Correlation of Pap Smear and Colposcopic Findings in Relation to Histopathology in Detection of Premalignant Lesions of Cervix

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Abstract

Background: Cancer develops from the premalignant lesions (CIN) over a period of time which can be diagnosed by screening tests. The Papanicolaou (Pap) smear was the initial screening test for CIN and invasive cervical cancer. However, the simultaneous use of Pap smear and colposcopy has been shown to increase the rate of the cervical cancer detection. So this study was done to assess the reliability of colposcopy by correlating the findings of colposcopy with cytology and colposcopic directed biopsy in women with unhealthy cervix .

Materials and Method: This was a prospective observational study conducted in 100 women aged between 18 to 65 years with unhealthy cervix. All were subjected to screening by Pap smear, colposcopy and colposcopic guided biopsy and their results were compared and correlated. Final correlation of the Pap smear and colposcopy were based on histopathology results.

Results: In the present study, the sensitivity of Cervical colposcopy was more than Pap smear (90.3% Vs 67.25%) but its specificity was only 64.9% compared to 97.7% of the Pap smear. This study demonstrated a high correlation between colposcopy and histology of 94.84%. The correlation between Pap smear and colposcopy was 99 %. The correlation between Pap smear and histology was 82%.

Conclusion: Colposcopy and colposcopic directed biopsy should be included along with Pap smear in screening for early detection of cancer of cervix since the accuracy of detection of cervical abnormalities is higher when they are used complementarily.

Keywords: *Cervical Cancer, Cervical Biopsy, Pap smear, Colposcopy, Unhealthy cervix*

Introduction

Cervical cancer is the fourth most common cancer affecting women and seventh overall world-wide after breast, colorectal and lung cancers.[1] It is also th e fourth most common cause of cancer deaths in women worldwide. Almost 70% of the global burden falls in areas with lower levels of development and more than one fifth of all new cases are diagnosed in India. The cervical cancers were an estimated 5,28,000 new cases & 2,66,000 deaths from cervical cancer worldwide in 2012, accounting for 7.5% of all female cancer deaths.[1]

The main cause of cervical cancer is a sexually transmitted infection by human papillomaviruses.(2) The worldwide human papiloma virus prevalence in cervical cancer is 99.7%.3 Cancer cervix has been considered preventable because it has a long pre-invasive state and availability of screening programs and treatment of preinvasive lesion is effective.(2) It has been well-established that well-organized screening by conventional cytology has substantially reduced

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the incidence of morbidity and mortality from cervical cancer in developed countries

Cervical cancer can be prevented and almost cured when diagnosed in early stages. So early detection and treatment of these premalignant lesions is the principal object of cervical cancer prevention program. In many developed countries, health education, early detection and appropriate management achieve 80% reduction in morbidity and mortality due to cervical cancer. These premalignant lesions can be detected with the help of screening tests which include Papanicolaou (pap) smear, colposcopy and histology. Pap smear is the initial simple, safe, non-invasive and effective screening test. In 1925 Hinselmann from Germany invented colposcopy for stereoscopic examination of the illuminated cervix and lower genital tract at a magnification of x6 to x40. It mainly demonstrates surface patterns and the terminal vascular network of the lesion. It is now routinely recommended for evaluation of women with abnormal Pap smear and for the diagnosis of suspicious invasive lesions in suspicious or unhealthy cervix. It identifies the appropriate sites for a biopsy and indicates the location of diseased tissue. The diagnosis of cervical neoplasia by colposcopy is based on recognition of four main features.

a. Intensity and colour tone of acetowhite areas.

b. Margins and surface contours of acetowhite area.

c. Vascular pattern.

d. Iodine staining.

Variation in quality and quantity of these atypical appearances help in differentiating CIN from other lesion or between types of CIN. In low-grade lesions, transparent to semi-transparent acetowhite areas with vague or feathery margins and fine punctation and/or mosaic seen. Opaque acetowhite areas with sharp margins and coarse punctation and/or mosaic are seen in high grade lesions. CIN lesions do not stain with iodine due to absence of glycogen. Colposcopic guided cervical biopsy can be taken from these abnormal areas. Combined with cytologic and histologic information colposcopy improves the accuracy of diagnosis of cervical cancer

. Objective of present study was to critically evaluate the sensitivity and specificity of PAP smear with Colposcopy in screening of Cancer Cervix by correlating with Histopathology in women with unhealthy cervix and abnormal symptoms.

Material and Method

This prospective study was conducted in the Department of Pathology Santosh medical college and associated hospital Ghaziabad, India. , from 1 July 2017 to July 2018 after taking approval from Institutional Ethical Committee.

The material of present study was collected from women who met the inclusion criteria and gave the consent for colposcopy and directed biopsy from the Department of Obstetrics and Gynecolog.y

Inclusion criteria

• Age- 20-60 years.

• Women with symptoms like white discharge, post coital bleeding, and inter-menstrual bleeding.

• Women with clinically unhealthy cervix (erosion, bulky cervix, bleeding on touch, ulcer, simple leukoplakia, keratinisation).

• Women with PAP smear showing dysplasia.

