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Histopathological diagnosis of cervical biopsy at tertiary care hospital

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Abstract
Introduction: Cervix is a gateway to numerous non neoplastic and neoplastic gynecological lesions. Cervical cancer is the leading cancer in Indian women and second most common cancer in women worldwide next to breast cancer.
Material and Method: A formalin fixed specimen of cervical biopsy received in histopathology section-pathology department. After receiving specimen fixation, grossing and staining was done. Histopathological examination with H&E stain followed by immunohistochemistry (IHC) done in special cases for differential diagnosis.
Result: In a total of 40 cases studied 17(42.5%) cases were non neoplastic, 1(2.5%) was of CIN 3 and 20 (55.0%) cases were malignant. Malignant lesion was most prevalent and more common in age group of 40-65 years.
Endocervical polyp was the most common non neoplastic lesion and squamous cell carcinoma was the most common cancer followed by adenocarcinoma and adenosquamous carcinoma.
Conclusion: Adequate cervical screening procedure with follow up cervical biopsies helps in early diagnosis and management of premalignant and malignant lesions and their prompt treatment.

Keywords: Endocervical polyp, non- neoplastic, neoplastic

Introduction
Cervix is the elongated fibromuscular lower portion of uterus measuring 2.5-3.0 cm. It divided into ecto-cervix and endo- cervix which is lined by squamous epithelium and mucin secreting columnar epithelium respectively with a characteristic transformation zone in between [1].
Uterine cervix is gateway to several non-neoplastic and neoplastic gynecological lesions [2].
A) Non neoplastic cervical lesions occur at all age groups but are more common in reproductive and sexually active women.

1. Inflammatory lesions
- Acute cervicitis, chronic cervicitis caused by various bacteria, viruses and fungi [3].
- Cervicitis caused by Human papilloma virus carries high risk for Condyloma acuminata,
- Cervical intraepithelial neoplasia (CIN) and carcinoma [4].

2. Non- neoplastic tumor like lesions
- Endocervical hyperplasia, endometriosis, polyps and Nabothian cysts [5].

B) Neoplastic lesions
Carcinomas of the female genital tract, particularly cervical carcinoma accounts for almost 12% of all cancers in women, and so represents the second most frequent malignancy in the world after carcinoma of breast [6].
The common cause of cervical cancer is Human Papilloma Virus (HPV). HPV is responsible for 99.7% of cervical cancer and infects 75 - 80% of sexually active adults at some point, however, it can be cleared by the body's immune system most of the time and is preventable. Over 100 types of HPV are currently known, most are not associated with cervical cancer or genital warts. The High-risk types (16, 18) are associated with cancer and the low risk types [6, 11] are associated with genital warts (WHO, 2022a).

Histopathological studies of cervix along with clinical correlation helps in early diagnosis of these cervical lesions.

Materials and Methods

All the uterine cervical biopsies received at the department of pathology of tertiary hospital over a period of January 2023 to December 2023, with a total of 40 cases included in the study. After receiving biopsy, gross examination was done, tissue preserved in 10% formalin. After fixation of the tissue grossing was done, processed in tissue processor and sectioned by microtome. Slides are stained with hematoxylin and eosin for microscopy. Histopathological examination was done to differentiate various cervical lesions followed by immunohistochemistry done in special cases for differential diagnosis.

Results

A total of 40 cases of cervical lesions were studied.

Table 1: Age wise distribution of patients in the study group

Age wise distribution	Number of patients	Percentage
< 20 years	00	0%
21-40 years	14	35%
41-60 years	16	40%
> 60 years	10	25%
	40	100%

In our study most common age group affected is 41-60 years comprising of 40%. The second most common group affected were in their reproductive age group of 21-40 years comprising 35%. The youngest and oldest patient in our study was 22 years and 65 years respectively.

Table 2: Distribution of cervical lesions

Cervical lesions	Total	Percentage
Non neoplastic (inflammatory and tumor like lesions)	17	42.5%
Pre-invasive cervical intraepithelial lesions	01	2.5%
Malignant lesions	22	55.0%

In our study, Malignant cervical lesions were 55%, followed by non-neoplastic cervical lesions were 42.5% and pre-invasive cervical lesions were 2.5%.

