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Prevalence of Abnormal Cervical Cytology based on the Bethesda System, at Phetchabun Hospital

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Abstract The objective of this study was to define the prevalence of abnormal cervical cytology based on the Bethesda System. All cytologic smears from the 1st April 2003 to the 31st March 2005 were reviewed and classified with the context of the Bethesda Classification System. Medical records of all patients with diagnoses of atypical squamous cell of undetermined significance (ASCUS), atypical glandular cell of undetermined significance (AGUS), low-grade squamous intraepithelial lesion (LSIL), high-grade squamous intraepithelial lesion (HSIL), squamous cell carcinoma (SCCA) or adenocarcinoma were reviewed for previous medical history, diagnostic study, histologic diagnosis and prior gynecologic disease. The most significant histologic diagnosis from all biopsy specimens submitted was compared with the abnormal cervical smear diagnostic categories in preinvasive and early stage cervical cancer. The prevalence of abnormal cervical cytology in 3,555 smears was 6.92 percent, which can be classified into ASCUS 52.03 percent (128 smears), HSIL 23.58 percent (58 smears), LSIL 11.79 percent (29 smears), squamous cell carcinoma 10.57 percent (26 smears) AGUS 1.63 percent (4 smears), and adenocarcinoma 0.40 percent (1 smear). Medical records of 223 new cases with abnormal cervical cytology were reviewed whereby 90 (40.36%) dropped out in the follow up and 39 (17.49%) underwent repeated pap smears. Colposcopes with or without biopsy were performed in 94 cases (42.15%). Cytologic diagnosis of histologically diagnosed as HSIL (CIN II or CIN III) and cancer of cervix was HSIL 82.61 percent ASCUS 13.04 percent and LSIL 4.35 percent, respectively. In conclusion the prevalence of abnormal cervical cytology in this study was slightly high relative to other studies. It is recommended that all women with HSIL cytology should undergo intensive evaluation including colposcopy with or without endocervical currettage. Failure to participate through the follow up period in Phetchabun Hospital was relatively high, therefore, the existing patient call and recall system should be re-evaluated.

Key words: **abnormal cervical cytology, Bethesda System**

Introduction

Cervical cytology screening has helped reduce cervical cancer rates dramatically since its implementation in the 1950s.[1,2] Pap test reporting classifications have evolved and been refined with the current standard, the Bethesda System (2001).

The incidence of abnormal cervical cytology under the Bethesda System was reported to be 5-6 percent.[3-6] ASCUS (atypical squamous cell of

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undetermined significance), accounting for 3 percent, was the most frequent cytologic finding. Generally, the incidence ratio of ASCUS to SIL (squamous intraepithelial lesion) was not greater than 2-3 times.[4,5] Evaluation of patients with abnormal cervical cytology usually consists of colposcopy with direct biopsy and or conization, followed by treatment based on the histologic diagnosis. There is an agreement that patients with cytology showing HSIL (high-grade squamous intraepithelial lesion) should undergo immediate colposcopic evaluation because they have a significant incidence of high-grade dysplasia.[7]

Evaluation of patients diagnosed as minimally abnormality as ASCUS or LSIL (low-grade squamous intraepithelial lesion) remains controversial.[8] Because the reported incidence of high-grade dysplasia in these patients varies.[9-11] Options include immediate colposcopy and repeated cervical smear every 3-6 months at least for a year, if the results are abnormal, the patients should undergo colposcopy. Immediate colposcopy increases colposcopist workload and cost whereas repeated cervical smear increases risk of no-show during follow up and high grade precursor or early invasive cancer lesion can not be detected early.

The goal was to study the management and estimate the prevalence of abnormal cervical cytology under the Bethesda System and to characterize the relative contributions of the different abnormal cervical cytology to the consequent histologic diagnoses in preinvasive and early stage cervical cancer.