Exclusion criteria

• Women with bleeding per vaginum at the time of examination.

• Women with frank invasive cancer.

• Women underwent hysterectomy.

• Pregnant women.

Written and informed consent was taken from all the patients after a brief explanation of the procedure. A careful history including demographic data like age, socioeconomic status, education, parity, age at marriage of the patient, was taken. General examination and systemic examination was done. Information is noted on pretested performa.

Prepared PAP smear slides were received fixed in 95% ethyl alcohol and ether. All the women were subjected to colposcopy and cervical biopsy. Biopsy specimens were received in 10% formalin fixative. The prepared PAP smears slides were then stained according to the conventional PAP technique and examined under a light microscope. The cytological interpretation of

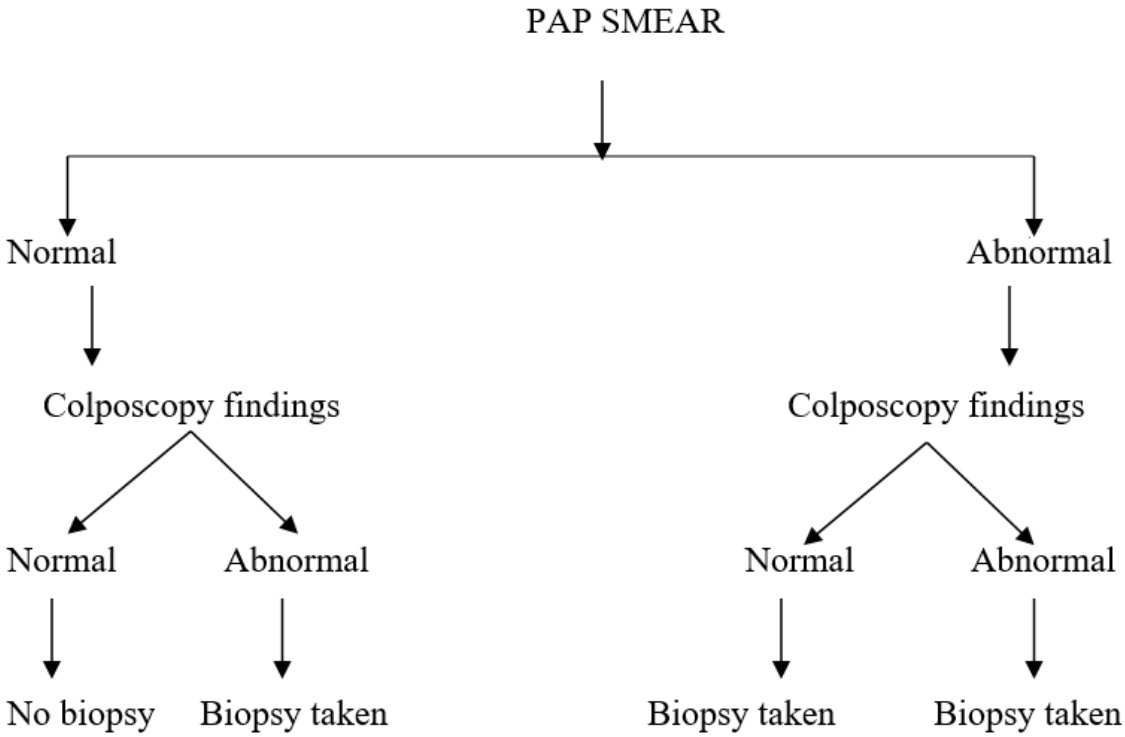
the smears was made according to the Bethesda system 2014.

Colposcopy-directed biopsies were processed, histopathological slides prepared and stained with hematoxylin and eosin and examined under a light microscope. Biopsy results were categorized as chronic cervicitis, cervical intraepithelial neoplasia I (CIN I), CIN II, CIN III, carcinoma in situ, squamous cell carcinoma (SCC) and adenocarcinoma according to WHO.

Statistical analysis

- Formulae used for calculation of efficacy
- Sensitivity= TP/TP + FN.
- Specificity= TN/ TN+FP.
- Positive predictive value= TP/TP+FP.
- Negative predictive value= TP/TP+FN.
- Accuracy= TP+TN/ Total.

Where, TP is true positive, TN is true negative, FP is false positive and FN is false negative.



Results

In the present study, women attending gynecology outpatient department had PAP smears were subjected to colposcopy and directed biopsy. The results of histopathology were compared and analyzed.

Total of 945 PAP smears were taken from june 2017 to June 2018, which is the time period of our study. Out of these 100 (10.5%) patients had also colposcopy and directed biopsies taken which were included in our study. Colposcopy findings and colposcopic-directed biopsy were received from the Department of Obstetrics and Gynecology and histopathological examination was done .

The peak age group was 40-55 years out of which 59% were menopausal cases. In our study the most common presenting complaint was white discharge per vaginum seen in (48%) Cases while 09% cases presented with complaints of post menopausal bleeding .

