

Histopathological Correlation with Cervical Cytology

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Abstract: The present study was undertaken with the aim to evaluate the histopathological correlation with cervical cytology among patients attending GOPD of Gauhati Medical College, Guwahati. It was a prospective, cross sectional study over a period of 1 year from July 2015 – June 2016. Total number of 280 patients with complaints of vaginal discharge, irregular bleeding, post coital bleeding, pain abdomen were randomly selected. Out of 280 cases 153 that is 55 % had NILM in PAP smear, 25% (70/280) had ECA, 15% (43/280) of the cases had inflammatory smear and 5% (14/280) were unsatisfactory for interpretation. Most commonly seen PAP abnormality was ASCUS that is 12%. 3% of the patients screened had LSIL, 7% had HSIL. AGC was seen in 1 case and adenocarcinoma was seen in 3 cases (1%). 2% of the total cases that is 6 cases had presented with squamous cell carcinoma. All the cases which were positive for PAP were taken up for biopsy and histopathological examination. The correlation between cytology and histology was calculated. Degree of freedom: 30. χ^2 -value: 167.43 (highly significant). Significance: $p < 0.01$

Keywords: Papanicolaou smear, cervical cytology, PAP test, ASCUS

I. Introduction

Cervical Cancer is one of the most common forms of cancer in women worldwide. It is preventable and curable if detected early. In developing countries, cancer of the uterine cervix is ranked second, with a relative frequency of 15% of all cancers in women, whereas in developed countries cervical cancer is ranked fifth, with a relative frequency of 4.4% [1],[2]. Screening asymptomatic women with regular Papanicolaou (PAP) smears allows diagnosis of treatable pre-invasive lesions.

Abnormal vaginal bleeding is a common symptom. This includes post-coital, inter-menstrual, or postmenopausal bleeding. In advanced cases, pelvic pain, pressure symptoms pertaining to the bowel or bladder, and occasionally urinary or faecal incontinence may be present.

The PAP smear test is used to screen asymptomatic women for cervical cancer and has been shown to reduce both the incidence and mortality related to this malignancy. Pre-malignant CIN lesions can be detected and treated by loop electrosurgical excision, cryosurgery, CO₂ laser, or hysterectomy. As studied by Walboomer et al, HPV infection is necessary for cervical carcinogenesis [3]. It is also established that specific high-risk human papilloma virus (HPV) types are causally involved in the pathogenesis of cervical cancer. The high-risk HPV types 16, 18, 45, and 56 are predominantly found in high-grade intraepithelial lesions and cervical cancers. Hence detection of high risk HPV DNA in cervical tissue can improve the efficacy of cervical cancer screening. Due to budget constraint, HPV DNA detection is not carried out regularly. But Pap smear study can be used for screening tool and many countries have cervical cancer prevention program by implementing Pap smear testing of women population.

Due to easy availability, cost effectiveness and reliability, cervical smears became a valuable tool in screening and diagnosing various pathologies of the cervix even at peripheral level in rural place. The present study was undertaken with the aim to evaluate the abnormal cytological entities detected by cervical Pap smears among patients reporting to outdoor department of Gynaecology Gauhati Medical College and Hospital, Guwahati.

II. Materials and methods

This is a prospective clinical study of women attending the Gynaecology OPD in Gauhati Medical College and Hospital, Guwahati. The Ethical Committee of Srimanta Sankardev University of Health Sciences, Guwahati, Assam, approved this cross sectional study. The study period was one year (July 2015 – June 2016). Non pregnant, married women of age 18 to 60 years with complaints of vaginal irritation or vaginal discharge of any kind or abnormal vaginal bleeding or with abnormal clinical findings were included in the study. Pap smear was taken using the Ayre's spatula and the cytobrush. The scrapped materials from each case were placed on two serially numbered grease free slides. Then the smears were made by thinning and gently spreading the materials. [4] Staining done with Papanicolaou staining procedure which employ, Haematoxylin as a nuclear stain and Orange G-6 and Eosin alcohol (Ea-36) as cytoplasmic counterstains. The slides are finally mounted in

Canada balsam and examined and interpreted. Classification of the smear was done as per The Bethesda 2001 classification system. Positively screened cases were called for biopsy. Punch biopsy was used. The site of biopsy is the region of the new SCJ which is the most likely area to harbour the worst abnormality. The specimens were preserved in 10% formalin and sent for histopathological examination

