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Original Research Article

Smear To Section: A Retrospective Comparative Study of Cyto-Histomorphology of Cervical Pathology

P.S. Sravani[1], C. Bhavani[2], M. Sreenivasulu[3], V. Siva Sankara Naik[4]

[1]Post graduate, Department of Pathology, Government Medical College, Ananthapuramu,
[2]Associate Professor, Department of Pathology, Government Medical College, Ananthapuramu
[3]Associate Professor, Department of Pathology, Government Medical College, Ananthapuramu
[4]Professor and HOD, Department of Pathology, Government Medical College, Ananthapuramu, Andhra Pradesh

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Corresponding author: Dr. V. Siva Sankara Naik
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Abstract

Introduction: Cervical cancer is the fourth most common cancer in women globally, and the second most common in India, where it accounts for a large portion of global cases and deaths. Most of these cases occur in low- and middle-income countries, where access to vaccines, screening, and treatment is limited. Among all Human papilloma virus plays a major role in cervical carcinoma pathogenesis. The progression of healthy cervix to cervical carcinoma have long phase of preceding cytological changes for over a decade. Hence through early diagnosis and intervention in precancerous stages, cervical cancers are preventable.

Materials and Methods: It is retrospective comparative study conducted on 3854 Pap smears received by Department of Pathology, in a Tertiary care hospital over a period of 18 months. Smears were processed, diagnosed and categorized according to Bethesda system of cervical cytology 2020. Among 207 abnormal smears identified, same cervical biopsies where examined, compared and analyzed.

Results: Out of 207 abnormal smears most common was reactive atypia (n=82, 39.61%) and least was adenocarcinoma (n=01,0.48%). Among histopathological examination most common was chronic cervicitis (n=98, 47.34%), and least was mixed neuroendocrine and non-neuroendocrine neoplasm. Both cytology and histopathology results compared and analyzed.

Conclusion: Histopathology is gold standard, it has more sensitivity and accuracy when compared to Pap smear. By combining Pap smear with histopathological examination can maximize the sensitivity and specificity in diagnosing of cervical cancer.

Keywords: Cervical Cancer, Precancerous, Human Papilloma Virus, Pap Smear, Cervical Biopsy.

Introduction

Cervical cancer constitutes the fourth most prevalent malignancy among women on a global scale. It is the second most common cancer both in the incidence and mortality in India making it as the major burden globally accounting for one fifth of the newly diagnosed and one fourth of the deaths.[2] Progression from healthy cervix to cervical cancer have long phase of preceding stages over decade. Hence through early diagnosis and intervening in precancerous stages it is preventable.[3]

Among all causes Human Papilloma Virus (HPV) plays a major role in cervical carcinoma pathogenesis. Prevention primarily through HPV vaccination at secondary level is screening and treating it.[4] Cervix is highly accessible for easy sampling, enabling high cure rates with timely treatment. Pap smear, pioneered by Sir. George Papanicolaou in late 1940's, revolutionized prevention of cervical carcinoma[5].

Pap smears are cytological tests for cervical morphology. Visual inspection with acetic acid and Visual inspection with Lugol's iodine are simple clinical screening methods for cervical abnormalities. Colposcopy with acetic acid allows for precise lesion identification and targeted biopsies.

Although Pap smear cytology is effective for detecting precancerous cervical conditions, false-negative results due to sampling and interpretation errors remain a concern. Hence, histologic examination is recommended to confirmation and cytohistopathological correlation advised by European guidelines to reduce false negatives diagnosis.[7]

Materials and Methods

It is retrospective and comparative study conducted on 3854 Pap smears received by Department of Pathology, in a Tertiary care hospital over a period of 18 months. Conventional smears were processed, stained with H&E, diagnosed and categorized according to Bethesda system of cervical cytology 2020.

Among 207 abnormal smears identified, same cervical biopsies received were fixed in 10% neutral buffered formalin, processed, stained with H&E, examined under light microscope and reported according to 5th edition of WHO classification of female genital tumors.

Cyto-histomorphological results were compared and analyzed. The aim of present study is to identify the accuracy of Pap smear in identifying various cervical pathologies.

Institutional ethical committee and scientific committee approval was taken. And data was analyzed by SPSS 23 and descriptive analysis were presented in frequencies and percentages.

Inclusion Criteria: Smears of symptomatic patients with available registered data Smears those showing atypical nuclear findings were correlated with histological findings.

Exclusion Criteria:

- Pregnant women.
- Smears with normal cytological results of Negative for intraepithelial lesion or malignancy (NILM) were excluded.

