) vs SLH (supracervical hysterectomy)[8, 9]. Those studies mostly performed in Western countries. Many cultural aspects, life style, social support and perceptions are different between Western and Eastern countries. Therefore, the aspect in quality of life may be different. For those reasons, this study was conducted to evaluate the quality of life of the patients who underwent TAH compare to TLH at King Chulalongkorn Memorial Hospital, Bangkok, Thailand.

Materials and Methods

After Ethical Board Committee of Chulalongkorn University approved the protocol, the study was conducted. The recruitment and data collection were performed during August 2016 and August 2017. Sample size calculation based on the data form previous study[9] with determined α error at 0.05, β error at 0.2. From the previous study, they found that the difference of EQ-5D score more than 5% was considered as significant. Ninety subjects per arm were required. We add 10% for dropout

rate, therefore; 99 subjects per group were collected.

Permission for the usage of EQ-5D was obtained from Euro-QOL group. EQ-5D was translated and verified into several languages include Thai language. We used Thai version of EQ-5D questionnaire to determine the quality of life of the subjects in this study.

The patients who were admitted and planned to perform TAH or TLH depended on their own decision at out patient department clinic after holistic counselling was given. However, their financial status and insurance coverage may influence their decision about the operation options. All the participants were counselled about the details of the trial and the questionnaire including follow-up visits. During preoperative period, general characteristics and clinical data of the participants were collected. Thai version EQ-5D questionnaire was given to the participants to read and answer by themselves (day 0; pre-operation). After the operation, the follow up questionnaires for day 1, day 7 and day 28 postoperation were given and the patients had to complete the questionnaires at home. The participants had to send back the entire questionnaire at follow-up visit.

General characteristics included age, parity, education, income, underlying disease and history of previous pelvic surgery. Operative data including diagnosis, pathologic report, weight of specimen, operative time, operative blood loss, conversion rate, blood transfusion and complications were also collected. Quality of life was measured with EQ-5D with VAS scale to determine their quality of life at before the operation then day 1, day 7 and day 28 postoperation.

After all data were collected, statistics analysis was performed with SPSS version 22. Unpaired t test, Chi square test, Fisher-Exact test, mean, median and percentile were used to analyze the date and presented in table or graph as appropriate.

Results

Total 100 cases of TAH and 102 cases of TLH were collected. Baseline characteristics of the participants including age, weight, height, body mass index (BMI), education, income, underlying disease, diagnosis and history of previous pelvic surgery were shown in Table 1. Weight, height, BMI, menopause status and diagnosis were similar in both groups. Educational level and income of TLH group were higher than TAH group. Previous pelvic surgery and age of the patients were slightly higher in TAH group. The most common reason to perform hysterectomy was myoma uteri in both groups. This study included precancerous and cancer cases. Precancerous cases included endometrial hyperplasia and CIN 3 with positive margin after proceeding excisional procedure. Cancer cases include cervical cancer stage Ia1 and early stage low risk endometrial cancer that can be treated by TAH or TLH.

Operative data and QOL data were presented in Table 2. Uterine size and operative time were not different in both groups. Blood loss was higher and length stay was longer in TAH group. Complication rate was similar. We found rectal injury one case in TAH group (1/100) and ureteric injury 1 case in TLH group (1/102). There was no conversion in this study. Transfusion rate in TAH group was 1% (blood loss 1,200 ml) and 1.96% in TLH group. For the transfusion in TLH group, one case had blood loss 800 ml and another one case had blood loss only 200 ml but she had anemia before the surgery. For the quality of life data, the less EQ-5D score means the better quality of life in that aspect. For domain 1 (mobility), TLH group had poorer score than TAH group. However, at day 1 after the operation mobility score was similar between group and TLH group was significantly higher ability to mobilize than TAH group in first week after the operation. Finally the different of mobility (domain 1) was not detected at 1 month after the operation. For domain 2 (self-care), there was no different between group in any point of time. Details of other aspects of quality of life in EQ-5D were presented in Table 2.

For VAS score, VAS in TLH group was slightly

higher than TAH in preoperative period and 1 week after the operation. However, the trend of VAS score in day 1 and day 7 after the operation decreased from the preoperative baseline and then finally achieved higher VAS score in 1 month after operation in both groups.

Table 1. General characteristic of the population in TAH and TLH group.

Characteristic	TAH (N=100)	TLH (N=102)	p value
Age (year): Mean (SD)	45.7 (9.2)	48.8 (7.5)	0.008
Weight (Kg): Mean (SD)	58.4(12.1)	59.5 (12.4)	0.547
Height (cm): Mean (SD)	157.2 (4.8)	157.9 (5.2)	0.378
BMI (Kg/m^2): Mean (SD)	23.7 (4.8)	23.8 (4.6)	0.783
Education: N (%)			
Primary	12 (12)	5 (4.9)	
Secondary	26 (26)	20 (19.6)	
Bachelor	50 (50)	2 (2.0)	
Higher than Bachelor	12 (12)	64 (62.7)	
Income (Baht): N (%)			
< 15001	19 (19)	12 (11.8)	
15001-30000	36 (36)	17 (16.7)	
30001-50000	41 (41)	38 (37.3)	
> 50000	4 (4)	35 (34.3)	
Menopause: N (%)			
No	77 (77)	75 (73.5)	
Yes	23 (23)	27 (26.5)	
Underlying disease: N (%)			
No	58 (58)	68 (63.7)	
Diabetes Mellitus	7 (7)	5 (4.9)	
Hypertension	16 (16)	8 (7.8)	
Dyslipidemia	2 (2)	4 (13.7)	
Other (Thyroid, CA breast)	17 (17)	17 (16.7)	
Previous pelvic surgery: N (%)			
No	59 (59)	68 (66.7)	
Yes	41 (41)	34 (33.3)	
Diagnosis: N (%)			
Myoma	58 (58)	65 (63.7)	
Adenomyosis	4 (4)	15 (14.7)	
Ovarian cyst	17 (17)	2 (2.0)	
Premalignant and malignant lesions*	21 (21)	20 (19.6)	

* Premalignant lesions included CIN I, II, III and Endometrial hyperplasia; Malignant lesions included cervical cancer stage Ia1 and early stage low risk endometrial cancer

Table 2. Surgical outcome and quality of life of the patients in TAH and TLH group.

	TAH (N=100)	TLH (N=102)	p value
Uterine size (g): Median (range)	195 (126-390)	214 (124-316)	0.234
Operative time (min): Mean (SD)	89.5 (37.7)	98.1 (27.7)	0.067
Estimate blood loss (ml); Median (range)	200 (85-300)	100 (50-200)	< 0.05
Length of stay (d): Mean (SD)	3.78 (1.06)	2.68 (0.73)	< 0.05
EQ-5D Day 0 (preoperative): Mean (SD)			
D0-1 (mobility)	1.01 (0.17)	1.11 (0.40)	0.024
D0-2 (self care)	1.10 (0.41)	1.07 (0.38)	0.575
D0-3 (usual activity)	1.13 (0.56)	1.06 (0.31)	0.265
D0-4 (pain/ discomfort)	1.53 (0.95)	1.23 (0.55)	0.007
D0-5 (anxiety/ depression)	1.71 (1.05)	1.31 (0.73)	0.002
VAS Day 0: Mean (SD)	76.95 (17.94)	83.16 (13.86)	0.006
EQ-5D Day 1 (after operation): Mean (SD)			
D1-1 (mobility)	2.45 (1.23)	2.35 (0.96)	0.531
D1-2 (self care)	2.10 (1.26)	2.10 (0.92)	0.960
D1-3 (usual activity)	1.90 (1.11)	1.85 (0.96)	0.851
D1-4 (pain/ discomfort)	2.44 (1.08)	2.24 (0.81)	0.148
D1-5 (anxiety/ depression)	1.65 (1.10)	1.40 (0.62)	0.050
VAS Day 1: Mean (SD)	70.80 (16.72)	75.03 (14.07)	0.053
EQ-5D week 1 (day 7): Mean (SD)			
W1-1 (mobility)	1.87 (0.69)	1.60 (0.64)	0.006
W1-2 (self care)	1.36 (0.61)	1.28 (0.51)	0.342
W1-3 (usual activity)	1.75 (0.89)	1.91 (1.10)	0.253
W1-4 (pain/ discomfort)	1.84 (0.86)	1.80 (0.61)	0.732
W1-5 (anxiety/ depression)	1.36 (0.77)	1.22 (0.49)	0.139
VAS week 1: Mean (SD)	77.50 (15.71)	82.2 (13.4)	0.023
EQ-5D month 1 (day 28): Mean (SD)			
M1-1 (mobility)	1.29 (0.48)	1.26 (0.47)	0.703
M1-2 (self care)	1.06 (2.78)	1.13 (0.50)	0.239
M1-3 (usual activity)	1.15 (0.39)	1.31 (0.53)	0.013
M1-4 (pain/ discomfort)	1.31 (0.48)	1.40 (0.65)	0.256
M1-5 (anxiety/ depression)	1.25 (0.59)	1.04 (0.26)	0.002
VAS month 1: Mean (SD)	84.90 (14.61)	87.83 (12.56)	0.127

Discussion

This study was conducted to compare quality of life of TAH and TLH patients by using EQ-5D questionnaire. In the aspect of mobility in the questionnaire reflects walking and moving abilities, patients in TAH group had better mobility score in preoperative period but the tendency of mobility score in TLH group was better than TAH group at postoperative day 1. However, there was no statistically significant at that point. The superiority of mobility score in TLH group was obviously showed in 1 week after operation. Finally, the score became similar at 1 month after the operation. From the result of several studies showed that pain in TLH was less than TAH. Therefore, the patients in TLH groups achieved faster mobility in recent post-operative period but the difference of mobility score disappeared after 1 month. This confirmed the short term benefit of TLH in mobility aspect.

For self-care aspect which represents any self-care activities such as bathing, tooth brushing and toileting, there was no different between groups in any point of time. During hospitalization (day 1 to day 3 postoperation), daily activity of the patients was usually assisted by nurse and the patient's relatives. Therefore, the interpretation of the difficulty of activity and translated into score may be interfered. After the patients went back home, Thai cultural and familial supporting system may have some influences in self-care and usual activity of the patients. In extended familial system like Thai or many Asian families, the patients usually received some assistances form their relatives to manage their self-care and daily activity during their recovery time which was different from Nuclear family system in Western countries. For that reason, the daily activity of our patients may be manipulated by their relatives. Therefore, the difficulties of daily activity in TAH and TLH which were represented by self-care score may not be significantly different. While, the nuclear family system of Western countries, the patients have to do nearly all daily and self-care activities by themselves. Without any assistant to manage activity, the different of the score became higher because of the difficult of daily activity was clearly showed in many Western studies[2, 6]. For the usual activity which means working, reading a book or doing hobbies, there were no differences between TAH and TLH in preoperative, 1st day and the 1st week after the operation but TLH group had worse score in the 4th week after the operation. Form many data, TLH patients returned to work earlier than TAH patients. TAH patients usually got sick leave for 4-6 week after the operation, while TLH patients already returned to work at that period of the time. Therefore, the actual daily activity at one month duration may be different between groups. Unfortunately, this study did not collect some data such as return to work duration and analgesic medication consumption. Collecting these factors in future research may be required. Moreover, the aspect of social and familial support may need in-depth interview to evaluate the detail of the support in each family.

For pain and discomfort aspect, TAH group felt more pain at the baseline. After the operation, pain and discomfort between groups were not different. However, in the 1st day after the operation, the anesthetic methods may influence the pain score because TAH patients in our hospital were mostly performed under spinal anesthesia but TLH was performed under General anesthesia. Spinal opioid that was added in spinal anesthesia can reduce postoperative pain. For that reason, the benefit of TLH in less pain aspect was obscured by different anesthetic technique at 1st day after operation. For 1 week and 1 month after operation pain and discomfort score were still similar. While, TLH had higher mobility score with same pain and discomfort score at the 1st week, it may represent some different activity of the patients. For anxiety and depression aspect, TLH group had less anxiety score than TAH group before the operation. Education and information can reduce the anxiety of the patients both before and after the operation. Due to the higher educational level in TLH group, the

preoperative anxiety score in TLH was less than TAH group. Then the score was similar at day 1 and day 7 after operation. Anxiety score of both groups in postoperative period were lower than preoperative period. After successful operation, the anxious level decreased and the decline was not depended on mode of the operation.

For VAS which reflected the overall health status perception of the patients, TLH group had higher VAS score in pre-operative period and at day 7 after the operation. However, the differences of the score between groups were not detected in day 1 and day 28 after the operation. TLH had short term benefit and then the benefit was faded down after time. Our results were different from some studies such as LACE trial[9], which claimed that TLH gave a greater improvement quality of life than TAH up to 6 months after surgery. Study of Garry, et al[2] found that laparoscopic hysterectomy had better quality of life at 6 week after surgery. On the other hand, our study result was similar to the study of Lumsden, et al[4] that found no difference at 1 month, 6 month and 1 year after surgery.

This study compared the quality of life between TAH and TLH in Thai patients and the results of our study were different from many Western studies. The different familial system and culture of taking care of the sick people by their relatives resulted on the quality of life of the patients. The results of this study can be used to counselling to the patient who is planning to performed TLH or TAH. However, there still had some limitations in this study. First, this study was not a randomized controlled trial.

The patients were not randomly assigned to perform TAH or TLH. Therefore, some baseline characteristics such as educational level and income were different between groups. For elimination these confounders in the future study, randomized controlled trial would be required to dilute the confounder effect of those factors. Second, the return to work duration should also be collected in the future study because it may have the effect on some aspect of quality of life. Moreover, the in-depth interview may be required to evaluate the details of the factors that result in recovery of the patients.

Conclusion

TLH may help in short term improvement in some aspect of quality of life after surgery. Long term benefit in quality of life is not significant. However, TLH still has benefits in reduce blood loss and hospital stay compare to TAH.

Potential conflicts of interest

The authors declare no conflict of interest.

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OBSTETRICS

Effect of Unfulfilled Standard Antenatal Care on Pregnancy Outcomes

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ABSTRACT

Objectives: To compare pregnancy outcomes between women who received unfulfilled standard versus fulfilled standard antenatal care (ANC) according to the Ministry of Public Health of Thailand (MOPH) guideline as the following; 1st visit as soon as possible but gestational age (GA) not later than 12 weeks of gestation, 2nd visit: GA between 16 - 20 weeks, 3rd visit: GA between 24 – 28 weeks, 4th visit: GA between 30 – 34 weeks and 5th visit: GA between 36 – 40 weeks.

Materials and Methods: A retrospective cohort study was conducted by recruiting medical records of all singleton pregnant women who delivered at the Department of Obstetrics and Gynecology, Faculty of Medicine, Vajira Hospital, Bangkok, Thailand from June 2015 to May 2016. All recruited pregnant women had singleton pregnancies, complete medical data record, certain GA by their last menstrual period or by early ultrasound before GA 28 weeks and GA at delivery equal to 28 weeks or more. Exclusion criteria were women with pre-existing medical conditions and fetal anomalies. Study outcomes were the rates of low neonatal birth weight (< 2,500 g), preterm delivery, low Apgar scores at 1 and 5 minute (< 7), neonatal intensive-care unit (NICU) admission, preeclampsia and postpartum hemorrhage.

Results: From 1,237 pregnant women who met to the eligible criteria, there were 1,170 cases included into the study. Six hundreds and three cases received fulfilled standard ANC and 567 cases received unfulfilled standard ANC. No statistical difference was found in the rates of low neonatal birth weight, preterm delivery, low Apgar scores, NICU admission, preeclampsia and postpartum hemorrhage between both groups. In addition, there were significantly higher rates of previous abortion, advanced maternal age, pre-pregnancy overweight and obesity and lower rates of teenage pregnancy, pre-pregnancy underweight in women who received fulfilled standard ANC.