Table 3: Distribution of non-neoplastic and pre-invasive cervical lesions

	Cervicitis	Endocervical polyp	Leomyomatous polyp	Pre-invasive lesion (CIN-3)
< 20 years	00	00	00	00
20-40 years	06	03	00	00
41-60 years	01	06	01	00
> 60 years	00	00	00	01
Total	07	09	01	01

In our study, endocervical polyp was the most common non-neoplastic lesion which is more common in the age group of 41-60 years, followed by cervicitis in the age group of 20-40 years.

Table 4: Distribution of malignant neoplastic lesions

	Squamous cell carcinoma	Adenocarcinoma	Adenosquamous carcinoma
< 20 years	00	00	00
20-40 years	05	00	00
41-60 years	06	02	01
> 60 years	08	00	00
Total	19	02	01

In our study, squamous cell carcinoma was the most common malignant neoplastic lesion in the age of >60 years, followed by adenocarcinoma and adenosquamous carcinoma.

Table 5: Distribution of squamous cell carcinoma

Age	Squamous cell carcinoma	
	Non keratinizing	Keratinizing
< 20 years	00	00
20-40 years	04	01
41-60 years	05	01
> 60 years	05	03
Total	14	05

In our study, non-keratinizing squamous cell carcinoma was more common than karatinizing squamous cell carcinoma.

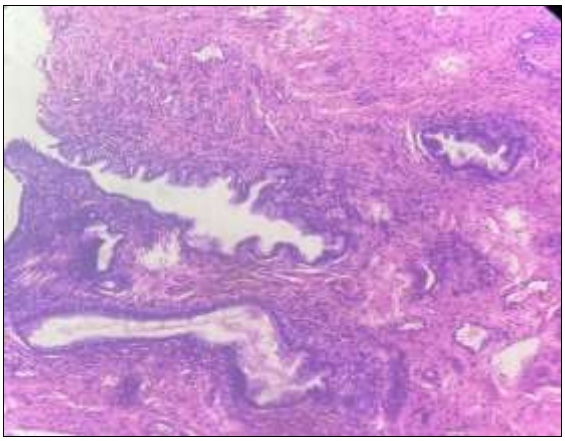


Fig 1: Chronic nonspecific cervicitis (H&E, 4X)

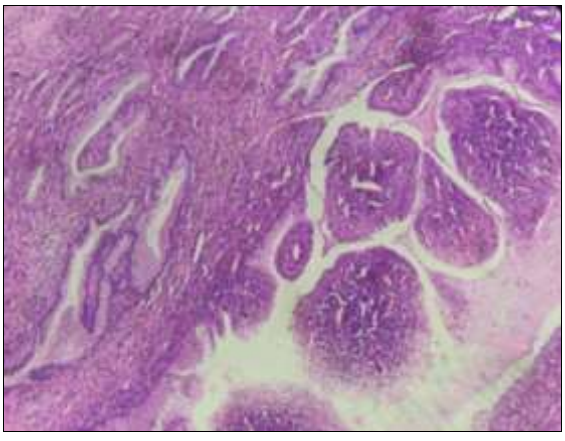


Fig 2: Papillary endocervicitis (H&E, 4X)

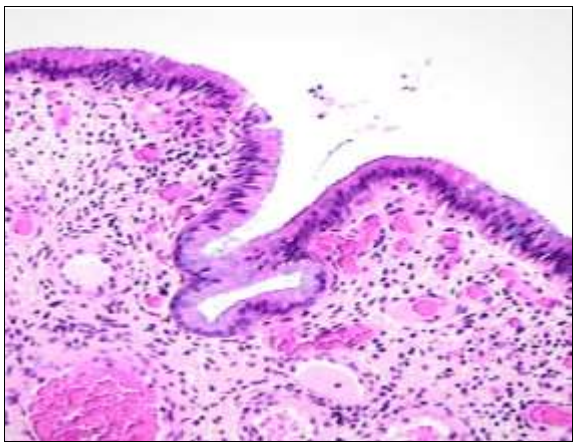


Fig 3: Endocervical polyp (H&E, 40X)

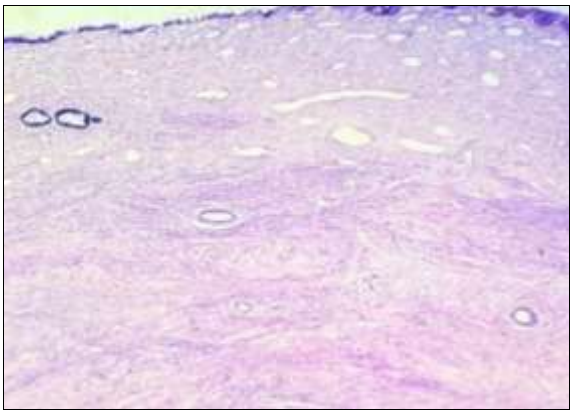


Fig 4: Leiomyomatous polyp (H&E, 4X)