Results

Among 3,854 Pap smears diagnosed, most common were inflammatory smears (n = 3276, 85.02%), followed by normal smears (n = 286, 7.42%). Inadequate smears were 88, 2.28%.

Among pathological, reactive changes (n = 82, 2.12%) (Fig.No:1) were most common, followed by low grade squamous intraepithelial lesion (LSIL) (n=53, 1.72%) (Fig.No.3), atypical squamous cells of undetermined significance (ASCUS) (n = 34, 0.2%) (Fig.No.2), High grade squamous intraepithelial lesion (HSIL) (n=27, 0.56%) (Fig.no.4) and squamous cell carcinoma (n= 04, 0.06%). Least was Adenocarcinoma (n=1, 0.03%). (Table 1).

Table 1: Pap smear pathological diagnosis distribution

Pap smear diagnosis	No. of cases (n)	Percentage (%)
Normal smears	286	7.42%
Inflammatory smears	3276	85.02%
Unsatisfactory smears	88	2.2%
Reactive changes	82	2.12%
Atypical squamous cells of undetermined significance(ASCUS)	34	0.2%
Low grade intraepithelial lesion (LSIL)	53	1.72%
High grade intraepithelial lesion (HSIL)	27	0.56%
Squamous cell carcinoma	04	0.06%
Atypical glandular cells of uncertain significance	04	0.12%
Atypical endocervical cells favoring neoplasm	02	0.05%
Adenocarcinoma	01	0.03%
Total	3854	100%

Out of 207 abnormal nuclear morphology, non-neoplastic conditions (n =120, 57.97%) were most common followed by Preneoplastic (n =82, 39.61%) and neoplastic conditions (n=05, 2.42%).

Histomorphologically chronic cervicitis (n = 98, 47.34%) (Fig no 5) was most common followed by mild dysplasia (n = 42, 20.28%), severe dysplasia (n = 23,11.12%), moderate dysplasia (n= 17, 8.24%), cervical polyp (n=12, 5.79%), squamous cell carcinoma insitu (n= 04,1.93%), invasive squamous cell carcinoma (n=07, 3.38%)(Fig no 6), adenosquamous carcinoma (n =03, 1.44%), mixed neuroendocrine and non-neuroendocrine carcinoma (n=1,0.48%) (Table no.2).

Comparison of cyto-histomorphological pathology: Totally out of 82 smears diagnosed as reactive atypia, 76 were chronic cervicitis predominantly, followed by 05 were endocervical polyp and 01 was mild dysplasia. Among ASCUS, 19 were chronic cervicitis, 07 were endocervical polyp, 06 were mild dysplasia, and 02 moderate dysplasia histologically.

04 cases of squamous cell carcinoma cytologically turned out to be 01 squamous cell carcinoma insitu and 03 were invasive squamous cell carcinoma.

02 cases of atypical endocervical cells favoring neoplasm cytologically, both were adenosquamous carcinoma histologically. 01 case of adenocarcinoma was turned out to be as mixed neuroendocrine and non-neuroendocrine neoplasm. (Table no. 3).

Table 2: Histopathological diagnosis – distribution of cases

Biopsy diagnosis	No. of cases(n)	Percentage (%)
Chronic cervicitis	98	47.34
Endocervical polyp	12	5.79
Mild dysplasia	42	20.28
Moderate dysplasia	17	8.24
Severe dysplasia	23	11.12
Squamous cell carcinoma insitu	04	1.93
Invasive squamous cell carcinoma	07	3.38
Adenosquamous carcinoma	03	1.44
Mixed neuroendocrine and non- neuroendocrine carcinoma	01	0.48
Total	207	100%

Overall sensitivity of this study was 98%, specificity was 72%, positive predictive value was 81% and negative predictive value was 97%.

