RESEARCH ARTICLE

Prevalence and Risk Assessment of Cervical Cancer Screening by Papanicolaou Smear and Visual Inspection with Acetic Acid for Pregnant Women at a Thai Provincial Hospital

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Abstract

Background: Cervical cancer is the second most common in Thailand, but the mortality rate may be rising yearly. It is a cancer that can be prevented by early screening for precancerous lesions, several methods being available. Objective: To identify the prevalence of abnormal Papanicolaou (Pap) smears and lesions with visual inspection with acetic acid (VIA) in pregnant women and assess risk factors for this group. Materials and Methods: This prospective study was performed at Prapokklao Hospital, Thailand during April-July 2016. All pregnant women of gestational age between 12-36 weeks who attended an antenatal clinic were recruited. All participants were screened for cervical cancer by Pap smear and VIA. If results of one or both were abnormal, colposcopic examination was evaluated by gynecologic oncologist. Results: A total of 414 pregnant women were recruited. Prevalence of abnormal Pap smear and VIA were 6.0 and 6.7 percent, respectively. The most common abnormal Pap smear was low grade intraepithelial lesion (LSIL, 44%). Factors associated with abnormal Pap smear in pregnant women were low BMI, multiple partners and being a government officer. In pregnancy, Pap smear had higher sensitivity and specificity than VIA for detection of precancerous cervical lesion. Patients with young coitarche or more than 25 years of active sexual activity were high risk groups. Conclusions: Prevalence of abnormal Pap smear and VIA in pregnant women was 6.0 and 6.7 percent, respectively. Factors associated with abnormal Pap smear were coitarche, years of sexual activity, low BMI, multiple partners and being a government officer.

Keywords: Papanicolaou smear - visual inspection with acetic acid - colposcopy - cervical cancer - pregnancy.

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Introduction

Cervical cancer was the second most common cancer of women in Thailand after breast cancer. Incidence of cervical cancer in Thailand was 23.4 in 100,000 (Ferlay et al., 1998). Cervical cancer mortality rate was rising from 0.66 - 0.94% between 2011 and 2014 (Department of Disease Control, Ministry of Public Health, 2015). Cervical cancer is preventable by screening for precancerous lesions. Available screening tools in Thailand are cervical cytology (Papaniculoau smear: Pap smear), visual inspection with acetic acid (VIA) and human papillomavirus (HPV) test. The cervical cancer screening coverage is now 68.4% of postpartum women in Prapokklao hospital. Increase screening coverage is desired as a part of a plan to reduce cervical cancer mortality rate in Thailand.

Cervical cytology is currently a standard for cancer screening. VIA is easy, cheap and compliance method. It is a suitable method for low resource setting areas. Because Prapokklao Hospital is a general hospital in eastern part of Thailand, it is located around 100 kilometers from Thai-Cambodia border. VIA may be considered to method of choice for cancer screening in this area.

Many factors were associated to cervical cancer such as multiple partners, history of sexually transmitted infection (STD), smoking, infection with human immunodeficiency virus, immunosuppression, long term contraceptive pills, etc., but the main cause of cervical cancer was infection with Human Papilloma Virus (HPV) (Moore et al., 2004; Perksanusak et al., 2015). The incidence of HPV infection in pregnant women is as high as 18% compared to 6.2% of non-pregnant women (Khanuja et al., 2014; Silvia et al., 2007). Because of hormone levels change and immunosuppressive status, the HPV infection is much higher in pregnant women.

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The aims of this study was to determine the prevalence of abnormal cervical cytology and the efficacy of VIA in pregnant women who attended the antenatal care clinic at Prapokklao hospital, Chantaburi, Thailand.

Materials and Methods

This was a prospective study approved by the Ethics committee of Prapokklao hospital. All pregnant women of gestational age between 12 and 36 weeks who attended the antenatal care clinic at Prapokklao hospital from April to July 2016 were recruited. Subjects with previous abnormal Pap smear or history of first half bleeding were excluded.

All subjects signed inform contents, then underwent cervical cancer screening by Pap smear and VIA. Modified Ayre's spatula was applied to the cervix for specimen collection. The cervical scrap specimen was smear on the glass slide and immediately fixed in 95% ethyl alcohol. The cervical sample was sent to be seen at the department of pathology, Prapokklao hospital. Cervical cytology was reported according to Bethesda classification 2001 (IARC, 2016).

Abnormal cervical cytology was then reported as cancer, high grade intraepithelial lesion (HSIL), low grade intraepithelial lesion (LSIL) and atypical smear. Atypical smear consisted of atypical squamous cell undetermined significance (ASC-US), atypical squamous cell cannot exclude high grade lesion (ASC-H), atypical glandular cell not otherwise specified (AGC-NOS) and atypical glandular cell favor neoplasia (AGC-FN).

