ประสิทธิภาพของการตรวจคัดกรองมะเร็งปากมดลูกที่ผลผิดปกติด้วยวิธีแป๊ปสามัญในโรงพยาบาลมหาสารคาม

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บทคัดย่อ

มะเร็งปากมดลูกเป็นมะเร็งที่พบบ่อยในหญิงไทยและทั่วโลก โรงพยาบาลมหาสารคามได้เข้าร่วมโครงการตรวจคัดกรองมะเร็งปากมดลูกระดับชาติตั้งแต่ปี 2548 จนถึงปัจจุบัน ปัจจุบันยังไม่มีการศึกษาประสิทธิภาพของการตรวจคัดกรองมะเร็งปากมดลูกที่ผลผิดปกติในโรงพยาบาลมหาสารคาม จึงเป็นที่มาของการศึกษานี้ที่มีวัตถุประสงค์เพื่อศึกษาประสิทธิภาพของการตรวจคัดกรองมะเร็งปากมดลูกที่ผลผิดปกติด้วยวิธีแป๊ปสามัญในโรงพยาบาลมหาสารคาม เป็นการศึกษาแบบ diagnostic test study โดยเก็บรวบรวมข้อมูลย้อนหลังจากผลการตรวจแป๊ปสามัญ (conventional pap smear) ตั้งแต่ พ.ศ.2558 ถึง 2562 จำนวน 139,268 ราย และผลที่ผิดปกตินำไปวิเคราะห์ร่วมกับผลพยาธิวิทยาของการตัดชิ้นเนื้อจากการส่องกล้องคอลโปสโคป

ผลการศึกษา จากการตรวจคัดกรองมะเร็งปากมดลูกด้วยวิธีแป๊ปสามัญจำนวน 139,268 ราย พบว่ามีกลุ่มที่ผลผิดปกติจำนวน 530 ราย ความไวและความจำเพาะของการตรวจคัดกรองมะเร็งปากมดลูกที่ผลผิดปกติด้วยวิธีแป๊ปสามัญ พบว่าในกลุ่ม low grade squamous intraepithelial lesion (LSIL) มีความไวร้อยละ 70 ความจำเพาะร้อยละ 64.57 ในกลุ่ม high grade squamous intraepithelial lesion (HSIL) พบความไวร้อยละ 73.25 ความจำเพาะร้อยละ 87.23 และในกลุ่มมะเร็งปากมดลูกมีความไวร้อยละ 54.17 และความจำเพาะร้อยละ 99.21

สรุป: พบว่าความไวและความจำเพาะปานกลางในกลุ่ม LSIL โดยมีความไวปานกลางแต่ความจำเพาะสูงในกลุ่ม HSIL และกลุ่มมะเร็งปากมดลูก ดังนั้นการพัฒนาคุณภาพการเก็บเซลล์ตัวอย่าง การอบรมเพื่อเพิ่มทักษะการแปลผล และมีแนวทางการปรึกษาผู้เชี่ยวชาญเพื่อช่วยอ่านผลแป๊ปสามัญที่ไม่ชัดเจนจะช่วยเพิ่มความไวและความจำเพาะของการตรวจคัดกรองมะเร็งปากมดลูกด้วยวิธีแป๊ปสามัญได้

คำสำคัญ: ผลแป๊บสามัญที่ผิดปกติ, ระยะก่อนมะเร็งปากมดลูก, มะเร็งปากมดลูก , ระบบบีเทสด้า

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Diagnostic Performance of Abnormal Conventional Cervical Pap smear result at Mahasarakham Hospital

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Abstract

Cervical cancer is commonly found in Thai women and worldwide. Mahasarakham hospital has implemented the national cervical cancer screening policy (conventional cervical Pap smear) since 2005. However, there is no previous study to evaluate the diagnostic performance of the abnormal Pap smear result at Mahasarakham hospital. This study was a diagnostic test study objective to evaluate the diagnostic performance of abnormal Pap smear (precancerous lesions and cervical cancer) at Mahasarakham Hospital. The data was retrospectively collected from 2015 to 2019. The abnormal Pap smear results were compared with the histopathologic reports. Then, the diagnostic performances were analysed.

