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CLINICOPATHOLOGICAL SPECTRUM OF PRENEOPLASTIC AND NEOPLASTIC CERVICAL LESIONS IN A TERTIARY CARE CENTER

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ABSTRACT

Background: Cervical cancer is one of the most frequent cancer affecting women worldwide. Developing countries account for 80% cases. In India, it is the 2nd leading cause of female cancer. Persistent infections and preneoplastic lesions establish over a period of 5-10 years and set the soil for neoplastic transformation. Spectrum of lesions can differ in various parts of the country. Hence we planned to study the frequency and clinicopathological spectrum of preneoplastic and neoplastic lesions of the cervix in our region. **Materials and Methods:** This cross sectional, observational study was carried out between July 2017 and June 2018 for a period of one year in the Department of Pathology, Indira Gandhi Medical College, Shimla.Ninety three patients diagnosed with preneoplastic and neoplastic cervical lesions were included in the study.The frequency and morphological spectrum of these lesions was evaluated. **Results**: Majority of the samples were cervical biopsies (81.72%). Age range of patients was 27-85 years (mean age 54.5 years) Maximum number of cases of both preneoplastic and neoplastic lesions were in the age group 41-50 years. Neoplastic lesions comprised 81.72% and preneoplastic lesions 18.28% of the total cases. Preneoplastic lesions included CIN I (58.82%), CIN III (23.53%) and CIN II (17.65%) in order of frequency .Majority of the neoplastic lesions were Squamous cell carcinoma**.** Most common subtype of Squamous cell carcinoma was Non keratinizing squamous cell carcinoma. **Conclusion**: This study can be taken as a small step providing the frequency, clinical presentation and histopathological spectrum of preneoplastic and neoplastic cervical lesions in our hill state. Emphasis is required on adequate cervical screening procedure with follow up cervical biopsies to help in early diagnosis and management of these lesions.

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KEYWORDS: Cervical cancer, preneoplastic, neoplastic.

INTRODUCTION

Cancer of the cervix uteri ranks 3rd among cancers afflicting women worldwide. An estimated 5,69,847 new cases and 311, 365 deaths due to cervical cancer were reported in 2018.[1] India alone accounts for significant global burden of cervical cancer. In India 96922 new cases increased annually with 60078 cervical cancer related deaths occurring every year.[1]

There is an established association between certain subtypes of Human Papilloma Virus (HPV), high grade precursors lesions and cervical carcinoma.[2] HPV causes more than 90% of cases of cervical cancer and is sexually transmitted. With onset of sexual activity, most people acquire HPV infection. Risk factors also include smoking, immunosuppression, use of contraceptive pills, multiple pregnancies, low socioeconomic status, STD like chlamydia infection, early sexual activity and multiple partners.[3] They act as cofactors and predispose to persistent infection with high risk HPVs and subsequent progression to preneoplastic and neoplastic stage.

Cervical cancer starts as a precancerous condition known as "dysplasia"/intraepithelial lesionand takes years to transform into invasive cancer.[4]

Histologically cervix is lined by two types of epithelia. Ectocervix is lined by stratified squamous epithelium and endocervix is lined by mucin secreting columnar epithelium with transformation zone in between. Squamous cell carcinoma usually arises from the ectocervix. Around 80- 90% of cervical cancer cases are of this type.[5] Other histologic types include adenocarcinoma, small cell carcinoma, adenosquamous carcinoma, which are less frequently encountered.

MATERIALS AND METHODS

Our study was a cross-sectional, observational study carried out for a period of one year (July 2017-June

2018) in the Department of Pathology, I. G. M. C, Shimla. Patient consent and approval from the Institutional Ethics Committee was obtained.

A total of 93 hysterectomy and cervical biopsy specimens were collected from patients diagnosed with cervical preneoplastic and neoplastic lesions. Morphology was assessed on H & E stained sections. Special stains were done where required. Cervical tumors were classified as per WHO classification 2016.[6]

Patients showing recurrence of cervical malignancies, undergoing treatment and HPV vaccinated patients with cervical malignancies were excluded from the study cohort.

RESULTS

We received 93 specimens out of which 76 (81.72%) were cervical biopsies and 17 (18.28 %) were hysterectomy specimens. Out of total 93 cases, 17 (18.28%) were preneoplastic and 76 (81.72%) neoplastic lesions.

Age of the patients varied from 27-85 years, the mean age being 54.5 years. The maximum number of patients were in the age group of 41-50 years, comprising 33 (35.48%) patients, followed by 51-60 years age group comprising 19 (20.43%) patients. (Table 1)

Table 1:- Age wise distribution of preneoplastic and neoplastic lesions.