Conclusions: There was no significant adverse pregnancy outcome in unfulfilled standard compared with fulfilled standard ANC group.

Keywords: antenatal care, pregnancy outcomes, low birth weight

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ผลของการฝากครรภ์ที่ไม่เป็นไปตามมาตรฐานต่อผลลัพธ์ของการตั้งครรภ์

ปาลิน พูลธนะนันท์, สมนิมิตร เหลืองรัศมีรุ่ง

บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาเปรียบเทียบผลลัพธ์ของการตั้งครรภ์ระหว่างสตรีตั้งครรภ์ที่เข้ารับการฝากครรภ์ครบและไม่ครบตามเกณฑ์ของกระทรวงสาธารณสุขไทย โดยการฝากครรภ์ครบตามเกณฑ์ 5 ครั้ง ของกระทรวงสาธารณสุขไทยมีดังนี้ : ครั้งที่ 1 ฝากครรภ์เร็วที่สุดเมื่อทราบว่าตั้งครรภ์ แต่อายุครรภ์ต้องไม่เกิน 12 สัปดาห์, ครั้งที่ 2 เมื่ออายุครรภ์ระหว่าง 16 – 20 สัปดาห์, ครั้งที่ 3 เมื่ออายุครรภ์ระหว่าง 24 – 28 สัปดาห์, ครั้งที่ 4 เมื่ออายุครรภ์ระหว่าง 30 – 34 สัปดาห์, ครั้งที่ 5 เมื่ออายุครรภ์ระหว่าง 36 – 40 สัปดาห์*

วัสดุและวิธีการ: *การศึกษาย้อนหลังจากข้อมูลในเวชระเบียนของหญิงตั้งครรภ์เดี่ยวทุกรายที่มีการเก็บข้อมูลครบถ้วน, อายุครรภ์แม่นยำ และคลอดที่อายุครรภ์มากกว่าหรือเท่ากับ 28 สัปดาห์ ที่คลอดในโรงพยาบาลวชิรพยาบาล ประเทศไทย ตั้งแต่มิถุนายน 2558 ถึง พฤษภาคม 2559 เกณฑ์การคัดออก ได้แก่ มีโรคประจำตัวที่ส่งผลกระทบต่อผลลัพธ์ของการตั้งครรภ์หรือทารกในครรภ์มีความพิการ ผลลัพธ์ของการตั้งครรภ์ที่ต้องการศึกษา ได้แก่ ความชุกของทารกแรกเกิดน้ำหนักตัวน้อย (< 2,500 กรัม), การคลอดก่อนกำหนด (< 37 สัปดาห์), คะแนนแอปการ์น้อยกว่า 7 คะแนน ที่นาทีที่ 1 และ 5 หลังคลอด, การส่งตัวทารกไปรักษาต่อในหอผู้ป่วยทารกแรกเกิดวิกฤต, ภาวะครรภ์เป็นพิษ และการตกเลือดหลังคลอด*

ผลการศึกษา: *จากผู้คลอดครรภ์เดี่ยวทั้งหมด 1,237 ราย เข้าเกณฑ์การวิจัยทั้งหมด 1,170 ราย จัดอยู่ในกลุ่มฝากครรภ์ครบตามเกณฑ์กระทรวงสาธารณสุขไทย 603 ราย และไม่ครบตามเกณฑ์กระทรวงสาธารณสุขไทย 567 ราย พบว่า ความชุกของทารกแรกเกิดน้ำหนักตัวน้อย, การคลอดก่อนกำหนด, คะแนนแอปการ์น้อยกว่า 7 คะแนน ที่นาทีที่ 1 และ 5 หลังคลอด, การส่งตัวทารกไปรักษาต่อในหอผู้ป่วยทารกแรกเกิดวิกฤต, ภาวะครรภ์เป็นพิษ และการตกเลือดหลังคลอด ไม่แตกต่างกันในสองกลุ่มอย่างมีนัยสำคัญทางสถิติ ในกลุ่มสตรีตั้งครรภ์ที่ฝากครบตามเกณฑ์ของกระทรวงสาธารณสุขไทยมีความชุกของประวัติการแท้งในครรภ์ก่อน, มารดาอายุมากกว่า 35 ปี และมีค่าดัชนีมวลกายก่อนตั้งครรภ์มากกว่ามาตรฐาน สูงกว่าอย่างมีนัยสำคัญทางสถิติ รวมทั้งมีความชุกของสตรีตั้งครรภ์วัยรุ่น และมีค่าดัชนีมวลกายก่อนตั้งครรภ์น้อยกว่ามาตรฐาน ต่ำกว่าอย่างมีนัยสำคัญทางสถิติ*

สรุป: *ไม่พบความความแตกต่างของผลลัพธ์ของการตั้งครรภ์ระหว่างสตรีตั้งครรภ์ที่เข้ารับการฝากครรภ์ครบและไม่ครบตามเกณฑ์ของกระทรวงสาธารณสุขไทย*

คำสำคัญ: *การฝากครรภ์, ผลลัพธ์ของการตั้งครรภ์, ทารกแรกเกิดน้ำหนักตัวน้อย*

Introduction

Antenatal care (ANC) is an important strategy that can help preventing adverse pregnancy outcomes which can occur with any mothers or any newborns. This includes many measures such as history taking, physical examination, fetal heart sound monitoring, laboratory investigation and ultrasonography in order to identify a pregnant woman or a fetus at risk that can lead to adverse pregnancy outcomes. Early detection of a pregnant woman at risk is useful for planning of treatment program. Closed monitoring, counseling pregnant woman and her husband, timing of delivery, planning route of delivery should be performed intensively and continuously. It is necessary for pregnant women to receive antenatal care as soon as possible and it must be continuous[1].

For low risk pregnancy, we have used Dame Janet Campbell's fixed pattern of antenatal visits since 1920, i.e. after first ANC visit patient will be appointed to ANC every 4 weeks until 28th week of gestation, then every 2 weeks until 36th week of gestation, then every week until delivery. If the patients are at risk, the doctor may follow up more frequently[1].

In 2002, the World Health Organization (WHO) has suggested pregnant women to have at least four visits referring to the gestational age (GA) range as the following; 1st visit as soon as possible but not later than 12 weeks of gestation, 2nd visit during 24 – 28 weeks, 3rd visit during 30 – 34 weeks and 4th visit during 36 – 40 weeks[2].

In 2013, Ministry of Public Health of Thailand (MOPH) adjusted the WHO guideline to be appropriate for Thai women by adding the visit at 16 - 20 weeks of GA, therefore suggestion for standard ANC in Thailand is as the following; 1st visit as soon as possible but not later than 12 weeks of gestation, 2nd visit between 16 - 20 weeks, 3rd visit between 24 – 28 weeks, 4th visit between 30 – 34 weeks and 5th visit between 36 – 40 weeks[3].

According to recent data, it was found that 57-64% of pregnant women in Thailand started first ANC after 12 weeks of gestation3 even MOPH has recommended to have ANC as soon as possible. From previous retrospective cohort studies, it was found that the more numbers of antenatal visits resulted in decreasing rate of low birth weight (LBW), NICU admission and neonatal death[4]. On the other hand, fewer ANC visits could result in late risk evaluation leading to late treatment, which eventually increases adverse pregnancy outcomes, e.g. low neonatal birth weight (< 2,500 g), birth asphyxia, neonatal endotracheal intubation, neonatal intensive-care unit (NICU) admission, neonatal death, postpartum hemorrhage, preeclampsia or gestational diabetes[4].

However another randomized controlled trial found that there were no differences in rates of NICU admission, low 1-minute Apgar scores (< 7), umbilical cord pH less than 7.0 and LBW between women who received ANC 10 or more and less than 10 visits 5. Villar and colleagues conducted multicenter randomized controlled trial between fixed pattern model and new model ANC according to WHO guideline 2002. They found no significant difference in rates of LBW and preeclampsia between both groups[6]. After their study had published, WHO guideline was widely used in state of fixed pattern model. In 2013, Vogel and colleagues reconsidered exploratory analysis using the same population in the study of Villar and colleagues. They found that there was significantly higher rate of fetal death between 32nd and 36th weeks of gestation (adjusted RR 2.24; 95% CI 1.42, 3.53) which could be related to reduced number of visits[7].

Until now, there is still no clear-cut information about pregnancy outcomes relating to the ANC guideline of MOPH. Therefore we conduct the present study in Thai pregnant women to investigate if there is any different result between women who receive fulfilled standard and unfulfilled standard ANC.

Materials and Methods

This retrospective cohort study was conducted

by recruiting medical records of all singleton pregnant women who delivered at the Department of Obstetrics and Gynecology, Faculty of Medicine, Vajira Hospital, Navamindradhiraj University, Thailand from June 2015 to May 2016. This study was approved by the Vajira Institutional Review Board.

Inclusion criteria were singleton pregnancy, complete data record, certain GA by their last menstrual period or by early ultrasound before GA 28 weeks, and GA at birth equal to 28 weeks or more. Exclusion criteria were women who had medical disorders or any conditions which may affect pregnancy outcomes (e.g. pre-existing diabetes, chronic hypertension, autoimmune diseases, renal disease, HIV infection and syphilis infection), severe fetal congenital anomalies or chromosomal abnormalities.

According to MOPH guideline, we divided population into two groups, i.e. the women who received fulfilled standard and unfulfilled standard ANC as the following; 1st visit as soon as possible but not later than 12 weeks of gestation, 2nd visit between 16 - 20 weeks, 3rd visit between 24 – 28 weeks, 4th visit between 30 – 34 weeks and 5th visit between 36 – 40 weeks[3].

Based on the data collected from the medical records, characteristic data were age, GA at first ANC visit, number of visits, parity, history of LBW delivery, history of abortion, ethnicity, pre-pregnancy body mass index (BMI), history of alcoholic drinking and smoking during pregnancy, and medical disorders. The primary objective was to study rate of low birth weight delivery defined as neonatal weight less than 2,500 g. The secondary objectives were the rates of preterm birth defined as delivery before 37 complete weeks, birth asphyxia by considering Apgar sores at 1 and 5 minute less than 7, NICU admission, preeclampsia diagnosed by blood pressure of 140/90 mmHg or more measuring apart for at least 6 hours together with urine protein more than 300 mg per 24 hours[8] and postpartum hemorrhage defined as blood loss 500 ml or more in vaginal delivery and 1,000 ml or more in cesarean delivery[1].

Sample size was calculated based on our pilot study with 5% chance of making a type I error and 20% of type II error. Number needed was 558 for each group. The data were analyzed by SPSS version 22.0 (IBM). Chi-square test and Fisher's exact test were used for comparing categorical data and study t-test was used for comparing continuous data. For multivariate analysis, the possible factors identified with univariate analysis were further entered into the logistic regression analysis to determine independent predictors of patient and presented as odds ratio (adjusted OR) and 95% confidence interval (CI). A p value of less than 0.05 was considered statistically significant.

Results

From all 1,512 pregnant women delivered in the studied period, 1,237 women were included in this study. After recruitment, 67 pregnant women were excluded, 9 of which due to fetal anomalies and 58 due to maternal previous medical conditions that could affect pregnancy outcomes. Therefore 1,170 pregnant women were enrolled to the study, 603 and 567 cases of which were classified in fulfilled standard and unfulfilled standard ANC group, respectively. Process of studied enrollment is shown in Fig 1.

Demographic data and antenatal characteristics of pregnant women were presented in Table 1. There were significant differences in maternal age, GA at first visit ANC, number of visits, history of abortion and pre-pregnancy BMI between fulfilled standard and unfulfilled standard ANC group. There were no differences in parity, history of LBW delivery, ethnicity and history of alcoholic drinking and smoking during pregnancy between both groups.

For the studied pregnancy outcomes, the results were no significant difference in rates of LBW delivery, preterm birth, low 1- and 5-minute Apgar scores, NICU admission, preeclampsia and postpartum hemorrhage (Table 2).

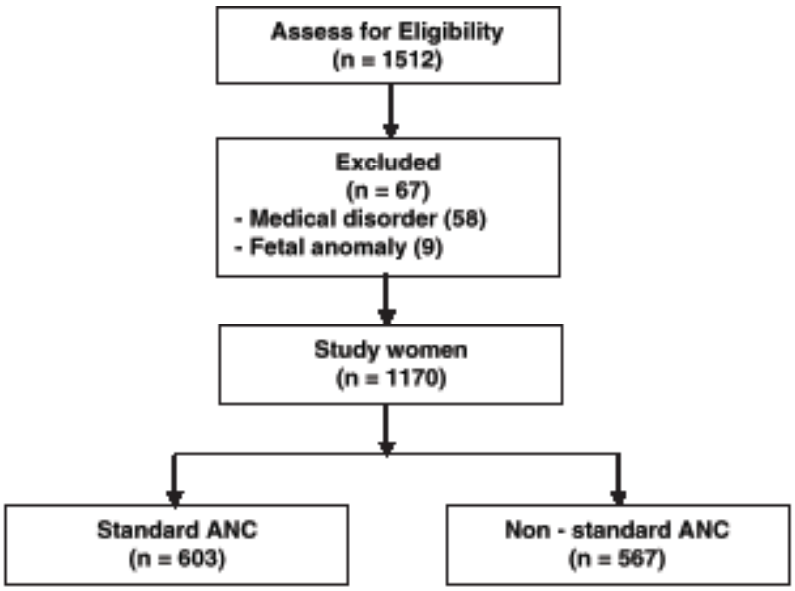

Fig. 1. Process of studied enrollment.

Table 1. Maternal demographic characteristics of fulfilled and unfulfilled antenatal care groups.

Characteristics	Fulfilled standard ANC	(n = 603)	Unfulfilled ANC standard	(n = 567)	p value
GA at 1st ANC (Median, IQR)	9	(7-11)	17	(15-21)	< 0.001
Number of visits (Median, IQR)	11	(10-13)	9	(7-10)	< 0.001
Maternal age, yrs (n, %)					< 0.001
Age < 20 years	49	(8.1)	104	(18.3)	
Age 20 - 34 years	418	(69.3)	379	(66.8)	
Age ≥ 35 years	136	(22.6)	84	(14.8)	
Nulliparous (n, %)	293	(48.6)	249	(43.9)	0.109
Previous LBW (n, %)	18	(3.0)	17	(3.0)	0.989
Previous abortion (n, %)	156	(25.9)	107	(18.9)	0.004
Thai ethnic (n, %)	565	(93.7)	514	(90.7)	0.052
Pre-pregnancy BMI (n, %)					<0.001
< 18.50	89	(14.8)	144	(25.4)	
18.50 - 24.99	345	(57.2)	316	(55.7)	
25.00 - 29.99	122	(20.2)	85	(15.0)	
≥ 30	47	(7.8)	22	(3.9)	
Alcohol (n, %)	1	(0.2)	2	(0.4)	0.528
Smoking (n, %)	2	(0.3)	7	(1.2)	0.077

IQR: interquartile range, ANC: antenatal care, LBW: low birth weight, BMI: body mass index

Table 2. Pregnancy outcomes of fulfilled and unfulfilled standard antenatal care groups.

Outcomes	Fulfilled standard ANC	(n = 603)	Unfulfilled ANC standard	(n = 567)	p value
LBW (n, %)	40	(6.6)	40	(7.1)	0.775
Preterm birth (n, %)	34	(5.6)	37	(6.5)	0.525
Low 1-min APGAR (n, %)	21	(3.5)	20	(3.5)	0.967
Low 5-min APGAR (n, %)	2	(0.3)	4	(0.7)	0.371
NICU admission (n, %)	10	(1.7)	8	(1.4)	0.731
Preeclampsia (n, %)	18	(3.0)	21	(3.7)	0.494
PPH (n, %)	14	(2.3)	12	(2.1)	0.812

ANC: antenatal care, LBW: low birth weight, NICU: neonatal care unit, PPH: postpartum hemorrhage

When multivariate analysis was used to adjust for maternal age, BMI and history of abortion, to exclude confounding factors that may affect pregnancy outcome, the outcomes were still not significantly different between the two groups (Table 3).