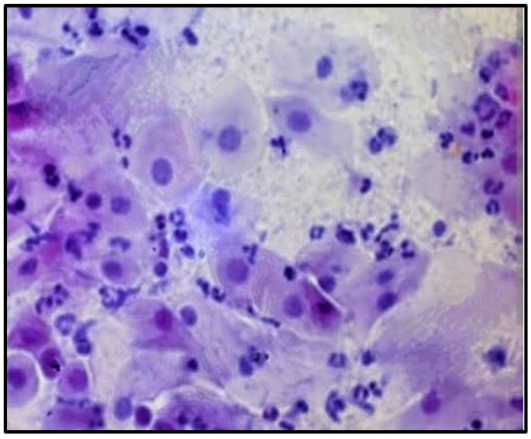

Figure 1: Reactive atypia

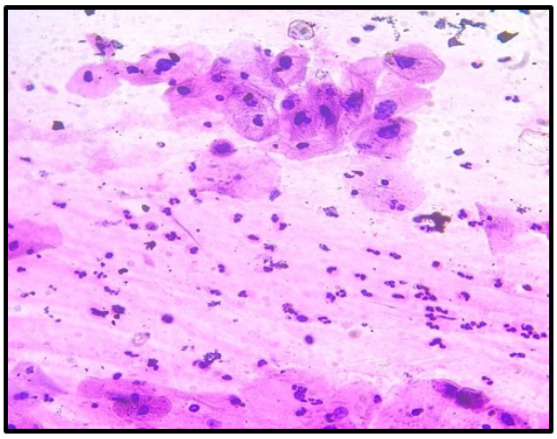

Figure 2: ASCUS

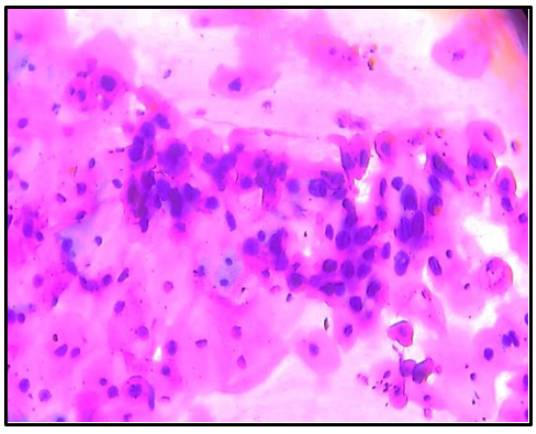

Figure 3: LSIL

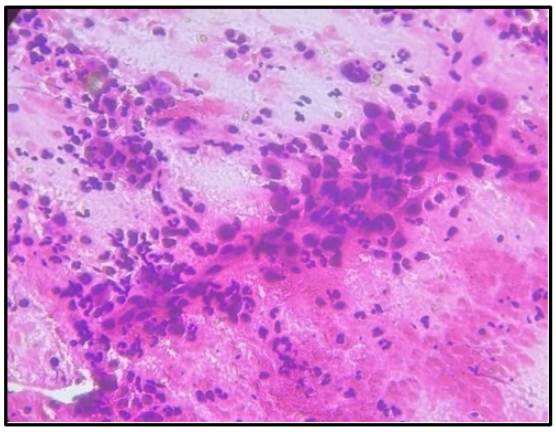

Figure 4: HSIL

Discussion

Cervical cancer is the fourth most common cancer in women globally and the second leading cause of cancer deaths among Indian women. Its slow growth allows for effective prevention through screening and HPV vaccination.[8]

The present study was conducted on 3854 Pap smears received with clinical diagnosis. For confirmation of abnormal nuclear features in Pap smear report all women underwent cervical biopsies. Final diagnosis was made according to the histopathology reports.

Through several studies the standard Pap smear test has a specificity of 98-99% but sensitivity ranging from 50-75% or lower. Its drawbacks include poor cell transfer, uneven distribution of abnormal cells, interference from inflammation and blood, and overlapping epithelial cells.[9] The present study aimed at finding out the efficacy of PAP smear in early detection of abnormalities in cervical morphology in preinvasive stage. The results are

mostly comparable with many other studies.

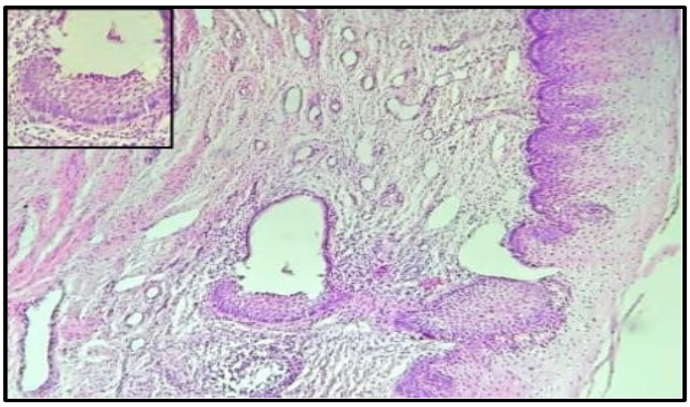

Figure 5: Chronic cervicitis (Insight- Squamous metaplasia of endocervical gland)

