Original Article

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Correlation of Pap Smear and Colposcopy in Relation to Histopathological Findings in Detection of Premalignant Lesions of Cervix in A Tertiary Care Centre

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Abstract

Objective: Correlation of papanicolaou (PAP) smear and colposcopy in the detection of premalignant lesions of cervix.

Materials and Methods: A prospective observational study was conducted in a tertiary care referral institute in 100 symptomatic, sexually active women of 20-65 years. PAP smears were performed by the conventional method and colposcopy was done for all 100 women who came with complaints of white discharge per vagina, intermenstrual, or postcoital bleeding, etc. Final correlation of the PAP smear and colposcopy were based on histopathology reports.

Results: In cytology and colposcopy-directed biopsy sensitivity is 65.38%, specificity is 95.83%. Positive predictive value 94.4%, negative predictive value 71.8% and accuracy are 80%.

Conclusion: In the present study, incidence of cervical intraepithelial neoplasia I (CIN I) was 28%, CIN II 11%, CIN III 4%, carcinoma *in situ* 2%, squamous cell carcinoma 5%, and adenocarcinoma 2%. This emphasizes the use of all 3 methods PAP cytology (conventional method), colposcopy, and histology is complementary to each other and helps to reduce false negative cases.

Key words: Adenocarcinoma, Colposcopy, Histopathology, Papanicolaou cytology, Squamous cell carcinoma

INTRODUCTION

According to the World Health Organization (WHO), cervical cancer is the second most common type of cancer among women's.[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 pre-invasive lesion is effective.[1] It has been well-established that well-organized screening by conventional cytology has substantially reduced the incidence of morbidity and mortality from cervical cancer in developed countries.[1]

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In developed countries such as the USA, 85% of women had at least one papanicolaou (PAP) test through their lifetime, but this rate is only 5% in the developing countries.[4] The goal of screening of carcinoma of cervix is to diagnose and treat carcinoma cervix in early pre-invasive states make the disease ideal for screening procedures.[1] The PAP smear is a simple, safe, non-invasive and effective method for detection of precancerous and noncancerous changes in the cervix and vagina.[5] In 1925 Hinsellman 1st hypothesized visualization of cervical epithelium under the magnification. Colposcopy provides a unique method to study the benign and premalignant lesions.[5] It is a simple noninvasive procedure which helps in determining the

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location, size and extent of abnormal cervical lesions and serves for detecting the site for biopsies. Colposcopy is complementary to cytology.[6] Cytology (PAP smear) is the lab method while the colposcopy is the clinical method of detection.[6] The final diagnosis must be made on histopathological examination.[6] PAP smear were interpreted according to The New Bethesda System 2014.[7] Histopathological slides were interpreted according to the WHO classification 2003.[8]

The aim of this study was to find a correlation of PAP smear and colposcopy in detecting the premalignant lesions of the cervix.

MATERIALS AND METHODS

This prospective study was conducted in the Department of Pathology Pt. J. N. M. Medical College, Raipur, Chhattisgarh, India, and Dr. Bhim Rao Ambedkar Memorial Hospital, Raipur, Chhattisgarh, India, from 15th July 2014 to 15th June 2015 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 Gynecology, Dr. Bhim Rao Ambedkar Memorial Hospital, Raipur, Chhattisgarh, India.

Inclusion Criteria

- Sexually active women of age group of 20-65 years
- Abnormal vaginal discharge, abdominal pain, irregular menstrual bleeding, post-menopausal bleeding, postcoital bleeding, prolapse, and burning micturition.

Exclusion Criteria

- Women >65 years and <20 years, women with frank cancer, pregnant women, and post total hysterectomy patients
- Unsatisfactory smears for evaluation.

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 proforma.

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 was carried out by for calculating sensitivity, specificity and positive and negative predictive value (NPV) of PAP smear, colposcopy, and histopathological examination.

