



A Study on Diagnostic Accuracy of Cervical Pap Smear by Correlating with Histopathology in a Tertiary Care Centre

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ABSTRACT

Objective: Analysis of various lesions detected on Cervical Pap smears and correlate it with histopathology to detect the diagnostic accuracy of Pap smears in detection of cervical lesions.

Methodology: The present study is a prospective study conducted from December 2015 to May 2017 for a period of 18 months which included 83 cases. All these patients underwent screening procedure with cervical smears and were directed for colposcopic guided biopsy.

Results: In the present study Pap smears showed sensitivity of 96.42%, specificity of 70.37% and diagnostic accuracy of 87.95 %.

Conclusion: Pap smear being minimally invasive showed significant correlation with Colposcopic directed biopsy. Pap smear still remains ideal screening procedure for early detection of cervical lesions.

Keywords: ?Cervical Pap Smear, Sensitivity, Specificity, Diagnostic Accuracy

Introduction

Cervical cancer is the second most common cancer in females worldwide and major cause of morbidity and mortality.^[1] Cervical cancer is preventable and cervical screening in many ways is an ideal screening test.^[2] Biopsy to confirm the presence of cervical cancer has long been used, but the more recent use of colposcopic directed biopsy on patients with abnormal Pap smear has allowed the recognition and treatment of cervical lesion at much earlier stage.^[3] Ideally, all patients with abnormal Pap findings should be subjected for colposcopy.^[4] Colposcopy used with Pap smear complement each other in detecting cervical lesion at earliest followed by histopathology which forms gold standard in confirming the diagnosis.^[5]

Hence, this study was undertaken. The objective of this study was analysis of the cervical pap smears for various abnormalities of cervix and co-relating cytology with histopathology.

Methodology

This is a hospital based 18 months prospective study conducted from December 2015 to May 2017 in S. Nijalingappa Medical College, Bagalkot, Karnataka after taking approval from Institutional Ethical Committee. 83 cases attending the hospital with the complaints of white discharge per vagina, pain abdomen and other gynecological complaints were included in the study. The following were the inclusion criteria :1) Sexually active women in reproductive age group (20-70 years).2) Women with symptoms of white discharge per vagina, post coital,

intermenstrual bleeding and post menopausal bleeding.3) Women who had undergone cytological screening of cervix. The following were the exclusion criteria : 1) Known case of carcinoma cervix.2) Patients undergoing chemotherapy and radiotherapy3) 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 and 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 was taken. Colposcopic directed biopsy specimens were received in 10% formalin fixative. The prepared Pap smear 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 for calculating sensitivity, specificity and positive and negative predictive value of Pap smear by correlating with histopathological examination.



Results

In the prospective study conducted from December 2015 to May 2017 for a period of 18 months 83 cases were analyzed and results are as shown in Tables 1 to 5.

Discussion

Premalignant and Malignant cervical lesions can be detected in Pap smears. Low grade squamous intraepithelial lesion (Koilocytosis or flat condyloma or CIN I) represents

Table 1: Presenting complaints of patients in present study.

Presenting complaints	No. of cases	Percentage
Pain abdomen	20	24.2
White discharge per vagina	51	61.4
Pain abdomen and white discharge per vagina	02	2.4
Irregular bleeding	08	9.6
Itching over genitals	02	2.4
Total	83	100

Table 2: Cytological Interpretation in present study as per Bethesda System 2014 classification.

Bethesda 2014	No. of cases	Percentage
NILM	21	25.30
ASCUS	17	20.48
ASC-H	05	6.02
LSIL	22	26.50
HSIL	09	10.84
SCC	05	6.02
AGC	04	4.81
Total	83	100

Table 3: Histopathological diagnosis of the cases.

Histopathological diagnosis	No. of cases	Percentage
Chronic cervicitis	27	32.53
CIN I	27	32.53
CIN II	14	16.86
CIN III	04	4.81
Squamous cell carcinoma (Well differentiated)	05	6.02
Squamous cell carcinoma (Moderately differentiated)	04	4.81
Squamous cell carcinoma (Poorly differentiated)	02	2.40
Total	83	100.00

Table 4: Co-relation of Cervical cytology with histopathologic diagnosis.