Age group (Years)	Preneoplastic lesion (n=17)	Neoplastic lesion(n=76)	Total (n=93)
21-30	1 (5.88%)	1 (1.31%)	2 (2.15%)
31-40	2 (11.76%)	9 (11.84%)	11 (11.83%)
41-50	8 (47. 06%)	25 (32.89%)	33 (35.48%)
51-60	2 (11.76%)	17 (22.37%)	19 (20.43%)
61-70	2 (11.76%)	16 (21. 05%)	18 (19.35%)
71-80	1 (5.88%)	7 (9.21%)	8 (8.60%)
81-90	1 (5.88%)	1 (1.31%)	2 (2.15%)

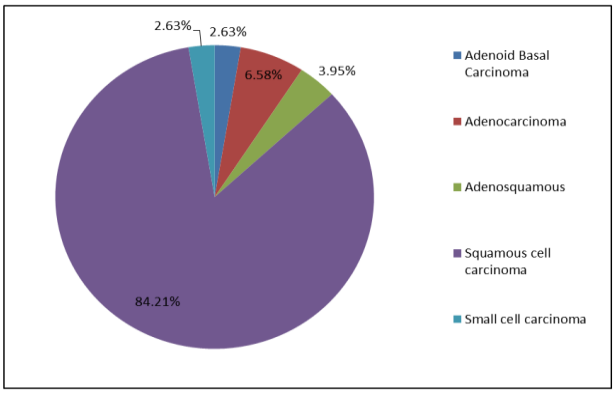
In patients with preneoplastic lesions most common symptom was metrorrhagia seen in 6 (35.29%) patients while post menopausal bleeding was the most common symptom seen in women with neoplastic lesions.(Table 2)

Table 2: - Distribution of cases on the basis of clinical features.

Clinical Features	Preneoplastic lesion	Neoplastic lesion	No. of cases	Percentage (%)
Post Menopausal bleeding	5	50	55	59.14
Metrorrhagia	6	5	11	11.83
Post –Coital bleeding	1	4	5	5.37
Foul Smelling Discharge	1	8	9	9.68
White Discharge	3	1	4	4.30
Mass per vagina	1	8	9	9.68
Total	17	76	93	100

In the present study, among 17 lesions of CIN , majority were CIN I accounting for 10 (58.82%) cases, followed by CIN III 4 (23.53%) cases and the least common being CIN II with 3 (17.65%) cases.

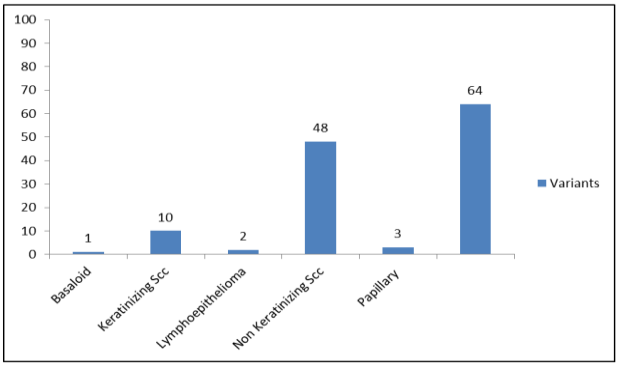
Out of 76 cases of neoplastic lesions, majority were Squamous cell carcinoma 64 (84.21%) cases followed by Adenocarcinoma 5 (6.58%) cases, Adenosquamous carcinoma 3 (3.95%) cases and 2 (2.63%) cases each of Adenoid basal carcinoma and Small cell (neuroendocrine) carcinoma.(Graph 1)



Graph 1: - Histological types of neoplastic lesions of cervix.

Of the 64 cases of Squamous cell carcinoma, 48 cases (75%) were diagnosed as Non- Keratinizing SCC and 10 (15.62%) cases as Keratinizing SCC. Three (4.68%)

were Papillary SCC, 2 (3.13%) Lymphoepithelioma like carcinoma and 1 (1.56%) was Basaloid SCC.(Graph 2)



Graph 2: Histopathological subtypes of Squamous cell carcinoma of cervix.

DISCUSSION

Cervical cancer is one of the leading causes of morbidity and mortality among women worldwide with a well defined preneoplastic stage. Studies have been done across the country to analyse the frequency and histopathologic spectrum of these neoplastic cervical lesions. No such data was available from our sub-himalayan region.

In the present study we received 93 specimens, out of which 76 were cervical biopsies and 17 hysterectomy specimens. Predominance of cervical biopsies (81.72%) is comparable to the number of specimens evaluated by Jain A et al[8] (74.77%), Krishnappa C et al[9] (80.8%)n their studies (Table 15) In our study, lesser number of hysterectomy specimens could probably be due to the fact that some of our patients went to higher centers for treatment.