Table 3. Pregnancy outcomes of fulfilled and unfulfilled antenatal care groups adjust for maternal age, BMI and history of abortion.

Outcomes	Fulfilled standard ANC	(n = 603)	Unfulfilled ANC standard	(n = 567)	Unadjusted Odds ratio	(95% CI)	Adjusted Odds ratio[a]	(95% CI)
LBW	40	(6.6)	40	(7.1)	0.94	(0.59-1.47)	0.93	(0.59-1.47)
Preterm birth	34	(5.6)	37	(6.5)	1.17	(0.72-1.89)	1.22	(0.75-1.98)
Low 1-min Apgar	21	(3.5)	20	(3.5)	1.01	(0.54-1.89)	1.05	(0.56-1.97)
Low 5-min Apgar	2	(0.3)	4	(0.7)	2.14	(0.39-11.70)	2.28	(0.41-12.71)
NICU admission	10	(1.7)	8	(1.4)	1.18	(0.46-3.01)	1.18	(0.46-3.04)
Preeclampsia	18	(3.0)	21	(3.7)	0.80	(0.42-1.52)	0.71	(0.37-1.36)
PPH	14	(2.3)	12	(2.1)	1.10	(0.50-2.40)	1.07	(0.4912.35)

Data presented as n, %

ANC: antenatal care, LBW: low birth weight, NICU: neonatal care unit, PPH: postpartum hemorrhage

[a] Adjusted for maternal age, BMI and history of abortion

Discussion

There were significantly higher rates of teenage pregnancy and pre-pregnancy underweight BMI in unfulfilled standard ANC group. These can reflect that the patients in this group have lower concern on health of themselves. Vice versa, the patients in fulfilled standard ANC group had significantly higher history of abortion, rate of advanced maternal age, overweight and obesity which might cause them to concern more than patients who did not have and result in early visit for ANC.

There might be other factors that effected

pregnancy outcome. Previous study by Triped O. found that maternal risk factors of low birth weight were low pre-pregnancy BMI, prior LBW delivery, number of ANC vists[9] and study by Sattayaruk S. found that there was significant relationship between less number of ANC visits and low 1-minute APGAR score[10]. Therefore we used multivariate analysis to adjust for maternal age, pre-pregnancy BMI and history of abortion to exclude confounding factors that may affect pregnancy outcomes. The outcomes were still not significantly different between the two groups.

In our study there were no differences in rates of LBW, APGAR score at 1 and 5 minute less than 7, and NICU admission which is correlated with previous study by Carter EB. in 2016 which compared between ANC more or equal to 10 visits and less than 10 visits in low risk pregnancy. As implied to our study it seems to be no difference in number of visits in both groups (9 vs. 11) from Carter EB.6 study cut point. These can result in no differences in pregnancy outcomes.

Although majority of pregnant women had regular and continuous ANC visits, they were assigned to unfulfilled standard ANC group due to first visit was late than 12 weeks of gestational age. We considered that the number of visits and continuance should be more concerned as an important predictor of pregnancy outcomes than gestational age at first visit.

This study might have some limitations. Firstly, there are selection biases, i.e. the inclusion criteria was GA at birth more than 28 weeks causing loss data on population who delivered at GA 24-28 weeks. It may result in lower rate of LBW than it should be in unfulfilled ANC group. Secondly, pregnant women who had history of abortion that could be from congenital or chromosomal anomalies tended to come to visit ANC earlier and then are enrolled in fulfilled standard rather than unfulfilled standard ANC group (25.9 vs 18.9%, P = 0.004). So, the result of fulfilled standard ANC group might be worse than it should be. Third, this study was a retrospective study, the result might not represent the effects of fulfilled standard versus unfulfilled standard ANC according to the MOPH guideline as good as randomized control trial.

Further study should be more concerned about GA at first visit cut point and continuance to achieve more accurate outcomes and to exclude pregnant woman who have history of abortion and non-Thai ethnicity in order to eliminate the selection bias. And new ANC guidelines should be adjusted by concern more about number of visits and GA at first visit to be as soon as possible. In case of late 1st ANC visit, the physician should encourage pregnant woman to take ANC as soon as possible and adequate amount.

Conclusion

There was no significant adverse pregnancy outcome in unfulfilled standard compared with fulfilled standard ANC group

Potential conflicts of interest

The authors declare no conflict of interest.

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OBSTETRICS

Prevalence of Exclusive Breastfeeding among Adolescent Mothers in Bangkok

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ABSTRACT

Objectives: To find the prevalence of exclusive breastfeeding (EBF) among adolescent mothers at 1 to 6 months postpartum and to evaluate the potential factors that encourage 6 months of EBF.

Materials and Methods: This prospective descriptive study was conducted from May to December 2016. A total of 192 adolescent mothers were interviewed directly at postpartum and interviewed by phone monthly over six months. The primary outcome was prevalence of EBF at 1 to 6 months postpartum. The secondary outcome was potential factors of 6 months EBF and reasons for discontinuation of EBF before 6 months.

Results: The prevalence EBF rates at 1 to 6 months postpartum were 97.4%, 54.7%, 32.3%, 25.5%, 20.8% and 19.8% respectively. The most common reasons for discontinuation of EBF were returning to school or work (58.4%). Significant predicting factors of 6 months EBF were maternal age 17-19 years old (adjust odds ratio (aOR) 5.96, 95% CI 1.62-21.92), marital marriage status (aOR 2.79, 95% CI 1.13-6.86), unemployment / housewives (aOR 10.08, 95% CI 2.00-50.75), and having income (aOR 3.98, 95% CI 1.35-11.72).

Conclusion: This study showed that EBF in adolescent mothers for 6 months was 19.8%. The most reasons of discontinuation of EBF before 6 months were returning to school or work. Significant predicting factors for 6 months EBF were maternal age, marital status, occupation and income.

Keywords: exclusive breastfeeding, adolescent, prevalence, factor

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ความชุกของการเลี้ยงลูกด้วยนมแม่เพียงอย่างเดียวในแม่วัยรุ่นที่กรุงเทพมหานคร

ณัฐนนท์ งามนิล, เกษมสิษฐ์ แก้วเกียรติคุณ

บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาความชุกของการเลี้ยงลูกด้วยนมแม่อย่างเดียวที่ 1 – 6 เดือนในแม่วัยรุ่น และเพื่อวิเคราะห์ปัจจัยที่มีผลต่อการเลี้ยงลูกด้วยนมแม่อย่างเดียว 6 เดือน*

วัสดุและวิธีการ: *ศึกษาเชิงพรรณนาไปข้างหน้าในแม่วัยรุ่น 192 คนที่คลอดบุตร ระหว่างวันที่ 1 พฤษภาคม ถึง 30 ธันวาคม 2559 ติดตามการเลี้ยงลูกด้วยนมแม่โดยการสัมภาษณ์โดยตรงก่อนออกโรงพยาบาลและสัมภาษณ์ทางโทรศัพท์ เมื่อ 1 ถึง 6 เดือนหลังคลอดบุตร ผลลัพธ์หลักคือความชุกของการเลี้ยงลูกด้วยนมแม่อย่างเดียวที่ 1 – 6 เดือนหลังคลอด ผลลัพธ์รองได้แก่ ปัจจัยที่มีผลต่อการเลี้ยงลูกด้วยนมแม่อย่างเดียว 6 เดือนและเหตุผลของการยุติการเลี้ยงลูกด้วยนมแม่อย่างเดียวก่อน 6 เดือน*

ผลการศึกษา: *อัตราการเลี้ยงลูกด้วยนมแม่เพียงอย่างเดียวในแม่วัยรุ่น ที่ 1 ถึง 6 เดือนหลังจากคลอดบุตรคือ ร้อยละ 97.4, 54.7, 32.3, 25.5, 20.8 และ 19.8 ตามลำดับ ซึ่งเหตุผลที่พบมากที่สุดที่ทำให้ยุติการเลี้ยงลูกด้วยนมแม่เพียงอย่างเดียวนั้น คือ การกลับไปเรียนหรือทำงาน (ร้อยละ 58.4) และปัจจัยที่มีผลต่อการเลี้ยงลูกด้วยนมแม่เพียงอย่างเดียว 6 เดือนอย่างมีนัยทางสถิติ ได้แก่ อายุแม่ 17 – 19 ปี (aOR 5.96, 95% CI 1.62-21.92) สถานภาพสมรส (aOR 2.79, 95% CI 1.13-6.86) การว่างงาน/แม่บ้าน (aOR 10.08, 95% CI 2.00-50.75) และการมีรายได้ (aOR 3.98, 95% CI 1.35-11.72)*

สรุป: *การศึกษานี้พบว่าความชุกของการเลี้ยงลูกด้วยนมแม่เพียงอย่างเดียวในแม่วัยรุ่น ครบ 6 เดือน ร้อยละ 19.8 เหตุผลที่พบมากที่สุดที่ทำให้ยุติการเลี้ยงลูกด้วยนมแม่เพียงอย่างเดียวนั้น คือ การกลับไปเรียนหรือทำงาน ปัจจัยที่มีผลต่อการเลี้ยงลูกด้วยนมแม่เพียงอย่างเดียว 6 เดือนอย่างมีนัยสำคัญทางสถิติ ได้แก่ อายุ สถานภาพสมรส การว่างงาน/แม่บ้าน และการมีรายได้*

คำสำคัญ: *การเลี้ยงลูกด้วยนมแม่อย่างเดียว, วัยรุ่น, ความชุก, ปัจจัย*

Introduction

Exclusive Breastfeeding, defined by the World Health Organization (WHO), is feeding infants breast milk only without any additional food or drink, not even water[1, 2]. WHO recommends that infants should be exclusively fed breast milk for at least 4-6 months because breast milk consists of essential nutrients and energy that infant needs. Breast milk promotes sensory and cognitive development, and protects the infant against infectious and chronic diseases. Exclusive breastfeeding reduces infant mortality due to common childhood illnesses such as diarrhea or pneumonia, and leads to a quicker recovery from illness. These effects can be measured in resource-poor and affluent societies[3]. There are also advantages for mothers. Breastfeeding contributes to the health and well-being of mothers, reduces risk of ovarian and breast cancer, increases family and national resources, and is environmentally safe[3, 4, 5]. While breastfeeding, infant suckling stimulate oxytocin release resulting in uterine contraction, reduction of blood loss and a temporary anxiolytic-like calming effect on postpartum maternal mood disturbances[4]. Breastfeeding reduces the risk of type II diabetes, hypertension, hyperlipidemia and cardiovascular disease[6, 7, 8]. Moreover, breastfeeding leads to weight loss due to the high energy use 500 Kcal more than usual to produce milk[4].

The United Nation International Children's Emergency Fund (UNICEF) recommends exclusive breastfeeding for 6 months. Thereafter infants should receive complementary foods with continued breastfeeding up to 2 years of age or beyond. UNICEF has launched ten steps to successful breastfeeding[9]. The Thai Ministry of Public Health is aware of EBF and has launched the Baby Friendly Hospital Initiative (BFHI) policy from 1979 to 1991 to promote exclusive breastfeeding in all hospitals in Thailand. According to this policy, all hospitals were prohibited from using powdered milk, bottle-feeding, teats and pacifiers. Between 2002-2006, the target rate of the 9th National Economic and Social Development Plan for 4-month-old infants should not be less than 30%; the 10th and 11th plans have changed from 4-months to 6-months EBF to comply with the WHO.

Adolescent pregnancy is a major global health problem. Adolescents are young people between the ages of 10 and 19 years old[10, 11]. Adolescent are often affected by unstable moods, socioeconomic problems, and health, education, and obstetric problems[12,13]. Santo E, et al., found that adolescent pregnancy was a factor in the discontinuation of exclusive breastfeeding (EBF)[14]. However, there are scanty report of prevalence of EBF in adolescents. The aims of this study were to find the prevalence of exclusive breastfeeding among adolescent mothers who delivered at Department of Obstetrics & Gynecology, Faculty of Medicine Vajira Hospital, Navamindradhiraj University, and evaluated the potential factors for 6 months EBF.

Materials and Methods

This prospective, descriptive, questionnaire-based study, was conducted from May 2016 to June 2017 at the Department of Obstetrics and Gynecology, Faculty of Medicine Vajira Hospital, Bangkok, Thailand. The research protocol was approved by the Vajira Institutional Review Board and Ethic Committee for research involving human subjects in April 2016.

The studied population consisted of all postpartum adolescent mothers (age 10-19 years) who hospitalized and gave birth at age not more than 20 years old at the Department of Obstetrics & Gynecology, Faculty of Medicine Vajira Hospital, Navamindradhiraj University from May 2016 to April 2017. Inclusion criteria were adolescent mothers who initiated breastfeeding within 48 hours after delivery and volunteered to answer questionnaire via telephone at 1, 2, 3, 4, 5 and 6 months postpartum. Exclusion criteria were twin pregnancy, preterm baby, sick baby and contraindication to breastfeeding. The sampling technique used in this study was computerized simple random sampling.

The sample size was calculated by using a formula for estimation of single population proportion with 95% confidence level and 5% margin of error. The population of adolescent mothers that delivered in Vajira Hospital in 2015 was 389. Based on a previous

study in Thailand, the prevalence of EBF at 6 months among adolescent mothers was 27.0%[15]. The calculated sample size of this study was at least 170. Participants who met inclusion and exclusion criteria were informed of the study process and signed an informed consent form in the early postpartum period.

All participants and their parents or legal guardians were informed about the processes of the trial on the postpartum ward before giving written informed consent. The following demographic data including maternal age, marital status, occupation, religion, parity, gestational age, route of delivery, antenatal care, knowledge of breastfeeding, neonatal birth weight and Apgar score were collected from obstetrics record. After hospital discharge, all participants would be phone interviewed at the scheduled time of 1, 2, 3, 4, 5 and 6 months postpartum about exclusive breastfeeding and reasons for EBF discontinuation by a research assistant. The participants would be phone interviewed for following up every 28 days. It was defined that 28 days equal to a month. The primary outcome of this study was the rate of EBF at 6 months. Secondary outcomes were the reasons for discontinuation of EBF and predicting factors for EBF at 6 months.

The term exclusive breastfeeding means feeding infants with milk from a woman's breast without any additional food or drink, not even water. The term of partial breastfeeding means giving other kinds of milk to the baby along with breast milk, regardless of liquids or solids provided. Bottled feeding was defined as the mother providing other kinds of milk without any breast milk[1, 2].

We evaluated knowledge about breastfeeding based on a previous study16 by asking the participants about the benefits of breastfeeding, the benefits and duration of EBF, and breastfeeding practice. No formal tool was used to assess the depth of participants' knowledge.

The data were analyzed by using SPSS version 22 (IBM). Associations between factors were analyzed by Chi-square test or Fisher's exact test for univariate analysis, and by multiple logistic regression for multivariate analysis. Results were presented as adjusted odds ratio with 95% confidence interval. A $p < 0.05$ was considered statistically significant.

Results

A total of 204 participants were enrolled in the study, 12 women loss to follow up. Therefore, 192 adolescent mothers were included for analysis. Most participants were 17-19 years old (69.3%), married (57.8%), had a secondary school education (66.1%), were Buddhist (99.0%), and had no knowledge about breastfeeding (88.5%) and vaginal delivery (86.5%). Half of them were housewives with no income (Table 1).

