Prevalence of Abnormal Cervical Cytology by Liquid Based Cytology in the Antenatal Care Clinic, Thammasat University Hospital

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Objective: *To determine the prevalence of abnormal cervical cytology by liquid based cytology(LBC) in pregnant women who attended the antenatal care clinic at Thammasat University Hospital*
Material and Method: *LBC was performed on specimens from the collecting vial containing preserved cell solution (Cytyc, Boxborough, MA) in pregnant women who attended antenatal care at the antenatal care clinic, Thammasat University Hospital between March and July 2010. One hundred forty three pregnant women were recruited in the present study. All cytological reports were reviewed by senior cytopathologists for accurate diagnosis using the Bethesda System 2001 criteria. Patients with abnormal results as "abnormal squamous/glandular cells of undetermined significant" or more over were referred for colposcopic examination.*
Results: *One hundred forty three pregnant women participated in the present study. The average age was 27.09 years. There were 10 abnormal Pap smear results with four, five, and one cases of ASC-US, LSIL and HSIL respectively. The prevalence of abnormal cervical cytology in this investigation was 7% with 0.7% high-grade cervical intraepithelial neoplacia. Only 6% of participants had the correct understanding of the necessity of Pap smear testing. Thirty-one percent of multiparous pregnant women in the present study had no previous Pap smear screening. The majority of participants had coitarche before the age of 20.*
Conclusion: *The prevalence of abnormal cervical cytology in pregnant patients attending the antenatal care clinic at Thammasat University Hospital was 7%. The cervical cytology and related education were highly recommended in antenatal care clinic to increase cervical cancer screening coverage among reproductive age women.*

Keywords: *Prevalence, Abnormal cervical cytology, Liquid based cytology, Pregnancy*

J Med Assoc Thai 2011; 94 (2): 152-8
Full text. e-Journal: *http://www.mat.or.th/journal*

Cervical cancer is the second most common cancer worldwide. It is the highest incidence cancer among Thai women[1,2]. It is found in sexually active women of all age. However, lately it is more commonly found in younger patients compared to other gynecological cancer[3]. Cervical cancer is a slow progressive disease. High-risk human papilloma virus (HPV) is the cause of cervical cancer. It is a curable disease if early detection and precancerous lesion is timely treated.

Pregnancy and prenatal care offer an excellent opportunity to implement the cervical cytology test for premalignant condition in young age group patients. In Thailand, the first antenatal care visit provides the majority of women the first opportunity to meet up with gynecological professionals.

Conventional Pap smear is the standard method for cervical cancer screening. Frequent screening per individual is needed due to the disease's long progression from precancerous to cancerous

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status. Unfortunately, only a small number of Thai women seem to be concerned about gynecological checkup and cervical cancer screening because of modesty[4].

Currently, a liquid based cytology offers some significant advantages over conventional Pap smear. The use of liquid based cytology preparation reduces some of the technical errors of conventional Pap smear, *i.e.*, lower contaminants of blood and mucous and circumventing the problematic air dry process. The monolayer of cells is also easier to examine under the microscope. This results in an increased rate of detection of abnormal cells for the liquid based sample.

The aim of the present study was to determine the prevalence of abnormal cervical cytology by liquid based cytology in pregnant patients who attended the antenatal clinic at Thammasat University Hospital.

Material and Method

The present research proposal received the approval of the Ethical Committee Clinical Research of Thammasat University Hospital in 2010. Participants consisted of first visit pregnant women who attended the antenatal clinic at Thammasat University Hospital between March and July 2010. An inclusion criterion was for patients with a gestational age of under 24 weeks. All 143 of the patients were recruited in the present study after their written informed consent form was signed.

Cervical cytologic screening was performed by liquid based cytology test. All the specimens were collected from the ectocervix with cytobrush 5-rounds in scraping pattern. The brush was immersed and manually stirred vigorously in the collecting vial containing preserved cell solution (Cytyc, Boxborough, MA). All specimens were submitted to the Department of Pathology, Thammasat University Hospital, where they were read by a certified cytopathologist to obtain accurate diagnoses using the Bethesda System 2001 criteria.

Patients who had abnormal results as "abnormal squamous/glandular cells of undetermined significant" (ASC-US/AGUS) or more over were referred to gynecologic oncologist for colposcopic examination.

Demographic, health specific and reproductive data were also collected from all participants using a structured questionnaire. The descriptive statistics were used to summarize the data in term of frequency, percentage, and the average mean. Chi-square test was used to compare categorical data which p-value was set at 0.05 for significant.