Majority of preneoplastic lesions were seen in 41 – 50 years age group which is similar to observations by Poste P et al[10] & Hebbar A et al. Patel M et al found majority of CIN cases a decade earlier. Carcinoma Cervix was seen commonly in 41- 50 years age group. This finding also correlated with that of Patel M et al,[11] Agarwal S et al[12] and various other researchers. Poste P et al[10] found most common age group of neoplastic lesions was 51-60 years. In our study mean age was 54.5 years similar to that of Olu Eddu.[22]

Very few studies have reported the clinical presentation of preneoplastic and neoplastic lesions of cervix. There is no uniformity observed in the clinical presentation of patients in various studies. In our patients of CIN, metrorrhagia was the commonest complaint which is similar to the study by Poste P et al.[10] However Gupta K et al[13] observed white discharge as the commonest symptom in CIN patients. This disparity in clinical presentation in our set of patients could probably be due to the less number of cases (17) of CIN in our study. Majority of our patients with SCC (90.91%) presented with post menopausal bleeding which is concordant with the observations of Gupta K et al[13] and Krishnappa C et al.[9]

Among 93 samples received, 17 (18.28%) cases were of preneoplastic lesions and 76 (81.72%) cases were of neoplastic lesions similar to that of Pujani M et al[14] and Krishnappa C et al.[9] Gupta M et al[15] observed 36 cases of CIN (32.7%) and 74 cases (67.3%) of invasive carcinoma.

In the present study, out of 17 Preneoplastic lesions, CIN I constituted the major group accounting for 10 cases (58.82%) followed by CIN III and II, accounting 4 (23.53%) and 3 (17.65%) cases respectively. (Figure 1, 2, 3) However Sangwaiya A[16] found highest frequency of CIN III lesions while Umar A et al,[17] Hebbar A et al[18] found equal cases of CIN I and CIN III. Less number of CIN II and CIN III cases in our study may be due to the patients presenting late during the course of disease with an overt malignancy.

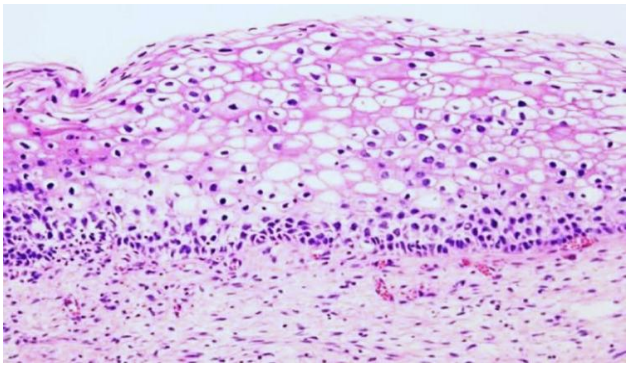


Figure 1:-Koilocytic Change. (CIN I) (H&E X 400).

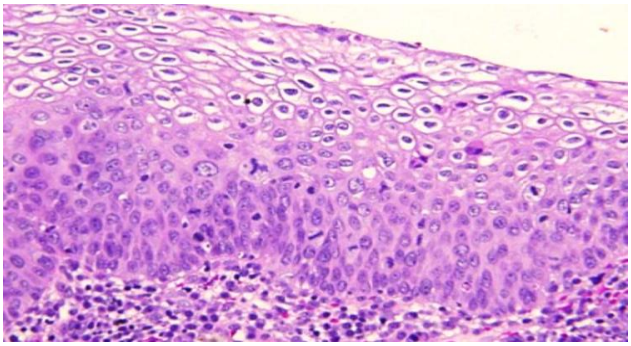


Figure 2:-CIN II. (H&E X 400).

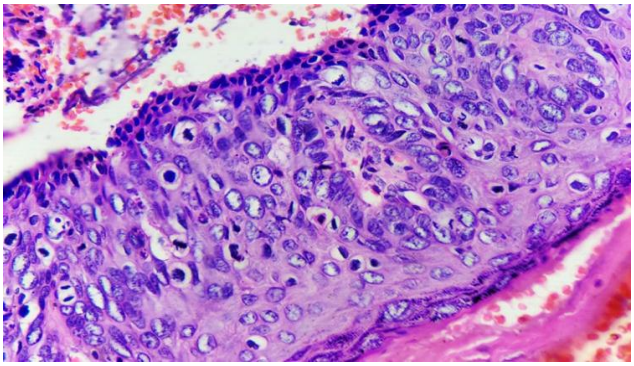


Figure 3:- CIN III. (H&E X 400)

Among Neoplasms, Squamous cell carcinoma was the most common type followed by Adenocarcinoma, both of these forming the major bulk.(Table 3) (Figure 4) We observed 3 (3.95%) cases each of Adenosquamous carcinoma similar to study by Krishnappa C et al[9] (3.8%).(Figure 5)There were 2 (2.63%) cases of Adenoid basal carcinoma and Small cell carcinoma (neuroendocrine) tumour similar to that observed by Krishnappa C et al[9] who found 3 (0.9%) cases of Adenoid basal carcinoma and 5 (1.55%) cases of neuroendocrine tumours. In a study by Gupta M et al[19] there were 4 (5.4%) cases of neuroendocrine tumours.

