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Prevalence of Abnormal Cervical Cytology According to The Bethesda System, at King Chulalongkorn Memorial Hospital

Tidaporn Yotwimonwat MD,
Ruangsak Lertkhachonsuk MD,
Surang Triratanachat MD,
Damrong Tresukosol MD,
Somchai Niruthisard MD.

Department of Obstetrics and Gynaecology, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand

ABSTRACT

Objective To define the prevalence of abnormal cervical cytology in The Bethesda System

Study All cytologic smears from October 1999 to June 2001 were reviewed and classified with the context of The Bethesda Classification System. Medical records of all patients with a diagnosis of ASCUS, AGUS, LSIL, HSIL, squamous cell carcinoma and 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.

Result The prevalence of abnormal cervical cytology in 61,701 smears was 0.85%, which can be classified into ASCUS 20.92%(114 smears), AGUS 8.44%(46 smears), LSIL 20.00%(109 smears), HSIL 34.68%(189 smears), squamous cell carcinoma 12.29%(67 smears) and adenocarcinoma 3.67%(20 smears). We reviewed 287patients medical records that were new cases with abnormal cervical cytology. One hundred (34.84%) were lost to follow up, thirty-four (11.85%) were repeated pap smear. Colposcopes with or without biopsy were performed in 153 cases (53.31%). Cytologic diagnosis of histologically diagnosed as HSIL (CIN II or CINIII) and cancer of cervix was HSIL 60.00%, AGUS 15.38%, LSIL 13.85 % and ASCUS 10.77%, respectively.

Conclusion The prevalence of abnormal cervical cytology in our study was low compare to other study. We recommended that all women with HSIL cytology should undergo intensive evaluation including colposcopy with or without endocervical currettage. The lost to follow up rate in King Chulalongkorn Memorial Hospital was relatively high, therefore, the patient call and recall system which is existed should be re-evaluated.

Key words: abnormal cervical cytology, The Bethesda System

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 (1991).

The incidence of abnormal cervical cytology in The Bethesda System was reported to be 5-6%.[3,4,5,6] ASCUS (atypical squamous cell of undetermined significance) was the most frequent cytologic finding at 3% 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 directed biopsy, 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.[9,10,11] Option includes immediate colposcopy and repeat cervical smear every 3-6 months at least 1 year, if the results were abnormal the patients should underwent to colposcopy. Immediate colposcopy increase colposcopist workload and cost whereas repeat cervical smear increase risk of lost to follow up and high grade precursor or early invasive cancer lesion can not be detected early.

Our goal was to estimate the prevalence of abnormal cervical cytology in 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.

Material and Methods

The Bethesda System was implemented in the Cytology laboratory in King Chulalongkorn Memorial Hospital since 1999. A total of 61,701 cervico-vaginal cytologic specimens obtained in a 2-year period between October 1999 and June 2001were reviewed. All cytologic smears were collected by the Ayre plastic spatula and slides evaluated at the Patho-cytology unit of Department of Obstetrics and Gynaecology, King Chulalongkorn Memorial Hospital. Routinely, the smears were screened by cyto-technicians, and when abnormal cells were found, the smears were further evaluated by the Cyto-pathologist. The laboratory performs quality control by reviewing 10% of the normal smear by Cyto-pathologist.

Five hundred and forty five medical records of patients in whom a diagnosis of abnormal cytologic finding (except for inflammatory atypia) were reviewed and the prevalence was calculated. Because the another objective in this research was to studied the management of abnormal cervical cytology and distribution of cytologic finding and final histologic diagnoses in preinvasive and early stage cervical cancer, the patients with a history of hysterectomy, a known history of genital tract cancer and visible cervical lesion were excluded. The medical records of 287 patients who met the criteria were reviewed for demographic data, medical history, diagnostic study and histologic diagnoses.