III. Results

In our study 153 that is 55 % of total 280 cases had NILM in PAP smear, 25% had ECA ,15% of the cases had inflammatory smear and 5% were unsatisfactory for interpretation. Highest PAP abnormalities were seen in the age group 41to 50 years.No significant association was found between the status of PAP positivity & age factor. It was observed that the incidence of CIN increases with increased duration of marriage. It was also noted that most of the patients who had early marriage before 20 years (29/101) had the highest PAP positivity. The present study reveals that there was a higher incidence of CIN with increased parity. There was high incidence of CIN in those who were para 3 and para 4 and above. In the present study, the most common complaint was white discharge P/V which comprised of 51% of the cases. But the highest incidence of PAP positive cases presented with non specific complaints like pain abdomen.(33%). CIN was found in cases presenting with post coital bleeding in 27% of cases. 24% of cases with irregular bleeding had positive PAP .23% of women presenting with white discharge had positive PAP finding. In the present study, most of the patients had leucorrhoea (24%), erosion (22%)or normal looking (22%) cervix.The highest incidence of ECA was observed in cases with pulled up cervix (85%). 76% of the cases who had cervical bleeding on touch had positive cytology. Ulcers were found in 30% of PAP positive cases. Patients who presented with erosion 24% had positive PAP.19% of patients presenting with leucorrhoea had abnormal PAP.13% had abnormal PAP with normal findings.

280 samples were as per Bethesda system of classification, NILM (Negative for Intraepithelial Lesion or Malignancy) with 153 (55%) samples and epithelial cell abnormality in 70 (25%) cases, inflammatory smears in 15% (43/280) (Table 1)

Table 1: Distribution of cases among adequate smears

Cytodiagnosis	No. Of cases	Percentage%
NILM	153	55%
ECA	70	25%
Inflammatory	43	15.%
Unsatisfactory	14	5%
Total	280	100%

Most commonly seen PAP abnormality was ASCUS that is 12% . 3% (7/280) of the patients screened had LSIL, 7% (19/280) had HSIL. AGC was seen in 1 case and adenocarcinoma was seen in 3 cases(1%). 2% of the total cases that is 6 cases had presented with squamous cell carcinoma.

Table 2: Analysis of samples reported as Epithelial cell abnormality (n=70)

PAP smear	No. Of cases	Percentage%
ASCUS	34	12%
LSIL	7	3%
HSIL	19	7%
AGC	1	0.3%
Adenocarcinoma	3	1%
SCC	6	2%

The total number of cases underwent biopsy and histopathological examination is 70. 31% of cases had Chronic non specific cervicitis . Squamous Metaplasia was found in 4 case (6%).21% of the cases presented with CIN 1,9 cases that is 13% of the cases had CIN II. CIN III was seen in 10% of cases. SCC was detected in 9 cases. Adenocarcinoma was found in 4 cases.

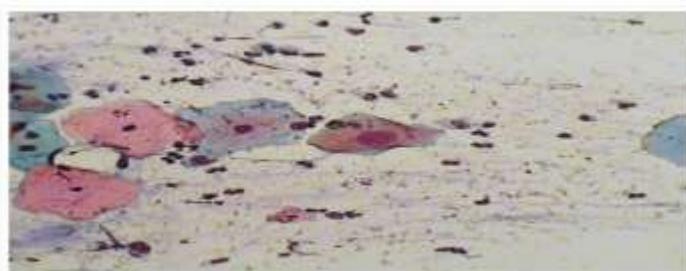


Fig i: Photomicrograph of ASCUS showing mildly enlarged nucleus in one mature squamous cell, Pap stain Out of 34 ASCUS cases 19/34 (55%) had histopathology report as chronic non specific cervicitis, 13/34 (38%) showed CIN 1, and 2 had CIN 2 (5%). Those who had LSIL on cytology showed 3/7 chronic non specific cervicitis, 1/7 squamous metaplasia, 2/7 CIN 1 and 1/7 CIN 2. Most of the HSIL (7/19) had CINIII, 6 had CIN II, 3/19 was diagnosed as SCC and 3/19 as squamous metaplasia. Cases that had SCC in cytology had SCC findings in histological examination too. All cases of Adenocarcinoma suspected in cytology was confirmed by HPE. Only one case of AGC was found to be adenocarcinoma in histopathology. The association between Cytology & Histology was found to be very significant. χ^2 -value: 167.43 (highly significant) Significance: $p < 0.01$.