Table 1. Demographic Characteristics And Prevalence of Abnormal Cervical Cytology Compared to Visual Inspection with Acetic Acid (VIA) in Pregnant Women at Prapokklao Hospital, Chanthaburi, Thailand

Characteristic	N=414 (%)	Pap smear (n (%))			VIA (n (%))		
		NILM	Abnormal	p-value	Negative	Positive	p-value
Age (years)†				0.384			0.098
<30	281 (67.9)	266 (68.4)	15 (60)		266 (68.9)	15 (53.6)	
≥30	133 (32.1)	123 (31.6)	10 (40)		120 (31.1)	13 (46.4)	
Residency†				0.15			0.239
Rural	188 (45.4)	173 (44.5)	15 (60)		172 (44.6)	16 (57.1)	
Urban	266 (54.6)	216 (55.5)	10 (40)		214 (55.4)	12 (42.9)	
Occupation‡				0.174			0.012*
Housewives	113 (27.3)	104 (26.7)	9 (36.0)		108 (28.0)	5 (17.9)	
Agriculture/Trade	57 (13.8)	51 (13.1)	6 (24.0)		54 (14.0)	3 (10.7)	
Government officer	164 (39.6)	158 (40.6)	6 (24)		154 (39.9)	10 (35.7)	
High school/college student	32 (7.7)	29 (7.5)	3 (12)		31 (8.0)	1 (3.6)	
Other	48 (11.6)	47 (12.1)	1 (4)		39 (10.1)	9 (32.1)	
Income (Baht)‡				0.354			0.541
<10000	111 (26.8)	105 (27.0)	6 (24.0)		106 (27.5)	5 (17.9)	
10000-20000	277 (66.9)	258 (66.3)	19 (76.0)		256 (66.3)	21 (75)	
> 20000	26 (6.3)	26 (6.7)	0 (0.0)		24 (6.2)	2 (7.1)	
Body mass index (kg/m^2)‡				0.12			0.003*
Underweight (BMI<18.5)	79 (19.1)	71 (18.3)	8 (32.0)		73 (18.9)	6 (21.4)	
Normal weight (BMI 18.5-24.9)	242 (58.5)	232 (59.6)	10 (40.0)		233 (60.4)	9 (32.1)	
Overweight and obese (BMI>25)	93 (22.5)	86 (22.1)	7 (28.0)		80 (20.7)	13 (46.4)	
Sexual partner(n)†				0.097			0.846
Single	187 (45.2)	180 (46.3)	7 (28.0)		175 (45.3)	12 (42.9)	
Multiple	227 (54.8)	209 (53.7)	18 (72.0)		211 (54.7)	16 (57.1)	
Parity†				0.388			0.531
Primigravidarum	134 (32.4)	124 (31.9)	10 (40)		127 (32.9)	7 (25.0)	
Multigravida	280 (67.6)	265 (68.1)	15 (60)		259 (67.1)	21 (75.0)	
Contraception†				0.654			0.2
Barrier	126 (30.4)	120 (30.8)	6 (24.0)		121 (31.3)	5 (17.9)	
Non-barrier	288 (69.6)	269 (69.2)	19 (76.0)		265 (68.7)	23 (82.1)	
Smoking†				1			1
No	411 (99.3)	386 (99.2)	25 (100.0)		383 (99.2)	28 (100.0)	
Yes	3 (0.7)	3 (0.8)	0 (0.0)		3 (0.8)	0 (0.0)	
Coitarche(years)‡				0.669			0.439
<15	21 (5.1)	19 (4.9)	2 (8.0)		21 (5.4)	0 (0.0)	
15-19	287 (69.3)	269 (69.2)	18 (72.0)		267 (69.2)	20 (71.4)	
≥ 20	106 (25.6)	101 (26.0)	5 (20.0)		98 (25.4)	8 (28.6)	
History of uterine curettage†				0.717			1
No	376 (90.8)	352 (90.5)	24 (96.0)		350 (90.7)	26 (92.9)	
Yes	38 (9.2)	37 (9.5)	1 (4.0)		36 (9.3)	2 (7.1)	
HIV infection†				0.004*			0.004*
Negative	412 (99.5)	389 (100.0)	23 (92.0)		386 (100.0)	26 (92.9)	
Positive	2 (0.5)	0 (0.0)	2 (8.0)		0 (0.0)	2 (7.1)	
History of STD†				1			0.653
No	392 (94.7)	368 (94.6)	24 (96.0)		366 (94.8)	26 (92.9)	
Yes	22 (5.3)	21 (5.4)	1 (4.0)		20 (5.2)	2 (7.1)	

