ORIGINAL ARTICLE

Variability study between Pap smear, Colposcopy and Cervical Histopathology findings

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Abstract

Objective: To determine the agreement/variability between colposcopic findings, Pap smear cytology and histopathological diagnosis in gynaecology patients.

Methods: The cross-sectional cohort study was conducted from October 2010 to September 2011 at the Fauji Foundation Hospital, Rawalpindi, and comprised women who presented to the out-patient department with various gynaecological complaints. Colposcopy was performed in all women with unhealthy cervix during gynaecological examination, abnormal Pap smear report, recurrent vaginal discharge and postcoital bleeding. Pap smear was performed before colposcopy if not done earlier. Colposcopic findings were recorded on a specially-designed proforma. Biopsies from abnormal areas were taken and sent for histopathology. Colposcopic findings were compared with histopathology and Pap smear reports The agreement between the methods was evaluated by using Kappa coefficient and chi square test at a significance level of 5%.

Results: The mean age of the 143 women was 44 8.5 years (range: 25-72 years). Colposcopic findings were normal in 66(46%) women, while 77(54%) had abnormal findings and among the latter, 62(80.5%) had abnormal histopathology, indicating strong agreement (K=0.65; p<0.001). Pap smear report was abnormal in 48(33.5%) cases and among them histopathology was abnormal in 28(58%). In the remaining 95(66.4%) patients with normal Pap smear, histopathology was abnormal in 44((46%), indicating weak agreement between Pap smear and histopathological diagnosis (K=0.10; p=0.08).

Conclusion: There was a strong agreement between colposcopic findings and histopathological diagnosis. However, agreement between cytological findings and colposcopic findings and cytology and histopathological diagnosis remained weak.

Keywords: CA Cervix, Colposcopy, Correlation. (JPMA 65: 1295; 2015)

Introduction

Colposcopy is a diagnostic procedure to examine an illuminated magnified view of the cervix and tissues of the vagina and vulva. Many premalignant and malignant lesions in these areas have noticeable characteristics which can be detected through colposcopy. Colposcope helps to visualise the cervix and distinguish normal from abnormal areas and to take direct biopsies from abnormal areas for further pathological evaluation. The main goal of colposcopy is to prevent cervical cancer by detecting precancerous lesions early and treat them.

The second most common cancer worldwide among women is carcinoma of cervix. Every year 50,000 new cases are diagnosed and 250,000 deaths are related to it.[1] Major burden of 80% new cases is borne by under-developed countries like Pakistan and in some of these countries carcinoma of cervix is the most common cancer.[1] The situation is further worsened by the fact that 75% women present with advanced stage. Lack of education and empowerment of women and inadequate screening programme for cervical cancer in these countries also partly affect this high burden.[2]

Carcinoma of cervix is a preventable condition and considerable effort goes into detecting and treating the preinvasive disease. Since 1943, Pap smear cytology has been used for the screening of cervical cancer.[3] However, the best method for cervical cancer screening still remains unclear. Literature recommends different methods ranging from simple cytology, colposcopy, and human papilloma virus (HPV) deoxyribonucleic acid (DNA) testing or even repeat cytology.[4-7] Developed world at present relies on cytology screening and treatment of high-grade cervical intra-epithelial neoplasia (CIN2 or CIN3), which is a precursor for cancer.[8] However, in developing countries like ours no proper cytology screening protocols are available. Also, cytological screening is not specificity sufficient to successfully identify the women with cancer precursors.[8] Hence, a good number of patients in pre-malignant stage are

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being missed. Colposcopy is used currently as a triage test in cervical cancer prevention. It helps to diagnose the patients in pre-malignant stage and categorise the women in a better way related to the need of treatment.[8]

Questions about the accuracy of colposcopy are on the rise. Loop excision studies after colposcopy have identified women with CIN 2+ and cancer missed colposcopically.[9]

The present study was planned to find the agreement/variability between colposcopic and histopathological findings, and also its agreement with Pap smear as the screening test.

Patients and Methods

The cross-sectional cohort study was conducted at the outpatient department (OPD) of Gynaecology and Obstetrics Unit 2, Fauji Foundation Hospital, Rawalpindi, from October 2010 to September 2011, and comprised women who presented with various gynaecological complaints. Colposcopy was performed on all those women who had recurrent vaginal discharge, postcoital or intermenstrual bleeding and unhealthy cervix on pelvic examination. The patients already diagnosed or treated for cervical cancer were excluded. Pap smear was taken before doing colposcopy by conventional method using Ayre's spatula and cervical biopsies were taken from suspicious areas for histopathology.