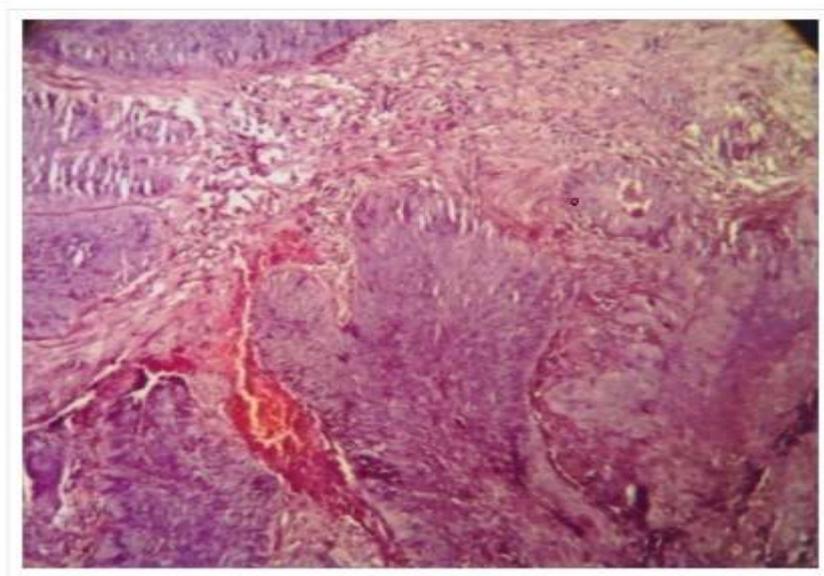


Fig-ii : Photomicrograph of SCC, H&E stain, 10x view

IV. DISCUSSION

In the present prospective study 280 cases were studied for cervical cytology after detailed history. Histopathological examination and there correlation to the cytological examination was done. The findings of the present study are recapitulated and compared with the results of other studies.

Cytodiagnosis

In the present study NILM was found to be 55%. Bal et al. [5] reported cases of NILM to be 91%. , Banik et al. [6] reported NILM cases to be 91.8%, Bukhari et al. [7] found the incidence of NILM to be 88%. Sherwani et al. [8] reported the incidence of NILM to be 85% .Gazal et al. [9] found NILM to be 84.5%.

Table 3: Incidence of NILM in different studies:

Pap report	Gazal et al	Sherwani et al	Bukhari et al	Banik et al	Bal et al	Present study
NILM	84.5%	85%	88.8%	91.8%	91%	55%

The incidence of NILM in the present study is low as compared to previous studies as the participants of the present study presented with specific complaints unlike previous studies where cases were included irrespective of complaints.

Epithelial cell abnormality:

In the present study ECA was present in 25% of the cases. Bal et al. reported the incidence of ECA as 5%, Banik et al. found the incidence to be 8.18%, Bukhari et al. found the incidence of ECA was 10.2%, Rubina

et al. [10] found the incidence as 6%, Gazal et al. reported the incidence as 12%. Sherwani et al. found the incidence of abnormality as 15%.

Table 4: Incidence of ECA in different studies:

Pap report	Radha aras et al	Gazal et al.	Sherwani et al.	Rubiana et al.	Bukhari et al.	Banik et al.	Bal et al.	Present study
ECA	15.1%	12%	15%	6%	10.2%	8.18%	5%	25%

The incidence of ECA in the present study is higher as compared to the other studies. This can be attributed to the fact that patients with specific complains attending the gynaecological OPD were included in this study. Other studies included cases irrespective of any complaints.

Squamous Cell Abnormality .

ASCUS was present in 12%, LSIL was present in 3% cases, HSIL in 7% cases and SCC was observed in 2% cases in our study. Aras et al.[11] (1992) found SIL in 14.35% cases and SCC in 0.82% cases. J S Misra (2004) [12] found the incidence of SIL as 6.1% and SCC as 0.5%. Rubina Sohail (2007-2008) found LSIL in 4% and HSIL in 2% cases. Sherwani et al .on conventional cytology found 10.6% cases of LSIL, HSIL was 0.6% and SCC in 3.7%. Bukhari et al. found the incidence of ASCUS as 1%, ASCH as 0.4%, LSIL as 4%, HSIL as 2.2% and SCC as 1.4%, Banik et al. reported ASCUS as 0.18%, ASCH as 0.12%, LSIL as 6.36%, HSIL as 1.18% and SCC as 0.35%. Bal et al. reported ASCUS as 0.3%, ASCH as 0.5%, LSIL as 5.78%, HSIL as 0.7% and SCC as 1.3%.