RESULTS

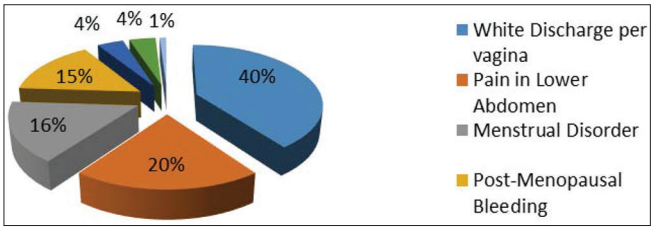
In the present study, women attending gynecology outpatient department had PAP smears were subjected to colposcopy and directed biopsy. The results of histopathology were compared and analyzed.

Total of 874 PAP smears were taken from 15th July 2014 to 15th June 2015, which is the time period of our study. Out of these 100 (11.4%) patients had abnormal PAP smear were interpreted. 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 between 41 and 50 years, 57% were menopausal cases, 93% women were from rural areas, and 20% were literate (Figure 1-6).

In Graph 1, it shows the most common presenting complaint was white discharge per vagina in 40% cases.

In Table 1, it shows the most common finding was acetowhite area in 43% cases under colposcopy.

In Graph 2, it shows that 64% PAP smears were interpreted as negative for intraepithelial lesion or malignancy (NILM).



Graph 1: Distribution of cases in relation to presenting complaint

Graph 3 depicts that out of 64 cases of NILM, 60 cases are of inflammatory smear, 2 are of trichomonas vaginalis, 1 of candida albicans and 1 of bacterial vaginosis.

In Table 2, it shows the most common histopathological finding was chronic cervicitis which accounts for 48% as compared to other findings.

In Table 3, it was seen that the most common biopsy result in inflammatory smear was chronic cervicitis which accounts for 46%.

Table 4 depicts the correlation of the PAP smear along with colposcopic finding out of which NILM accounted for 65%.

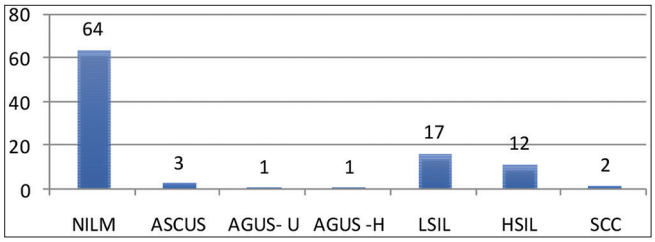
In Table 5, it was shown the correlation between histopathological findings with colposcopic finding.

Table 6 showed about the correlation between PAP smear and histopathological diagnosis in which positive accounted for 36% and negative for 64%.

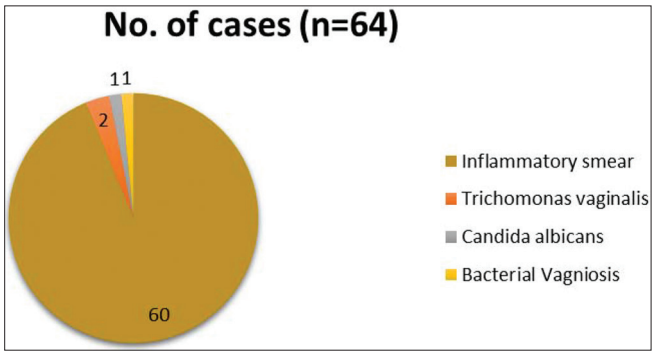
Table 7 depicts about sensitivity and specificity of PAP smears along with the positive predictive value (PPV), NPV and accuracy.

DISCUSSION

In the present study, the maximum number of cases were in the age group of 41-50 years (50%), similarly reported by Sharma *et al.*,[9] and by Algotar *et al.*[10] In study of Goyal *et al.*,[11] the mean age was 39.38 years.