Table 2 shows prevalence of exclusive breastfeeding among adolescent mothers. All participants initiated EBF within first day of postpartum. However, the prevalence rate gradually decreased over time. EBF rate at first to fifth months among adolescent mothers were 97.4%, 54.7%, 32.3%, 25.5% and 20.8% respectively. By the sixth month after birth, only 19.8% of the infants were being nourished with breast milk exclusively.

A total 154 of 192 adolescent mothers discontinued EBF before 6 months. The most common reasons for discontinuation of EBF before 6 months were working and studying (58.4%). The other reasons were insufficient milk (39.6%) and mother-infant separation (2%).

Predicting factors for 6 months EBF included maternal age group, marital status, education level, occupation, income, parity, breastfeeding knowledge, amount of antenatal care, gestation age at first ANC, gestation age at delivery, route of delivery and neonatal birth weight (low birth weight is defined by the World Health Organization as a birth weight of an infant of less than 2500 gram)[10]. After analysis of prevalence of EBF for 6 months, this study found that predictive factors associated with 6 months EBF were maternal age, marital status, occupation, income (money earned from doing work or received from investments) and breastfeeding knowledge (Table 3).

Table 1. Baseline Characteristic (192 participants).

Characteristics	n (%)
Age (years)	
12-16	59 (30.7)
17-19	133 (69.3)
Marital Status	
single	74 (38.6)
married	111 (57.8)
divorced	7 (3.6)
Education	
primary	34 (17.8)
secondary	127 (66.1)
college	31 (16.1)
Occupation	
unemployed/housewives	96 (50.0)
studying	41 (21.4)
employed	32 (16.6)
merchant	23 (12.0)
Having income	
yes	Having income
no	yes
Religion	
Buddhism	190 (99.0)
Muslim	2 (1.0)
Parity	
primipara	155 (80.8)
multipara	37 (19.2)
Route of delivery	
vaginal delivery	166 (86.5)
cesarean section	26 (13.5)
Breastfeeding Knowledge	
yes	22 (11.5)
no	170 (88.5)

Table 2. Rate of exclusive, partial breastfeeding and bottled feeding (192 participants).

Timing after delivery	Exclusive breastfeeding	Partial breastfeeding	Bottled feeding
	n (%)	n (%)	n (%)
At 1 months	187 (97.4)	4 (2.1)	1 (0.5)
At 2 months	105 (54.7)	53 (27.6)	34 (17.7)
At 3 months	62 (32.3)	75 (39.1)	55 (28.6)
At 4 months	49 (25.5)	80 (41.7)	63 (32.8)
At 5 months	40 (20.8)	86 (44.8)	66 (34.4)
At 6 months	38 (19.8)	88 (45.8)	66 (34.4)

Table 3. Association between related factors and 6-month exclusive breastfeeding (192 participants).

Factors	Exclusive breastfeeding		p value
	6 months (n=38), n (%)	< 6 months (n=154), n (%)	
Age (years)			
12-16	3 (5.1)	56 (94.9)	0.001*
17-19	35 (26.3)	98 (73.7)	
Marital Status			
married	29 (26.1)	82 (73.9)	0.010*
single / divorced	9 (11.1)	72 (88.9)	
Education			
secondary / college	34 (21.5)	124 (78.5)	0.195*
primary	4 (11.8)	30 (88.2)	
Occupation			
studying	2 (4.9)	39 (95.1)	0.023*
employed/ merchant	12 (21.8)	43 (78.2)	
unemployed/ housewives	24 (25.0)	72 (75.0)	
Income			
yes	25 (26.0)	71 (74.0)	0.030*
no	13 (13.5)	83 (86.5)	
Parity			
1	28 (18.1)	127 (81.9)	0.219*
2 or more	10 (27.0)	27 (73.0)	
Number of delivery			
none	29 (17.9)	133 (82.1)	0.127*
1 or more	9 (30.0)	21 (70.0)	
First antenatal care (weeks)			
≤ 12	9 (23.1)	30 (76.9)	0.564*
> 12	29 (19.0)	124 (81.0)	
Number of ANC			
< 4	5 (15.6)	27 (84.4)	0.517*
> 4	33 (20.6)	127 (79.4)	
Breastfeeding Knowledge			
yes	9 (40.9)	13 (59.1)	0.019**
no	29 (17.1)	141 (82.9)	
Route of delivery			
vaginal	34 (20.5)	132 (79.5)	0.544*
cesarean	4 (15.4)	22 (84.6)	
Neonatal birth weight			
low birth weight	1 (7.1)	13 (92.9)	0.310**
normal	37 (20.7)	141 (79.2)	
Gestational age			
full term	38 (20.7)	146 (79.3)	0.360**
post term	0 (0.0)	8 (100)	

data presented as number (%), * Chi-square test, **Fisher's exact test

After adjusted odds ratio (aOR) estimated by multiple logistic regression adjusting for age, marital status, income, occupation and knowledge were analyzed. This study revealed that adolescent mothers aged 17-19 years old were 6 times higher 6 months EBF than those aged group 12-16 years old (aOR 5.96, 95% CI 1.62-21.92). Married adolescent mothers showed 2.8 times higher 6 months EBF rate than those who were single or divorced (aOR 2.79, 95% CI 1.13-6.86). Unemployed adolescent mothers / housewives showed 10 times higher 6 months EBF rate than working adolescents or students (aOR 10.08, 95% CI 2.00-50.75). Adolescent mothers who had income were 4 times higher 6 months EBF rate than those had no income (aOR 3.98, 95% CI 1.35-11.72) (Table 4).

Table 4. Univariate and multivariate analysis of factors related to 6-month exclusive breastfeeding.

Factors	Exclusive breastfeeding			Multivariate analysis		
	OR[1]	95%CI	p value	aOR[2]	95%CI	p value
Age (years)						
12-16	1.00	Reference		1.00	Reference	
17-19	6.67	(1.96-22.67)	0.002	5.96	(1.62-21.92)	0.007
Marital Status						
single / divorced	1.00	Reference		1.00	Reference	
married	2.83	(1.26-6.37)	0.012	2.79	(1.13-6.86)	0.025
Occupation						
studying	1.00	Reference		1.00	Reference	
employed/ merchant	5.44	(1.15-25.86)	0.033	1.77	(0.33-9.61)	0.509
none/ housewives	6.5	(1.46-28.96)	0.014	10.08	(2.00-50.75)	0.005
Income						
no	1.00	Reference		1.00	Reference	
yes	2.25	(1.07-4.72)	0.032	3.98	(1.35-11.72)	0.012
Breastfeeding Knowledge						
no	1.00	Reference		1.00	Reference	
yes	3.37	(1.32-8.61)	0.011	2.91	(0.98-8.65)	0.055

OR: odds ratio, aOR: adjusted odds ratio, CI: confidence interval
[1] OR estimated by Binary logistic regression
[2] aOR estimated by multiple logistic regression

Discussion

This study found that prevalence of exclusive breastfeeding in adolescent mothers was only 19.8% at 6 months postpartum while the first month after postpartum was 97.4% and gradually decreased over time to the 6 months postpartum cut-off. This finding was lower than the target rate of the 11th National Economic and Social Development Plan (2012-2016) for the 6-month-old infants that should not be less than 30%. Compared with those of earlier studies of EBF in adolescents, the 6-month EBF rate in this study was lower than other studies. However, there were scant reports of EBF among adolescent mothers. A study from Ecuador found that the rate of EBF at 6 months in adolescents was up to 62.9%[16]. Another report from Srinakharinwirot University in Thailand found that 6 months EBF in adolescent was 27.0%[15].

This low prevalence rate of EBF in the present study leads to the consideration of strategies for increasing EBF rates in adolescents, such as peripartum policies and practices to promote EBF, eliminate obstacles to continue EBF, cooperation with school or workplace to support EBF and home visit to encourage longer EBF.

The most common reasons for discontinuing EBF before 6 months in adolescent mothers were the necessity of returning to school or going to work (58.4%) and insufficient milk (39.6%). This finding was consistent with the results of a study in Ecuador. Nevertheless, there are not yet maternity leave policies for students and day care centers for adolescent mothers in Thai schools. This results in decreasing EBF and a switch to partial breastfeeding or bottled feeding. Cooperation between hospitals and schools to offer a specific room for collecting milk or breastfeeding may increase EBF and reduce household expenses as well.

After analyzing factors associated with 6 months EBF, this study found that significant predictive factors of 6 months EBF among adolescent mothers were age, marital status, occupation and income. Adolescent mothers aged 17-19 years old showed 6 times greater EBF rate than those aged 12-16 years old. This might be due to more responsibility and maturity among older adolescents than younger adolescents, resulting in longer EBF. This study also found that adolescent mothers who were married tended to EBF 2.8 times more than single mothers. This might be because married adolescents were more prepared for pregnancy and breastfeeding. Moreover, this study revealed that unemployed mothers or housewives had a 10 times greater rate of EBF than employed and studying mothers. This finding was consistent with a study in Thailand which found that the most common reason that caused mothers to discontinue EBF was the obstacle of an occupation[17]. This finding could explain why unemployed mothers or housewives had more time for breastfeeding than working mothers or students.

Although breastfeeding knowledge was not significant predictor for 6 months EBF in this study, but a previous study in Ecuador found that adolescent mothers who had breastfeeding knowledge were 3 times more likely to stick to EBF than those who didn't have breastfeeding knowledge[16]. In the authors opinion, breastfeeding knowledge should be an important factor for continuing EBF because it is the primary essential element for the initiation and maintenance of breastfeeding. Breastfeeding knowledge should include not only awareness of the benefits of, and barriers to EBF, but also attitude, practice and husband/family support of breast feeding. Thus, healthcare providers should design and implement breastfeeding knowledge for proper timing and content to increase the likelihood of prolonged EBF to 6 months.

The strength of this study included that it was a prospective study. However, this study was limited to adolescent mothers living in an urban area where they mostly had higher education level and higher income. Thus, this study may not represent all adolescent mothers in Thailand. Moreover, multiple logistic regression was analyzed in only 38 adolescent mothers who were 6 months EBF; that might be a limitation in the sample size for analysis. Future research should study among a population of adolescent mothers living in rural areas.

Conclusion

This study found that EBF in adolescent mothers was 19.8% at 6 months. The most common reasons for discontinuing EBF before 6 months were returning to school or work. Significant predictive factors for 6 months EBF were maternal age, marital status, occupation and income. The EBF rate in Thai adolescents who lived in Bangkok was still low in present study. Family members and healthcare providers should encourage adolescent

mother to aware of the benefits and importance of EBF to increase 6 months EBF rate.

Potential conflicts of interest

The authors declare no conflict of interest.

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Rectal Misoprostol in Women Undergoing Myomectomy for Intraoperative Blood Loss Reduction: A double-blinded randomized placebo-controlled study

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ABSTRACT

Objectives: To compare amount of intraoperative blood loss between patients using preoperative rectal misoprostol versus placebo group.

Materials and Methods: A randomized double-blinded placebo-controlled trial, 46 women with uterine leiomyoma indicated for myomectomy, both abdominal and laparoscopic approach were randomly assigned and received rectal misoprostol (400 µg) or placebo at 30 minutes before operation, then estimation of blood loss was recorded as primary outcome. Changes in hemoglobin, hematocrit, rate of transfusion and adverse events were also recorded.

Results: Median and interquartile range of intraoperative blood loss in misoprostol group was 350 (613) ml and 500 (663) ml in placebo group. Mann-Whitney U test showed no statistical significance (p = 0.136). Univariate analyses showed significant factors of intraoperative blood loss were intramural type, type of operation and larger size of mass. But after multivariate analyses, the only significant factor affecting more blood loss was intramural type of leiomyoma (odds ratio 23, 95% confidence interval 1.96-271.9, p = 0.013). Changes of hemoglobin, hematocrit, transfusion rate and other complications were not significant.

Conclusion: There was no significant benefit in blood loss reduction after using preoperative rectal misoprostol in the study.

Keywords: Leiomyoma, myomectomy, misoprostol, blood loss, hemoglobin.

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การเหน็บยาไมโซพรอสตอลทางทวารหนักก่อนผ่าตัดเนื้องอกมดลูก เพื่อลดการเสียเลือดจากการผ่าตัด: การศึกษาเปรียบเทียบกับยาหลอก

พฤฒพร มณีรัตน์, สิริกาญจน์ ทองใหม่

บทคัดย่อ

วัตถุประสงค์: *เพื่อเปรียบเทียบการเสียเลือดระหว่างผ่าตัดเนื้องอกมดลูกระหว่างกลุ่มที่ได้ยา ไมโซพรอสตอล กับยาหลอก*
วิธีดำเนินการทำวิจัย: *การศึกษาทดลองแบบสุ่มโดยมีกลุ่มควบคุมในสตรีไทยที่เป็นโรคเนื้องอกกล้ามเนื้อมดลูกชนิดไม่ใช่มะเร็ง และจะเข้ารับการผ่าตัดแบบนัดที่โรงพยาบาลราชวิถีระหว่างวันที่ 1 ตุลาคม พ.ศ. 2559 จนถึง 31 สิงหาคม พ.ศ. 2560 ทั้งหมด 46 ราย จากนั้นแบ่งเป็น 2 กลุ่มได้แก่ กลุ่มที่ได้รับยา ไมโซพรอสตอล 400 ไมโครกรัม และกลุ่มที่ได้รับยาหลอก โดยจะเหน็บยาทางทวารหนักก่อนผ่าตัด 30 นาที แล้วเปรียบเทียบการเสียเลือดระหว่างผ่าตัดใน 2 กลุ่ม*
ผลการวิจัย: *มัธยฐานของการเสียเลือดระหว่างผ่าตัดในกลุ่มที่ได้ยาไมโซพรอสตอลเท่ากับ 350 มิลลิลิตร เปรียบเทียบกับยาหลอกที่ 500 มิลลิลิตร (p = 0.136) แต่จากการวิเคราะห์ในกลุ่มย่อยพบว่าการใช้ยาอาจได้ประโยชน์ในการผ่าตัดเนื้องอกมดลูกผ่านกล้อง ผู้ป่วยที่มีก้อนเนื้องอกที่พื้นที่น้อยกว่า 30 ตารางเซนติเมตร และผู้ป่วยที่มีก้อนเนื้องอกที่ปริมาตรน้อยกว่า 40 มิลลิลิตร แต่จากการวิเคราะห์แบบโลจิสติกพบว่าปัจจัยที่มีผลกับการเสียเลือดมากได้แก่ เนื้องอกมดลูกชนิด Intramural (p = 0.013) ภาวะแทรกซ้อน และการได้รับเลือดไม่แตกต่างกันระหว่างสองกลุ่ม*
สรุป: *การเหน็บยาไมโซพรอสตอลทางทวารหนักก่อนผ่าตัด 30 นาทีไม่ช่วยลดการเสียเลือดจากการผ่าตัดเนื้องอกมดลูกอย่างมีนัยสำคัญ*

คำสำคัญ: *เนื้องอกกล้ามเนื้อมดลูก, การผ่าตัดเนื้องอกมดลูก, การเสียเลือดระหว่างผ่าตัด, ไมโซพรอสตอล ฮีโมโกลบิน*

Introduction

Leiomyoma of uterus is the most common benign gynecologic tumor of all ages. In Rajavithi hospital, more than 200 patients are newly diagnosed in each year. Clinical manifestations are varied based on size and location of tumor, such as pelvic pain, heavy menstrual bleeding, urinary frequency and inability to pregnant successfully.

Myomectomy is a favorable choice of treatment because symptoms will be relieved effectively. But the main challenging problem is the intraoperative bleeding that contributes to blood transfusion and unintended hysterectomy. Studies regarding morbidity of myomectomy showed transfusion rate in myomectomy were about 9-20%[1, 2]. Vasoconstrictors and uterotonic drugs were applied to decrease blood loss during myomectomy, such as intravenous oxytocin[3], intramyometrial bupivacaine and adrenaline[4], tranexamic acid[5, 6] and prostaglandin analogues[7].