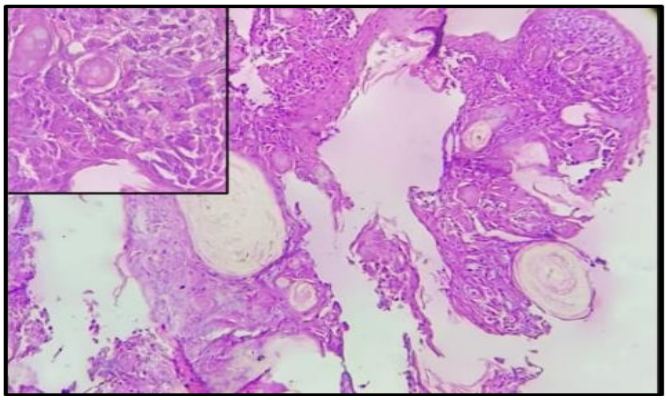

Figure 6: Squamous cell carcinoma

In our study abnormal nuclear features in Pap smear reports were 207 (5.4%), whereas in study conducted by Kalyankar VY et al.[11] (25.46%) reports were abnormal. In study conducted by Garg P et al. [12] abnormal Pap smear reports were 18 (5.46%).

Inflammatory smear reports were 3276 (85.02%) in our study, whereas in study conducted by Rampuria S et al.[13] 79(79%) reports were inflammatory and in study conducted by Ashmita D et al.[14] inflammatory Pap smear reports were 43(81.13%). Smears showing ASCUS were 34(0.2%) in our study. In study conducted by Bamanikar SA. [10]11(0.77%) reports showed ASCUS and in study conducted by Garg P et al.[12] reports showing ASCUS were 06 (1.86%). Smears showing LSIL were 53 (1.72%) in our study which is less when compared to other studies conducted by Kalyankar VY et al.[11] 12 (21.4%), Ashmita D et al.[14] 03(5.7%) and Garg P et al.[12] 08 (2.46%).

In our study HSIL reports were 14(0.7%), whereas in study conducted by Sunita et al.[15] 2(0.3%) reports gave HSIL. In study conducted by Patel et al. [3] HSIL reports were 1(0.1%). Smears showing squamous cell carcinoma were 2(0.1%) in our study. In study conducted by Sunita et al.,[15] 3(0.5%) reports gave squamous cell carcinoma and in study conducted by Patel et al.[3] reports showing squamous cell carcinoma were 7(0.7%).

Keeping in view of the importance of carcinoma and the precancerous lesion (CIN) of the cervix, early detection of abnormalities in cervix with close regular follow-up is recommended for prevention of malignancy.

Table 3: Comparative distribution of cytohistomorphological correlation

Pap / Biopsy	Reactive Change	ASC US	LSI L	HSI L	SC C	AG US	Atypical endocervical cells favoring neoplas m	Adenocarci noma	Tot al
Chronic cervicitis	76	19	03	-	-	-	-	-	98
Endocervical polyp	05	07	-	-	-	-	-	-	12
Mild dysplasia	01	06	32	03	-	-	-	-	42
Moderate dysplasia	-	02	13	02	-	-	-	-	17
Severe dysplasia	-	-	05	17	-	01	-	-	23
Squamous cell carcinoma insitu	-	-	-	03	01	-	-	-	04
Invasive squamous cell carcinoma	--	-	-	02	03	02	-	-	07
Adenosquamous carcinoma	-	-	-	-	-	01	02	-	03
MiNEN	-	-	-	-	-	-	-	01	01
Total	82	34	53	27	04	04	02	01	207

Biopsy is the gold standard when taken from the correct site, while the pap smear is cost effective, non-invasive, and similarly sensitive. However, biopsy is recommended if abnormalities are found in the pap smear, with sampling errors being the leading cause of false negatives.

Table 4: Comparison of distribution of cases according to Pap findings.

Name of the study	Inflammatory smear	ASCUS	LSIL	HSIL	SCC
Bamanikar SA et al. [10]	735 (51.6%)	11(0.8%)	00	05 (0.35)	02(0.14%)
Kalyankar VY et al. [12]	41(73.2%)	00	12 (21.4%)	03(5.35%)	00
Garg P et al. [12]	305(94.13%)	06(1.9%)	08 (2.5%)	01(0.34%)	03(0.93%)
Rampuria S et al. [13]	79(79%)	15(15%)	01(01%)	03(03%)	00
Ashmita D et al. [14]	43(81.13%)	03(5.7%)	03(5.7%)	02(3.7%)	00
Present study	3276 (85%)	34(0.2%)	53(1.7%)	27(0.6%)	4(0.06%)

Conclusion

Our study shown the overall sensitivity and specificity of Pap smears diagnosis is significant enough to reduce the incidence and preventing malignancy by early detection of abnormality.

The discordance between the cyto-histomorphological diagnoses can be reduced by adequate and precise sampling from lesion proper.

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