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Pap Smear and Histopathological Correlation: is it Worth Screening Women for Cervical Lesions?

Medical Science

KEYWORDS :

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ABSTRACT

BACKGROUND:

Conventional cervical cytology is most commonly used cervical cancer screening test in the world . Squamous intraepithelial lesion (SIL) and cervical cancer are a major health concern worldwide.

AIMS:

- *To classify cervical lesions into malignant and benign group.*
- *To correlate cytological with histopathological findings.*

MATERIALS AND METHODS:

- *100 cases of pap smears and cervical biopsies (including hysterectomy specimens) were included in the study. The patients in whom both pap smear and cervical biopsy was available ,were taken into the study.*
- *The cyotological interpretation of smears was done according to the NEW 2001 BETHESDA system.*

RESULTS and CONCLUSION:

Our srudy showed overall sensitivity 60%, specificity 93.75% and accuracy 84.3% for abnormal pap smear when compared with gold standard histological diagnosis. Study shows good cyto-histological correlation for abnormal test results. Regular screening should be adviced for the early detection of cervical carcinoma.

INTRODUCTION:

Carcinoma cervix ranks third amongst the commonest malignancies for women. The aim of cervical screening by cytology using Papanicolaou (Pap) stain is performed to detect precancerous, cancerous and non-cancerous changes in the cervix. The incidence of the carcinoma cervix in the developed countries is 90,000 and in the developing countries is 340,000 per year.[1]

According to estimates an average woman under 40yrs of age has 2% chance of developing cervical carcinoma. Cervical carcinoma does not arise suddenly from normal epithelium but is presented by a spectrum of intraepithelial neoplastic changes that are precancerous and also known by the term cervical intraepithelial neoplasia, if these lesions were left untreated; up to one third of them would develop into carcinoma.1

Cervical cytological screening using PAP stain is designed to detect over 90% of cytological abnormalities. It has also been established that most cervical cancers can be diagnosed at the preinvasive stage with adequate and repetitive cytological screening.

The epithelium lining the cervix is constantly under the influence especially at the squamocolumnar transformation zone of hormone ,bacteria and other factors.It responds by altering the number ,maturation and differentiation of its cells ,in an attempt to sustain and minimise the damage by changing it into a more suitable type.

Exfoliative cytology deals with the study of cells spontaneously shed from the skin, mucous and serous membranes. Cytodiagnostics of the vaginal-cervical-endocervical (VCE) smear by volume is the largest in exfoliative cytology, since it is done for both the healthy and sick women. These smears include epithelial and non epithelial cells . In the universal effort for combating cervical cancer are available several possible methods, including measures of primary and secondary prevention. These measures could bring out only modest effects on the incidence and mortality of cervical cancer with the only exception being organized screening based on the use of cytological examinations of the cervix (Pap test), which proved to be very useful in reducing the incidence and mortality of cervical cancer in countries where it is implemented.[2]

The definition of Cervical Intraepithelial Neoplasia includes a spectrum of intraepithelial cellular atypia of mild degree originating at the base of the cervical squamous epithelium or squamous like metaplastic columnar epithelium of cervix to severe degree involving the full thickness of the epithelial lining .The original terms dysplasia and carcinoma in situ was replaced by the new term cervical intraepithelial neoplasia proposed by (WHO) classification in order to stress a continuum of disease. Recently the Bethesda system of terminology has been introduced inorder to sub-classify the lesions into different grades: atypical squamous cells of undetermined significance (ASCUS),high grade and low grade squamous intraepithelial lesions (SIL). [1]

ASCUS show nuclear enlargement 2.5-3 times that of an intermediate squamous cell nucleus,with slight increase in nuclear/cytoplasmic ratio.There may be an occasional binucleation observed.The nuclear outline are generally smooth with rare irregularity and the chromatin distribution within it is even.

Squamous intraepithelial lesions again classified into two types High grade SIL and Low grade SIL.LSIL show nuclear enlargement atleast 3 times that of an intermediate squamous cell nucleus,with moderate increase in nuclear/cytoplasmic ratio. Binucleation is a frequently observed phenomenon.The nuclear outline is slightly irregular and the chromatin distribution within it is even but may be smudged also.

