Prevalence of High-Grade Cervical Intraepithelial Neoplasia (CIN) in the Patients with Atypical Squamous Cells of Undetermined Significance (ASC-US) Pap Smears: Hospital Based, Dynamic Population Area

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Objective: *To determine the prevalence of cervical intraepithelial neoplasia (CIN) 2-3 (high-grade CIN) among women with Atypical Squamous Cells of Undetermined Significance (ASC-US) Pap smear.*
Material and Method: *A retrospective medical record review of 220 women with ASC-US cervical Pap smear, including age, menstruation status, parity, placed of residence, occupation, main complaint, and definite histopathological result between July 2007 and January 2010 was done.*
Results: *The prevalence of high-grade CIN 2 and CIN 3 in Thammasat University Hospital were 8.6% and 3.2% respectively. No cancer was found in the present study. There was no statistically significant difference in the prevalence of high-grade CIN between the patients who were 50 years old or more and those who were younger.*
Conclusion: *Prevalence of high-grade CIN in women with ASC-US was 11.8%. Immediate colposcopy is recommended in women with ASC-US.*

Keywords: *Pap smear, ASC-US, High grade CIN*

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Cervical cancer is the most common gynecologic cancer in Thailand found in 24.7 in 100,000 women, with an increasing trend of morbidity and mortality[1]. A papanicolaou (Pap) smear is a test for early detection and treatment of premalignant cervical cancer. In 2001, Bethesda system "Atypical squamous cell" ASC were classified into two categories, namely ASC-US, Atypical squamous cells of undetermined significance and ASC-H, Atypical squamous cells cannot exclude high-grade squamous intraepithelial lesions[2].

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Prevalence of ASC-US should be noted. However, the data collected was subject to individual personal experience of each cyto-screener and cytopathologist involved in the data collection[3]. Thus, diagnosis was difficult to confirm. The diagnosis of histopathology with ASC-US may vary from normal histology, cervicitis, cervical intraepithelial neoplasia (CIN) 1, CIN2, CIN3 and invasive cancer. However, the rate reports of high-grade CIN (CIN 2/3) worldwide vary from 4 to 18.5%[4-11].

Management options of ASC-US cases have been either to follow-up under closed surveillance, HPV (human papillomavirus) testing, or immediate colposcopy[12]. In Thammasat University Hospital, Pathumthani, Thailand HPV testing is not available at present. The physician may choose to follow-up ASC-US cases under closed surveillance or prepare an

immediate colposcopy based on his personal experience and the wishes of the patient.

The present study looked into the prevalence of CIN2/3 diagnosis in women with ASC-US Pap smear to suggest criteria for systemic management option for health care facilities in a dynamic population area.

Material and Method

This retrospective research proposal was reviewed and approved by the Faculty of Medicine, Thammasat University Ethical Committee on Clinical Research in 2008. Case of patients with ASC-US by either conventional or liquid-based cervical cytology at Department of Obstetrics and Gynecology, Thammasat University Hospital, Pathumthani, Thailand between July 2007 and January 2010 were reviewed. Sample size of 220 cases was calculated from using prevalence (17%) of ASC-US cytology in previous studies[4] with alpha of 0.05 and an acceptable error of 10%. Patients with ASC-US that underwent colposcopic examination and had histopathological reports were reviewed. Exclusion criteria were immuno-compromised women, anti- HIV positive, women with history of chemotherapy treatment, and women with prior CIN cytology.

Process of study

Pap smear was screened by cyto-screener. The unusual slides were picked out to be presented. The diagnosis was done by the cytopathologist. This diagnosis was then confirmed and counter-signed by the pathologist in charge. All subjects with ASC-US were sent to gynecologic oncologists for colposcopic examination. Tissue from colposcopic-directed-biopsy was obtained from the most suspicious lesions. Endocervical curettage was carried out when colposcopic examination provided unsatisfactory results. Normal cases were the ones with satisfactory colposcopy and no suspicious lesions including non-CIN histopathological result.

Demographic data was collected from the outpatient chart regarding age, parity, menstruation status, place of residence, main complaint for requesting Pap smear, and definite cervical histopathology.

Statistical analysis

The data was analyzed using the program SPSS version 17.0. Descriptive statistics were used for demographic data and summarized as frequencies, percentages, and mean with standard deviation. Difference between variables were evaluated with Chi-square test and Fisher's exact test, significance only if the p-value ≤ 0.05.

Results

The medical records reviewed were between July 2007 and January 2010. Two hundred fifty six women were diagnosed with ASC-US. Thirty-six women were excluded per the above-mentioned criteria, resulting in inclusion of 220 cases. Socio-demographic characteristics and reproductive data for 220 ASC-US subjects were presented in Table 1.