One hundred and fifty-three patients underwent colposcope in our 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 repeat cervical smear every 3-6 month at least 1 year. If colposcopic evaluation was unsatisfactory, endocervical curettage was undertaken. Patients then received further investigation or surgical procedures by cold-knife conization or LEEP and/or hysterectomy, when histologic reports suggested the possibility of preinvasive or early invasive cervical cancer. Surgical specimens were evaluated by Pathologist at Cyto-pathology unit of King Chulalongkorn Memorial Hospital. The most severe histologic diagnosis from all surgical specimens (biopsy, conization, LEEP or hysterectomy specimens) was compared with category of the cervical smear obtained from each patients. Some patients who were inconvenient to colposcopy were underwent repeat cervical smear every 3-6 month at least 1 year.

Result

From our study, the prevalence of abnormal cervical cytology classified by The Bethesda System was 0.85%(545 in 61,701 smears) which can separated into ASCUS 20.92%(114 smears), AGUS 8.44%(46 smears), LSIL 20.00%(109 smears), HSIL 34.68%(189 smears), squamous cell carcinoma 12.29%(67 smears) and adenocarcinoma 3.67%(20 smears) as shown in Table 1.

After patients with a history of hysterectomy, a known history of genital tract cancer and a visible cervical lesion were excluded, 287 of 61,706 cases were evaluated for cytologic results. The mean age was 44 years (range 15-86 years). Two- hundred sixteen patients (75.3%) were premenopause with the remaining (24.7%) being menopause as shown in Table 2. The frequencies of ASCUS, AGUS, LSIL, HSIL, squamous cell carcinoma and adenocarcinoma were 21.60%(62), 9.41%(27), 21.95%(63), 35.89% (103), 8.36%(24) and 2.79%(8) respectively, as shown in Table 3.

Table 1. Prevalence and distribution of abnormal cervical cytology in King Chulalongkorn Memorial Hospital

Cytologic diagnosis	No.(%)	%Total
ASCUS	114(20.92)	0.18
AGUS	46(8.44)	0.07
LSIL	109(20.00)	0.17
HSIL	189(34.68)	0.30
SCCA	67(12.29)	0.10
Adeno CA	20(3.67)	0.03
Total	545(100)	0.85

ASCUS= atypical squamous cell of undetermined significance;
AGUS= atypical glandular cell of undetermined significance;
LSIL= low-grade squamous intraepithelial lesion;
HSIL= high- grade squamous intraepithelial lesion;
SCCA = squamous cell carcinoma; AdenoCA = adenocarcinoma.

Table 2. Demographic data of 287 studied cases

Variable				%
Age	Mean ± SD	44±13	years	
	Range	15-86	years	
Parity	Mean ± SD	2 ± 2	(0-9)	
Oral	contraception	28	persons	9.76
History of STD* (HIV)		25	persons	8.71
Premenopause		216	persons	75.26

*STD = sexuallly transmitted disease

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

Cytologic diagnosis	No.	%
ASCUS	62	21.60
AGUS	27	9.41
LSIL	64	22.30
HSIL	103	35.89
SCCA	24	8.36
Adeno CA	7	2.44
Total	287	100.00

Of the 287 patients, 100(34.84%) were lost to follow up, which were ASCUS 30%(30), AGUS 7%(7), HSIL 29%(29), LSIL 23%(23), squamous cell carcinoma 8%(8) and adenocarcinoma 3%(3)(Table 4). When the lost follow up rate in each group was considered, ASCUS showed the highest rate for 48.39%(30 in 62). It should be noted that the lost follow up rate was also high in other groups, squamous cell carcinoma 33.33% (8 in 24), adenocarcinoma 37.50%(3 in 8) and HSIL cytology group 28.16%(29 in 103), eventhough our hospital has notifying system by mail.

Thirty-four of 287 patients had repeat cervical smear which all results were negative.