Colposcopic findings ware normal in 20% cases , while presence of acetowhite areas was the most common abnormal colposcopic finding seen in 48% cases. (table 1)

On histopathological report , CIN was found in 33% cases , CIN II and CINII in respectively 09% and06% cases . Histopathology showed features of chronic

cervicitis in 45 % cases. (table 2)

Table 3 depicts the correlation of PAP smears along with Colposcopic findings , out of which NILM accounted for 62% cases on pap smears most of which were either normal on colposcopy or showed acetowhite areas19% and 28% respectively

On correlation of PAP smears and histopathology 62% cases were negative on PAP smear while 38% were variously positive . 4 cases of squamous cell carcinoma on PAP smears were confirmed as invasive squamous cell carcinoma on histopathology (100%)

Comparing the PAP smear screening result with the final histopathological diagnosis and putting it to statistical evaluation , out of 38 cytology positive smears 37 (97.3%) were also positive on histopathology , while 1 case was false positive . 62 Cytology negative cases were seen in the study out of which 44 were also negative on biopsy while there were 18 false negative cases on PAP smear. (Table 4)

Table 5 shows the sensitivity and specificity of PAP smear as calculated from the present study and using the stastical formulae already defined . Pap smear had a sensitivity of 67.27% with a 97.3% positive predictive value .

The mean age of women in Our study was 35 years. This corresponds to 34.5, 36 and 36 in studies done by Pandey et al, Goel et al, Durdi G et al respectively.3-5

The mean parity of women in Our study was 3. This corresponds to 2.7, 2 and 3 in studies done by Goel et al, Durdi G et al and Ashmita D et al respectively. 4-6

In our study the PPV of PAP smears was calculated to be 97.3% while this had a NPV of 70.9% . This was found to be comparable to earlier studies (Table 6)

Pap smear had an accuracy of 81% in the present study , while similar studies done earlier had an accuracy of 80.5% and 80% Chaudhary et al ([7]) and Mallur et al([8]).

Table 1: Distribution of cases according to colposcopic findings

Colposcopic findings	Number of cases	Percentage
Normal	20	20
Acetowhite area	48	48
Punctations	16	16
Mosaic pattern	16	16
TOTAL	100	

Table 2 : Histopathological findings

Histopathological Findings	Number of cases	Percentage
Chronic cervicitis	45	45
CIN I	33	33
CIN II	09	09
CIN III	06	06
CIS	01	01
SCC	04	04
Adenocarcinoma	02	02
Total	100	100

Table 3 Correlation of PAP smear and Colposcopic findings PAP SMEAR COLPOSCOPIC FINDINGS

	Normal	Acetowhite area	Mosaic	Puncta-tions	Total
NILM	19	28	02	13	62
ASCUS	-	02	02	01	05
LSIL	01	12	04	02	19
HSIL	-	02	06	-	08
SCC	-	02	02	-	04
AGUS-U	-	01	-	-	01
AGUS-H	-	01	-	-	01
TOTAL	20	48	16	16	100

Table 4 Comparison of PAP smear and histopathology

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Histopathology	POSITIVE	NEGATIVE	TOTAL
PAP smear			
Positive	37	01	38
Negative	18	44	62
Total	55	45	10

Table 5: Sensitivity and specificity of PAP smear

Sensitivity	TP/TP+FN	67.27%
Specificity	TN/TN+FP	97.7%
PPV	TP/TP+FP	97.3%
NPV	TN/TN+FN	70.9%
Accuracy	TP+TN/TP+TN+FP+FN	81%

PAP: Papanicolaou, PPV: Positive predictive value, NPV: Negative predictive value

Table 6: On comparison with other studies the following results were obtained

Study	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Present study)	67.27%	97.7%	97.3%	70.9%
Chaudhary *et al.*(7)	79.37	81.02	65.79	89.52
Ashmita *et al(6)*	90.24	72.73	66.6	86.54
Mallur *et al.*(8)	80	81.54	66.67	89.83
Goyal *et al.*(4)	86	40.5	66.18	66.18

PPV: Positive predictive value, NPV: Negative predictive value

Conclusion

Cervical cancer is one of the preventable and highly curable disease when diagnosed in early stages. Early diagnosis of CIN and invasive cervical cancer in the adult women is a desirable goal. CIN lesion and early invasive cancer are asymptomatic. So, it is important to develop an accurate screening tool to detect the disease in an early stage when it is amenable to treatment.

In countries like India, Pap smear cytology, being a less expensive procedure, is used for screening of

cervical cancer. Findings in this prospective study showed that colposcopy is definitely more sensitive than the Papanicolaou smear as a screening tool for CIN. But the Papanicolaou smear was, however, more specific as a screening tool for CIN than colposcopy. Colposcopy by magnifying 40 times helps in determining the appropriate site of cervical biopsy.

Hence, the accuracy of detection of cervical abnormalities is higher when cytology, colposcopy and colposcopic directed cervical biopsy are used complementarily in the evaluation of women with unhealthy cervix .

Colposcopy and cytology are not competitive method, but complementary to each other. Best result in early detection of pre-invasive carcinomas could be obtained by combined use of cytology and colposcopic directed biopsy.

The PAP smear screening should be carried out in all women of reproductive and menopausal age group

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Ethical approval: The study was approved by the Institutional Ethics Committee

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