Methodology

The Bethesda System was implemented in the Cytology laboratory Phetchabun Hospital since 2003. A total of 3,555 cervico-vaginal cytologic specimens obtained within a 2-year period, between the 1st April 2003 and the 31st March 2005, were reviewed. All cytologic smears were collected by the Ayre spatula and slides evaluated at the Patho-cytology Unit of Phetchabun Hospital. Routinely, the smears were screened by cyto-technicians, and when abnormal cells were identified, the smears were further evaluated by the cyto-pathologist. The laboratory adhere to quality control by reviewing 10 percent of the normal smear by cyto-pathologist.

Two hundred and forty six medical records of patients of whom a diagnosis of abnormal cytologic finding (except for inflammatory atypia) were reviewed and the prevalence was calculated. The patients with a history of hysterectomy, a known history of genital tract cancer and visible cervical lesion were excluded. The medical records of 223 patients who met the criteria were reviewed for demographic data, medical history, diagnostic study and histologic diagnoses.

Ninety four patients underwent colposcope in this study. The patients were biopsied in case that the following abnormal findings: leukoplakia, acetowhite lesion, punctuation, mosaic and abnormal vessels were detected. But patients with adequate colposcopy and no significant lesion were considered to be disease-free and were not biopsied. In this group the patients were reminded to undergo repeated cervical smear every 3-6 month for, at least a year. If colposcopic evaluation was unsatisfactory, adenocarcinoma 0.40 percent (1 smears) as endocervical curettage was undertaken. Patients then received further investigation or surgical procedures by cold-knife conization and/or hysterectomy, when histologic reports suggested the possibility of preinvasive or early invasive cervical cancer. Surgical specimens were evaluated by a pathologist at Cyto-pathology Unit of Chiangmai Medical University. The most

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severe histologic diagnosis from all surgical specimens (biopsy, conization, or hysterectomy specimens) was compared with category of the cervical smear obtained from each patients. Some patients who found inconvenient colposcope underwent repeated cervical smear every 3-6 month for, at least a year. Data study was analyzed by descriptive statistical analysis.

Result

The prevalence of abnormal cervical cytology classified by the Bethesda System was 6.92 percent (246 in 3,555 smears) which can be separated into ASCUS 52.03 percent (128 smears), HSIL 23.58 percent (58 smears) and LSIL 11.79 percent (29 smears) (Table 1).

After patients with a history of hysterectomy, a known history of genital tract cancer and a visible cervical lesion were excluded, 223 of 3,555 cases were evaluated for cytologic results. The mean age was 45 years (range 17-84 years). Onehundred and fifty eight patients (70.85%) were premenopause as shown in Table 2. The frequencies of ASCUS, HSIL, squamous cell carcinoma and adenocarcinoma were 54.26 percent (121), 23.77 percent (53), 10.76 percent (24) respectively (Table 3)

Of the 223 patients, 90(40.36%) failed to participate through out the follow up, including ASCUS 71.11 percent (64), HSIL 13.33 percent (12), LSIL 7.78 percent (7) (Table4).

When the lost follow up rate in each group was considered, ASCUS showed the highest rate for 52.89 percent (64 in 121). It should be noted that the lost follow up rate was also high in other groups, AGUS 1 in 3, LSIL 33.33 percent (7 in 21), SCCA 25 percent (6 in 24) and HSIL 22.64 percent (12 in 53), even though our hospital has a notifying system by mail.

Thirty-nine of 223 patients had repeated cervical smears of which the results were all negative.

Colposcope with or without biopsies, cervi-

Table 1 Prevalence and distribution of abnormal cervical cytology, Phetchabun Hospital

Cytologic diagnosis	Number (%)	Prevalence
ASCUS	128 (52.03)	3.6
AGUS	4 (1.63)	0.11
LSIL	29 (11.79)	0.82
HSIL	58 (23.58)	1.63
SCCA	26 (10.57)	0.73
Adeno CA	1 (0.40)	0.03
Total	**246 (100)**	**6.92**

Table 2 Demographic data of the 223 subjects

Variable		Percent
Age(years) Mean ± SD	45±12	
Range	17-84	
Parity Mean ± SD	2±2	
Oral contraception (persons)	32	14.35
History of STD*(HIV) (persons)	12	5.38
Premenopause (persons)	158	70.85