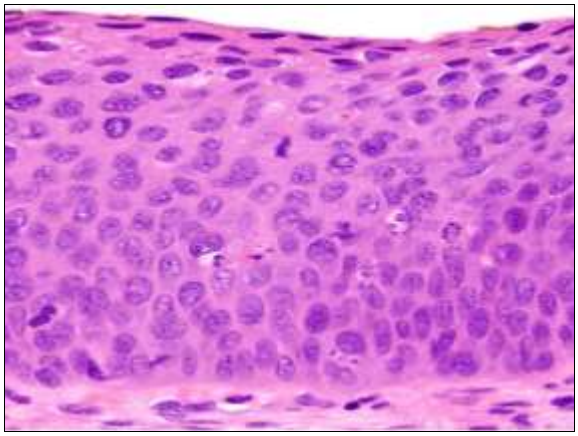


Fig 5: High grade squamous intraepithelial lesion (HSIL/CIN3) (H&E, 40X)

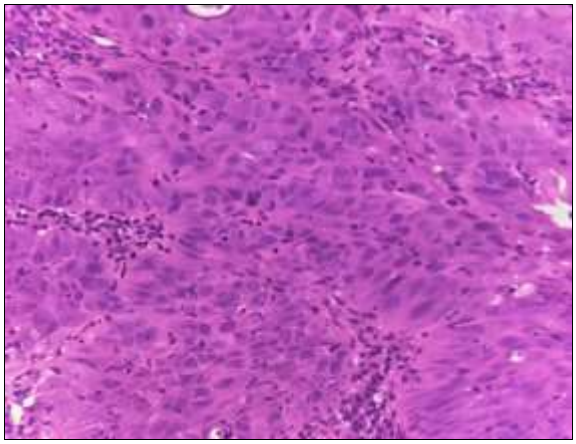
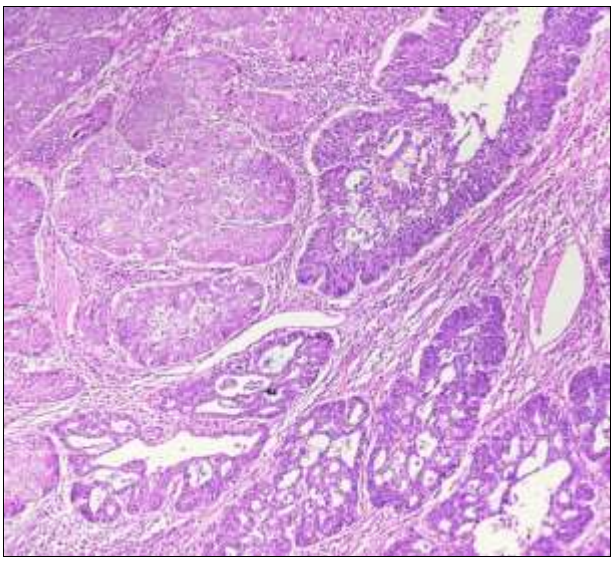


Fig 6: Nonkeratinizing SCC (H&E, 40X)



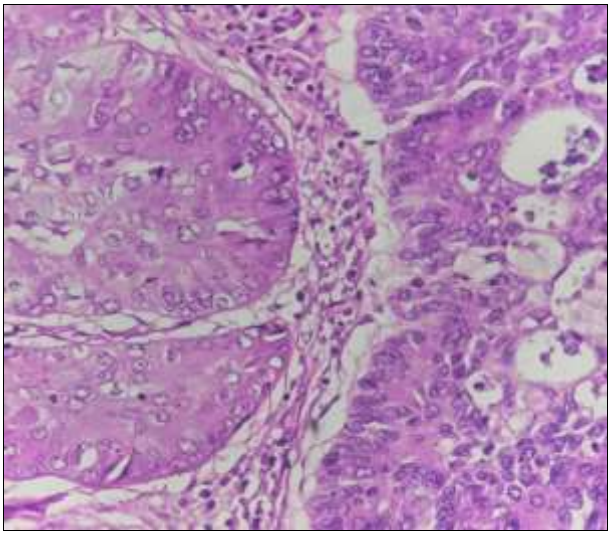


Fig 7: Adenosquamous carcinoma (H&E, a.10X, b.40X)

IHC for adenosquamous carcinoma

CK5/6, p16 and p63 positive - for squamous component
CK7 and EMA positive - for glandular component.