Cytology	Histopathology				
	Chronic cervicitis	CIN I	CIN II & CIN III	SCC	TOTAL
NILM	19	02	00	00	21
ASCUS	03	11	03	00	17
ASC-H	00	01	02	02	05
AGC	03	00	01	00	04
LSIL	02	12	07	01	22
HSIL	00	01	05	03	09
SCC	00	00	00	05	05
Total	27	27	18	11	83

Table 5: Comparison of statistical parameters of Pap smears:

Studies	Sensitivity	Specificity	PPV	NPV	Diagnostic accuracy
Present study (2017)	96.42%	70.37%	87.09%	90.40%	87.95%
Chaudhary et al (2016)	25.40%	99.27%	94.12%	74.32%	80.5%
Ashmita et al (2013)	19.51%	83.33%	80.00%	23.26%	86.54%
Malur et al (2009)	41.66%	81.2%	86.21%	78.26%	80%
Jain et al (2010)	78%	91.1%	26.9%	11.3%	73.2%

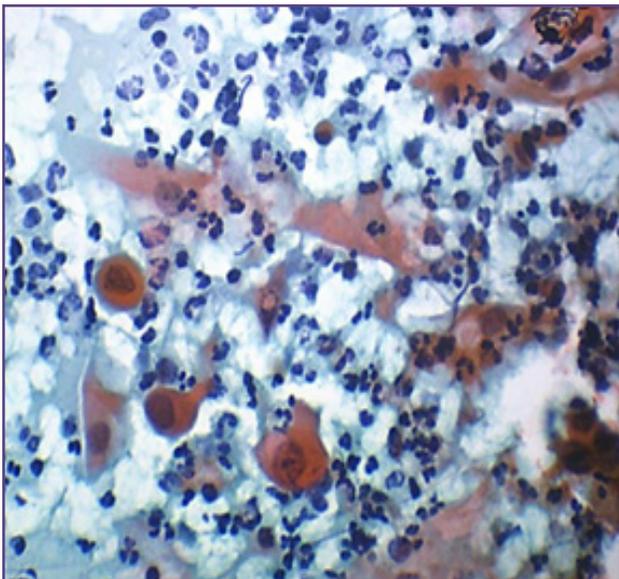


Fig. 1: High grade squamous Intraepithelial lesion cells with enlarged, hyperchromatic nuclei and irregular nuclear outline, (PAP stain, 400 X).

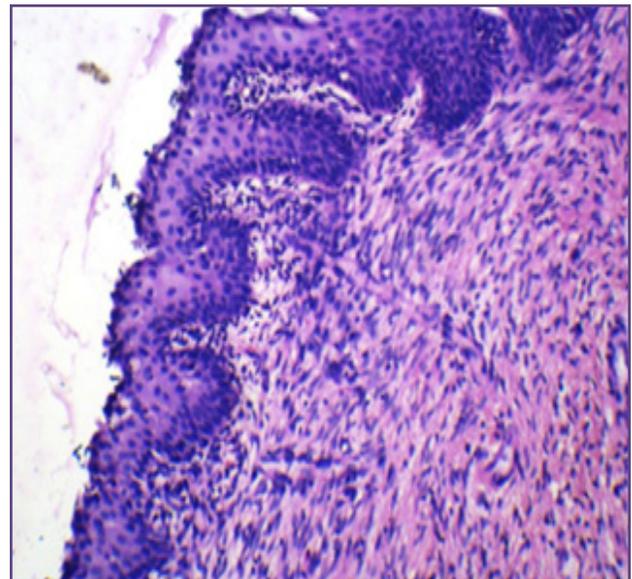


Fig. 2 :Section showing Chronic cervicitis with Severe dysplasia - CIN III, (H & E Stain , 100 X).