STD = sexually transmitted disease

Table 3 Distribution of abnormal cervical cytology in preinvasive and early stage cervical cancer

Cytologic diagnosis	Number (%)
ASCUS	121 (54.26)
HSIL	53 (23.77)
SCCA	24 (10.76)
LSIL	21 (9.41)
AGUS	3 (1.35)
Adeno CA	1 (0.45)
Total	**223 (100.00)**

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cal conization and hysterectomy were performed in 94, 33 and 21 patients, respectively. Six patients were referred to Cancer Institute because of cervical biopsied specimen were beyond carcinoma in situ. One hundred twenty one patients in ASCUS group, after excluding those lost in the follow up, thirty-five patients (28.93%) underwent colposcope, nine patients (7.44%) conization, four patients (3.31%) hysterectomy, one patient (0.83%) was referred and twenty two patients (18.18%) repeated cervical smear. Twenty one patients in LSIL group, colposcope,cervical conization, hysterectomy and repeat cervical smear were performed in 8(38.10%), 2(9.52%), 1(4.76%) and 6(28.57%) patients respectively.

In the AGUS group, there was only three patients, one patient underwent colposcope and one repeated cervical smear. In HSIL group colposcope, cervical conization, hysterectomy, refer and repeat cervical smear were performed in 31(58.49%), 11(20.75%), 8(15.09%), 3(5.66%) and 10 (18.87%) patients respectively (Table 4-5).

Comparison of cytologic finding and final histologic diagnosis among patients who underwent colposcopic examination with or without biopsy (94 cases) was shown in Table 6.

Table 4 Management of patients with abnormal cervical smear at Phetchabun Hospital in preinvasive and early stage cervical cancer

Cytologic diagnosis	Colposcope	Loss in follow up	Repeated cervical smear	Total
ASCUS	35	64	22	121
HSIL	31	12	10	53
SCCA	18	6	-	24
LSIL	8	7	6	21
AGUS	1	1	1	3
Adeno CA	1	-	-	1
Total	**94**	**90**	**39**	**223**

Table 5 Management after colposcopic examination in patients with abnormal cervical smear

Cytologic diagnosis	Colposcope	Conization*	TAH**	Refer***
ASCUS	35	9	4	1
AGUS	1	-	-	-
LSIL	8	2	1	-
HSIL	31	11	8	3
SCCA	18	10	8	2
Adeno CA	1	1	-	-
Total	94	**33**	**21**	**6**

Conization = cold-knife conization*
*TAH** = total abdominal hysterectomy*
*Refer*** = refer when cervical biopsied specimens were beyond carcinoma in situ*

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Table 6 Distribution of cytologic findings and final histologic diagnosis among patients undergoing colposcopic examination with or without biopsy

Cytology	Histologic Diagnosis (%)				
	Negative & cervicitis	LSIL*	HSIL**	Cancer of the cervix	Detection rate*** percent
ASCUS	32(91.4)	-	3(8.6)	-	8.6(3/35)
AGUS	1	-	-	-	-
LSIL	5	2	1	-	(3/8)
HSIL	9(29)	3(9.7)	11(35.5)	8(25.8)	71(22/31)
SCCA	1(5.6)	-	7(38.9)	10(55.6)	94.4(17/18)
Adeno CA	-	-	-	1	(1/1)
Total	48	5	22	19	

LSIL = CINI = cervical intraepithelial neoplasia I,*
*HSIL** = CINII or CINIII = cervical intraepithelial neoplasia 2 or 3,*
*Detection rate*** = percent of patients who histologic diagnosed as low-grade squamous intraepithelial lesion (CINI), high-grade squamous intraepithelial lesion (CINII or CINIII), and cancer of the cervix*

In the ASCUS group (n=35), three patients (8.6%) were finally diagnosed as HSIL (CINII or CINIII).

In the LSIL group (n=8), two patients (25%) were histologically diagnosed as LSIL and one patient (12.5%) as HSIL. Of 31 patients with HSIL cytology, three (9.7%) had LSIL lesion, eleven (35.5%) had HSIL lesion, which were CINII 4 cases (12.9%) and CINIII 7 cases (22.6%); eight (25.8%) had cancer of cervix which six patients (19.4%) were microinvasive carcinoma and two patients (6.4%) were invasive squamous cell carcinoma.