Graph 2: Papanicolaou smear interpretation by the 2014 Bethesda system



Graph 3: Pattern of negative for intraepithelial lesion

Table 1: Distribution of cases according to colposcopic finding

Colposcopic finding	Number of cases	Percentage
Normal	27	27
Acetowhite area	43	43
Punctation	16	16
Mosaic pattern	14	14
Total	100	

Table 2: Histopathological findings

Histopathological findings	Number of cases	Percentage
Chronic cervicitis	48	48
CIN I	28	28
CIN II	11	11
CIN III	4	4
CIS	2	2
SCC	5	5
Adenocarcinoma	2	2
Total	100	100

CIN: Cervical intraepithelial neoplasia, CIS: Carcinoma *in situ*, SCC: Squamous cell carcinoma

Table 3: Correlation of PAP smear and histopathological diagnosis

PAP smear	Histopathological finding							
	CC	CIN I	CIN II	CIN III	CIS	SCC	Adenocarcinoma	Total
NILM	46	11	4	1		2		64
ASCUS		3						3
LSIL	1	14	2					17
HSIL	1		5	3	2	1		12
SCC						2		2
AGUS-U							1	1
AGUS-H							1	1
Total	48	28	11	4	2	5	2	100

PAP: Papanicolaou, NILM: Negative for intraepithelial lesion or malignancy, AGUS: Atypical glandular cells of undermined significance, CC: Chronic cervicitis, ASCUS: Atypical squamous cells of undetermined significance, LSIL: Low-grade squamous intraepithelial lesion, HSIL: High-grade squamous intraepithelial lesion

Table 4: Correlation of PAP smear and colposcopic finding

PAP smear	Colposcopic finding				
	Normal	ACW	Mosaic	Punctation	Total (%)
NILM	25	22	04	14	65
ASCUS		01	01		02
LSIL	02	10	03	02	17
HSIL		08	04		12
SCC			02		02
AGUS-U		01			01
AGUS-H		01			01
Total	27	43	14	16	100

PAP: Papanicolaou, NILM: Negative for intraepithelial lesion or malignancy, AGUS: Atypical glandular cells of undermined significance, ASCUS: Atypical squamous cells of undetermined significance, SCC: Squamous cell carcinoma, HSIL: High-grade squamous intraepithelial lesion, LSIL: Low-grade squamous intraepithelial lesion

Table 5: Correlation between histopathological finding with colposcopic finding

Histopathological findings	Colposcopic finding				
	Normal	ACW	Mosaic pattern	Punctuation	Total
Chronic cervicitis	25	17	02	09	51
CIN I	04	12	04	06	26
CIN II		07	03	01	11
CIN III		03			03
CIS			02		02
SCC			03		05
Adenocarcinoma		02			02
Total	29	43	14	16	100

CIN: Cervical intraepithelial neoplasia, CIS: Carcinoma *in situ*, SCC: Squamous cell carcinoma

Table 6: Correlation between PAP smear and histopathological diagnosis

Histopathology	Positive	Negative	Total
PAP smear			
Positive	34	02	36
Negative	18	46	64
Total	52	48	100

PAP: Papanicolaou

Table 7: Sensitivity and specificity of PAP smear

Sensitivity	TP/TP+FN	65.38%
Specificity	TN/TN+FP	95.83%
PPV	TP/TP+FP	94.44%
NPV	TN/TN+FN	71.86%
Accuracy	TP+TN/TP+TN+FP+FN	80.00%

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

In present study white discharge per vaginum (40%) was most common complaint similarly reported by Chaudhary *et al.*,[6] 39%.

In present study, the most common colposcopy finding was acetowhite area (43%), similar study reported by Krishnegowda and Veena[12] 22%.

On PAP smear 64% were reported NILM, and frank malignancy was reported as 2% cases, low-grade squamous intraepithelial lesion and high-grade squamous intraepithelial lesion was reported 17% and 12%, respectively (Graph 2 and Table 8).

A maximum number of cases on histopathological examination were those of infection among them majority had chronic cerivicitis (48%). Cervical Intraepithelial lesions were seen in 43 cases. CIN I were seen in 28 cases and CIN II and CIN III were reported 15%, and SCC and adenocarcinoma were reported 2% cases, respectively. Similar study reported by Bodal and Brar[18] reported adenocarcinoma in 2% cases only (Tables 9 and 10).