Women who came for Pap smears in this investigation were between 20 to 70 years old. Seventy-five percent were between 30-50 years old. The mean age of the women was 38.92. Most of them had at least one child and were pre-menopause. More than half of the subjects lived in Pathumthani, which is the

Table 1. Socio-demographic characteristics and reproductive data for 220 ASCUS subjects at Thammasat University Hospital, Pathumthani, Thailand

Characteristics	n = 220	%
Age (years):		
20-29	28	12.7
30-39	91	41.4
40-49	72	32.7
50-59	26	11.8
60-70	3	1.4
Parity:		
0	19	8.6
≥ 1	201	96.4
Menopausal status:		
Pre menopause	197	89.5
Post menopause	23	10.5
Place of residence:		
Pathumthani	151	68.6
Bangkok	10	4.5
Ayudhaya	9	4.1
Nontaburi	8	3.6
Other	42	20.1
Occupation:		
Office worker and daily wage earners	99	45.0
Unemployed	50	22.7
Proprietary business owners	29	17.2
Government employees	16	7.3
Other	26	11.8
Chief complaint:		
Check up	209	95.0
Post partum	8	3.6
Abnormal leukorrhea	2	0.9
Vaginal bleeding	1	0.5

province where the hospital was located. Twelve percent lived within two hours driving range. The largest occupation group (45%) was office employees and daily wage earners. Ninety five percent (209/220) came in for Pap smear check up.

Cervical histopathologic results with ASC-US cytology in our study are shown in Table 2. Fifty-six, 32, and 12% of colposcopic examination was negative for intraepithelial lesion and malignancy (NILM), CIN 1, and high-grade CIN (CIN 2/3) respectively (Table 2). No case of invasive cancer was found among our subjects.

The present study also wanted to find out whether any socio-demographic/reproductive characteristics had any correlation with the histopathology of CIN2/3 in our ASC-US subjects. Results are shown in Table 3.

Age related prevalence of cervical histopathology in 220 ASCUS subjects was then investigated. Results are shown in Fig. 1. It is notable to find both NILM/CIN1 and CIN 2/3 cases in all age groups up to 49 years of age. In 50-59 years old group there were 14 cases of NIML/CIN 1 but no CIN 2/3, while 60-70 years old group had two cases of CIN 2 and one case of CIN 3 but no case of NILM/CIN 1.

Table 2. Cervical histopathologic results for 220 ASCUS subjects at Thammasat University Hospital

Histopathology	n	%
NILM	124	56.3
Low-grade CIN (CIN 1)	70	31.8
High-grade CIN		
CIN 2	19	8.6
CIN 3	7	3.2

NILM = negative for intraepithelial lesion and malignancy

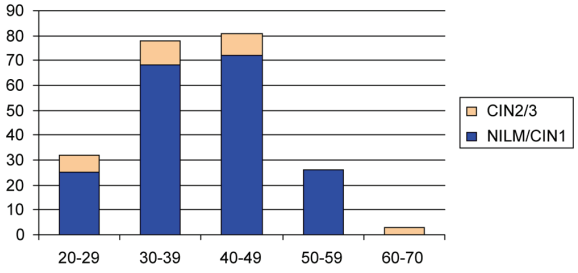

Fig. 1 Low/high grade CIN in 220 ASC-US subjects categorized by age characteristic, Thammasat University Hospital 2007-2010

Table 3. Prevalence of low/high grade CIN in 220 ASC-US subjects categorized by socio-demographic and reproductive characteristic, Thammasat University Hospital 2007-2010

Characteristics	Histopathology n (%)		p-value (Chi-square)
	NILM/CIN 1 (n = 194)	CIN 2/3 (n = 26)	
Age			
< 50 yr	168 (87.96)	23 (12.04)	1[(A)]
≥ 50 yr	26 (89.66)	3 (10.34)	
Parity			
0	15 (78.95)	4 (21.05)	0.253[(A)]
≥ 1	179 (89.05)	22 (10.95)	
Menopausal status			
Pre menopause	174 (88.32)	23 (11.68)	0.741[(A)]
Post menopause	20 (89.46)	3 (13.04)	
Chief complaint			
Check up	184 (88.46)	24 (11.54)	0.638[(A)]
Others	10 (83.33)	2 (16.67)	
Occupation			
Office worker and daily wage earners/unemployed/others	151 (88.30)	20 (11.60)	0.660[(B)]
Proprietary business owners/government employees	45 (91.84)	4 (8.16)	

A = Fisher's exact test
B = Yate's correction for Chi-square

Table 4. Prevalence of ASC-US cytology from previous studies

Authors	Country	n	Histopathology (%)	
			CIN2/3	Cancer
Lachman et al 1998[4]	USA	560	16.8	0
Lousuebsakul et al 2000[5]	USA	421	4	1
Massad et al 2001[6]	USA	399	17	1
Chichareon et al 2002[7]	Thailand	83	16.5	0
ALTS Group 2003[8]	USA	849	12.5	0
Limpvanuspong et al 2008[9]	Thailand	287	9.1	1.2
Gupta et al 2010[10]	India	153	9.2	5.3
Suntornlimsiri 2010[11]	Thailand	254	18.5	7.9
Panyanupap 2010	Thailand	220	11.8	0

Discussion

The ASC-US defined by 2001 Bethesda system gives an unclear cytological report between normal and precancerous status. Pap smear of Thammasat University Hospital reports 2.7% ASC-US. The ASC-US diagnostic rate from the present study follows the findings worldwide.