Results: There were 139,268 cases of conventional Pap smear with 530 cases of abnormal result (precancerous and cancer) within the study period. The sensitivity and specificity of low grade squamous intraepithelial lesion (LSIL) from Pap smear report were 70.00% and 64.57%, respectively. The sensitivity and specificity of high grade squamous intraepithelial lesion (HSIL) from Pap smear report were 73.25% and 87.23%, respectively. The sensitivity and specificity of cervical malignancy from Pap smear report were 54.17% and 99.21%, respectively.

Conclusion: This study shows moderate sensitivity and specificity diagnosis in LSIL and moderate sensitivity, but high specificity diagnosis in HSIL and cervical cancer. Improving sampling collection, specimen preparation, cytological interpretation of cytologist and expert consultation are essential to achieve concurrently high sensitivity and specificity.

Keywords: Abnormal conventional cervical Pap smear, cervical precancerous lesion, cervical cancer, LSIL, HSIL, Bethesda system

Introduction

Cervical cancer (CC) is the fourth most common cancer in women globally (528,000 new cases each year) and the second most common in developing areas (445,000 new cases each year). CC is also the fourth most lethal cancer in women worldwide (266,000 deaths) and the third cause of cancer-related death in developing countries (230,158 deaths)[1], which means that more than 80% of the global burden occurs in developing areas. Hospital-based cancer registry annual report at National cancer institute department of medical services ministry of public health Thailand, CC is the second most common (14.2% or 245 new cases of female cancer in 2018). New case cancer affecting women after breast cancer (40.8% or 704 new cases of female cancer in 2018)[2]. CC screening using conventional Pap smear has been conducted to reduce the incidence and mortality of this disease[3]. Liquid based cytology (LBC) and HPV testing can improve specimen quality, higher sensitivity, specificity and accuracy of low-grade precancerous lesion detection but it has similar effectiveness in CC detection[4]. The cost-effectiveness of conventional Pap smear is the reason that it is the main tool for CC screening at Mahasarakham Hospital and Mahasarakham Province. The cytological report of conventional Pap smear uses the Bethesda System, 2001[5]. When the abnormal Pap smear (precancerous and CC) is detected, the colposcopy and histological examination should be performed for diagnosis confirmation.

The diagnostic performance of our conventional Pap smear is important for monitoring of Pap smear quality. The previous studies, from difference countries, reported various sensitivity and specificity of Pap smear.[6-9] However, no study was conducted in Mahasarakham Hospital. Therefore, this study aims to evaluate the diagnostic performance of Pap smear in the detection of precancerous lesions and CC at Mahasarakham hospital which can be used for monitoring and improving of our cancer screening system.

Materials and Methods

This diagnostic test study was conducted at Mahasarakham Hospital. The retrospective review of the Pap smear data, from November 1st2015 to December 31th 2019, was done. The sample size was calculated using the formula for proportion estimation of descriptive study by N4studies program. The estimated sensitivity was 0.425[4], the estimated error was 0.0425 and the alpha error was 0.05. The calculated sample size was 520. All retrospective data between study period (530 cases) was included in this study.

All conventional Pap smear reports during the study period were reviewed. Patient characteristics and clinical data were reviewed. The Pap smear reports were categorized according to the Bethesda System 2001[5]. The negative cytology was defined as inflammatory changes and squamous metaplasia. The positive cytology was defined as atypical cells in the squamous or glandular epithelium and more severe lesions. The Bethesda system classifies lesions in the squamous epithelium as atypical squamous cells of undetermined significance (ASC-US), which are probably not neoplastic, and atypical squamous cells cannot exclude the diagnosis of high grade squamous intraepithelial lesion (ASC-H), low grade squamous intraepithelial lesion (LSIL), high grade squamous intraepithelial lesion (HSIL), and squamous cell carcinoma. The glandular epithelium lesions are classified as atypical glandular cells (AGC), atypical glandular cells favor neoplasia (AGC-FN) and adenocarcinoma[5].