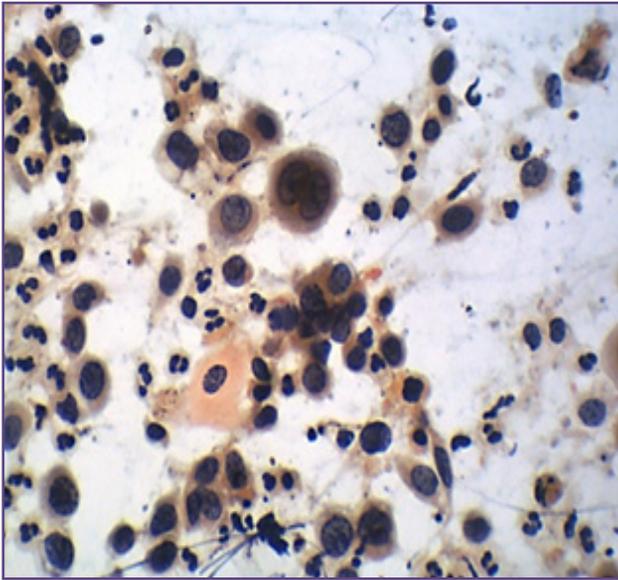


Fig. 3 : Pap smear of cervix showing Invasive squamous cell carcinoma .(PAP Stain, 400 X).

the clinical and morphological manifestation of productive HPV infection. It is characterized by proliferation of basal/parabasal like cells that may be minimal but at most extends no more than one-third of the way up the epithelium. Mitotic activity is confined to this zone. Upper three –quarters to two thirds of the epithelium , the cells differentiate and gain cytoplasm however nuclear enlargement persists with nuclear hyperchromasia and nuclear membrane irregularities. Often there is development of a well defined halo like vacuole around the nucleus , this change along with cytoplasmic change is termed as koilocytosis, koilocytotic atypia or HPV cytopathic effect.^[6] High-grade squamous Intraepithelial lesions includes CIN II, CIN III. There is proliferation of squamous cells most frequently in the zone of metaplasia and near the squamo-columnar junction. In CIN II there is maturation present in upper half of the epithelium with nuclear atypia persisting to the surface. Nuclear abnormalities are more marked than in CIN I and extend further through the epithelium. Mitotic figures are present and are confined to the basal two-thirds of the epithelium. Abnormal forms may be seen. In CIN III there is maturation which maybe absent or confined to the superficial third of the epithelium. Nuclear abnormalities are marked throughout most of the thickness of the epithelium. Mitotic figures are numerous and are found at all levels of the epithelium. Abnormal mitosis are frequent.^[7]

According to the international Committee on histological Terminology for lesions of the uterine cervix, “ any lesion in which the epithelial formations invade the underlying

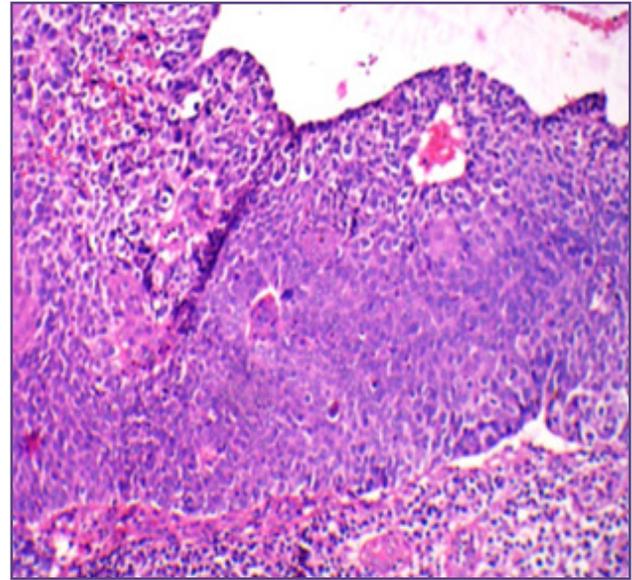


Fig. 4 : Section showing Poorly differentiated invasive squamous cell carcinoma (H & E Stain, 100 X).

stroma by infiltration or destruction is to be classified as invasive carcinoma.” A modification of the Border’s method based on the degree of differentiation is currently the most widely used histologic grading system. According to this method squamous cell carcinoma are graded as well differentiated (grade I), moderately differentiated (grade II) and poorly differentiated (grade III). Most common is moderately differentiated squamous cell carcinoma.^[7]

Out of 83 cases most common age group which was affected was found to be in the range of 31 – 40 years, similar to the study conducted by Algotar K et al.^[8] The age group in which carcinoma cervix was reported was of higher age group. Most common presenting complaint in our study was white discharge per vagina similar to the Chaudhary et al. ^[1] Other complaints being pain abdomen and irregular bleeding.