WHO system (Dysplasia terminology)	CIN Terminology	Bethesda Terminology
Mild dysplasia	CIN I	Low grade SIL
Moderate dysplasia	CIN II	High grade SIL
Severe dysplasia	CIN III	High grade SIL
Carcinoma in situ	CIN III	High grade SIL

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Materials and Methods:
This is a prospective study conducted in a tertiary hospital at the department of Pathology. A complete clinical history of the subject was recorded as per the proforma.

The inclusion criteria were: symptomatic patients with normal cervix on clinical examination and symptomatic patients with suspicious cervical lesion. Cases excluded from the study were: pregnant women, patients who have undergone hysterectomy, excessive vaginal bleeding at the time of examination and patients on therapy.

Conventional Pap smears were taken by the gynaecologists at the squamocolumnar junction using Ayer's spatula in clockwise direction for 360°.The endocervical smears were made by rotating the endocervical brush. Two separate smears were made from the squamocolumnar junction and endocervical area on a single glass slide. The smears were immediately fixed in 95% Isopropyl alcohol for 30 minutes.

Biopsy was taken from cervix mainly in cases with epithelial cell abnormality on pap smears and badly eroded cervix, by applying 3% acetic acid (acetowhite areas).They were fixed in 10% formalin, routinely processed and stained with haematoxylin and eosin.

The pap smears were reported by adopting "The revised Bethesda System of Classification (2001 TBS)" and histopathology "WHO classification of tumours of uterine cervix (2003)". The cytological findings were correlated with histopathological findings.

RESULTS:
Table-1: Cytological Diagnosis:

Diagnosis	Distribution (n = 86)	Percentage (%)
Inflammatory	50	58
ASCUS	10	11.6
LSIL	10	11.6
HSIL	4	4.8
SCC	6	7
Unsatisfactory	6	7

Table 1 shows the different cytological diagnosis.The most commonly diagnosed condition was inflammatory lesion covering more than half of the cases (58%). In 10 cases ASCUS was diagnosed. (11.6%). LSIL 11.6%,HSIL 4.8% and malignancy in 7%. 7% smears were reported to be unsatisfactory.

Table-2: Cytological and histopathological correlation:

Cytology patterns on PAP	No. of cases on PAP	Histopathology				
		Non-neoplastic	CIN-I	CIN-II	CIN-III	Malignancy
Inflammatory	50	47	2	-	1	-
ASCUS	10	7	2	1	-	-
LSIL	10	1	7	2	-	-
HSIL	4	-	1	1	1	1
SCC	6	-	-	-	-	6
Unsatisfactory	6	6	-	-	-	-

Table 2 shows cyto histological correlation. LSIL cytology diagnostic category was histologically equivalent to HPV/ mild dysplasia/CIN 1. HSIL category histologically equivalent to moderate and severe dysplasia, CIN 2 and CIN 3, CIS and with features suspicious for invasion according to Bethesda 2001 classification .

Concordance rates for different cytological categories were calculated as below

Table-3: Sensitivity, Specificity, PPV and NPV:

Epithelial Abnormality	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Diagnostic Accuracy (%) [Efficiency]
LSIL	58.3	96.2	70	93.8	91.2
HSIL	33.3	97.6	50	95.5	93.3
Carcinoma	85.7	100	100	98.8	98.9
Overall(for abnormal smears)	60	93.75	51.7	85.7	84.3

Table 3 shows the different statistical values of Pap-smear for different grades of diseases. Diagnostic accuracy was 93.3% for HSIL and 98.9% for malignancy . PPV in HSIL was 50% and was 100% in carcinoma. Pap smear was least sensitive in diagnosing HSIL (33.3%), but specificity (96.2%) and diagnostic accuracy was good (91.2%).

DISCUSSION:
The incidence of cervical carcinoma is incredibly high. 80% of all its cases are attributed to developing countries, because prevention programmes are either non existent or not properly implemented.[2]

It is a well established fact that papsmear had been the most effective cancer screening test ever introduced. This screening test has helped achieve a reduction in the death rate of more than 70% for a prevalent cancer.1

Carcinoma cervix is thoght to be an ideal gynaecological malignancy for screening as it

fulfils both test and disease criteria for screening. As it has a long latent phase, it can be detected as identifiable and treatable premalignant lesions which precede the invasive disease and it is more than worth its cost.3

In this study, 58% of the cases had the cytological diagnosis of benign/ inflammatory and malignancy was present in 7% of the cases. This is comparable to Bodal and Brar in which benign cases were 59% and carcinoma was diagnosed in 10% of the cases. Similar results were seen in Saha and Thapa study in which benign cases were 51.16% and carcinoma was seen in 6.97% cases.3

One of the case diagnosed as severe dysplasia in pap smear turned out to be malignancy which was confirmed by the biopsy.