Results

Details of cytological reports from the 143 pregnant women participating in the present study are presented in Table 1. All 143 specimens were adequate for further evaluation.

The prevalence of abnormal cervical cytology in the present investigation was 7%. There were four, five, and one cases of ASC-US, low-grade squamous intraepithelial lesion (LSIL), and high-grade squamous intraepithelial lesion (HSIL), respectively. Among normal subjects, 48 cases showed infection, namely *Candida* spp.(62.5%), *Gardnella* spp.(35.4%), and *Trichomonas vaginosis* (2.1%).

The colposcopic examination and colposcopic directed biopsy without endocervical curettage was performed in every case with abnormal cervical cytology. All ASC-US patients had pathologic diagnosis of cervicitis. All five LSIL patients were then diagnosed as CIN 1 while the HSIL patients were diagnosed with CIN 2. All abnormal cervical cyology cases had satisfactory colposcopic findings with no significant bleeding.

The demographic data of the participants distributed by the cervical cytology results are shown in Table 2. Participants in the present investigation were between 15-41 years old with the mean of 27.09 years. Sixty-three percent of the study group was aged between 20-29 years old. Sixty six percent of patients completed the secondary level and 15% had an undergraduate degree or with higher education. The majority (34%) were office workers or factory daily wage earners while the second largest group (28%) was housewives. Sixty-two percent earned a monthly income of 10,000 Baht or less (around 300 USD). This is

Table 1. Prevalence of abnormal cervical cytology by liquid based cytology in 143 subjects at the antenatal care clinic, Thammasat University Hospital, 2010

Results	n (%)
Normal	133 (93.0)
Without infection	85 (59.4)
With Infection	48 (33.6)
Abnormal Pap smear	10 (7.0)
ASC-US	4 (2.8)
LSIL	5 (3.5)
HSIL	1 (0.7)

ASC-US = atypical squamous cells of undetermined significance; LSIL = low grade squamous intraepithelial lesion; HSIL = high grade squamous intraepithelial lesion

the lowest wage earner group in the Thai tax structure and received tax exemption under the current government.

This group of participants had excellent personal habits. Ninety-four percents of participants never smoked, and 78% did not consume alcohol. Only 5% lived in households where they were secondhand smokers (Table 2).

Half of the participants were nulliparous. Among multiparous participants, 77% of this group had normal delivery. Fifty-seven percent of participants never had any Pap smear test. Those who previously

Table 2. Demographic data of the patients attending the antenatal care clinic at Thammasat University Hospital and the results of their liquid based cervical cytology

Results	Pap smear results (%)		
	Normal (%) n = 133	Abnormal (%) n = 10	Total (%) n = 143
Age			
< 20	11 (100.0)	0 (0)	11 (7.7)
20-29	81 (90.0)	9 (10.0)	90 (62.9)
30-39	34 (98.0)	1 (2.0)	35 (24.5)
≥40	7 (100)	0 (0)	7 (4.9)
Education			
Primary school	24 (92.4)	2 (7.6)	26 (18.2)
Secondary school	87 (91.6)	8 (8.4)	95 (66.4)
Undergraduate degree +	22 (100.0)	0 (0)	22 (15.4)
Occupation			
Government officer	6 (100.0)	0 (0)	6 (4.1)
Employee	45 (91.9)	4 (8.1)	49 (34.3)
Market woman	24 (92.4)	2 (7.6)	26 (18.2)
housewife	37 (92.5)	3 (7.5)	40 (28.0)
Student	4 (100.0)	0 (0)	4 (2.8)
Others	17 (94.5)	1 (5.5)	18 (12.6)
Income per month(Baht)			
5,000-10,000	80 (89.9)	9 (10.1)	89 (62.2)
>10,000-20,000	37 (100.0)	0 (0)	37 (25.9)
>20,000-30,000	9 (100.0)	0 (0)	9 (6.3)
>30,000	7 (87.5)	1 (12.5)	8 (5.6)
Smoking			
Never	126 (93.4)	9 (6.6)	135 (94.4)
Smoked	1 (100.0)	0 (0)	1 (0.7)
Family member smoked	6 (85.8)	1 (14.2)	7 (4.9)
Alcohol consumption			
Never	104 (93.7)	7 (6.3)	111 (77.6)
Rarely	10 (83.4)	2 (16.6)	12 (8.4)
Often	19 (95.0)	1 (5.0)	20 (14.0)
History of delivery			
Nulliparous	69 (95.9)	3 (4.1)	72 (50.3)
Multiparous	64 (78.5)	7 (21.5)	71 (49.7)
Normal labor	50 (91.0)	5 (9.0)	55 (77.5)
Cesarean section	14 (87.5)	2 (12.5)	16 (22.5)
History of Pap smear			
Never	77 (95.1)	4 (4.9)	81 (56.6)
Existing history	56 (90.4)	6 (9.6)	62 (43.4)
Normal result	56 (90.4)	6 (9.6)	62 (100.0)
Abnormal result	0 (0)	0 (0)	0 (0)

had the tests all reported normal result with the present study (Table 2).