Table 8: On comparison with other studies the following results were obtained

Study	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Present study (2015)	65.38	95.83	94.44	80
Chaudhary *et al.*[6]	79.37	81.02	65.79	89.52
Ashmita *et al.*[13]	90.24	72.73	66.6	86.54
Mallur *et al.*[14]	80	81.54	66.67	89.83
Pimple *et al.*[15]	74.5	92.9		
Goyal *et al.*[10]	86	40.5	66.18	66.18
Kushtagi *et al.*[16]	78			

PPV: Positive predictive value, NPV: Negative predictive value

Table 9: Accuracy of PAP smear

Study	Accuracy (%)
Present study (2015)	80
Chaudhary *et al.*[6]	80.5
Ashmita *et al.*[13]	86.54
Mallur *et al.*[14]	80
Boicea *et al.*[17]	98.3

PAP: Papanicolaou

Table 10: Correlation between PAP smear and colposcopy on comparison with other studies

Study	ASCUS (%)	AGUS (%)	LSIL (%)	HSIL (%)	SCC (%)
Present (2015)	3 (3.0)	2 (2.0)	17 (17)	12 (12)	2 (2.0)
Goyal *et al.*[10]	9 (3.0)	1 (0.33)	17 (5.67)	1 (0.33)	
Chaudhary *et al.*[6]	17 (8.5)		10 (5.0)	5 (2.5)	2 (1.0)
Sharma *et al.*[9]	1 (0.04)		214 (9.28)	5 (0.21)	

PAP: Papanicolaou, ASCUS: Atypical squamous cells of undetermined significance, SCC: Squamous cell carcinoma, AGUS: Atypical glandular cells of undermined significance, LSIL: Low-grade squamous intraepithelial lesion, HSIL: High-grade squamous intraepithelial lesion

14% cases were malignant in PAP smear turned out to malignant in histopathology showing strong correlation between PAP smear and histopathology ($P < 0.0001$) by Pearson correlation coefficient factor.

Some of the cases were obscured by blood and inflammation which were missed on PAP smear but proved to be malignant on histopathology.

Table 8 shows sensitivity, specificity, PPV and NPV compared with other studies.

Table 9 shows accuracy of PAP smear compared with other studies.

Table 10 shows correlation between PAP smear and colposcopy on comparison with other studies.

CONCLUSION

The result on current study support, PAP smear demonstrates of premalignant and malignant lesions,

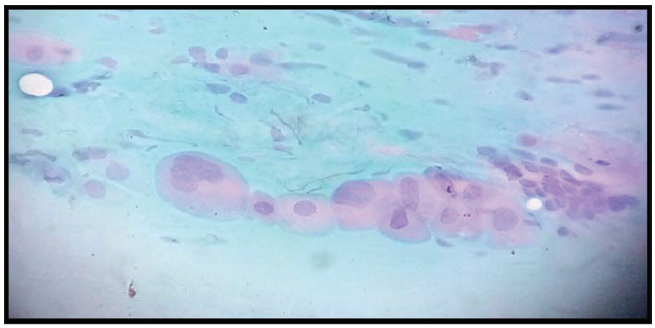


Figure 1: Photomicrograph of papanicolaou (PAP) smear of a case of high grade squamous intraepithelial lesion showing cytoplasm reduced cell borders may be angular or rounded, disproportionate nuclear enlargement, irregular nuclear membrane, abnormal chromatin pattern and tumor giant cell (PAP, ×400)

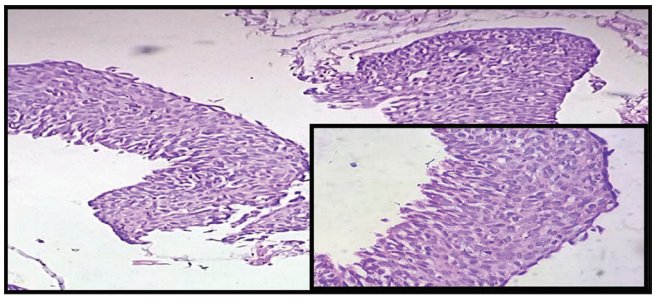


Figure 2: Photomicrograph of histopathology section of a case cervical intraepithelial neoplasia III showing complete replacement of normal squamous cells by crowded abnormal cells with marked nuclear pleomorphism, hyperchromasia, and loss of polarity. No evidence of cell maturation can be seen and the basement membrane is intact (H and E ×100 and ×400)