Colposcopic examinations were performed in all positive cytology cases. Cervical biopsy was routinely done in the suspected cases and the histological tissue was prepared by hematoxylin/eosin straining technique, then submitted to a histopathological examination by a pathologist. Histopathologic results were classified into seven categories of disease severity: Normal/no neoplastic abnormalities, HPV, LSIL, HSIL (CIN2, CIN3 and CIS), squamous cell carcinoma, endocervical glandular dysplasia, adenocarcinoma in situ (AIS), adenocarcinoma and other CC[10].

The diagnostic performance (sensitivity, specificity, accuracy, positive predictive value; PPV and negative predictive value; NPV) of Pap smear were analysed, based on three group of disease (LSIL, HSIL and CC). The gold standard was the histopathological reports. The statistical program was SPSS version 21, KKU license. This research protocol was approved by the Ethics Committee on Human Research, Mahasarakham Hospital (MSKH REC No.61-01-039).

Results

There were 139,268 conventional Pap smear during the study period with 530 (0.38%) positive cytology results. The demographic characteristics were shown in Table 1. The mean age was 44.25 years old (S.D. 10.32, range 16-71). Most cases were pre-menopause and have two children.

The Pap results. were: ASC-US in 26.8%, ASC-H in 9.4%, HPV in 14.9%, LSIL in 17.3%, HSIL in 11.5%, AGC in 16.6% and adenocarcinoma in 0.8% , ASC-US and SIL ratio was 1:2.08 (Table 1, 2).

Table 1 Demographic characteristics and Pap results (N=530)

Characteristics	N (%)
Age (yr) (mean± SD)	44.25±10.32
Parity	
0	65 (12.3)
1	107 (20.2)
2	254 (47.9)
>2	104 (19.6)
Menopausal status	
Pre-menopause	398 (75.0)
Menopause	132 (25.0)
Total Pap smear	139,268
Abnormal cervical Pap smear	530 (0.38)
diagnosis	
ASC-US	142 (26.8)
ASC-H	50 (9.4)
HPV	79 (14.9)
LSIL	92 (17.3)
HSIL	61 (11.5)
SCC	13 (2.5)
AGC	88 (16.6)
AIS	1 (0.2)
Adenocarcinoma	4 (0.8)
ASC-US: SIL ratio	1:2.08

Table 2 Cytology diagnosis by TBS 2001 classification compare with histopathology

Cytology \ Histopathology	Neg	HPV	LSIL	HSIL	SCC	AIS	Adeno carcinoma	Other CC	total
ASC-US	82	34	14	10	1	0	1	0	142
ASC-H	13	8	6	22	1	0	0	0	50
HPV	23	34	19	3	0	0	0	0	79
LSIL	22	35	24	10	0	1	0	0	92
HSIL	3	3	9	41	4	0	1	0	61
SCC	-	-	0	2	10	0	1	0	13
AGC	54	12	7	10	1	2	1	1	88
AIS	0	0	0	0	0	1	0	0	1
Adenocarcinoma	2	0	0	0	0	0	2	0	4
Total	199	126	79	98	17	4	6	1	530

The sensitivity, specificity, accuracy, PPV and NPV were shown in Table 3. The sensitivity, specificity, accuracy, PPV and NPV of LSIL lesion of Pap smear were 70.00%, 64.57%, 65.34%, 24.64% and 92.86%, respectively. The sensitivity, specificity, accuracy, PPV and NPV of HSIL lesion of Pap smear were 73.25%, 87.23%, 85.25%, 48.71% and 95.17%, respectively. The sensitivity, specificity, accuracy, PPV and NPV of CC were 54.17%, 99.21%, 92.81%, 91.90% and 92.90%, respectively. The test performance for LSIL, HISL and malignancy were 1.08, 0.83 and 0.54 respectively.

Table 3 Diagnostic performance of cervical Pap smear

	Cervical Pap smear diagnosis		
	LSIL (95% CI)	HSIL (95% CI)	Malignancy (95% CI)
Sensitivity(%)	70.00 (62.26-76.98)	73.25 (62.62-82.23)	54.17 (32.82-74.45)
Specificity(%)	64.57 (55.59-72.85)	87.23 (83.14-90.64)	99.21 (97.99-99.78)
Accuracy(%)	65.34 (59.52-70.83)	85.25 (81.47-88.52)	92.81 (90.27-94.86)
Positive Predictive Value(%)	24.64 (20.20-29.69)	48.71 (41.06-56.42)	91.90 (79-.98-96.99)
Negative Predictive Value(%)	92.86 (90.85-94.45)	95.17 (93.27-96.56)	92.90 (89.44-95.28)
Positive Likelihood Ratio	1.98 (1.53-2.55)	5.74 (4.21-7.82)	68.52 (24.14-194.48)
Negative Likelihood Ratio	0.46 (0.5-0.61)	0.31 (0.22-0.44)	0.46 (0.30-0.71)