Misoprostol, a synthetic prostaglandin E1 analogue, promotes myometrial contraction after binding at EP3 and EP4 receptor that increase amount of intracellular calcium. Pharmacokinetic properties of misoprostol were studied and showed different onset of action and serum level depending on route of administration. Rectal misoprostol achieves maximal level at less than 30 minutes with narrowest serum level variation[8] resulting in the safest route. Thus, this study aimed to investigate the effective of misoprostol in blood loss reduction, transfusion rate and other postoperative complications comparing with placebo.

Materials and Methods

The study was a double-blind clinical trial with balanced allocation into two parallel groups and registered in Clinicaltrial.gov with registration number: NCT02908295. No protocol amendment was made after the trial commenced. Ethical committee of Rajavithi Hospital approved the study with registration number: 59147.

Women provisional diagnosed as uterine leiomyoma that myomectomy was scheduled, either abdominal or laparoscopic approach, during October 2016 to August 2017 in Rajavithi Hospital were enrolled in the study. Exclusion criteria included (1) medical diseases which increase bleeding tendency (2) history of antiplatelet and anticoagulant exposure less than seven days (3) exposure of prostaglandin analogue and/or non-steroidal anti-inflammatory drugs (NSAIDs) less than seven days (4) medical diseases which may become worsen after prostaglandin exposure, such as uncontrolled hypertension, asthma, glaucoma and heart diseases (5) preoperative platelet count less than 100,000 /cm3 or abnormal coagulation tests (6) allergy to misoprostol or other prostaglandin analogues (7) abnormal pathologic diagnosis unless leiomyoma and (8) mass in abnormal location, such as broad ligament or cervical leiomyoma.

The sample size was calculated by using a formula for continuous data[9].

$$N = \frac{(Z_{1-\alpha/2} + Z_{1-\beta})^2 \times \left[\frac{\sigma^2_{int} + \sigma^2_{con}}{n_{con}/n_{int}}\right]}{(\mu_{int} - \mu_{con})^2}$$

Mean blood loss of misoprostol group and placebo were 230.60 and 322.39 ml, respectively. Standard deviations of blood loss of 55.72 and 88.13 ml respectively[10] were used in calculation. A sample size of 14 women per group was required to determine difference of this amount of blood loss (power = 0.9 and α = 0.05). But no adjunctive procedures were restricted in the study and expected loss rate of 10%, 20 participants per group were enrolled.

The randomization was performed by simple computer-generated random number table (Microsoft Excel) with ratio 1:1 divided into 2 parallel groups. The sequence of randomization was kept in sealed opaque envelope sequentially and sent to operating room. Thus, participants and operators were blinded to treatment assignment.

Flow diagram was showed in Fig. 1. 48 women were recruited then counselling about intervention and written informed consent were completed. 2 patients refused to join the study due to private cases. All 46 participants were interviewed, physically examined

and taken blood test for complete blood count (CBC) and coagulation test to exclude disorders contraindicated in the protocol. Then, they were randomized to the study group received 400 mg misoprostol (Cytotec™, 200 mg; Pfizer, USA) rectally at 30 minutes before operation and placebo group received 200 mg of vitamin B6, Pyridoxine hydrochloride (Besix®, 100 mg; Charoon Bhesaj, Thailand) rectally at the same time.

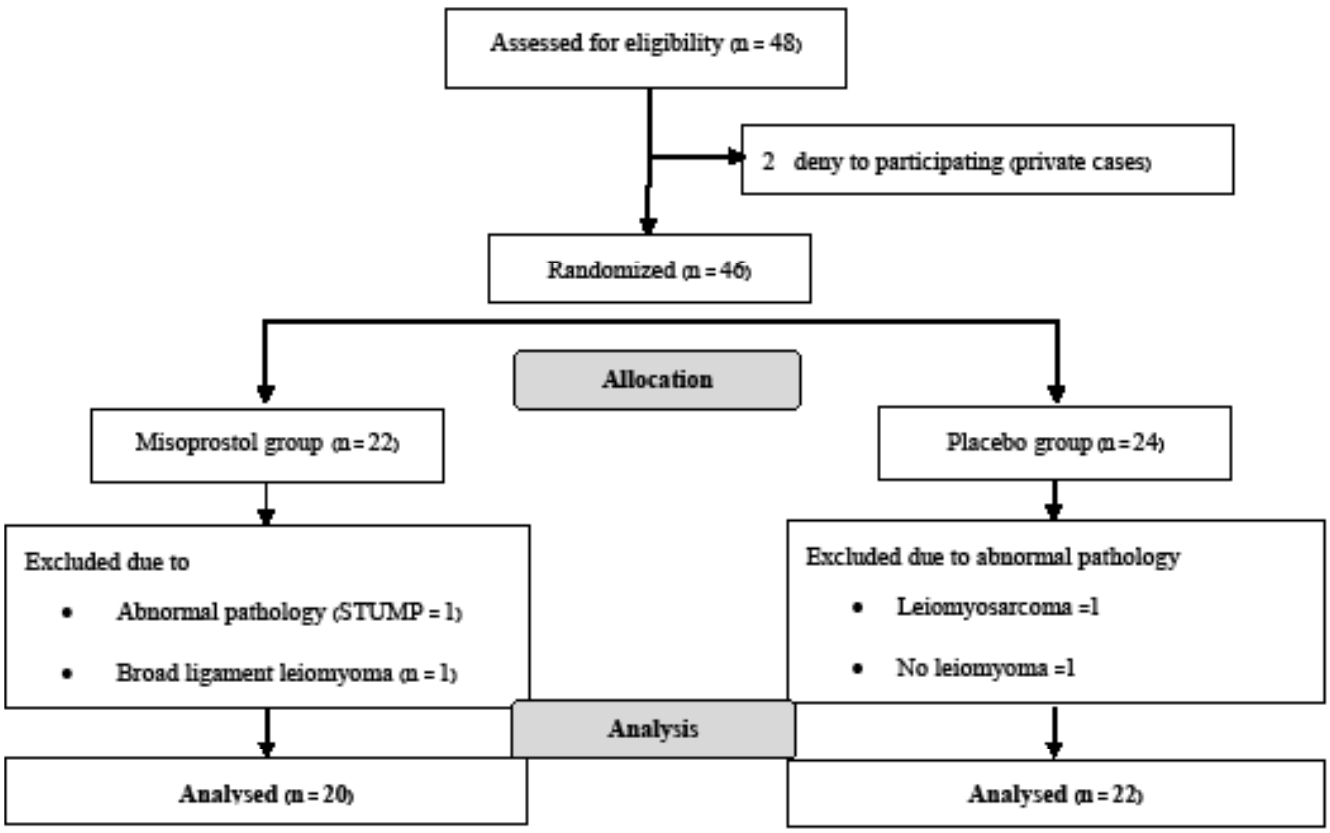

Fig. 1. Flow diagram of study allocation

During preoperative period, participants in both groups were omitted to use NSAIDs, prostaglandin and other drugs that contribute to bleeding tendency. In those undergoing laparoscopic myomectomy, the authors substituted preoperative misoprostol for cervical priming by hygroscopic cervical dilator (Dilapan-S®, 4mm x 55 mm; HPSRx, Virginia) to avoid exposure to prostaglandin.

On the date of surgery, a sealed envelope labelled by numeric code consisting of drug and data recorder was sent to operative theatre. The drug was inserted rectally at 30 minutes before operation by a trained doctor assigned to accompany the surgery. Few drops of normal saline were used to dissolve tablets before insertion. Intraoperative blood loss was recorded by measuring amount of blood on the surgical gauzes and swabs[11] compared with visual analog scale[12]. Another was recorded from blood in suction container after subtracted water using for irrigation and washing. Blood transfusion was considered if blood loss was more than 1,500 ml and/or the intraoperative hemoglobin was less than 8 g/dl. Duration of operation, intraoperative findings, adjuvant procedures, intraoperative complications

and blood transfusion were recorded.

After the operation, CBC was repeated within 24 hours. Pain and other adverse effect of misoprostol uses, such as diarrhea, abdominal cramp, flushing and fever (more than 38°C in body temperature) were recorded by research nurses and doctors attending in each case. Abdominal cramping was categorized into mild, moderate and severe using visual analog scale and amount of opioid requests was recorded as an objective data that represents pain. One patient had a broad ligament leiomyoma, so she was excluded. After pathologic diagnoses were reported, another 3 participants with abnormal pathology were excluded; one for uterine smooth muscle tumors of uncertain malignant potential (STUMP), one for leiomyosarcoma and another one without leiomyoma in pathologic tissue.

Statistical analysis was performed using IBM SPSS Statistics version 20 (IBM© Corp., Armonk, NY, USA) with intention-to-treat analysis. Data were presented as frequencies with percentage in categorical variables and statistical significance was determined by Pearson's chi square and Fischer's exact test. Means ± standard deviation (SD) or median with interquartile ranges (IQR) are used to demonstrate continuous variables based on distribution of data. Student's t-test and Mann-Whitney U-test were used in analyses. The distribution of blood loss was right skewed and normalized by logarithmic transformation. Univariate and multivariate linear regression analysis were used to estimate factors influencing the primary outcome. Finally, meta-analysis was used to summarize pool effects with other studies.

The primary outcome was estimated intraoperative blood loss (EBL). Secondary outcome measures were postoperative hemoglobin difference, blood transfusion rate, duration of surgery, complication of surgery and postoperative adverse events.

Results

48 patients were recruited. After exclusion of 6 patients, 42 participants were in final analysis. Table 1 shows patient demographic data, characteristics of leiomyoma and operative factors. There were no significant differences in both groups.

The primary outcome was presented in Table 2, the median (IQR) of EBL in misoprostol and placebo were 350 (613) and 500 (663) ml, respectively. Nonetheless, no significant difference was found in both groups (p = 0.136). Grouped by operation type, EBL in misoprostol group was significant lower in patients undergoing laparoscopic myomectomy with median EBL difference 200 ml, 150 versus 350 ml (p = 0.022). Due to positively skewed distribution of EBL showed in Fig. 2, it was logarithmic transformed, termed Log EBL, then student t-test was used and resulted in the same way as in Mann-Whitney U-test. Changes in hemoglobin/hematocrit, intraoperative transfusion rate, duration of surgery, hysterectomy conversion rate and adjuvant procedures used during surgery were not different in both groups. There had one patient in placebo group converted to hysterectomy due to huge leiomyoma, 16-cm in largest diameter, with severe pelvic adhesion after her previous abdominal myomectomy for 2 times.

Univariate analysis of significant factors contributed to EBL at cut point of more than 250 mL was used then demonstrated in Table 3. Intramural type, larger diameter, area and volume and type of operation were significant factors of more than 250 ml of blood loss.

Figure 3 shows subgroup analyses, mioprostol uses in laparoscopic myomectomy could reduce EBL more than 250 ml with OR 0.03 (95%CI 0.002 – 0.68, p = 0.025), but not in abdominal myomectomy group (p = 0.535). Furthermore, largest mass with area less than 30 cm2 or volume less than 40 cm3 had significant benefit in reduction of EBL more than 250 ml from misoprostol uses, OR 0.12 (95%CI 0.02 – 0.97, p = 0.037).

But after performing binary logistic regression, the only significant variable was intramural type leiomyoma (Table 4).

Postoperative adverse events were showed in Table 5. Nausea and vomiting were most common. No significant difference of frequencies between two groups (p = 0.925).

Table 1. Demographic and clinical characteristics of enrolled women.

	Misoprostol group (n = 20)	Placebo group (n = 22)	p value
Age (yr), mean ± SD	35.9 ± 5.30	36.3 ± 5.18	0.774
Body mass index (kg/m^2), mean ± SD	22.3 ± 3.89	22.9 ± 2.95	0.556
Preoperative hemoglobin (g/dl), mean ± SD	11.6 ± 1.31	11.8 ± 1.31	0.595
Preoperative hematocrit (%), mean ± SD	36.2 ± 3.72	36.9 ± 3.35	0.691
Previous abdominal surgery, n (%)			0.418
• Cesarean delivery	0 (0)	1 (4.5)	
• Ovarian surgery	1 (5)	0 (0)	
• Appendectomy	0 (0)	1 (4.5)	
• Others	0 (0)	1 (4.5)	
Operation, n (%)			0.582
• Abdominal myomectomy	14 (70)	15 (68.2)	
• Low midline	6 (42.9)	6 (40)	
• Pfannenstiel	8 (57.1)	9 (60)	
• Laparoscopic myomectomy	6 (30)	7 (31.8)	
Surgeon, n (%)			0.574
• Gynecologic oncologists	15 (75)	17 (77.3)	
• General gynecologists	5 (25)	5 (22.7)	
Hormonal uses in 3 months, n (%)			
• No	12 (41)	17 (77.3)	
• COCs	1 (5)	1 (4.5)	
• DMPA	5 (25)	3 (13.6)	
• GnRH agonist	2 (10)	1 (4.5)	
Type of leiomyoma, n (%)			0.435
• Intramural	15 (75)	17 (77.3)	
• Subserous	5 (25)	5 (22.3)	
Largest mass diameter (cm), mean ± SD	7.7 ± 2.36	8.3 ± 2.28	0.408
Median number of leiomyoma	2 (3)	3 (3)	0.303
Number of resected leiomyoma, n (%)			0.424
• 1	8 (40)	5 (22.7)	
• 2 - 3	7 (35)	8 (36.4)	
• 4 – 5	1 (5)	5 (22.7)	
• 5 – 10	2 (10)	3 (13.6)	
• > 10	2 (10)	1 (4.5)	

Table 2. Primary and secondary outcomes.

	Misoprostol group (n = 20)	Placebo group (n = 22)	p value
EBL (ml), median (IQR)‡	350 (613)	500 (663)	0.136
• Abdominal myomectomy	500 (713)	500 (1000)	0.505
• Laparoscopic myomectomy	150 (163)	350 (450)	0.022
Changes in hemoglobin (g/dl), mean ± SD	- 0.4 ± 0.84	- 0.8 ± 1.23	0.305
Changes in hematocrit (%), mean ± SD	- 1.9 ± 3.29	- 2.72 ± 3.93	0.445
Intraoperative transfusion rate, n (%)	3 (15)	5 (22.7)	0.406
Duration of surgery (minutes)			
• Abdominal myomectomy	132.9 ± 38.77	139.0 ± 50.01	0.714
• Laparoscopic myomectomy	210 ± 40.67	167.1 ± 100.41	0.342
Hysterectomy conversion rate, n (%)	0 (0)	1 (4.5)	0.524
Adjuvant treatment used, n (%)			
• Tranexamic acid	9 (45)	10 (45.5)	0.610
• Tourniquet	1 (5)	0 (0)	
• Bupivacaine and epinephrine	2 (10)	2 (9.1)	0.563

EBL: estimated blood loss; SD: standard deviation

‡ Mann-Whitney U test

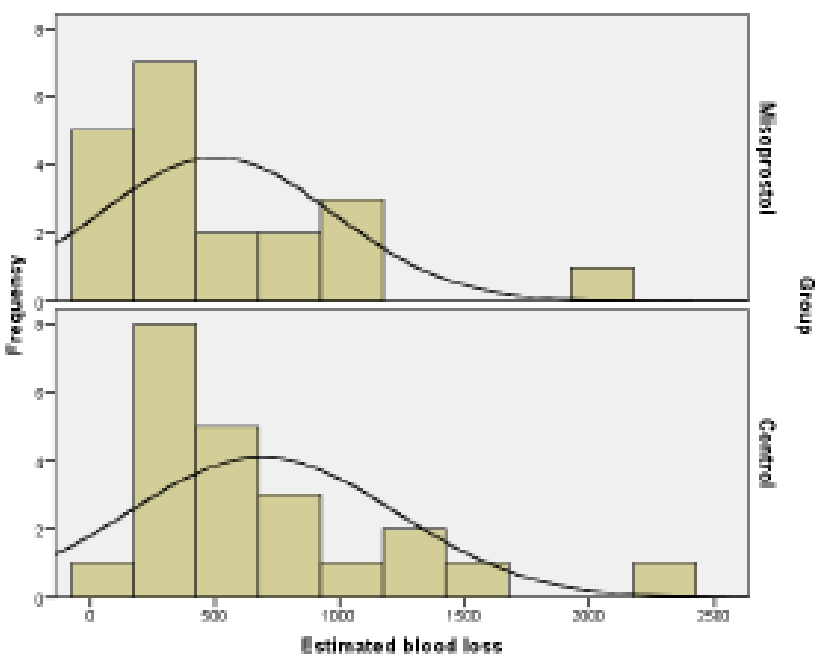

Fig. 2. Histogram of EBL distribution in two groups.