Sample size was calculated using Power Analysis & Sample Size (PASS) software based on sample size determination technique mentioned in literature[10] and its trial version is freely available on the internet. The sample size was also confirmed using Correlation calculator available at the College of Physicians and Surgeons Pakistan (CPSP). To calculate the sample size we also considered studies already done to observe agreement between colposcopy, Pap smear and histopathology.[11-15] To observe agreement between Pap smear and histopathology, we set in calculator Null kappa[11] = 0 alternate kappa > 0.3, power of test = 0.95, significance level = 0.05. This gave us a minimum sample size of 116. For sample size between colposcopy and histopathology, null kappa = 0.3 and alternate kappa[14,15] = 0.61 was taken while keeping the same significance level and power of test. This resulted in a sample size of 143. Similarly, the sample size for colposcopy and Pap smear was calculated to be 115. Finally, keeping in view the fact that the software calculates minimum sample size, we decided to for n=143 for each of the three comparisons.

Colposcopy findings, cytology report and histopathology reports were entered in a specially-designed proforma. Abnormal cytologies included were atypical sqamous cells of undetermined significance (ASCUS), low-grade intraepithelial lesions (LSILs), high-grade intraepithelial lesions (HSILs) and invasive carcinoma.

Colposcopy was considered abnormal when there was presence of acetowhite areas and abnormal vessels irrespective of the grade of these changes. Biopsies were taken in all the women for histopathological analysis. The histopathological changes were classified as normal, CIN1, CIN2, CIN3 or invasive carcinoma. There were no patients with borderline or HPV changes.

The significance of association was assessed by chi square test with a significance level of 5% and the strength by kappa statistics. Kappa coefficients (K) were calculated and the agreement was analysed between cytological and histopathological findings, the presence of abnormal colposcopic findings and cytology, and abnormal colposcopic findings and histopathological diagnosis. Kappa is a concordance index ranging from 0 to 1, and the maximum value of 1 expresses the perfect agreement, and 0 corresponds to the complete absence of agreement.

Results

The mean age of the 143 women was 44±8.5 years (range: 25-72 years). Mean parity was 5±3. Colposcopic findings were normal in 66(46%) women, while 77(54%) had abnormal findings. Among the latter, 62(80.5%) women

Table-1: Colposcopy and histopathology.

Colposcopy	Histopathology		Kappa	p-value
	Abnormal	Normal		
Abnormal	62 (80.5%)	15 (19.5%)	0.65	<0.001
Normal	10 (15%)	56 (85%)		

Table-2: Colposcopy and pap smear (n=143).

Colposcopy	Pap Smear		Kappa	p-value
	Abnormal	Normal		
Abnormal	27(56.2%)	50(53%)	0.03	0.34
Normal	21(43.7%)	45(47%)		

Table-3: Pap smear and histopathology (n=143).

Pap smear	Histopathology		Kappa	p-value
	Abnormal	Normal		
Abnormal	28 (58.3)	20(47.6%)	0.10	0.08
Normal	44(46%)	51(53.6%)		

had abnormal histopathology and in 15 (19.5%) women the histopathology was normal (K=0.65; p<0.001) (Table-1).

Out of 66 women with normal colposcopy, histopathology was abnormal in 10(15% false negative) cases. The calculated sensitivity and specificity of colposcopy findings were 86% and 79% respectively.

Pap smear taken before colposcopy was abnormal in 48(33.5%) women and 95(66.5%) had normal Pap smear (K=0.03; p=0.34) (Table-2).

Analysis of women with abnormal smear report showed that 21(43.7%) had normal colposcopy and histopathology was also normal in 15(31% false positive). On the other hand 50(52.6%) women with normal smear had abnormal colposcopy and abnormal histopathology in 40 (42% false negative).

Comparison of Pap smear with histopathology showed that out of total 48 patients with abnormal Pap smear, 28(58.3%) had abnormal histopathology, while of the 95 patients with normal smear, 51(53.6%) had normal histopathology. The remaining 44(46%) women had abnormal histopathology (p=0.08). False positive cases were 20(28%). The calculated sensitivity and specificity for Pap smear was 38.8% and 71.8%, indicating the low accuracy of Pap smear (Table-3).

Discussion

Due to various well recognised inherent limitations of cervical cytology, a percentage of high-grade lesions are missed on Pap test.[16-20] Studies suggest a wide variation in the parameters of accuracy, sensitivity and specificity of cytology stained by the Papanicolaou method. In our study, out of 72 patients with abnormal histopathology, smear was normal in 44. Similarly, colposcopy was abnormal in 50 patients out of 95 with normal smear. So no significant agreement of Pap smear was found with colposcopy and histopathology.

