

A Relationship between Uterine Cervical Cytopathology and Histopathology in Mongolia

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Objectives: This study aimed to evaluate the correlation between uterine cervical squamous cell abnormalities by conventional cytology and corresponding histopathology, and to assess the accuracy between them. **Methods:** A total of 192 cytological smears of patients with squamous cell abnormalities who underwent colposcopy examination from April – December 2015 were included in this study. The final agreement between cytology and histopathology was defined by the evaluation of histology as a golden standard. **Results:** The agreement between cytology and histopathology evaluation was 65.6%, and the discrepancy was 33.6% ($k=0.512$). When the classes of cytology were evaluated for accuracy, it was discovered that NILM* had a higher sensitivity of 77.0%, a specificity of 87.0%, a false positive of 23% and a false negative of 13.0% ($k=0.711$). Among the LSIL cases a sensitivity was discovered of 39.0%, a specificity of 82.7%, a false positive of 61.0% and a false negative of 17.3% ($k=0.392$). However, in HSIL sensitivity dropped to 37.8%, specificity increased to 91.6%, false positive were 62.0% and false negative were 8.4% ($k=0.501$). **Conclusion:** The agreement for diagnosis of uterine cervical cytology and histopathology was 65.6% ($n = 126$) and the discrepancy was 33.6% ($n = 64$) ($p = 0.001$). The correlation between cervical cytology and histopathology remained moderate ($kappa=0.512$). Thus, it is proposed that an appropriate quality control system for the cytopathological confirmation may contribute to the further detection and treatment for uterine cervical cancer in Mongolia.

Keywords: Cervical cytology, Squamous cell abnormalities, Sensitivity, Cervical cancer, Mongolia

Introduction

World-wide cervical cancer is one of the most common cancers. Approximately 10% of women are diagnosed with cervical cancer during their lifetime. The incidence of cervical cancer has been increasing every year. More than 85% of the global burden

of cervical cancer occurs in developing countries [1]. Therefore, cervical cancer is an important public health problem especially among poorer adult women. Cervical cancer is the third most common cancer in women causing an estimated 528 000 new cases and 226 000 deaths in 2018 [2]. The risk is high in regions such as Eastern and Western Africa, Southern Africa, South-

Central Asia, South America and Middle Africa [3].

Papanicolaou testing or cytology and colposcopy is a widely used screening tool in asymptomatic populations and following potentially curable lesions of the lower female genital tract [4-6]. Therefore, cytology is the most effective technique to prevent and detect precancerous conditions of the uterine cervix. However, due to inaccuracy of cervical cytology, the final diagnosis should be made on cytohistologic examination [7, 8]. That is to say that although the cervical cytology method represents a feasible test to prevent and detect precancerous lesions of the uterine cervix before they become invasive, its high false-negative results due to sampling and interpretation errors are still a reason for concern [9]. Thus, the final diagnosis should be made on cytohistological correlation to assess the accuracy of the cervical cytology [10].

Since cancer of the cervix is a leading cause of death among women worldwide, it is important to use the best detection tool. The best screening method for cervical cancer is the Papanicolaou (Pap) test. The Bethesda system 2014 is a system for reporting cytological interpretation of Pap smear results [11,12]. Data on assessing the quality of cervical cytology testing is limited in our country. Thus, this study aims to evaluate the correlation between uterine cervical squamous cell abnormalities by cytology and corresponding histopathology and to evaluate the corresponding accuracy between them in Mongolia.

Materials and Methods

This hospital-based retrospective study was conducted from smears of women aged between 19-65 with squamous cell abnormalities that underwent colposcopic examination at the National Center for Cancer in Mongolia. Total of 192 smears were collected during April – December, 2015. Cytological smears without a histopathologic diagnosis were excluded from this study. Microscopic review examinations were performed by experienced cytologic and pathologic fellows. The cytological smears were classified according to The Bethesda system 2014 and the histological findings were classified according to The WHO classification 2003. The concordance rate was considering on the evaluation of histology as a golden standard.

Statistical Analysis

Data was analyzed by SPSS version 17 (SPSS Inc, Chicago, IL, USA) and presented as mean \pm SD, numbers, and percentages. The overall accuracy and agreement between cytology and

histopathology results were represented by the sensitivity, specificity, and positive and negative predictive values. The chi-square test was used to analyze the association between categorical variables in the overall diagnoses. A p-value of 0.05 or less was considered for statistical significance. Cronbach's alpha was used to measure the reliability of the relationship between diagnoses of the cytology and histopathology as a group in our study. The reliability is acceptable if the alpha is 0.7 or higher.