In the AGUS group (n=1), the tissue diagnosis was negative.

The detection rate of ASCUS, LSIL, HSIL cervical cytology report were 8.6 percent, 3 in 8 and 71 percent respectively. The most common cytologic diagnosis of histologic HSIL (CINII and CINIII) and cancer of cervix was HSIL 82.61 percent (19 in 23) followed by ASCUS 13.04 percent (3 in 23) and LSIL 4.35 percent (1 in 23).

Discussion

The prevalence of abnormal cervical cytology based on the Bethesda System in Phetchabun Hospital was slightly high (6.9%) when compared to 5-6 percent reported in other studies. This may result from the different sexual behaviors and cultures among countries. ASCUS identified as the most frequent abnormal cervical cytology in the study as well as in other reports.[4] The ratio of ASCUS to SIL did not exceed 2-3 times and the prevalence of ASCUS was not greater than 5 percent of all cervical smears,[4,5] which considered acceptable rate for most screening cytology laboratories.

The detection rate were found in ASCUS and LSIL cytology group 8.6 percent and 3 in 8 respectively, which were lower than 45 percent of biopsy confirmed SIL in 398 patients presenting with cytologic ASCUS or LSIL reported by Wright et al.[10] In that connection, it included significant proportion of patients (34%) who had been treated previously for histologic SIL. It should be

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observed that such patients were excluded in this study. Similarly, Cox et al[11] reported high prevalence of histologic SIL in 217 patients with minimally abnormal cervical smears, under the context of only young adult patients were included while this study included patients of all age-group. Other studies[6,12,13] have indicated high rates of histologic SIL, but these rates were observed when colposcopy was performed only after repeated smears were abnormal. Although the detection rate in ASCUS group was lower than LSIL cytology group, but the histologic lesion was not quite different.

The prevalence of AGUS was 0.11 percent and was not found significant pathology because the number of patients was very low[4]. The other studies have demonstrated that 17-52 percent of women with an AGUS cytologic diagnosis will prove to have cervical or uterus lesion.[14,15] Goff et al[4] reported the serious abnormalities of the cervix or the uterus upto 50 percent, which could be subdivided into SIL 39.7 percent, adenocarcinoma in situ 7.9 percent, adenocarcinoma of cervix 32 percent and endometrial hyperplasia 3.2 percent.

The detection rate in HSIL cytology group was 71 percent, which corresponds well with the study reported by Kinney et al,[5] describing the incidence of 70.9 percent of biopsy confirmed SIL in patients presenting with HSIL cytology. The detection rate in HSIL cytology group was relatively higher than those in ASCUS and LSIL indicating the importance of a careful and complete evaluation to these patients, such as immediate colposcope with biopsy.

The loss during the follow up was considered very high in this study (40.36%), therefore, further investigation is reqiured. The existing patients call and recall system, should be re-evaluated.

The limitation to our study should be acknowledged as all retrospective studies procedures are not standardized and patients were managed by various physicians. The final histologic diagnosed in every abnormal cervical smear included in the sample, could not be indentifyed because all abnormal smears were not followed directly by colposcopy and histology. It is anticipated that this study provides the management giudeline for gynecologist at Phetchabun Hospital to further investigate after cytologic diagnosis and provide precolposcope counselling.

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บทคัดย่อ **ความชุกของเซลล์ปากมดลูกผิดปรกติตามระบบ Bethesda ในโรงพยาบาลเพชรบูรณ์**

สุรัตน์ โรจน์แสงเรือง

แผนกสูติ-นรีเวชกรรม โรงพยาบาลเพชรบูรณ์

วารสารวิชาการสาธารณสุข ๒๕๔๙; ๑๕:๖๗-๗๔.