Data concerning sexual and reproductive behaviors of participants are shown in Table 3. The majority of participants (69%) had their coitarche between ages 16 and 19 while two percent had it before age of 16. Almost half (49%) only had one sexual partner. Among participants with more than one partner, 68 people had 2-4 partners. Few had more than four partners (3.5%).

Participants' knowledge of cervical cancer was examined in the questionnaire. The result is shown in Table 4. The majority of participants (34.97%) said cervical cancer screening was necessary for all women, while only 5.59% gave the right answer that the screening was necessary for all sexually active women. Fifty-three percent (25.17 and 27.97) believed that Pap smear was necessary when some conditions occurred, *i.e.*, vaginal bleeding, leucorrhea, and after delivery period.

Table 5 shows the participant's history of cervical cancerous screening. Not only that 55.5% of first time pregnant women had not previous Pap smear screening but also 31% of multiparous subjects were also blind to the significance of cervical cancer treating. Since this latter group had at least once passed through the hands of a gynecological professional, it indicated an oversight in our women's health care system.

Table 6 shows the reason for no history of Pap smear from the negative group in Table 5. It is understandable for the nulliparous group that some (75% in this group) had no awareness of cervical cancer and its preventive measure. However, 45% in the multiparous group had no awareness of this second most common cancer in women in Thailand despite their meeting with gynecologic health care providers during antenatal care.

Table 3. Sexual behavior of the patients attending the antenatal care clinic at Thammasat University Hospital and the result of their liquid based cervical cytology

	Normal (%) n = 133	Abnormal (%) n = 10	Total (%) n = 143
Age of coitarche (years)			
< 16	3 (100.0)	0 (0)	3 (2.1)
16-19	92 (92.9)	7 (7.1)	99 (69.2)
> 19	38 (92.6)	3 (7.4)	41 (28.7)
Number of sexual partners			
1	67 (95.7)	3 (4.3)	70 (49.0)
2-4	63 (92.6)	5 (7.4)	68 (47.5)
> 4	3 (60.0)	2 (40.0)	5 (3.5)

Table 4. Knowledge of cervical cancer screening among pregnant participants attending antenatal care clinic at Thammasat University Hospital

Significant of Pap smear testing	n (%)
Necessary for all women	50 (34.97)
Necessary for all sexually active women	8 (5.59)
Necessary for women with leukorrhea or vaginal bleeding	36 (25.17)
Necessary for women with previous Pap smear abnormal result	4 (2.80)
Necessary for women after delivery	40 (27.97)
Not necessary	5 (3.50)
Total	143 (100.0)

Table 5. History of Pap smear check up and parity of pregnant participants attending the antenatal care clinic at Thammasat University Hospital

	History of Pap smear, n (%)		
	Yes	No	Total
Nulliparous	32 (44.5)	40 (55.5)	72 (100.0)
Multiparous	49 (69.0)	22 (31.0)	71 (100.0)

Chi-square p-value = 0.005

Discussion

Prevalence of abnormal cervical cytology in pregnant women in 2010

Cervical cancer in pregnancy is a very rare occurrence[5,6]. The problem found in pregnant women was more of a precancerous lesion type. First visit of antenatal care is the excellent time for precancerous condition, sexual transmitted diseases, and general gynecologic problem screening. In many Thai women, the first visit to antenatal care was their first encounter to a gynecological professional[4]. However, many Thai women refused pelvic examination and cervical cancer screening during such visits. Some gynecologists believe that the incidence of cancer in reproductive aged women is rare based on old data. As a result, physicians respect patients' request and order cervical screening for the postpartum visit instead.