Table 3. Univariate analysis on factors affecting EBL more than 250 mL.

Factors	EBL > 250 ml (n, %)	OR (95% CI)	p value
Group			
• Misoprostol	13 (65)	0.41 (0.10, 1.71)	0.188
• Placebo	18 (81.8)	1	
Age			
• ≥ 35 yr	14 (70)	0.69 (0.17, 2.73)	0.426
• < 35 yr	17 (77.3)	1	
BMI			
• ≥ 25 kg/m^2	6 (85.7)	2.40 (0.26, 22.56)	0.398
• < 25 kg/m^2	25 (71.4)	1	
Operation			
• Abdominal	24 (82.8)	4.11 (0.96, 17.63)	0.049
• Laparoscopic	7 (53.8)	1	
Types of leiomyoma			
• Intramural	28 (84.8)	11.2 (2.09, 60.16)	0.005
• Subserous	3 (33.3)	1	
Number of leiomyoma			
• ≥ 3 myomas	10 (71.4)	0.83 (0.20, 3.52)	0.541
• < 3 myomas	21 (75)	1	
Largest diameter			
• ≥ 8 cm	19 (90.5)	7.13 (1.31, 38.77)	0.016
• < 8 cm	12 (57.1)	1	
Largest area			
• ≥ 30 cm^2	21 (91.3)	9.45 (1.70, 52.10)	0.006
• < 30 cm^2	10 (52.6)	1	
Largest volume			
• ≥ 40 cm^3	21 (91.3)	9.45 (1.71, 52.10)	0.006
• < 40 cm^3	10 (52.6)	1	

EBL: estimated blood loss

Table 4. Predictive factors of EBL > 250 ml from binary logistic regression.

Factors	Total	EBL > 250 mL			
		Coefficient	n (%)	Adjusted OR (95% CI)	p value
Misoprostol	20	-0.71	13 (65)	0.49 (0.08, 2.99)	0.441
Intramural type	33	3.14	28 (84.8)	23.08 (1.96, 271.87)	0.013
Largest volume < 40 mL	19	-2.31	10 (52.6)	0.10 (0.008, 1.20)	0.070
Constant		0.79			

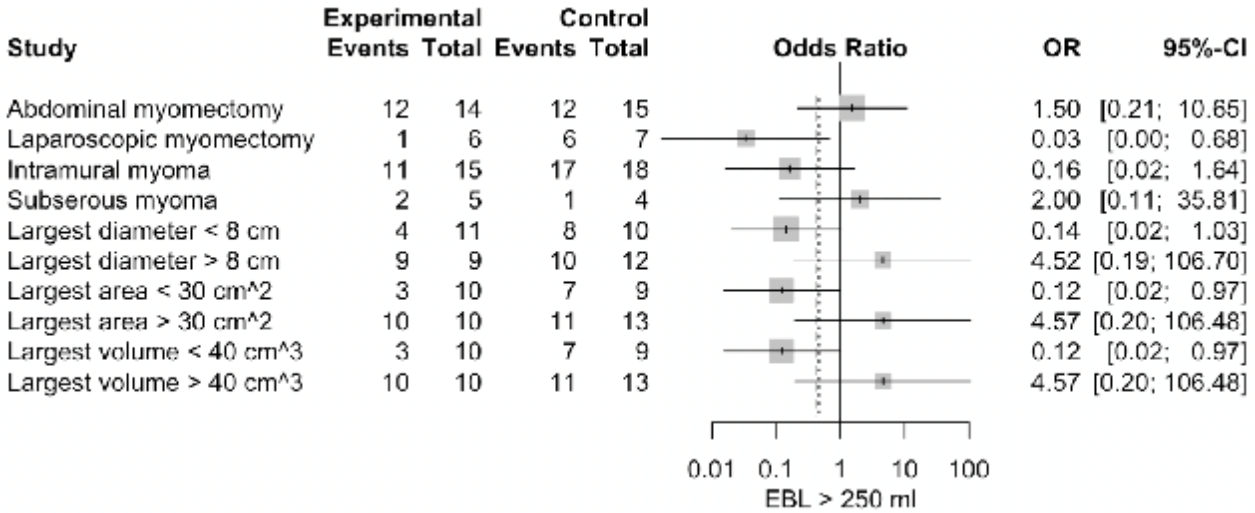

Fig. 3. Subgroup analysis on factors affecting EBL > 250 ml after using misoprostol.

Table 5. Postoperative adverse events.

	Misoprostol group (n = 20)	Control group (n = 22)	p value
Nausea and vomiting, n (%)†	5 (25)	6 (27.3)	0.574
Diarrhea, n (%)	0 (0)	0 (0)	
Fever, n (%)†	1 (5)	2 (9.1)	0.537
Abdominal pain, n (%)‡			0.422
• Mild	1 (5)	0 (0)	
• Moderate	15 (75)	15 (68.2)	
• Severe	4 (20)	7 (31.8)	
Vaginal bleeding, n (%)†	4 (20)	3 (13.6)	0.444
Total analgesic requests, mean ± SD‡‡	1.9 ± 0.67	2.1 ± 0.84	0.414
• Abdominal myomectomy	1.8 ± 0.84	2.1 ± 0.90	
• Laparoscopic myomectomy	2.06 ± 0.90	2.0 ± 0.71	

† Fischer's exact test, ‡ Pearson chi-square, ‡‡ t-test

Discussion

Several mechanisms of misoprostol were proposed. Releasing of prostaglandin induces myometrial contraction that constricts spiral vessels resulting in bleeding control. Besides, prostaglandin has vasoactive effect demonstrated by uterine Doppler study[13].

The study concluded that preoperative rectal 400 ug of misoprostol at 30 minutes prior to surgery had no significant benefit in decreasing amount of intraoperative blood loss. Because Rajavithi Hospital is the referral and training center that crowed of complicated cases, especially in abdominal myomectomy, with many different surgical team. Moreover, there were no restrictions of other procedures that could be confounders. Variation of blood loss in both groups were

noticed and lowering the power of study. Thus, more participants were needed. The result was inconsistent with Abdel H[14] and Celik[15]. They studied in women undergoing abdominal myomectomy then compared effectiveness of misoprostol versus placebo and the result showed that blood loss and operation time were significantly decreased in misoprostol group. Kalgoiannidis[16] included only laparoscopic myomectomy participants, the results were similar. Characteristics of masses in these three studies were comparable with the study (Table 6). Meta-analysis was performed to summarize pool effect (Fig. 4), and found significant benefit of misoprostol use in random effects model with mean difference of -182.41 mL (95% CI -274.71, -90.11).

Table 6. Comparison of previous studies on misoprostol in myomectomy.

Study, year	n	Inclusion criteria	Intervention (route/dose)	Operation	EBL (SD), mL
Celik, 2003	25	Mean diameter 15 cm Median number 5	Misoprostol (Vg, 400 ug)	Abdominal myomectomy	472 (77) vs 621 (121) p < 0.05
Abdel, 2015	50	Mean area 150 cm^2 ≤ 5 myomas	Misoprostol (RS, 400 ug)	Abdominal myomectomy	574 (195) vs 874 (172) p < 0.05
Niroomand, 2015	80	Mean diameter 8 cm	Misoprostol (Vg, 200 ug)	Abdominal myomectomy	458 (287) vs 696 (411) p < 0.05
Kalgoiannidis, 2011	6	Mean diameter 5 cm	Misoprostol (Vg, 400 ug)	Laparoscopic myomectomy	126 (41) vs 217 (74) p < 0.05
This study	42	Median diameter 8 cm Median number 2.5	Misoprostol (RS, 400 ug)	Abdominal, laparoscopic myomectomy	502 (475) vs 686 (535) p = 0.248

Vg: per vagina, RS: per rectal

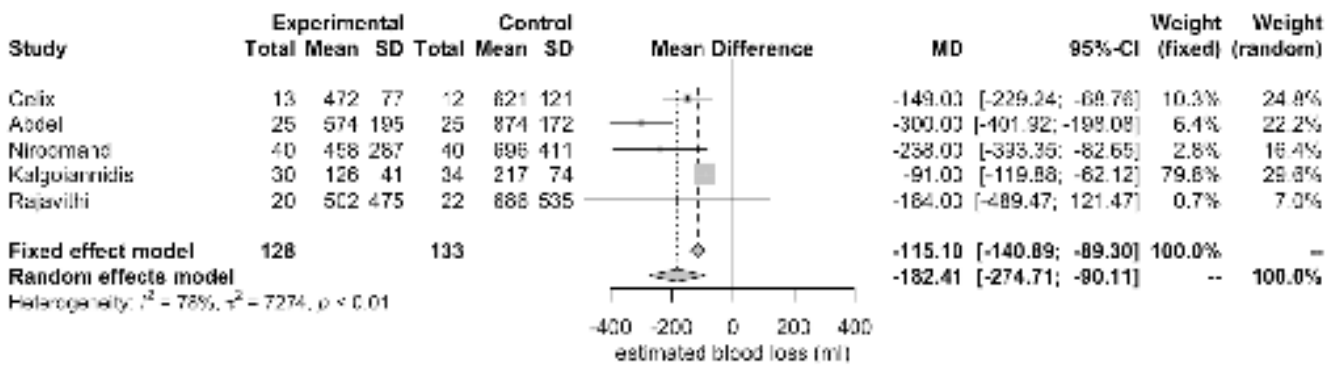

Fig. 4. Meta-analysis of studies focusing on misoprostol in reduction of EBL.

In laparoscopic subgroup, misoprostol uses could decrease intraoperative blood loss (p = 0.022). This could be explained by the fact that there have many interventions that can be performed rapidly to stop bleeding, such as suturing and clamping. These were confounders affecting variation of EBL in each

case. Also, difficulty in laparoscopic group was lower than in abdominal myomectomy, because patients with complicated diseases tended to choose abdominal myomectomy after counselling risk of uncontrolled bleeding leading to hysterectomy conversion.

Changes of hemoglobin and hematocrit showed no significant difference in both groups, differ from those in Celik that mean hemoglobin difference was 0.9 g/dl ($p < 0.05$) and Abdel summarized mean changes of hemoglobin and hematocrit as 0.4 g/dl and 1.3%, respectively ($p < 0.05$). Also, blood transfusion rate was not significantly increased in control group of Abdel, but difference in Celik was significant (4 versus 2 patients in total of 13 in each group). In this study showed 5 participants (22.7%) in control group whereas 3 (15%) in misoprostol group that received perioperative blood transfusion but no significant difference ($p = 0.406$)

Common adverse effects of misoprostol were abdominal cramp, fever with chill, vomiting and diarrhea. The authors recorded these events and found 5 participants in each group experienced mild nausea and vomiting that recovered with supportive treatment. Postoperative opioid uses might contribute to incidence of nausea and vomiting, however no significant difference of opioid uses between two groups.

Different administration time prior to surgery and route might affect the outcome, after the authors reviewed study protocol of previous studies and found that time of administration was at least 60 minutes before operation started. This difference was also a possible cause of the discrepant result that further evaluation is needed.

The study was a prospective study with placebo-controlled and clearly defined study protocol based on patient safety, but due to a brief period, the study recruited smaller group of participants than previous studies with limited of restriction criteria that lowering power of the study. However, despite the diversity of patients, randomization can divided participants properly (Table 1). Thus, confounding bias was decreased.

Another weak point was the means evaluating amount of blood loss that were based on counting, not the most accurate way but concomitant with postoperative hemoglobin, hematocrit and transfusion rate that determined clinical significance.

For clinical applications, overall data showed that use of misoprostol tended to be benefit in decreasing intraoperative blood loss with acceptable adverse effects, especially in laparoscopic myomectomy which mechanical hemostatic procedures were limited.

Conclusion

A 30-minute preoperative dose of rectal misoprostol had no significant benefits in reducing amount of intraoperative blood loss in myomectomy, but it could help in small leiomyoma (less than 30 cm^2 or 40 ml). In a small laparoscopic subgroup, misoprostol might be useful. Adverse events were mild and acceptable. Clear benefit on abdominal myomectomy, and different protocol of administration need further investigations with larger participants. Either abdominal or laparoscopic myomectomy should be selected.

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Potential conflicts of interest

The authors declare no conflict of interest.

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OBSTETRICS

The Surge of Maternal and Congenital Syphilis in a Tertiary Care Center in Bangkok, Thailand

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ABSTRACT

Objectives: Globally, syphilis in pregnancies remains a significant health concern, because the infection results in numerous maternal and fetal complications. However, in Thailand, documented evidence regarding the disease in the mothers and their newborns is scarce. Therefore, we conducted the study to explore the disease's trends in the aforementioned populations.

Materials and Methods: A 10-year retrospective descriptive study (1st January 2006 – 31st December 2015) was conducted at King Chulalongkorn Memorial Hospital, Bangkok, Thailand. Hospital records of syphilis-infected pregnant women and their infants were extensively reviewed by 2 obstetricians and a neonatologist. Descriptive statistics was leveraged to present patient's demographic and syphilis-related data.

Results: The percentage of syphilis-infected pregnant women increased from 0.05% in 2006 to 0.5% in 2015. Following the same trend, the percentage of infants with proven or possible congenital syphilis rose from 0% in 2006 to 0.06% and 0.13% in 2015, respectively. Interestingly, teenage pregnant women were particularly affected by the disease in the recent years; the incidence escalated from 10% to 30%. There were 16.4% (n = 12) of infected pregnant women who did not receive treatment antenatally, half of them were asymptomatic with positive serologic results (CMIA+, RPR-, TPPA+ results).

Conclusion: This study adds new information regarding the surge of maternal and congenital syphilis cases particularly in young pregnant women. This update will help to increase the awareness of obstetricians regards to syphilis screening and treatment during pregnancy period. Moreover, it emphasizes the importance of medical personnel's' familiarity with the reverse syphilis screening algorithm before applying to clinical practice.

Keywords: syphilis, pregnancy, congenital infection.