Comparison of our pap smear study with other studies is shown in table-4 in terms of sensitivity, specificity, efficiency, ppv and npv.

Reports of cytology sensitivity in the study in detecting cervical neoplasia ranged from 50%-98% . Biopsy report is considered as the gold standard provided biopsy is taken from the appropriate site. Pap smear test is found to be inexpensive, non-invasive and closely as sensitive, specific and effective as biopsy however it is said and expected to perform biopsy if any abnormalities are detected in pap smear.

The limitation of the study was short time period of 1.5 years and smaller sample size. Automated liquid based pap cytology test was not performed.

Low sensitivity of the test can be improved by adequate sampling and avoiding technical errors.

Table-4: Comparison of Pap smear values in different studies(%). 4

Study	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Diagnostic Accuracy (%)
Naik et al.,2015	79.4	58.3	86.1	46.6	74.5
Jain et al.,2012	78	26.9	91	11.3	73.2
Saha et al.,2005	76	83.3	86.4	71.4	79.1
Tuon et al.,2002	77	-	74	45	-
Bruce et al.,1996	89.4	64.8	88.9	-	-
Present study	60	93.75	51.7	85.7	84.3

Conclusion:

To conclude, we can say that pap smear can be used to detect most common problem of infection in cervical region causing white discharge. The other important aspect is screening for cancer. Previoudly recommended and proven good test – PAP smear is less invasive and simple procedure to perform. As it is cheap; it is affordable for governments of developing country, NGOs and poor people to detect early onset abnormalities on regular bases. Abnormal smears can be confirmed further by biopsy.

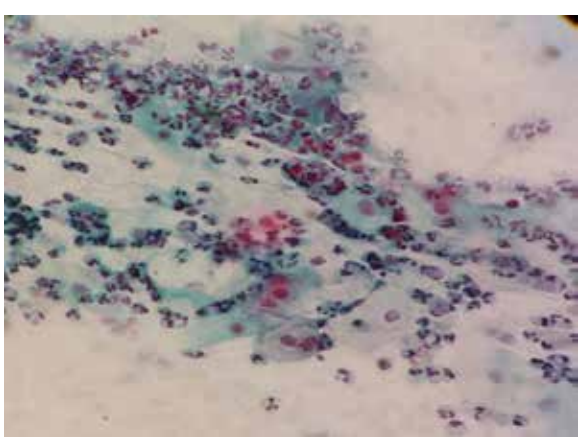


Figure-1: showing inflammatory smear

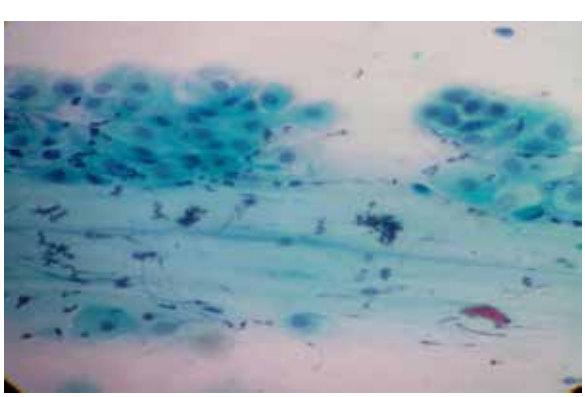


Figure-2: pap smear showing HSIL in which hyperchromatic parabasal cells show Nucleomegaly and overlapping nuclei.

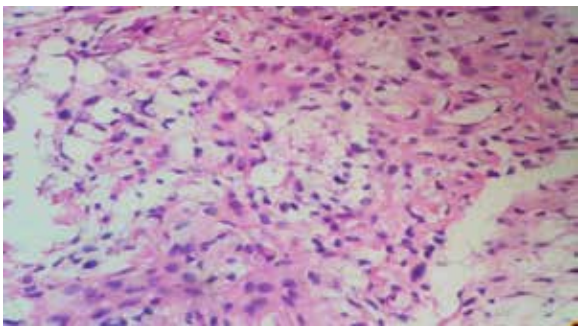


Figure-3: H&E slide showing CIN-3

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