วัตถุประสงค์ของการศึกษานี้ เพื่อหาความชุกของเซลล์ปากมดลูกที่ผิดปรกติตามระบบ Bethesda โดยทบทวนข้อมูลเซลล์ปากมดลูกจากผู้ป่วยที่มาตรวจระหว่าง ๑ เมษายน ๒๕๔๖ จนถึง ๓๑ มีนาคม ๒๕๔๙ ที่ได้วินิจฉัยว่าเป็น atypical squamous cell of undetermined significance (ASCUS), atypical glandular cell of undetermined significance (AGUS), low-grade squamous intraepithelial lesion (LSIL), high-grade squamous intraepithelial lesion (HSIL), squamous cell carcinoma (SCCA) and adenocarcinoma โดยดูประวัติข้อมูลพื้นฐาน วิธีการตรวจวินิจฉัยขั้นต่อไป ผลการตรวจทางพยาธิวิทยาจากชิ้นเนื้อ และโรคทางนรีเวชที่เคยเป็น โดยดูความสัมพันธ์ระหว่างผลการวินิจฉัยทางพยาธิวิทยาจากชิ้นเนื้อกับผลการตรวจเซลล์ปากมดลูก ในกลุ่มเซลล์ก่อนเป็นมะเร็งและเซลล์มะเร็งระยะต้น พบว่าความชุกของเซลล์ปากมดลูกที่ผิดปรกติ เท่ากับร้อยละ ๖.๔๒ จากการตรวจสเมียร์ ทั้งหมด ๓,๕๕๕ แผ่น ซึ่งแบ่งเป็น ASCUS ร้อยละ ๕๒.๐๓ (๑๒๘ แผ่น), HSIL ร้อยละ ๒๓.๕๘ (๕๘ แผ่น), LSIL ร้อยละ ๑๑.๗๕ (๒๕ แผ่น), squamous cell carcinoma ร้อยละ ๑๐.๕๗ (๒๖ แผ่น) AGUS ร้อยละ ๑.๖๓ (๔ แผ่น) และ adenocarcinoma ร้อยละ ๐.๔๐ (๑ แผ่น) ได้ทบทวนผู้ป่วยรายใหม่ที่พบเซลล์ปากมดลูกผิดปรกติจำนวน ๒๒๓ ราย เป็นผู้ป่วยที่ไม่ได้มาตรวจติดตาม ๙๐ ราย (๔๐.๓๖%) เป็นกลุ่มที่ได้รับการตรวจเซลล์ปากมดลูกซ้ำ ๓๕ ราย (๑๗.๔๕%) มีผู้ป่วย ๕๔ ราย (๔๒.๑๕%) ได้รับการส่องกล้องตรวจปากมดลูก ผู้ป่วยที่ได้รับการวินิจฉัยขั้นสุดท้ายจากผลชิ้นเนื้อว่าเป็น HSIL และมะเร็งปากมดลูก เมื่อย้อนกลับไปดูผลตรวจเซลล์ปากมดลูกพบว่าเป็น HSIL ร้อยละ ๘๒.๖๑ ASCUS ร้อยละ ๑๓.๐๔ และ LSIL ร้อยละ ๔.๓๕ ตามลำดับ จึงสรุปได้ว่า ความชุกของเซลล์ปากมดลูกที่ผิดปรกติในการศึกษานี้ค่อนข้างสูงเล็กน้อยเมื่อเทียบกับการศึกษาอื่นๆ และในรายผู้ป่วยที่มีความผิดปกติของเซลล์ปาก-มดลูกในระดับ HSIL ควรได้รับการตรวจติดตามสืบค้นต่อไปอย่างใกล้ชิด ไม่ว่าจะเป็นการส่องกล้องตรวจปากมดลูก หรือขูดชิ้นเนื้อจากคอมดลูกก็ตาม นอกจากนี้ผู้ป่วยที่ขาดการตรวจติดตามของโรงพยาบาล มีค่อนข้างมาก ซึ่งอาจจะต้องมีการประเมินและปรับปรุงระบบการติดตามผู้ป่วย

คำสำคัญ: **เซลล์ปากมดลูกที่ผิดปรกติ, ระบบ Bethesda**

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