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การเพิ่มขึ้นของมารดาที่ติดเชื้อซิฟิลิสในระหว่างการตั้งครรภ์และทารกที่ติดเชื้อแต่กำเนิด

ญดา คุนผลิน, อนงค์นาถ ศิริทรัพย์, สุรสิทธิ์ ชัยทองวงศ์วัฒนา

บทคัดย่อ

วัตถุประสงค์: เพื่อศึกษาอัตราการติดเชื้อซิฟิลิสในมารดาระหว่างการตั้งครรภ์ และทารกที่มีการ ติดเชื้อซิฟิลิสแต่กำเนิด ในระยะเวลา 10 ปี ตั้งแต่ปี พ.ศ. 2549 ถึงปี พ.ศ. 2558 ที่โรงพยาบาลจุฬาลงกรณ์

วัสดุและวิธีการ: ผู้วิจัยทำการศึกษาแบบเก็บข้อมูลย้อนหลัง โดยเก็บข้อมูลจากเวชระเบียนของ หญิงตั้งครรภ์ที่มาคลอดที่โรงพยาบาลจุฬาลงกร์ ตั้งแต่วันที่ 1 มกราคม พ.ศ. 2549 ถึงวันที่ 31 ธันวาคม พ.ศ. 2558 เวชระเบียนของหญิงตั้งครรภ์ที่มีการติดเชื้อซิฟิลิสในระหว่างการตั้งครรภ์ และเวชระเบียนของทารกถูกทบทวนโดยสูติแพทย์ 2 ท่าน และแพทย์ผู้เชี่ยวชาญด้านทารก ปริกำเนิดจำนวน 1 ท่าน ผลการเก็บข้อมูลจะถูกนำเสนอโดยสถิติเชิงพรรณนา

ผลการศึกษา: อัตราการติดเชื้อซิฟิลิสของมารดาระหว่างการตั้งครรภ์เพิ่มขึ้นจากร้อยละ 0.05 ในปี พ.ศ. 2549 เป็นร้อยละ 0.5 ในปี พ.ศ. 2558 เช่นเดียวกันกับอัตราการติดเชื้อซิฟิลิสแต่กำเนิด ซึ่งเพิ่มจากไม่มีการติดเชื้อในปี พ.ศ. 2549 เป็นร้อยละ 0.06 ใน ปี พ.ศ. 2558 นอกจากนี้ ร้อยละของทารกที่น่าจะมีการติดเชื้อในปี พ.ศ. 2558 ยังมีจำนวนถึงร้อยละ 0.13 การศึกษาพบ ว่าในจำนวนของมารดาที่มีการติดเชื้อซิฟิลิสทั้งหมดพบเป็นมารดาวัยรุ่นถึงร้อยละ 30 นอกจากนี้ การศึกษายังพบว่าร้อยละ 16 ของมารดาที่ติดเชื้อทั้งหมดไม่ได้รับการรักษาในระหว่างการตั้งครรภ์ ซึ่งเกือบครึ่งของมารดาเหล่านี้ไม่มีอาการแสดงขณะตั้งครรภ์แต่มีผลเลือดที่ผิดปกติ (CMIA+, RPR-,TPPA+)

สรุป: จากการศึกษาพบว่ามีการเพิ่มขึ้นของอัตราการติดเชื้อซิฟิลิสของมารดาในระหว่างการตั้ง ครรภ์ และการติดเชื้อแต่กำเนิดของทารกโดยเฉพาะในมารดาวัยรุ่น จากผลการศึกษาจะช่วยเพิ่ม ความตระหนักเกี่ยวกับการเกิดโรคและการรักษาซิฟิลิสในระหว่างการตั้งครรภ์แก่สูติแพทย์ นอกจากนี้ผลการศึกษายังเน้นย้ำถึงความสำคัญในการทำความเข้าใจการตรวจคัดกรองซิฟิลิสด้วยวิธี reverse screening ก่อนจะนำมาปรับใช้ในทางคลินิก

คำสำคัญ: ซิฟิลิส, การตั้งครรภ์, การติดเชื้อแต่ปริกำเนิด

Introduction

Despite the availability of effective and safe antibiotic regimens, syphilis remains an ineradicable sexually transmitted infection[1,2]. The disease is caused by a spirochete, Treponema pallidum which has affected the human race for more than half a century[3]. Globally, syphilis in pregnancies remains a significant health issue. In 2012, approximately 930,000 pregnant women worldwide were estimated to have syphilis[4]. This number rivals the number of HIV-infected pregnant women. If syphilis is left untreated during pregnancy, it can result in numerous adverse maternal outcomes; miscarriages, premature deliveries, low birth weights, stillbirths, congenital syphilis and neonatal deaths. Additionally, these outcomes incur public health burdens[5-7]. Fetuses can extract syphilis from their mothers at any stage of the disease; however, transmission most commonly occurs during the early stages which leads to fetal hepatic dysfunction, placentomegaly, hematologic abnormalities and eventually hydrops fetalis[8].

Unfortunately, in Thailand, documented evidence regarding maternal and congenital syphilis is scarce; therefore, we conducted this study to examine the disease's trends in a large referral center in Bangkok, Thailand in order to increase obstetricians' awareness of syphilis, the almost neglected maternal infection, to improve the screening coverage and treatment strategy during the pregnancy period.

Materials and Methods

This is a 10-year retrospective descriptive study conducted in a tertiary care center (King Chulalongkorn Memorial Hospital, KCMH) in Bangkok, Thailand. Electronic clinical records of women who were diagnosed with syphilis during current pregnancy and who delivered at KCMH between 1st January 2006 and 31st December 2015 were retrieved. Chart records of the potentially affected infants were also extracted from the hospital database. The study was approved by the institutional review board, the Faculty of Medicine, Chulalongkorn University.

All pregnant women who attended antenatal clinic at KCMH were evaluated for syphilis in the first and third trimesters using rapid plasma reagent (RPR) test until February 2011, after which the testing was substituted by the treponemal chemiluminescence immunoassay (CMIA) (ARCHITECT Syphilis TP, Abbott Laboratories, Abbott Park, Illinois, USA). Treponema pallidum particle agglutination (TP-PA) test was leveraged to confirm the diagnosis during both periods. Pregnant women who were diagnosed with syphilis received standard treatment according to sexually transmitted diseases treatment guidelines published by the Center for Diseases Control and Prevention (CDC), USA[9-11]. Neonatologists were well aware of the maternal conditions; therefore, the infants were treated with standard antibiotic regimens accordingly.

Diagnoses of maternal and congenital syphilis obtained from the hospital database was extensively reviewed by 2 experienced obstetricians and a neonatologist[9-11]. In addition, demographic, clinical and laboratory data of these pregnant women and their infants were collected.

Data was analyzed by IBM SPSS software version 22 (IBM Corp, Armonk, NY, USA). Patient's demographic and syphilis-related data were presented by descriptive statistics.

Results

A total number of 56,475 pregnant women delivered and 57,637 infants were born at KCMH between 2006 and 2014. Syphilis was diagnosed during current pregnancy in 73 pregnant women (0.13%). The mean age of the infected pregnant women was 27.7 years old (SD 8.3 years) and the median gestational age at the time of diagnosis was 18 weeks (range 6-40 weeks). There were 71 singletons, one set of twins and one set of triplets contributing to 76 infants born to the

infected pregnant women. Nine infants were proved to have congenital syphilis (0.016%). Maternal and infant characteristics are shown in Table 1 and Table 2, respectively.

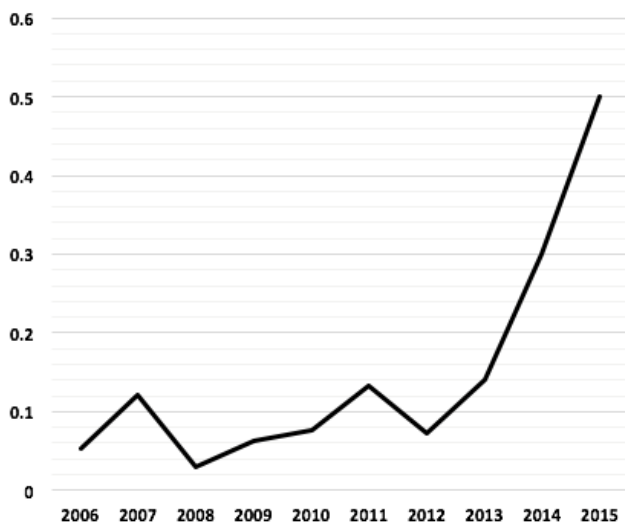
Between 2006 and 2014, the percentage of pregnant women identified as having syphilitic infection during current pregnancy had increased from 0.05% in 2006 to 0.50% in the final year (Fig. 1.). The percentage of infants with proven or possible congenital syphilis (Fig. 2.) also followed the same trend rising from 0% in 2006 to 0.06% and 0.13%, respectively, in 2015.

Table 1. Maternal characteristics.

Maternal characteristics	n=73 (%)
Gestational age at diagnosis	
• First trimester	24 (32.9)
• Second trimester	25 (34.2)
• Second trimester	24 (32.9)
Number of pregnancy	
• Primigravida	29 (39.7)
• Multiple gravida	44 (60.3)
Number of ANC	
• ≤ 4 times	22 (30.1)
• > 4 times	51 (69.9)
Maternal syphilis stage	
• Early syphilis (primary, secondary, early latent)	6 (8.2)
• Late latent/unknown duration	67 (91.8)
Maternal treatment regimen before delivery	
• None	12 (16.4)
• Benzathine penicillin G	57 (78.1)
• Ceftriaxone	3 (4.1)
• Erythromycin	1 (1.4)
Maternal co-infection	
• HIV	3 (4.1)
• Hepatitis B	1 (1.4)
Gestational age at delivery	
• < 37 weeks of gestation	17 (23.3)
• ≥ 37 weeks of gestation	56 (76.7)
Route of delivery	
• Vaginal delivery	53 (72.6)
• Cesarean delivery	20 (27.4)

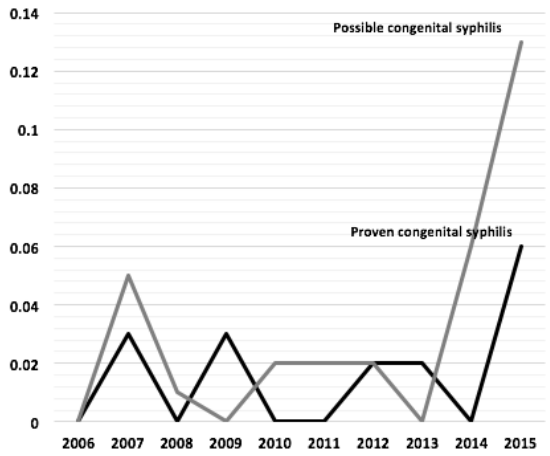
Table 2. Infant characteristics.

Infant characteristics	n=76 (%)
Birth weight	
• Very low birth weight	3 (3.9)
• Low birth weight	16 (21.1)
• Normal weight	57 (75.0)
Sex	
• Male	41 (53.9)
• Female	35 (46.1)
Syphilis related birth outcomes	
• Stillbirth	4 (5.3)
• Neonatal death	1 (1.3)
Infant syphilis status	
• Not infected	50 (65.8)
• Possible congenital infection	17 (22.4)
• Proven congenital infection	9 (11.8)



Year	Sypilis-infected pregnant women (total pregnant women = 56,475)	
	n	%
2006	3	0.053
2007	8	0.121
2008	2	0.030
2009	4	0.063
2010	3	0.077
2011	5	0.133
2012	4	0.073
2013	7	0.140
2014	14	0.300
2015	23	0.500

Fig. 1. Maternal syphilis.



Year	Proven congenital syphills		Possible congenital syphills	
	n	%	n	%
2006	0	0.00	0	0.00
2007	2	0.03	4	0.05
2008	0	0.00	1	0.01
2009	2	0.03	0	0.00
2010	0	0.00	1	0.02
2011	0	0.00	1	0.02
2012	1	0.02	1	0.02
2013	1	0.02	0	0.00
2014	0	0.00	3	0.06
2015	3	0.06	6	0.13

Fig. 2. Congenital syphilis.

Fig. 3. provides maternal age at the time of diagnosis divided into 2 different time periods; 2006-2010 and 2011-2015. Between 2006 and 2010, 10% (n=2) of the syphilis-infected pregnant women were younger than 20 years of age which escalated to 30% during 2011-2015. Notably, the percentage of early-stage syphilis cases also increased from 0% in 2006-2010 to 11.3% (n=6) in 2011-2015. Among women affected by early-stage syphilis, 83.3% (n=5) were under 25 years old.

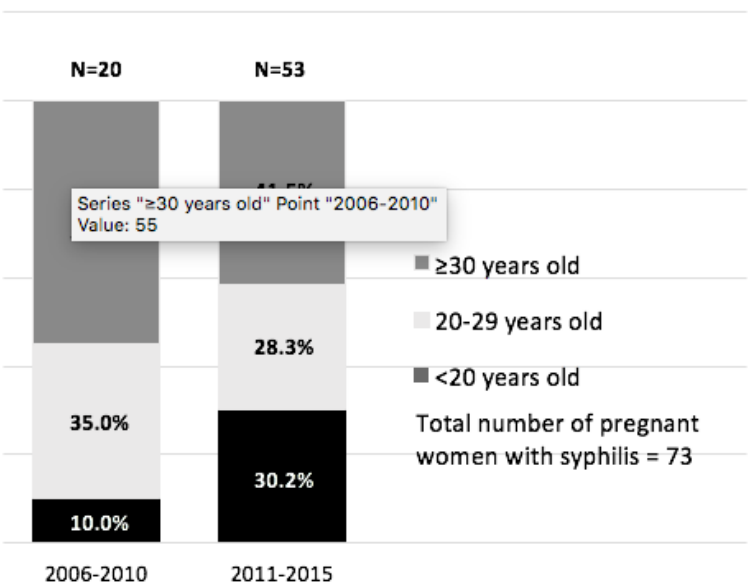


Fig. 3. Maternal age at diagnosis.

Overall, there were 16.4% (n=12) of infected pregnant women who did not receive any treatment before delivery. Table 3. provides clinical characteristics of untreated syphilis-infected pregnant women.

Of the 76 infants born to syphilis-infected pregnant women, 11.8% (n=9) of them were diagnosed with congenital syphilis. Out of the 9 affected infants, there were 7 singletons and one set of twins. Considering their maternal clinical characteristics, 55.6% (n=5) did not attend antenatal clinics and were newly diagnosed as having syphilis during intrapartum period. In addition, almost all of them (n=8) were diagnosed with syphilis in the third trimester and 77.8% (n=7) gave birth prematurely. The median interval from the diagnosis to delivery was 1 week (range 0-13 weeks).

Table 3. Diagnosis of untreated syphilis-infected pregnant women.

Diagnostic characteristic	n=12 (%)
Latent phase of unknown duration (CMIA+,RPR-,TPPA+)	5 (41.7%)
Diagnosis at delivery	4 (33.3%)
RPR: weekly reactive, TPPA+	3 (25.0%)

Discussion

According to our study, the percentages of pregnant women diagnosed with syphilis fluctuated around 0.1% during 2006-2013 which is well correlated with previous reports from Thailand and other Southeast Asia countries[4, 12, 13]. However, our recent data revealed that the number of syphilis-infected pregnant women had significantly increased for 2 consecutive years to 0.5% in 2015 which synchronizes with syphilis infection in particular population in the region; men who have sex with men[14, 15]. Not only did the number of infected pregnant women increase, but also the number of affected infants. The percentage of proven congenital syphilis cases remained stable between 0-0.03% during 2006-2014. Unfortunately, by the final year, the percentage sharply rose to 0.6%. In 2008-2009, previous study regarding congenital syphilis prevalence in Thailand unveiled that there were 0.1 case of congenital syphilis per 1,000 live births[16]. In consistent with the aforementioned study, we also demonstrated approximately similar incidence (0.01%) of congenital syphilis during the same period. However, we found a surge of congenital syphilis cases during the last 2 years.

In addition, we also discovered that during recent years, the number of syphilis-infected pregnant women who were younger than 20 years of age had increased from 10% to 30%. This trend correlates with other studies which evidence an escalating number of young women diagnosed with sexually transmitted diseases[17, 18]. Among syphilis-infected pregnant women who missed their treatment opportunities, majority of them were asymptomatic with positive serologic results as described; CMIA+, RPR-, TPPA+ results. This occurrence could be explained by the complicated interpretation of reverse syphilis screening algorithm as described by other studies[19-22]. Therefore, before applying the reverse syphilis screening algorithm, clinicians and medical personnels should be aware of and familiar with this approach.