† Fisher's Exact Test, * statistic significant, ‡t-test, NILM: negative for intraepithelial lesion or malignancy, ASC-US: atypical squamous cells of undetermined significance, LSIL: low grade squamous intraepithelial lesion, HSIL: high grade squamous intraepithelial lesion, STD: sexual transmitted disease

Table 2. Comparison between Pap Smear, Visual Inspection with Acetic Acid and Colposcopy (N = 414)

Screening result		Colposcopy		Sensitivity	Specificity	Accuracy	PPV	NPV
		Positive**	Negative	(%)	(%)	(%)	(%)	(%)
VIA				59.26	96.89	94.44	57.14	97.15
	Positive	16	12					
	Negative	11	375					
Pap smear				70.37	98.45	96.62	76	97.94
	Positive*	19	6					
	NILM	8	381					

VIA: Visual inspection with acetic acid, NILM: negative for intraepithelial lesion or malignancy, * positive = ASC-US: atypical squamous cells of undetermined significance, LSIL: low grade squamous intraepithelial lesion, HSIL: high grade squamous intraepithelial lesion, PPV: positive predictive value, NPV: negative predictive value, ** low grade lesion

After completion for cervical sample collection, a cotton swab was soaked in three percent acetic acid. The cotton swab was then applied around the cervix for 1 minute. Then the cervix was thoroughly inspected with naked eye. When thickened white plaques appearance (acetowhite lesion) was shown, it was considered as positive for VIA. If the cervix appearance was smooth, pink, uniform, featureless, ectropion, polyp, cervicitis, inflammation and nabothian cysts, the VIA test was negative. The presence of cauliflower-like growth, ulcer or fungating mass were classified as suspected cancer (IARC, 2016). All cases who had abnormal Pap smear or positive VIA were appointed for colposcopic examination.

Colposcopic examination was reported according to the modified Reid colposcopic index (RCI) (Ferris et al., 1994).Cervical biopsy was performed in case of high grade precancerous cervical lesion. Endocervical curettage (ECC) was omitted in the study. If the indication of cervical conization was met, the operation would be postponed until after labor and delivery. Cervical conization during pregnancy was performed only in case of highly suspicious of cancer.

Participants data were collected directly from medical record and questionnaire include age, residency, occupation, income, weight, height, body mass index(BMI), number of partner, gestational age, number of pregnancy, contraception, smoking, coitarche, history of uterine curettage, history of sexually transmitted diseases (STD) and Human immunodeficiency virus (HIV) infection were all recorded.

Statistical analysis was performed using Statistical Package for the Social Sciences version 19.0 (SPSS v.19). Range and mean were used to describe characteristics of the study population. Frequency and percentage were interpreted by descriptive statistic. Chi-square test and Fisher's exact test were used to analysed categorical data and t-test was used for continuous data. The p-value of less than 0.05 was statistic significant.

Results

Four hundreds and fourteen pregnant women were recruited for this study.Average age, BMI and gestational age of participants were 26.7±6.9 years, 22.3±4.39 kg/m2 and 25.4±6.36 weeks, respectively. Monthly income and age of first sexual experience were 13,307±6105.7 baht and18.2±3.44 years. Nearly half of cases (187/414) were monogamy. One tenth of cases (38/414) had history of uterine curettage. Other demographic characteristics of all participants were represented in Table1.

The prevalence of abnormal Pap smear was 6 percent (25/414). The abnormal Pap smear finding of ASC-US, ASC-H, LSIL and HSIL were 36% (9/25), 12% (3/25), 44% (11/25), 8% (2/25), respectively.The prevalence of positive VIA was 6.7 percent (28/414).

There was no cancer or high grade precancerous lesion reported from colposcopy. Two cases of HSIL from Pap smear showed low grade lesion appearance during colposcopic examination. Postpartum cervical cytology of them were normal result. Comparison between Pap smear, VIA and colposcopy were showed in Table 2. Low grade cervical precancerous lesion was 6.5% (27/414) in the present study. Sensitivity and positive predictive value (PPV) of Pap smear were higher than VIA with statistical significant (70.4 *vs* 59.2% and 76 *vs* 57.1%, respectively). Both VIA and Pap smear had no different significant specificity, accuracy and negative predictive value (NPV).

Low BMI, multiple partner and government officer were associated with abnormal conventional cytology. Positive VIA was related to the higher income, overweight, and daily worker. The correlation of demographic character and colposcopy result was represented in Table3.

Table 4 showed correlation between coitarche and Pap smear screening. Data suggested subjects who started sexual engagement in younger years (12-14 years old) had the higher percentage of positive Pap smear. The percent positive result decrease as the coitarche increased (see Table 4.). Our data showed at the time of the study people who started as sexual lives after 30 years old had 0 percent positive Pap smear.

Table 5 showed about the years of sexual activity engagement. It reported that patients who were sexually active for more than 25 years had a higher risk of positive Pap smear (25% among same age group peer).