Cervical smear analysis showed higher number of Low grade intraepithelial lesion (LSIL) cases comprising 26.50 % of case, followed by Negative for intraepithelial malignancy (NILM) accounting for 25.30 % cases. We reported Atypical squamous cells of undetermined significance (ASCUS) in 20.48 % cases, Atypical squamous cells cannot exclude an HSIL (A SC-H) in 6.02 % cases, High grade squamous intraepithelial lesion (HSIL) in 10.84 % , Squamous cell carcinoma (SCC) in 6.02 % cases and Atypical glandular cells (AGC) in 4.81 % of cases. On Histopathological examination chronic cervicitis was found in 32.53 % cases, CIN I in 32.53 % , CIN II in 16.86 % , CIN III in 4.81 % cases and 11 cases were confirmed to have malignancy.

Cervical smear analysis showed higher number of Low grade squamous intraepithelial lesion (LSIL) cases comprising 26.50 % of cases with the cells in singles or in clusters with large cells having fairly abundant mature well defined cytoplasm with nuclear enlargement of more than 3 times the area of normal intermediate nuclei with coarsely granular chromatin with some cells having binucleation inconspicuous nucleoli and koilocytosis, followed by Negative for intraepithelial malignancy (NILM) with the smears displaying normal cellular elements that is superficial cells with pyknotic nucleus abundant eosinophilic cytoplasm, few intermediate cells having slightly larger nuclei compared to the superficial cells and abundant amount of cyanophilic cytoplasm accounting for 25.30 % cases. We reported Atypical squamous cells of undetermined significance (ASCUS) in the smears showing few cells with features of LSIL and cellular changes with nuclear enlargement 2.5-3 times of normal intermediate cell, slightly increased ratio of nuclear to cytoplasmic area, and minimal nuclear hyperchromasia, and irregularity in chromatin distribution and nuclear membrane abnormality, with these features ASCUS was diagnosed in 20.48 % cases. Atypical squamous cells cannot exclude an HSIL (ASC-H) was interpreted in the smears with the cells in singles or in small groups and individual cells were of the size of metaplastic cells with the nuclei of about 1.5 – 2.5 times that of normal cells and increased nuclear to cytoplasmic ratio was approximating of that of High grade squamous intraepithelial lesion (HSIL) in 6.02 % cases. HSIL with smears showing small and less mature cells, scant cytoplasm either as single or in syncytial aggregates with high nuclear cytoplasmic ratio, nuclear membrane irregularity and hyperchromasia coarsely granular evenly distributed chromatin was found in 10.84 % , Squamous cell carcinoma (SCC) was interpreted in 6.02 % cases with the features of isolated cells and few clusters with marked variation in cellular size and shape with dense orangeophilic cytoplasm and increased nuclear cytoplasmic ratio, irregular nuclear membrane having coarsely granular irregularly distributed chromatin with macronucleoli with few cases associated with hyperkeratosis and parakeratosis. and smears with Atypical glandular cells (AGC) showed crowded sheets of cells with distinct cell border having abundant cytoplasm but increased nuclear to cytoplasmic ratio and enlarged nucleus up to 3 – 5 times of normal endocervical nuclei with mild nuclear hyperchromasia mild chromatin irregularity and some cells showed nucleoli in 4.81 % of cases. On Histopathological examination chronic cervicitis was found in 32.53 % cases, CIN I in 32.53 %, CIN II in 16.86

%, CIN III in 4.81 % cases and 11 cases were confirmed to have malignancy. As with the other studies, the percentage of carcinoma was lower than the percentage of dysplasia in present study. With the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of 96.42%, 70.37%, 87.09%, 90.47% and 87.95% respectively Pap smear definitely showed a significant correlation with gold standard histopathology, which was comparable with the other studies Chaudhary et al^[1], Ashmita et al^[9], Malur et al^[10] and Jain et al^[11] as shown in Table 5.

Conclusion

Pap smear is an ideal screening procedure being minimally invasive, cost effective and accurate enough to demonstrate pre-malignant and malignant lesion of cervix. Complimentary to the Pap smears is the colposcopy which helps in visualization and aid us in identifying exact site for biopsy to be taken for histopathological diagnosis. With this study we conclude that there is definitely a significant correlation between Pap smear and histopathology and hence forth continues to be ideal procedure to identify the cervical lesion and initiate the therapy.

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