Ethical Statements

The present study was approved by the Ethics and Research Committees of the Mongolian National University of Medical Sciences (N^o13-10/1A).

Results

A total of 192 conventional smears of patients with histopathological biopsies were included in this study. The mean age of the patients was 41.8 ± 9.4 years. A majority of the women 89.6% (n=175) were aged between 30-60 years old.

Two out of the total 192 smears were excluded due to being unsatisfactory for study. Table 1 shows that the concordance rate between cytology and histopathology was 65.6% (n=126), a discrepancy was 33.6% (n=64). Overall concordance rate includes benign 37.3% (n=47), cervical interepithelial neoplasia (CIN) 61.9% (n=78), and squamous cell carcinoma 0.8% (n=1).

Table 2 shows the histopathological results according to different cytologic categories. A majority of abnormal cytology was LSIL (26.8%), followed by ASCUS, HSIL, ASC-H and SCC (18.9%, 13.7%, 5.3%, and 1.5%, respectively), while other cytology was NILM (33.7%).

NILM or normal cytology was histopathologically benign in 24.7% (n=47), CIN1 in 7.9% (n=15), CIN2/3 in 0.5% (n=1) and cancer in 0.5% (n=1) of the overall cases. ASCUS cytology yielded a diagnosis of NILM in 0.5% (n=1), low-grade lesions in 13.2% (n=25), CIN2/3 in 5.3% (n=10) of the cases. LSIL cytology was confirmed to be CIN1 in 16.3% (n=31) or no intraepithelial lesions in 5.8% (n=11) of patients but coexisting high-grade lesions (CIN2/3) occurred in 4.7% (n=9) of cases. HSIL and ASC-H cytology yielded high-grade lesions in 6.3% (n=12) and 2.6% (n=5), respectively. Coexisting low-grade lesions were diagnosed in 4.2% (n=8) and 2.1% (n=4), respectively, while

Table 1. Concordance rate between the cytology and histopathology results

Evaluation of diagnoses	Number (n)	Percent (%)
Concordance	126	65.6
Discrepancy	64	33.6
Total	190	100.0

Table 2. The histopathological results according to different cytologic categories

Cytological category	Total		Histopathology							
	Benign		LSIL (CIN 1)		HSIL (CIN 2/3)		SCC (Carcinoma)			
	N	%	N	%	N	%	N	%	N	%
NILM	64	33.7	47	24.7	15	7.9	1	0.5	1	0.5
ASCUS	36	18.9	1	0.5	25	13.2	10	5.3	0	0
LSIL	51	26.8	11	5.8	31	16.3	9	4.7	0	0
ASC-H	10	5.3	1	0.5	4	2.1	5	2.6	0	0
HSIL	26	13.7	4	2.1	8	4.2	12	6.3	2	1.1
SCC	3	1.5	0	0	1	0.5	2	1.1	0	0

NILM -Negative for intraepithelial lesion or malignancy; ASC-US -Typical squamous cells of undetermined significance; LSIL -Low-grade squamous intraepithelial lesion; HSIL -High-grade squamous intraepithelial lesion; SCC -Squamous cell carcinoma.

Table 3. Comparative results of statistical analysis between the cytological categories

Cytology categories	True positive % (Sensitivity)	True negative % (Specificity)	False positive % (PPV ^a)	False negative % (NPV ^b)	Cronbach's Alpha ^c	p-value
NILM	77.0	87.0	23.0	13.0	0.711	0.001
ASC-US	72.2	93.6	27.8	6.4	0.794	0.001
LSIL	39.0	82.7	61.0	17.3	0.392	0.001
ASC-H	60.0	97.3	40.0	2.7	0.708	0.001
HSIL	37.8	91.6	62.2	8.4	0.501	0.001
SCC	0	98.4	100.0	1.6	-0.032	0.587

^aPositive predictive value; ^bNegative predictive value; ^cMean Cronbach's Alpha=0.512

cancer was confirmed in 1.1% (n=2) of HSIL cases. CIN1 and CIN2/3 was diagnosed in patients with SCC cytology in 0.5% (n=1), and 1.1% (n=2), respectively.