Discussion

The prevalence of abnormal conventional Pap smear among pregnant women in this study was 6 percent. The previous literature in Thailand reported the prevalence of abnormal cervical cytology in pregnancy varied from 0.4 to 7 percent (Ingprasarn et al., 2014; Ngaojaruwong et al., 2008; Sueblinvong et al., 2005; Khaengkhor et al., 2011). Our current result falls into the previously published prevalence.

Selected works in pregnant women from some US localities, China and India showed the prevalence of abnormal Pap smear at 8%, 12.5% and 18%, respectively

(Hong et al., 2014; khanuja et al., 2014; Loomis et al., 2009). Reports from Turkey and Brazil had lower prevalence than our current at 0.9% and 1.9%, respectively (Xavier-Júnior et al., 2014; Dinc et al., 2012). The different of abnormal cervical cytology in pregnancy varied with incidence of cervical cancer. People of different countries have different age of coitarche and sexual habits. We cannot compare the prevalent rate of abnormal Pap smear across different countries without more demographic data.

The prevalence of positive VIA in this study was 6.7% compare to 8.5% from India (Priyadhashini et al., 2013). Both studies reported similar percentage.

Pregnancy condition is the cause of cervical change extension or eversion of proliferative endocervical tissue. Cervical glands become hypertrophic and hyperplasia, correlated with increased gestational age (Cunningham et al., 2014). Pap smear samples in pregnant women can be more easily obtained than that of non-pregnant women because the transitional zone is more easily obvious. In nulliparous subjects, the transitional zone is more difficult to see. There may be some cancerous tissue but not easily seen or accessed during the Pap smear procedure. VIA interpretation requires naked eye observation at transitional zone. Cervical eversion should be extremely expanded. As a result, if the transitional zone of the cervix cannot be seen in its entirely for complete evaluation period, this result in the possibility of more false negative case in VIA of pregnant women compared to non-pregnant women.

In this study, sensitivity and PPV of VIA were less than that of conventional Pap smear (59.26% *vs* 70.37% and 57.14% *vs* 76%, respectively). Both methods used in this study were comparable in their specificity, accuracy and NPV. VIA can be applied for cervical screening in pregnant women. Positive results would be valid but bear in mind that false negative are common. However, Pap smear is more highly recommended to be a method of choice for cervical screening in pregnant women.

The conventional cervical cytology had significant characteristic; multiple partners, government officer and low BMI.

In participants with low BMI may be related to low nutrition. If pregnant women were in low nutritional status, they had low antioxidants. Antioxidant from fruit and vegetables, such as beta-carotene, lycopene, and vitamins A, C, and E (alpha-tocopherol) can interact with free radicals and prevent cancer (Bouayed et al., 2010; Moore et al., 2004; Diplock et al., 1998). In diet which lacks fruit, vegetable and fiber, Free radicals can damage cell component include DNA, protein and cell membrane (Valko et al., 2007). Nutrition played an important role in pregnant women health. Good nutrient might improve function of the immune system.

Pap smear result is an early detection for cervical cancer. Our study revealed that our population with lower coitarche had the highest percentage of abnormal Pap smear result among their peer at 9.6% (Table4.). The group with young adolescence and early adulthood age (14-19 and 20-24 years) had similar percentage of abnormal Pap smear of 6.2 and 5.4 percent, respectively. The number went down with the higher coitarche age we followed, the lower abnormal Pap smear found (3.3 and 0 percent at 25-29 and 30+ age group). It seemed to follow the common knowledge that the earlier one started to be sexually active the more likely she would develop cervical cancer. Furthermore, higher income and overweight were impact to VIA. That was different from characteristic that significant in cervical cytology.

To study our data a bit further, number of sexually-active years was calculated in all subjected by subtracting their age with their coitarche. Table5 showed similar percentage of abnormal Pap smear result between 0-4, 5-9, 10-14, 15-19 and 20-24 years at 5.98, 4.6, 6.67, 5.12 and 6.67 percent, respectively. However, the data for more than 25 years shot up to 25 percent. It comfirmed the long known fact that HPV virus had a long incubating period. This data suggests that older women who had been sexually active should have Pap smear screening in their 50+ (sexually active for more than 25 years) so if there is a cervical cancer development it could be detected at its earliest stage.

In Conclusion, prevalence of abnormal Pap smear and VIA in pregnant women was 6 and 6.7 percent, respectively. Factors associated with the abnormal Pap smear was coitarche, years of sexual activity, low BMI, multiple partner and government officer.

In pregnancy, VIA can be applied for cervical screening in pregnant women for low resource country. Positive VIA was found more than abnormal Pap smear. However, Accuracy, sensitivity and specificity of Pap smear were more than that of VIA.

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