Colposcope with or without biopsies, cervical conization, hysterectomy and radical hysterectomy were performed in 153, 47, 35 and 11 patients, respectively. Sixty-two patients in ASCUS group, after excluding the lost follow up cases, twenty-five patients (40.32%) underwent colposcope, six patients (9.68%) conization, three patients (4.84%) hysterectomy, one patient (1.61%) radical hysterectomy and fourteen patients (22.58%) repeat cervical smear. Sixty-three patients in LSIL group, colposcope, cervical conization, hysterectomy and repeat cervical smear were performed in 27(42.86%), 4(6.35%), 2(3.17%) and 14(22.22%) patients respectively.

In the AGUS group, eighteen (66.67%) patients underwent colposcopy, six (22.22%) patients conization, seven (25.93%) patients hysterectomy, two (7.40%) repeat cervical smear and the remaining (25.93%) were lost to follow up. In HSIL group colposcope, cervical conization, hysterectomy, radical hysterectomy and repeat cervical smear were performed in 63(61.17%), 22(21.36%), 15(14.56%), 5(4.85%), 11(10.68%) patients respectively as shown in Table 4 -5.

Table 4. Management of patients with abnormal cervical smear at King Chulalongkorn Memorial Hospital in preinvasive and early stage cervical cancer

Cytologic diagnosis	Colposcope	Loss follow up	Repeat cervical smear	Total
ASCUS	25	30	7	62
AGUS	18	7	2	27
LSIL	27	23	14	64
HSIL	63	29	11	103
SCCA	16	8	-	24
adeno CA	4	3	-	7
Total	153	100	34	287

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

Cytologic diagnosis	Colposcope	Conization£	TAH*	RHND¶
ASCUS	25	6	3	1
AGUS	18	6	7	-
LSIL	27	4	2	-
HSIL	63	22	15	5
SCCA	16	9	7	2
adeno CA	4	-	1	3
Total	153	47	35	11

£conization = cold-knife conization or LEEP
*TAH = total abdominal hysterectomy
¶ RHND = radical hysterectomy and pelvic node dissection

Comparison of cytologic finding and final histologic diagnosis among patients who performed colposcopic examination with or without biopsy (153 cases) was shown in Table 6.

In the ASCUS group (n=25), four patients (16%) were finally diagnosed as HSIL (CINII or CINIII), two (8%) as microinvasive, one(4%) as invasive squamous cell carcinoma.

In the AGUS group (n=18), seven (38.90%) patients were histologically diagnosed as HSIL, two (10.66%) as microinvasive carcinoma and one (5.33%) as adenocarcinoma of cervix. Of 27 patients with cytologic LSIL, two (7.4%) had LSIL (CIN I) histologic lesion, nine (33.33%) had HSIL lesion, which were CINII 1 case (3.70%) and CINIII 8 cases (29.63%). And of 63 patients with HSIL cytology, five (7.9%) had LSIL (CIN I) lesion, twenty- three (36.5%) had HSIL lesion, which were CINII 3 cases (4.75%) and CINIII 20 cases (31.75%); eight(12.8%) had microinvasive carcinoma, seven(11.29%) had invasive squamous cell carcinoma and one(1.61%) had adenocarcinoma of cervix.

The detection rate of ASCUS, AGUS, LSIL, HSIL cervical cytology report were 28.0%, 55.6%, 40.7% and 71.4% respectively. The most common cytologic diagnosis of histologic HSIL (CINII and CINIII) and cancer of cervix was HSIL 60.00%(39 in 65) followed by AGUS 15.38%(10 in 65), LSIL 13.85%(9 in 65) and ASCUS 10.77%(7 in 65).