The results of the present study has shown slightly raised incidence of ASCUS as compared to other studies. This can be due the reason that the present study included females coming with some gynaecological problem and hence more chances of positive result. Sherwani et al, Rubina et al., Bukhari et al., Banik et al. and Bal et al. had found LSIL as the most common ECA whereas ASCUS was found as the most common ECA in the present study. In the present study squamous cell carcinoma was found in 2% of cases which is similar to the study by Sherwani et al.

Table 5: Showing Squamous cell abnormality in different studies:

Pap report	Radha et al	JS Misra et al.	Sherwani et al.	Rubiana et al.	Bukhari et al.	Banik et al.	Bal et al.	Present study
ASCUS					1%	0.18%	0.3%	12%
LSIL			10.6%	4%	4.6%	6.36%	2.7%	3%
HSIL			0.6%	2%	2.2%	1.8%	0.7%	7%
SIL	14.35%	6.1%						
SCC	0.82%	0.5%	3.7%					2%

In the present study ASCUS and HSIL was found to be more as patients with complaints were included. Differences in other results may be attributed to inter-observer variation. In the present study 4 glandular cell abnormality was detected ,1 AGC and 3 adenocarcinoma.

Cytological findings and Histopathological correlation:

In the present study an effort was made to correlate the cytological findings with their histopathological findings. As we can see in the table below maximum cases which showed ASCUS on PAP smear had CNSC (55%) on histopathology, although 38% showed CIN 1. Patients with LSIL had CNSC as well as CIN 1 and 2. Patients who had HSIL on PAP had squamous metaplasia, CIN 2, CIN 3 and even 3 cases of SCC. 6 cases of SCC on cytology were proved the same in histology. The association between Cytology & Histology was

calculated. There was high degree of freedom:30. The χ^2 -value by Pearson's chi square test was : 167.43 which is highly significant. Significance: $p < 0.01$

Table 6: Showing the cytology and histological correlation in different studies.

CYTOLOGY	HISTOLOGY	Yeoh et al. 1996[14]	Kalyani et al. 2016[13]	Present study
ASCUS	chronic non specific cervicitis,	6/66(9%)		19 /34(55%)
	Atypia	30/66(45%)		
	CIN I	19/66(28%)		13/34(38%)
	CIN II	10/66(15%)		2 /34(5%)
	CIN III			
	SCC	1/66(1.5%)		
LSIL	chronic non specific cervicitis,	3/81(4%)		3/7(42%)
	Atypia	8/81(10%)		1/7(14%)
	CIN I	37/81(45%)		2/7(28%)
	CIN II	32/81(39%)		1/7(14%)
	CIN III			
	SCC	1/81(1%)		
HSIL	chronic non specific cervicitis,	8/104(8%)	1/6(16%)	
	Atypia	2/104(2%)		3/19(15%)
	CIN I	19/104(18%)		
	CIN II	72/104(69%)		6 /19(31%)
	CIN III		1/6(16%)	7/19(36%)
	SCC	3/104(3%)	4/6(66%)	3/19(15%)
AGC				1adenocarcinoma
SCC	CIN II,III	4/10(40%)		
	SCC	6/10(60%)	2/2(100%)	6 (100%)
Adeno carcinoma	Adenocarcinoma		1/1(100%)	3 (100%)

From the above table we can see that the SCC results in cytology was confirmed by histology in 100% of the cases in all the studies. Other studies mentioned above have also correlated the association of cytology and histology significantly. In the ASCUS category our histology report showed benign lesions in 55% of cases. The reason behind this was that those cases had erosion or ulcers, hence there was inflammatory atypia for which in PAP smear those cells were considered as atypical squamous cell.

V. Conclusion

Pap smear screening has increased the detection of early stage preinvasive lesions and cancers that are potentially curable. High parity, early age of marriage, low socioeconomic status, illiteracy are the risk factors of Cervical lesions including CIN and Ca cervix. All symptomatic patients must be screened for cervical cytology. The correlation between cytology and histopathology is found highly significant ($p < 0.01$). So an organized cervical cytology screening programme is the mainstay for control of cervical cancer.

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