With regards to congenital syphilis, in this study, nearly all infants were born to late presenters; pregnant women diagnosed in the third trimester or during delivery. Furthermore, a third of untreated women did not attend antenatal care. This finding emphasizes the importance of antenatal care in order to early detect any infection, to improve their health conditions and to prevent their infants from contracting the disease. As late treatment in third trimester, short interval between treatment initiation to delivery, preterm labor and inadequate antenatal care were

associated with syphilis-related adverse pregnancy outcomes and a greater number of congenital syphilis cases[23-25].

Conclusion

The strength of the study is that it adds new information with regards to the surge of maternal and congenital syphilis cases particularly in young adults. This updated insight will help increase the awareness of obstetricians regarding the importance of syphilis screening strategy and the treatment during pregnancy period. Timely identification of syphilis-infected women can substantially improve pregnancy outcomes, maternal health and prevent the infants from contracting the disease[26, 27]. However, the review was conducted in a single tertiary care center; therefore, further research is needed to confirm the rising trend of syphilis infection during pregnancy throughout the country.

Potential conflicts of interest

The authors declare no conflict of interest.

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Voiding Pattern in Thai Female without Lower Urinary Tract Symptoms

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ABSTRACT

Objectives: To study the parameters of voiding patterns in Thai women without lower urinary tract symptoms (LUTS) and to compare the voiding parameters between different age groups and menopausal status.

Materials and Methods: Seventy Thai women who lived or worked in various communities in Thailand without LUTS were invited to participate in the study during May-September, 2015. The volunteers were asked to complete Thai version Urogenital Distress Inventory for screening of LUTS for exclusion. All cases were trained how to collect and record in 3-day bladder diary.

Results: Two hundreds and ten bladder diaries (70 women; 3 days/1 person) were completed by seventy women. The mean ± standard deviation (SD) of age was 48.4 ± 7.9 years, the body mass index was 23.3 ± 4.0 kg/m^2, 25.7% were postmenopausal. The mean ± SD of voiding parameters were: 7.4 ± 2.3 times (24 hrs voiding frequency), 6.5 ± 2.0 times (daytime frequency), and 1,560 ± 627 ml (daily voided volume). The median (interquartile range) of night time frequency was 0.7 (0-3) times. The increasing age was associated with higher 24-hr voiding frequency and daytime voiding frequency.

Conclusion: The voiding parameters of Thai women without LUTS were reported. This data can be used as the tools for selecting Thai women with LUTS for further investigations and treatments. This result can be used as the reference for future research for the LUTS management.

Keywords: bladder diary, Thai women, voiding patterns.

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รูปแบบการถ่ายปัสสาวะในผู้หญิงไทย ที่ไม่มีอาการทางเดินปัสสาวะส่วนล่าง

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บทคัดย่อ

วัตถุประสงค์: *เพื่อหาค่าปกติของรูปแบบการถ่ายปัสสาวะในผู้หญิงไทย โดยหาค่าต่อไปนี้ : จำนวนครั้งที่ปัสสาวะใน 24 ชม., จำนวนครั้งที่ปัสสาวะในช่วงเวลากลางวัน, จำนวนครั้งที่ปัสสาวะในช่วงเวลานอน, ปริมาตรปัสสาวะตลอด 24 ชม., ปริมาณเฉลี่ยของปัสสาวะแต่ละครั้ง, ปริมาตรปัสสาวะที่มากที่สุดต่อครั้ง และหาความสัมพันธ์ของตัวแปรเหล่านี้กับกลุ่มอายุและภาวะวัยทอง*

วัสดุและวิธีการ: *หญิงไทย 70 คน ที่อาศัยอยู่ในประเทศไทย และไม่มีอาการของทางเดินปัสสาวะส่วนล่าง จะได้รับเชิญให้เข้าร่วมศึกษา ในช่วงเดือน พฤษภาคม – กันยายน 2558 อาสาสมัครทำแบบสอบถาม Urogenital Distress Inventory (UDI) ฉบับภาษาไทย จากนั้นได้รับการสอนให้เก็บและบันทึกปัสสาวะในใบบันทึกปัสสาวะ*

ผลการศึกษา: *ได้รับแผ่นบันทึกปัสสาวะคืนรวม 210 แผ่น จากหญิงอาสาสมัคร 70 คน อายุเฉลี่ย 48.4 ปี, ดัชนีมวลกาย 23.3 kg/m^2, มีผู้ที่หมดประจำเดือนแล้ว 18 คน (25.7%) พบว่า ค่าเฉลี่ยของจำนวนครั้งที่ปัสสาวะเท่ากับ 7.4 ± 2.3 ครั้งในหนึ่งวัน การปัสสาวะช่วงกลางวัน 6.5 ± 2.0 ครั้ง และปริมาตรปัสสาวะในหนึ่งวัน เท่ากับ 1,560 ± 627 ซีซี ค่ามัธยฐานของการปัสสาวะช่วงเวลานอน 0.7 (0-3) ครั้ง พบความสัมพันธ์ของอายุและจำนวนครั้งที่ปัสสาวะตลอดวัน และปัสสาวะช่วงกลางวัน*

สรุป: *การศึกษานี้ได้นำเสนอข้อมูลพื้นฐานของลักษณะรูปแบบของการขับถ่ายปัสสาวะในผู้หญิงไทยที่ไม่มีอาการของทางเดินปัสสาวะส่วนล่าง และค่าอ้างอิงที่จะช่วยในคัดเลือกผู้ป่วยที่จะตรวจเพิ่มเติมและดูแลรักษา ทั้งในทางคลินิกและในการวิจัยต่อไป*

คำสำคัญ: *ปัสสาวะ, ผู้หญิงไทย, รูปแบบการถ่ายปัสสาวะ*

Introduction

Lower urinary tract dysfunction is a common problem affecting reproductive and postmenopausal women around the world. Overall prevalence of urinary incontinence was found to range from 25-45%[1]. In Asian population, the prevalence of lower urinary tract symptoms (LUTS) was about fifty-three percent in reproductive-age females[2]. In a community-based study, the urinary incontinence prevalence was reported at 36.5%[3]. The annual cost-of-illness estimation for urinary incontinence in Canada, Germany, Italy, Spain, Sweden, and the United Kingdom was about 7 billion Euro[4]. The steps of investigation in these patient include history and physical examination, patient questionnaires, voiding diaries, urinalysis, post voiding residual urine volume, urodynamic study and pad testing[5]. Only in some situation that initial investigations provide inadequate data, imaging are required. The most LUTS diseases can be diagnosed by initial evaluation.

Voiding diary (sometime called frequency volume chart or bladder diary) is a useful and valuable tool for evaluating patient with lower urinary tract dysfunction such as urgency, urinary incontinence and overactive bladder. This diary is relatively low cost, high effective and non-invasive tool compared to urodynamic studies. However, this tool was not used frequently and the adherence was low[6]. The reasons were lack of standardization (many recording formats), lack of normal value of voiding parameter in each population group, and poor compliance to complete diary. In order to encourage the use of voiding diary, the International Continence Society (ICS) decide to published the standardized voiding diary for international use[7].

The roles of voiding diary include: facilitating history-taking, developing the differential diagnosis, understanding LUTS and complexity of voiding difficulty, assessment the nocturia and provide biofeedback following interventions[8]. Up to now there is no data about the normal voiding pattern in Thai women. The ICS suggested for the publishing of the normal value of voiding pattern in each population group/country so that there will be reference value of the voiding diary to differentiate normal/abnormal pattern for further investigation in the women with LUTS. The aim of this study was to study the parameters of voiding patterns in Thai women without LUTS and to compare the voiding parameters between different age groups and menopausal status.

Materials and Methods

After the Institute Research Ethics Committee approval, 70 Thai women who lived or worked in various communities in Thailand without lower urinary tract symptoms (LUTS) were invited to participate in the study during May - September, 2015. Distributions of samples were matched to the Thai ages and occupation distribution structure from National Statistical Office, 2014. The age distributions were: age 30-39 years: 31%, 40-49 years: 31%, 50-59 years: 23.6%, 60-70 year: 13.8%. The occupation distribution were: officer 37%, farmer 33%, housewife 15%, government officer 15%[9]. The exclusion criteria were: any positive answer (score more than or equal to 1) by Thai version Urogenital distress inventory questionnaires (UDI)[10], recent use of medications with anticholinergic effect, relevant neurologic disorders, uncontrolled medical diseases (e.g. diabetes), previous surgery for incontinence or pelvic organ prolapse, current vaginal pessary use, those who worked primarily at night, and pregnancy or within 3-month postpartum women.

After the written informed consent was obtained and the personal characteristics were recorded, the research nurse explained the study process and answered any additional questions. Volunteers were asked to complete Thai version UDI, then were trained how to collect and record the 3-day Thai version voiding diary by research nurse. The complete records were sealed in pre-paid registered envelope and returned to the researchers.

Sample size calculation

Sample size estimation was calculated based on our pilot study in 10 Thai women without LUTS by Thai version UDI. The parameter that yielded maximum sample size was the number of 24-hr frequency (mean ± standard deviation (SD) = 6.73 ± 1.4 times). The acceptable error was 5 percent of mean of 24-hr frequency (0.34). The calculation sample size was 65.13 (1.96^2*1.4^2 / 0.34^2). Assuming that the 10 percent may loss to follow up or incomplete the voiding diary or having any error in recording the data, the estimation sample size was about 70 cases.

Data analysis and statistics

Statistical analysis was done by using SPSS program version 22.0. Descriptive statistics [mean (SD) or median (interquartile range) and percentage] were used for baseline characteristics. The correlations between age and various voiding parameters were calculated by using Pearson's correlation coefficient. Multivariate analysis with linear regression was applied to determine the effects of menopause and age on the voiding patterns.

Results

Ninety five women were invited into the study, 24 were excluded due to positive UDI and one subject was postpartum woman. Seventy women completed the voiding diaries. The mean age was 48.4 years (35-63 years), the body mass index (BMI) was 23.3 kg/m^2 (18.1-35.8 kg/m^2), and 18 women (25.7%) were menopause. Seventeen women (24%) worked as housekeeper, twenty women (29%) performed agriculture, twenty-three women (33%) were employees and ten (14%) were government officers. Majority of subjects in this study (75%) were sexually active women. (Table 1)

Table 1. Demographic characteristics.

	Mean	SD	Range
Age (years)	48.4	7.9	(35.0 - 63.0)
BMI (kg/m^2)	23.3	4.0	(18.1 - 35.8)
Parity (n)	1.8	1.0	(0.0 - 5.0)
Profession	n (%)		
Housewife	17 (24)		
Agriculture	20 (29)		
Employees	23 (33)		
Government officer	10 (14)		
Menopause	18 (25.7)		
Active sexual intercourse	53 (75.7)		

BMI: body mass index, SD: standard deviation

Subjects voided with a mean ± SD was 7.4 ± 2.3 times in 24 hours, while 95% of women voided less than 12 times. The daytime and night time frequencies were 6.5 ± 2.0 times and 0.7(0-3) times, respectively. The daily voided volume was 1,560 ± 627 ml. The mean ± SD of the voided volume was 191.8 ± 71.1 ml, and the maximum voided volume was higher (381.1 ± 137.2 ml) (Table 2)

Higher age was associated with higher 24-hr

and daytime voiding frequencies (Pearson correlation coefficients = 0.2 and 0.2, p value = 0.015 and 0.028, respectively). A significant negative correlation also found between BMI and these parameters (correlation coefficients = -0.2 and -0.2, p value = 0.02 and 0.06, respectively).

Table 2. Voiding parameter outcome (N=70).

Parameter	Mean ± SD	Range	95th Percentiles
24-hr frequency (times)	7.4 ± 2.3	(3 - 14)	12
Daytime frequency (times)	6.5 ± 2.0	(2 - 11)	10
Night time frequency (times)	0.7	(0 - 3)	3
24-hr voided volume (ml)	1560.5 ± 627.7	(250 - 3550)	2750
Average voided volume (ml)	191.8 ± 71.1	(50 - 500)	306
Maximum voided volume (ml)	381.1 ± 137.2	(100 - 900)	600

SD: standard deviation

Discussion

Voiding diary (or bladder diary) is the important instrument to accurately assess clinical of LUTS. Most guidelines recommend using the diary adjunct to subjective evaluation. There is a clear evidence that a bladder diary is a valid and reliable measurement technique by the psychometric validation[7]. However, until now the literatures of the normative value of voiding parameter have been still sparse. The present study was conducted in community based and using national demographic distribution of age and profession to select the cases that could represent the Thai women in this age group. Previous studies used the simplified questions of the voiding condition for the inclusion criteria[11, 12]. But we decided to use the standardized questionnaire UDI (Thai version) to exclude women with LUTS for the more precise case selection.

From our results, we found the cut off (95th percentiles) for: "increase daytime frequency" as more than 10 times during daytime period, "urinary frequency" as voiding > 12 times in a 24-hr period and "nocturia" define as voiding more than 3 times that preceded and followed by sleep to select case for further investigation in Thai women that suffer for LUTS symptoms.

We found that the cut off value of voiding frequency from our study was similar to some reports (about 7-8 times a day)[12-14] and different in some studies (5-6 times a day)[11, 15]. And the mean voided volume (192±71 ml) from our study was slightly lower than previous studies in Caucasian women[11, 12]. These can be explained by the variations of drinking habit, BMI and races in each population group.

The studies in UK and Taiwan consistent found the mean voiding volume was significantly higher for the night time than in the daytime[13, 15], but not in our study (Table 3). We found the night time voided volume in about the half amount of daytime voided volume (192 ±71 ml vs. 83±97 ml). This can be explained by the sleep disorder, anatomic, lifestyle or climatic differences of Thai female. We also found the higher daytime and 24-hr voiding frequency that increased with increasing age. This aging effect on voiding patterns can be explained by the aging effect: the detachment of urothelial cells, an increase in connective tissue, intermingled with the smooth

muscle fibers in the muscle layer, increased innervation and neurotransmitter release[16], ischemic change[17] and fibrotic change of urinary bladder[18].

Table 3. Comparison of results of present study to other normative studies with asymptomatic women.

Parameter	Larson (1988)	Kassis (1993)	Homma (2000) Percentiles	FitzGerald (2002)	Huang (2006)	Present study
Subjects (N)	151	33	32	300	68	70
24-hr voided volume (ml) (mean ± SD)	1430±487	1473±386	1332±59	1759± 797	1529± 60	1560.5±627.7
Voids per 24 hr (times) (mean ± SD)	5.8±1.4	5.6±1.3	8±0.4	8.3±2.4	7.34±1.63	7.4±2.3
Voided volume (ml) (mean ± SD)	250±79	-	175±8	216±87	225±81	191.8±71.1
Maximum voided volume (ml) (mean ± SD)	460±174	-	277±16	362±161	-	381.0±627.7
Nocturia (% of subjects who reported ≥1 episodes)	15	rare	-	44	-	41

SD: standard deviation

The strength of this study was that we use the new proposed ICS-standardized voiding diary in Thai version, so the finding may be compared with other new studies. And we also used the standardized questionnaires (UDI) to exclude women with LUTS to make the inclusion criteria more accurate.

The limitation of our study was that as our study was designed for the study the normal voiding pattern but not for testing the correlations in each parameters and potential associated factors. Further studies are required to clarify these factors.

Conclusion

The voiding parameters of Thai women without LUTS were reported. This data can be used as the tools for selecting Thai women with LUTS for further investigations and treatments. This result can be used as the reference for future research for the LUTS management in Thai women.

Potential conflicts of interest

The authors declare no conflict of interest.

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