Table 6. Distribution of cytologic findings and final histologic diagnoses among patients who underwent colposcopic examination with or without biopsy

	Histologic Diagnosis				
Cytology	**Negative& cervicitis**	**LSIL***	**HSIL****	**Cancer of the cervix**	**Detection rate #**
ASCUS	18(72.0%)	-	4(16%)	3(12.0%)	28.0% (7/25)
AGUS	8(44.4%)	-	7(38.9%)	3(16.7%)	55.6%(10/18)
LSIL	16(59.3%)	2(7.4%)	9(33.3%)	-	40.7%(11/27)
HSIL	18(28.6%)	6(9.5%)	23(36.5%)	16(25.4%)	71.4%(45/63)
SCCA	1(6.2%)	-	7(43.8%)	8(50.0%)	93.8%(15/16)
AdenoCA	-	-	1(25.0%)	3(75.0%)	100.00%(4/4)
	61	8	51	33	73

* LSIL = CINI = cervical intraepithelial neoplasia I,
**HSIL = CINII or CINIII = cervical intraepithelial neoplasia2 or 3
#Detection rate = percent of patients who histologic diagnosed as low-grade squamous intraepithelial lesion (CIN 1), high-grade squamous intraepithelial lesion (CINII and CINIII), and cancer of the cervix

Discussion

From our study, the prevalence of abnormal cervical cytology according to The Bethesda System in King Chulalongkorn Memorial Hospital was very low when compared to 5-6% found in other reports. However, it was very closed to the prevalence (0.71%) at Ramathibodi Hospital between 1993-1997.[12] This may results from the different sexual behavior and culture among countries. HSIL was the most frequent cytologic finding in our study, whereas ASCUS was found at the highest rate in other reports.[4] It is assume that this study was hospital base. As a result, patients in this study were mostly middle aged and they came to the hospital after the present of gynecologic problem. The ratio of ASCUS to SIL did not exceed 2-3 times and the prevalence of ASCUS was not greater than 5% of all cervical smears,[4,5] which were considered acceptable rate for most screening cytology laboratories.

The detection rate were found in ASCUS and LSIL cytology group 28.0% and 40.7% respectively, which were lower than those reported by Wright et al,[10] that study described an overall incidence of 45% of biopsy confirmed SIL in 398 patients presenting with cytologic ASCUS or LSIL , but that study includes a significant proportion of patients (34%) who had been treated previous for histologic SIL. Our study excluded such patients. Cox et al[11] reported similar high prevalence of histologic SIL in 217 patients with minimally abnormal cervical smears, but that study included only young adult patients. Our study included patients of all ages. Other studies[6,13,14] have found 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, more serious lesions were demonstrated, microinvasive 8% (2) and invasive 4%.[1]

The prevalence of AGUS was 0.07% and significant pathology was found in 55.6%, which corresponds with other studies which have demonstrated that 17-52% of women with an AGUS cytologic diagnosis will prove to have cervical or uterus lesion.[15,16] For instance, Goff et al.[16] reported the serious abnormalities of the cervix or the uterus upto 50%, which could be subdivided into SIL 39.7%, AIS (Adenocarcinoma in situ) 7.9%, adenocarcinoma of cervix 32% and endometrial hyperplasia 3.2%. However, our histologic studies were HSIL 38.5%,[7] microinvasive 11.16%[2] and adenocarcinoma of cervix 5.58%[1] without any uterine abnormality after complete investigation.

The detection rate in HSIL cytology group was 71.4%, which corresponds with the study reported by Kinney et al,[5] that study described incidence of 70.9% of biopsy confirmed SIL in patients presenting with HSIL cytology.

The prevalence of abnormal cervical smears in King Chulalongkorn Memorial Hospital was low which is interesting for further study. The detection rate in HSIL cytology group was relatively higher than in ASCUS and LSIL indicating the importance of a careful and complete evaluation to these patients, such as immediate colposcope with biopsy.

The lost follow up rate was considered very high in this study (34.8%), therefore, further studies should investigate this point. The patients call and recall system, which exists, should be re-evaluated.

The limitation to our study should be acknowledged like all retrospective studies, procedure are not standardized and patients were managed by various physicians. We could not identify final histologic diagnosed in every abnormal cervical smear present in the study population because all an abnormal smears were not followed directly by colposcopy and histology. It is anticipated that this study provides the line of management for gynecologist at King Chulalongkorn Memorial Hospital to decide further investigation after cytologic diagnosis and use for precolposcope counseling.

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