The results of the statistical analysis between the cytological categories varied (Table 3). According to the overall cytological data, TP ranges were 37.8-77.0%, TN ranges were 82.7-98.4%, FP ranges were 23.0-100%, and FN ranges were 1.6-17.3%. Among the cytological categories, TP of the NILM at 77.0% and ASC-US at 72.2% were higher than others. The agreement between the NILM, ASC-US, and ASC-H findings were substantial (k=0.708-0.794), HSIL was a moderate (k=0.501), and LSIL was fair (k=0.392), however, the agreement of the SCC was

slight (k=0.032). Over all, a moderate (k=0.512) agreement was found by defining the concordance and discordance rates between cervical cytology and histopathology findings.

Discussion

Cervical cytology is the most common and reliable test for the detection and prevention of cervical cancer in a world. However, multiple studies evaluating the performance of cytology in detecting cervical abnormalities have various results. This might be due to different methods of cervical cytology sampling, or skills and experience of the screener, and quality control of

the testing in some studies. Therefore, our study aimed to evaluate the performance of cytology in detecting cervical cell abnormalities in Mongolia.

According to our data, concordance and discordance rate between cervical cytology and histopathology was 65.6% and 33.6%, respectively. These findings are in line with the ranges reported in the literature from similar studies, i.e. 51.2–77.5% for cytohistological concordance and 22.5–48.8% for discrepant cases of pap smears [13-15]. According to this data, health care providers should pay close attention to improving quality control for those discrepant results, to further prevent cervical cancer in Mongolia.

The accuracy of the major cytological diagnosis of LSIL was confirmed to be CIN1 in 16.3% of cases, followed by ASCUS yielding a diagnosis of low-grade lesions in 13.2% of the cases. These numbers were comparable to ASCUS cytology, and this could probably support the suggestion that LSIL is equivalent to ASCUS [16]. HSIL cytology yielded high-grade lesions in 6.3% of cases and coexisting cancer was confirmed in 1.1% of cases, which was similar to the study done in Thailand where the incidence of cervical cancer is very high [17,18]. Our study revealed that squamous cell carcinoma cases were confirmed to be low-grade and high-grade intraepithelial lesion, while benign were 1.5% (1/64) and HSIL were 7.6% (2/26) cytology cases yielded pathologic carcinoma. Similar studies showed up to 16.6% invasive cancer in HSIL cytology [18,19]. Therefore, cervical cancer should be another consideration in caring for high-grade lesions in cervical cancer in high incidence countries.

The accuracy of conventional cytology for detecting cervical abnormalities in this study was in similar range compared to previous studies which was about 59-78% [20]. However, accuracy was different from the cytological categories. In the study of Pava P.F et al. [21], sensitivity and specificity found for LSIL were 78.9% and 95.0%, positive and negative predictive value were 93.7% and 82.6%; Therefore, the sensitivity and specificity found for HSIL were 60.0% and 95.5%, positive and negative predictive value were 66.6% and 94.2%, respectively. However, the study by Atla et al. [22], sensitivity and specificity found for LSIL were 92.9% and 67.3%, respectively. The present study found that the diagnosis of LSIL was 60.8% and 65.4% for sensitivity and specificity, negative predictive value was 35.5% and false-positive was 39.2% and the in the diagnosis of HSIL was 50.0% and 86.1% for sensitivity and specificity, false-

negative was 13.9% and false-positive was 50.0%, respectively. The diversity of study results in different countries is likely to be associated with a diversity in the health of the country's economy and health care systems [23-25]. Therefore, this may lead to of differences in conventional cytology that result in obscuring the abnormalities on cytological smears.

Whereas a previous study reported a kappa coefficient is in range 0.40- 0.632 for LSIL and HSIL [26,27], the present study revealed kappa coefficient is in range 0.213-0.311 which is markedly different. These findings suggest that cytology testing for the screening and detection of cervical cancer still needs more improvement in Mongolia.

Limitation

There are several limitations in our study. First, we used a small number of cases, with only corresponding histopathologic diagnosis. Some smears with lost information in the registration system have error. However, normal histological findings were reviewed to confirm a true negative result. Second, demographic factors including age, marital status, number of children, etc. are not considered in this study. Since this study was a retrospective it was difficult to get complete information about patients, however, only preserved smears and histology blocks were used.

Conclusion

The concordance for diagnosis of cervical cytology and histopathology was 65.6% (n = 126) and the difference was 33.6% (n = 64) (p = 0.001). The correlation between cervical cytology and histopathology remained moderate (kappa=0.512). Thus, an appropriate quality control system for the cytopathological confirmation may contribute to the further detection and prevention of cervical cancer in Mongolia.

Conflict of Interest

The authors declared no conflict of interest.

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