Table 6. Reason of no history of Pap smear and parity of pregnant participants attending the antenatal care clinic at Thammasat University Hospital

	Reason of no history of Pap smear, n (%)		
	No awareness*	Awareness with hindrance**	Total
Nulliparous	30 (75.0)	10 (25.0)	40 (100.0)
Multiparous	10 (45.5)	12 (54.5)	22 (100.0)

Chi-square p-value = 0.04

* No symptom, do not make time to go

** Not going because of out of date belief, namely shyness, or other hindrance like relocation away from familiar health care provider

The prevalence of abnormal cervical cytology and CIN in pregnancy varies from one study report to the others. Yamazaki et al in year 2006[7] reported abnormal cervical cytology in 1.13% pregnant women in Japan, while local reports from Thailand showed 0.8 and 0.52 percent in 2005 and 2008 respectively[8,9]. In the present investigation, abnormal cervical cytology among pregnant women with first antenatal visit at Thammasat University Hospital was 7%.

This is the first report of abnormal cervical cytology in pregnant women with prevalence greater than 3 percent[7-11]. The present investigation employed liquid based preparation. Liquid based technique is known to increase the rate of abnormal cells detection due to the lower contaminants of blood and mucous and circumventing the problematic air-dry process. The monolayer of cells is also easier to examine under the microscope. Sensitivity of this technique is higher than conventional Pap smear (92 compared to 51% respectively)[12]. However, this improved technique alone would not account for more than 8-fold increase in pregnant women (0.8-7%) abnormal cytology prevalence between Sueblinvong's[8] and the present study done to a population of the same location. Further look into demographic, health specific and reproductive data may shed some light on this alarming high prevalence of cervical precancerous incidence among reproductive age women in Thailand.

Sueblinvong's[8] reported 3.6 and 1.7% abnormal Pap smear incidence among pregnant women aged below 20 and 20-29 years of age respectively. The present study found none in the former age group but 10 percent in the latter population. Table 3 indicates that 71% of the participants had coitarche at below 20 years of age. However, 66.4% of participants finished high school at the age around 18-19 years. This indicated that many had their first sexual experience while attending high school. Since abnormal cytology in subjects below age 20 was zero percent in its own age group, it implied that sex education information might have reached its intended target. This also showed in reduction of teen pregnancy rate from 18 to 7.7% in year 2005 and the present time[8].

Questionnaire requested sexual history information revealed data of great interest (Table 3). Pregnant women with one, 2-4, and > four partners had 4.3, 7.4, and 40% abnormal cervical cytology compared to their own age group. Peters R et al in 1986[13] mentioned a total number of four sexual partners or more increase a relative risk of abnormal cervical cytology for such an individual 3.6-fold. The present data totally agreed with the report.

Knowledge of cervical cancer and self-care in pregnant women

Very few participants (5.59%) had the correct understanding of necessity of Pap smear testing. Fifty-three percent (25.17 and 27.97) believed that a Pap smear was necessary when some conditions occurred, *i.e.*, vaginal bleeding, leucorrhea, and after delivery period. This showed that women of reproductive age of low income (majority of the presented participants) did not receive cervical cancer information concerning prevention and screening. Table 5 and 6 exemplified the above statement.

The study of cervical cytology in pregnant women from the same Thammasat University Hospital locus between 2005 (conventional Pap smear)[8] and 2010 (liquid based cytology) showed that the prevalence of abnormal cervical cytology was increasing. The authors found cases of multiparous women who had no prior cervical cancer screening. Some had no awareness of cervical cancer screening's significance and the others had some unreasonable negative connotation about the procedure. The former group should have been educated in the antenatal care clinic and had the cervical cancer screening performed while they attended antenatal care. Ob & Gyn professionals should all spend some resources with pregnant women to raise women's reproductive health care standard in the population of reproductive age women.

The latter group (women with unreasonable phobia) is a difficult group to work with. Changing

people's attitude is more difficult than educating them. More information is needed to understand the cause of their reluctance and fear before they could be reached.

The present finding indicated that most pregnant subjects started their active sexual lives before the age of high school graduation. As a result, sex and reproductive health education programs are highly recommended for children before the end of primary education. However, presentation of such a program needs to be appropriate to children in this age group to be the most effective. Contraception, sexual transmitted disease prevention, and cervical cancer vaccination should be campaigned to the target group before their coitarche. The same information should be presented to parents of these children to introduce them to the idea of HPV vaccination in the near future.