The present study excluded 18 cases (7.6%) with ASC-US Pap smear that were monitored every 4 to 6 months without colposcopic exam. The present study found prevalence of high-grade CIN with ASC-US cytology at 11.8%. This figure is in the range reported in previous studies, which found the high-grade CIN ranged from 4 to 18.5%[4-11], details shown in Table 4.

In Limpvanuspong et al 2008 study of Bangkok subjects, found a prevalence of high-grade CIN and invasive cancer at 9.1% and 1.2%[9] compared to 11.8% and 0% in the present study. Their subjects were mostly city dwellers. The population is not similar to our study. Therefore, prevalence of high grade CIN may not to be similar too. Suntornlimpsiri et al studied a high incidence location in Chiang Mai. They found the prevalence of high-grade CIN and invasive cancer at18.5% and 7.9%, respectively[11]. However, the Chiang Mai location contained people who were known to participate in sexual business. Since the population in Chiang Mai and Pathumthani had distinct characteristics, the differences seen between this report and Chiang Mai are explainable.

In the present study, there was no significant test for the difference in the prevalence of high grade CIN between who were 50 years old or more and those who were younger ($p = 0.792$). The result is different from US data from Flynn et al 2001[13]. In the US, where health care is accessible to most people, it is convenient to follow-up on a patient. Thammasat University Hospital is located in an area with a dynamic migrant population. The present study also found three women with ASC-US cytology who were more than 60 years old. All of them were high-grade CIN (2 cases with CIN 2 and one with CIN3). Therefore, immediate colposcopy was recommended to 60+ years old ASC-US cytology patient to prevent disease progression if the follow-up fail.

Conclusion

Prevalence of high-grade CIN in women with ASC-US cytology in Thammasat University Hospital is 11.8%. In migrant population areas, immediate colposcopy is recommended in women with ASC-US.

Potential conflicts of interest

None.

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ความชุกของรอยโรคระยะก่อนเป็นมะเร็งปากมดลูกชนิดความเสี่ยงสูงในสตรีที่มีผลการตรวจคัดกรองมะเร็งปากมดลูกชนิด ASC-US ในประชากรที่มีการโยกย้ายถิ่นฐานบ่อย

อนุสรณ์ ปัญญานุภาพ, ยุทธเดช ทวีกุล, เย็นฤดี ภูมิถาวร, กริชา ไม้เรียง, คมสันติ์ สุวรรณฤกษ์, จรรยา ภัทรอาชาชัย, กรณ์กาญจน์ ภมรประวัติ

วัตถุประสงค์: *เพื่อศึกษาความชุกของการเกิดภาวะก่อนเป็นมะเร็งปากมดลูกชนิดความเสี่ยงสูงในผู้ป่วยที่มีผลการตรวจคัดกรองมะเร็งปากมดลูกชนิด ASC-US ในประชากรที่มีการโยกย้ายถิ่นฐานบ่อย*

วัสดุและวิธีการ: *เก็บข้อมูลโดยย้อนหลังจากเวชระเบียนของสตรีที่มีผลการตรวจคัดกรองมะเร็งปากมดลูกชนิด ASC-US ที่ได้รับการตรวจวินิจฉัยเพิ่มเติมด้วยการส่องกล้องขยายปากมดลูกร่วมกับการตัดชิ้นเนื้อตรวจทางพยาธิวิทยา จำนวน 220 คน ระหว่างเดือนกรกฎาคม พ.ศ. 2550 ถึง มกราคม พ.ศ. 2553*

ผลการศึกษา: *ในสตรีที่มีผลการตรวจคัดกรองมะเร็งปากมดลูกชนิด ASC-US พบความชุกของภาวะก่อนเป็นมะเร็งปากมดลูกชนิด CIN 2 และ CIN 3 คิดเป็นร้อยละ 8.6 และ 3.2 ตามลำดับ ไม่พบมะเร็งปากมดลูกในการศึกษานี้ อีกทั้งไม่พบว่ามีความแตกต่างอย่างมีนัยสำคัญของภาวะก่อนเป็นมะเร็งปากมดลูกชนิด CIN 2/3 ระหว่างสตรีที่มีอายุมากกว่า 50 ปี กับสตรีที่อายุน้อยกว่า 50 ปี*

สรุป: *ร้อยละของความชุกของภาวะก่อนเป็นมะเร็งปากมดลูกชนิดความเสี่ยงสูงในผู้ป่วย ที่มีผลการตรวจคัดกรองมะเร็งปากมดลูกชนิด ASC-US เท่ากับ 11.8 การตรวจด้วยกล้องคอลโปเพิ่มเติมทันทีร่วมกับการตัดชิ้นเนื้ออาจจะมีประโยชน์ในผู้ป่วยเหล่านี้*