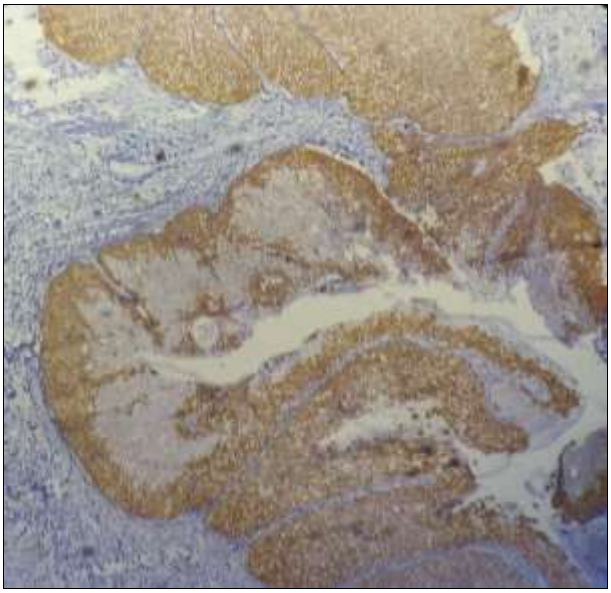


Fig 8: CK5/6 (10x) -Positive for squamous component in Adenosquamous carcinoma

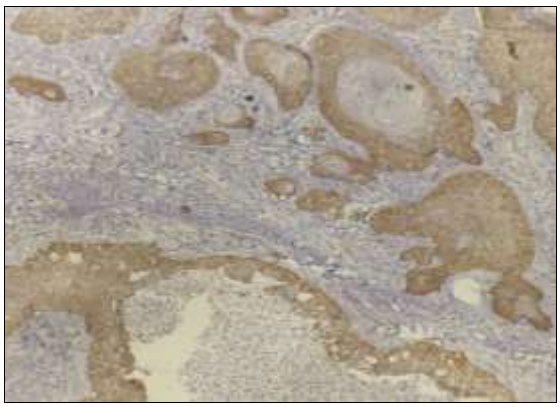


Fig 9: P16(4x) - Positive for squamous component in Adenosquamous carcinoma

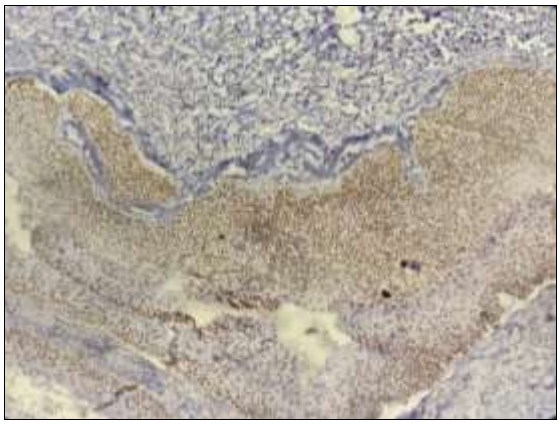


Fig 10: P63 (10x) - Positive for squamous component in Adenosquamous carcinoma

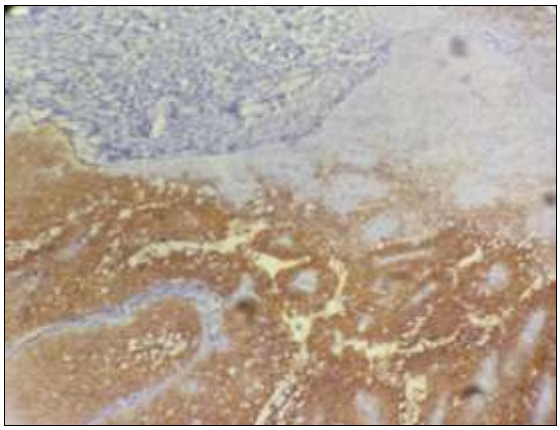


Fig 11: CK7 (10x) -Positive for glandular component in Adenosquamous carcinoma

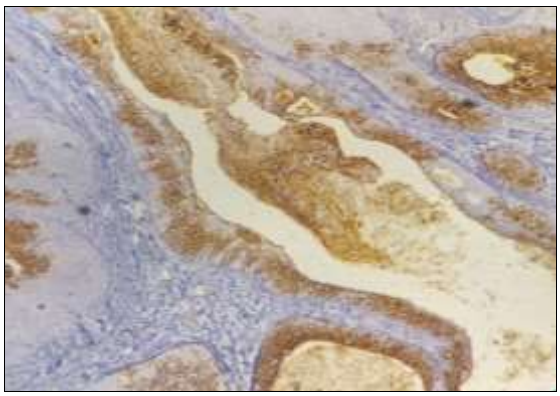


Fig 12: CEA (4x) -Positive for glandular component in Adenosquamous carcinoma

Discussion

Non-neoplastic tumors such as endocervical/ leiomyomatous poyps were most common non neoplastic lesion seen in 10(25%) cases. Maximum cases were seen in age group of 40-60 yrs. But a study done in tertiary care hospital by Saravanan *et al.* [7] found polyps in only 6.5% of cases. Histopathological features of presence of dilated endocervical glands and blood vessels in the stroma shows diagnosis of endocervical polyp. Leimyomatous polyp showed subepithelial smooth muscle arranged in interlacing fascicles.

Chronic non- specific cervicitis lesion seen in 7 cases (17.5%), comparable to the study done by Badge *et al.* [8]. Maximum cases were seen in age group of 20-40 yrs. Presence of lymphoplasmacytic infiltrate indicates chronic cervicitis with few cases showed squamous metaplasia.

Infective causes of cervicitis includes organisms such as viral, bacterial, fungi and protozoan, microorganisms commonly encountered in Sexually Transmitted Infections (STIs) and Urinary Tract Infections (UTIs). Studies have shown that chronic granulomatous cervicitis is mostly caused by tuberculosis [9].

Human Papilloma Virus (HPV) infection causes the clinical and morphological manifestation of Squamous intraepithelial lesions.

In our study 1 case (2.5%) showed cervical squamous intraepithelial lesions, which were high grade lesions seen in 5th decade. Cervical biopsies showing cytological abnormality in lower 1/3rd of the epithelium indicated as Low Grade Squamous Intraepithelial Lesion (LSIL). Dysplasia in lower 2/3rd or full thickness of the cervical epithelium were indicated as High Grade Squamous Intraepithelial Lesion (HSIL). The outcome for patients with LSIL is excellent as regression is expected within approximately one year. In the management of these lesions, a more aggressive approach has to be, because progression to invasive carcinoma is higher in these lesions.