Conclusion

The prevalence of abnormal cervical cytology in pregnant patients attending the antenatal care clinic at Thammasat University Hospital was 7% with 0.7% high-grade CIN prevalence. Thirty-one percent of multiparous pregnant women in the present study had no previous Pap smear screening. The cervical cytology is highly recommended for the routine screening in the antenatal care clinic for women who had no prior cervical cancer screening because no one can tell when the women will meet up with gynecological professionals again. Education in antenatal care clinic and post partum ward would be one of the easiest ways to increase cervical cancer screening coverage among reproductive age women. However, the present study was limited by the number of population, which was too small to be representative of the entire population. Furthermore, this subject requires further studies.

Potential conflicts of interest

None.

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ความชุกของความผิดปกติในการตรวจคัดกรองมะเร็งปากมดลูกโดยวิธีเซลล์วิทยาอิงของเหลวในสตรีตั้งครรภ์ที่โรงพยาบาลธรรมศาสตร์เฉลิมพระเกียรติ

ปรานี แข็งข้อ, กริชา ไม้เรียง, คมสันต์ สุวรรณฤกษ์, ยุทธเดช ทวีกุล, เย็นฤดี ภูมิถาวร, จรรยา ภัทรอาชาชัย, กรณ์กาญจน์ ภมรประวัติ

วัตถุประสงค์: *เพื่อศึกษาความชุกของความผิดปกติในผลการตรวจคัดกรองมะเร็งปากมดลูก โดยวิธีเซลล์วิทยาอิงของเหลว (liquid based cytology) ในสตรีตั้งครรภ์ที่มารับการฝากครรภ์ที่โรงพยาบาลธรรมศาสตร์เฉลิมพระเกียรติ*

วัสดุและวิธีการ: *สตรีตั้งครรภ์ที่มาฝากครรภ์ที่โรงพยาบาลธรรมศาสตร์เฉลิมพระเกียรติในช่วงเดือนมีนาคม ถึงเดือนกรกฎาคม พ.ศ. 2553 ได้ถูกคัดเลือกเพื่อรับการตรวจคัดกรองปากมดลูกโดยวิธีเซลล์วิทยาอิงของเหลว โดยตัวอย่างทั้งหมดจะถูกส่งไปแปลผลที่หน่วยพยาธิวิทยา โรงพยาบาลธรรมศาสตร์เฉลิมพระเกียรติ สตรีที่มีผลการตรวจผิดปกติตั้งแต่ "abnormal squamous/glandular cells of undetermined significant (ASC-US)" ขึ้นไปจะได้รับการส่องกล้องขยายปากมดลูกและตัดชิ้นเนื้อบริเวณปากมดลูกเพื่อยืนยันการวินิจฉัย*

ผลการศึกษา: *ผลการตรวจวิเคราะห์พบความผิดปกติจากการตรวจคัดกรองมะเร็งปากมดลูก โดยวิธีเซลล์วิทยาอิงของเหลวในสตรีตั้งครรภ์ที่มารับการฝากครรภ์ทั้งหมด 10 ราย จากสตรีที่รับการตรวจทั้งหมด 143 ราย คิดเป็นความผิดปกติร้อยละ 7 โดยแยกเป็นความผิดปกติชนิด ASC-US, LSIL และ HSIL จำนวน 4 ราย, 5 ราย และ 1 ราย ตามลำดับ จากการศึกษาพบว่าสตรีตั้งครรภ์ที่เคยมีบุตรแล้วอย่างน้อย 1 คน จำนวนถึงร้อยละ 31 ที่ไม่เคยรับการตรวจมะเร็งปากมดลูกเลย และจากสตรีที่รับการตรวจทั้งหมด 143 ราย มีผู้ที่เข้าใจอย่างถูกต้อง ถึงความจำเป็นในการตรวจคัดกรองมะเร็งปากมดลูกเพียงร้อยละ 6 และส่วนใหญ่ของสตรีตั้งครรภ์ที่ศึกษามีเพศสัมพันธ์ครั้งแรกก่อนอายุ 20 ปี*

สรุป: *ความชุกของความผิดปกติในผลการตรวจคัดกรองมะเร็งปากมดลูกในสตรีตั้งครรภ์ โรงพยาบาลธรรมศาสตร์เฉลิมพระเกียรติ ในการศึกษานี้คิดเป็นร้อยละ 7 ซึ่งค่อนข้างสูงเมื่อเทียบกับในการศึกษาอื่น การให้ความรู้ ความเข้าใจที่ถูกต้องเกี่ยวกับการตรวจคัดกรองมะเร็งปากมดลูกจึงยังควรแนะนำในสตรีตั้งครรภ์ เพื่อผลในการลดอุบัติการณ์การเกิดมะเร็งปากมดลูก*