Discussion

From this study, the positive cytology was found in 0.38% of test. This result was similar as Teresa D et al (0.76%)[11] and Nawaz FH et al study (0.68%)[12]. but other studies were generally higher than what we found in our study (range, 1.7 to 4.05%).[7,13-16] In our study, Pap smears were collected from no symptom patients who participated in a Province Screening Program and patients presented with gynecological symptom causing low positive cytology. Some studies collected the test results from patients with gynecological symptom resulting in a higher positive test result.

In the LSIL group, the sensitivity of conventional Pap smear in our center was 70.00%, specificity was 64.57%, PPV was 24.64% and NPV was 92.86%. The sensitivity was close to Verma et al[6], but was lower than Kanjanavirojkul et al[7] study which reported sensitivity at 76.9% and 86.5%, respectively.[6-7] The specificity was lower than 70.0% and 96.2% from Verma et al[6] and Kanjanavirojkul et al[7] study. The PPV was also lower than 90.9% of Verma et al[6] study but the NPV was similar. However, Kanjanavirojkul et al[7] used conventional Pap smer method and thin Prep method to collect cytology data, while Verma et al[6] using endocervical cytology might contribute result from our study.

In the HSIL group, the sensitivity, specificity, PPV, and NPV of our study were 73.25%, 87.23%, 48.71% and 95.17%, respectively. In the CC group, the sensitivity, specificity, PPV, and NPV were 54.17%, 99.21%, 91.90% and 92.90%, respectively. Our data, in these groups, is similar with other studies[6-9].

The overall diagnostic performance of Pap smear in our center was similar rate as a systematic review study to evaluate the diagnostic accuracy of the Pap smear by Nanda et al.[17] that found its sensitivity was 51% (range 30% to 87%), and specificity was 98%, (range 86% to 100%). A study from Cochrane review[18] showed pooled sensitivity for CIN 2+ diagnosis from conventional Pap smear was 62.5% and pooled specificity was 96.6%.

Most women in our study were multiparous women. The mean age of the participants was 44.25±10.32 years old. It is thought that the average age of women population in study was appropriate considering the fact that the common age to develop HSIL lesion[19-20] ASC-US: SIL ratio was 1:2.08, it is normal limit of standard PAP report (ratio 3:1)[21].

The different in cytohistologic correlation of this study with other various studies may be due to many factors;[9-13] such as the different population, collection methods (LBC or conventional), the diagnostic criteria, the experience and the skill of the cytotechnologists and cytopatho logists[22]. The Pap smear limitations also include failure to acquire adequate specimens, intra-observer bias, and misinterpretations. The quality of smear, such as Inflammation, scant cellularity, mucin, blood contaminating samples and thick smears, have been cited as reasons for inadequate samples.[16] Percentage of inadequate samples in Pap smear were 5-9% in the national standard range.[23] Overlapping epithelial cells decrease the sensitivity to as low as 50% with rising false negative rate to 14-33%[24].

The limitation of this study was retrospective study design. We could not collect some clinical data from patients such as abnormal leucorrhea, intercourse period, vaginal douche, vaginal bleeding and other factors which influenced the Pap interpretation. The data of associated factors such as specimen collectors (nurse, medical student, intern or staff), adequacy of specimen were also absent. Another limitation was the negative Pap smear cases which were not enrolled in this study due to no tissue biopsy and histological examination, so the false negative rate might be higher.

Conclusion

This study shows moderate sensitivity and specificity diagnosis in LSIL and moderate sensitivity, but high specificity diagnosis in HSIL and CC. Improving sampling collection, specimen preparation, cytological interpretation of cytologist and expert consultation are essential to

achieve concurrently high sensitivity and specificity.

Potential conflicts of interest

None.

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