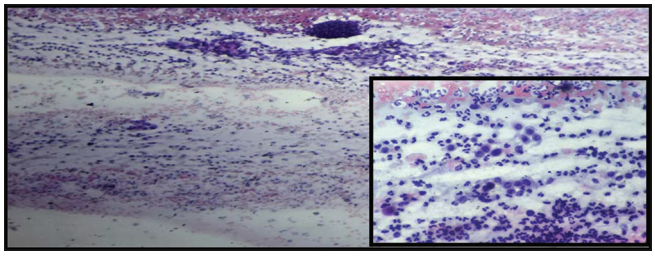


Figure 3: Photomicrograph of papanicolaou (PAP) smear of a case of squamous cell carcinoma showing variation in size and shape dyskaryotic cells with scanty cytoplasm. The chromatin is abnormally clumped (PAP, ×100 and ×400)

whereas colposcopy shows the exact site for biopsy for histopathological diagnosis and for further management. 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 at least once in a lifetime.

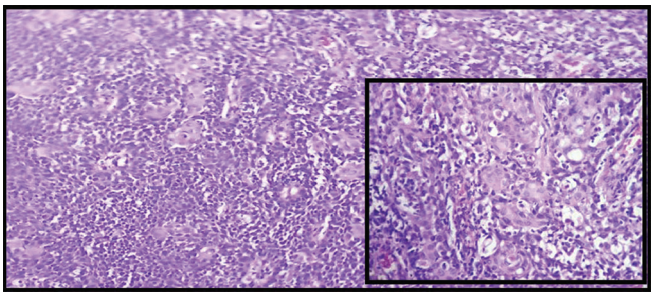


Figure 4: Photomicrograph of histopathology section of a case of squamous cell carcinoma (SCC) showing nests of SCC are invading downward and undermining the mucosa (H and E, ×100 and ×400)

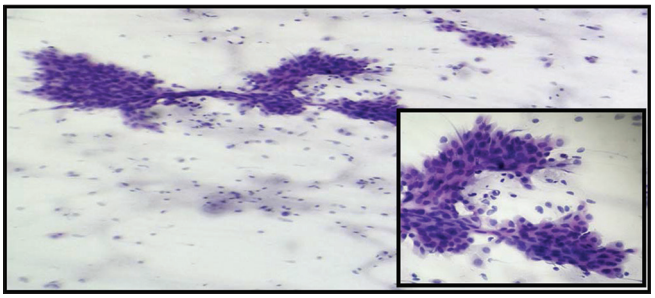


Figure 5: Photomicrograph of papanicolaou (PAP) smear of a case of atypical glandular cells of undermined significance-H showing the individual atypical endocervical cells are hyperchromatic with coarsely clumped chromatin. They show the characteristic feathering of the nuclei at the edge of the cluster (PAP, ×100 and ×400)

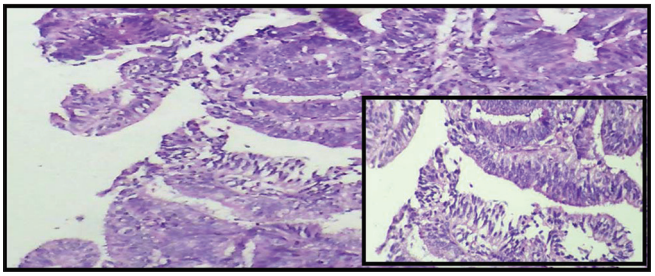


Figure 6: Photomicrograph of histopathology section of a case of adenocarcinoma showing the lining epithelium is stratified and crowded, and it consists of moderately enlarged nuclei with coarse chromatin (H and E, ×100 and ×400)

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