In a study[19] cytohistological correlation was obtained in 77.5% of high-grade lesions. A retrospective review[21] found accuracy of cytology to be 62.7%. A systematic review with meta-analysis that included 94 observational studies with conventional cytology evaluated the accuracy of the Pap test for screening and monitoring of cytological abnormalities. It concluded that studies of accuracy for Pap smears had many biases and the best selected studies showed only moderate agreement without high accuracy, a sensitivity ranging between 30 and 70% and specificity 86 to 100%.[22]

Another meta-analysis that included nine studies reported sensitivity and specificity of conventional cytology for high-grade lesions to be 55.2 and 75.6%, and for low-grade lesions of 96.7 and 81.2% respectively.[23]

In the present study, there was a poor concordance between cytology and histology and a poor agreement between cytology and colposcopy. A prospective analytical study conducted in India in 2008 also showed lack of agreement of cytology with histopathology and the study concluded that even the patients with persistent inflammatory Pap smear can harbour a high proportion of CIN.[11] A study showed fair agreement between Pap smear and cervical biopsy (k=0.5).[12] Similarly, another study also showed a high cyto-histopathological accordance of 82%[13] but it mainly comprised patients with LSIL.

A prospective study to evaluate the agreement between Ried colposcopic index impression and biopsy histology said the agreement between colposcopic impression and histological diagnosis was highly significant. The negative predictive value of a benign colposcopic impression was 70.5%, the sensitivity was 74% and the specificity was 90.7%.[14] A similar study showed a good agreement between Reid colposcopic impression and histopathology (k= 0.66).[15] Another study to find out the strength of agreement between colposcopic impression and biopsy histology said the association between impression and histology was significant but the strength of agreement was poor (k=0.20).[24] A study of accuracy of colposcopic grading for detection of high-grade cervical intraepithelial neoplasia concluded that finding of acetowhite lesions identify the women with CIN2+, and biopsy of all these lesions maximises the sensitivity and specificity of colposcopic diagnosis.[8] A study conducted in India found colposcopy a good sensitive test for detection of CIN with sensitivity up to 74.7% and specificity up to 92.9%.[25]

Colposcopic findings were normal in 56(79%) cases of patients with normal histopathology, indicating a specificity of 79%. It was concluded that colposcopy does help to identify the best site for biopsy and diagnosis of intraepithelial neoplasia. It is noteworthy that colposcopy with directed biopsy detects intraepithelial neoplasia grade III in two-third cases, with greater sensitivity when two or more biopsies are performed.[26] A study analysed three clinical trials to find out the accuracy of colposcopic biopsy and concluded that more than one biopsy improved the colposcopic accuracy.[27]

A meta-analysis that included eight longitudinal studies observed a high accuracy of colposcopy (89%) with a concordance in 61% cases when compared to histopathology. However, there were an equal proportion

of false-positives and false-negatives, although the false-positive results are more frequent in low-grade lesions.[28] Biopsy was not performed in all patients included, but only in patients with abnormal colposcopic findings so it is not possible to calculate the validation diagnostic tests (accuracy, sensitivity and specificity) since the gold standard (histopathology) for all women (normal and abnormal colposcopic findings) is not available in these studies.

The abnormal colposcopic findings showed a good correlation to histopathology than the correlation of cytology with histopathological findings. Thus, it is suggested that although the colposcopy served mainly to find the best place to proceed to biopsy, it also helped to improve the diagnosis of cervical intraepithelial lesions. In a study that assessed the inter-observer variability of colposcopic diagnosis according to the histological results, the presence of abnormal colposcopic findings showed a sensitivity for cervical intraepithelial neoplasia of 90.2% and a specificity of 48.6%.[29]

There was good agreement[30-32] (k=0.65) between colposcopic findings and histopathological diagnosis, but weak agreement[30,31] between cytology and colposcopic findings (k=0.03). The agreement between cytology and histopathology was fair[30-32] (k=0.10).

Conclusion

The high specificity and sensitivity of colposcopy indicated that colposcopy has an important role in the diagnosis of cervical intraepithelial neoplasia. More studies that allow the determination of sensitivity and specificity of colposcopy are needed for a better assessment of the importance of colposcopy as a method of detecting cervical intraepithelial neoplasia and not just as a resource for locating the best site for biopsy.

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