Most of the Patients with HSIL are cured by Loop electrosurgical Excision Procedure (LEEP) and surgical conization procedure but size of the lesion, completeness of excision predicts recurrence. HPV DNA at 12 months post therapy is the best predictor of recurrence or relapse of residual disease [10].

Out of the different histopathological types of cervical cancer, squamous cell carcinomas account for 75-80% of cervical cancers, adenocarcinoma 15-25%, and adenosquamous carcinomas 3-5% [11].

Amongst the neoplastic lesions Squamous Cell Carcinoma (SCC) was the commonest (47.5%) lesion, comparable to study done by Gupta *et al.* [12] (94.26%). SCC was seen predominantly seen in age group of 50-60 years and above. Diagnosis of SCC was made based on the Presence of invasive nests of dysplastic squamoid cells infiltrating the basement membrane and invading the stroma, keratin pearl formation made diagnosis of SCC. Few cases showed moderately and poorly differentiated squamous cell carcinoma.

In the present study only 2(5%) cases of adenocarcinoma (Figure no 2) and 1(2.5%) case of adenosquamous carcinoma were noted.

For confirmation of both glandular and squamous component in adenosquamous carcinoma, Immunohistochemistry (IHC) was done, which shows positivity for CK5/6, p16 and p63 confirmed squamous component and positivity for CK7 and EMA confirmed

glandular component.

Conclusion

Cervical malignancies were common in the age group of 40-60 years and presented most commonly with bleeding per vagina. Hence women in the older age group with bleeding per vagina should be suspected for cervical malignancy and should be examined for the same.

Adequate cervical screening procedure by pap smear, HPV screening with follow up cervical biopsies helps in early diagnosis and management of premalignant and malignant lesions as they are major source of mortality and morbidity in women.

Low grade squamous intraepithelial lesions should be followed up with HPV DNA testing and p16 immunohistochemistry and observation and HSIL with LEEP, conization and HPV DNA testing.

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