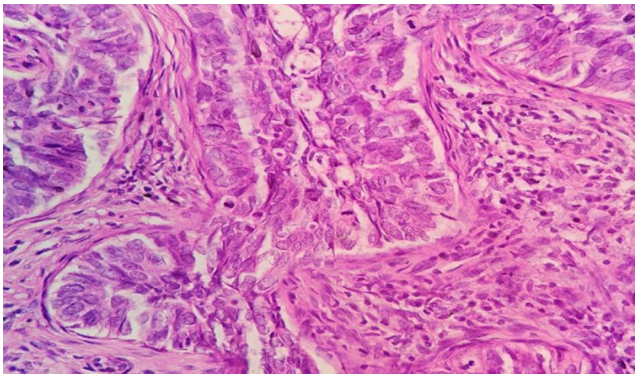


Figure 5:-Adenoid Basal carcinoma of cervix. (H&E X 400)

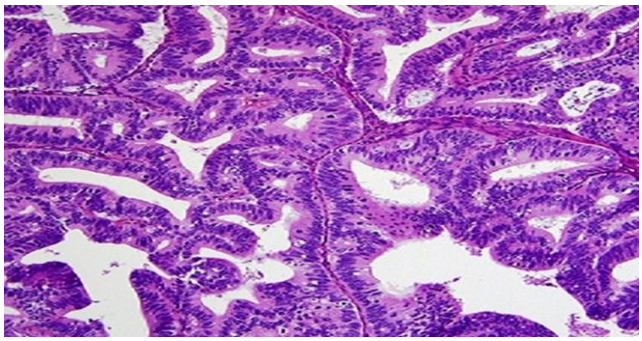


Figure 4:-Adenocarcinoma of cervix. (H&E X 100).

Table 3:-Comparison of different morphological types in various studies.

Author (year)	SCC	Adenocarcinoma	Adenosquamous carcinoma
Krishnappa C et al[9] (2014)	158 (84.5%)	24 (11.7%)	8 (3.8%)
Hebbar A et al[18](2017)	6 (50%)	6 (50%)	-
Umar A et al1[17](2016)	53 (68%)	6 (7.7%)	2 (2.5%)
Kishore V et al[15](2017)	45 (95.74%)	2 (4.26%)	-
Pujani M et al[14](2018)	36 (72%)	7 (14%)	2 (4%)
Gupta M et al[19](2018)	63 (85.2%)	6 (8%)	1 (1.3%)
Present study	64 (84.21%)	5 (6.58%)	3 (3.95%)

In our study we followed 2 tiered classification system proposed by WHO.[6] Among SCC, majority of cases were of non- keratinizing squamous cell carcinoma (75%) followed by keratinizing squamous cell carcinoma (15.62%).(Figure 6 & 7) Jain A et al,[8] Krishnappa C et al,[9] Gupta M et al,[19] Jedpiyawongse A et al[21] followed 3 tiered classification system of Squamous cell carcinoma (SCC) by Wentz and Reagan i. e. Large cell keratinizing squamous cell carcinoma (LCK SCC), Large cell non- keratinizing squamous cell carcinoma (LCNK SCC), and Small cell non keratinizing squamous cell carcinoma (SCNK SCC).[6] In these studies LCNK SCC was the most common variant of SCC followed by LCK SCC. This is comparable to our observations. However Bisht D et al[20] found LCK SCC as the most common subtype (45.45%) different from all other studies.

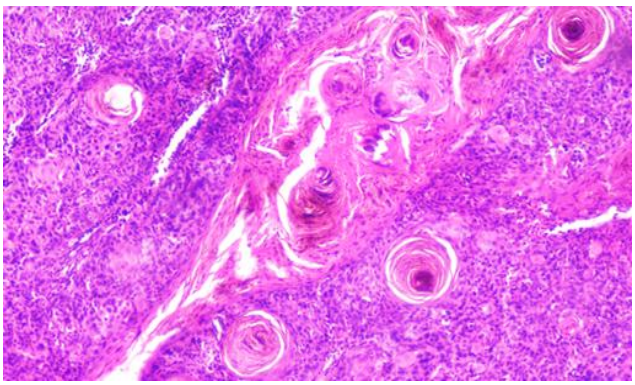


Figure 6:- Keratinizing squamous cell carcinoma of cervix. (H&E X 100).

We also found 2 (3.13%) cases of Lymphoepithelioma like carcinoma, 3 (4.68%) cases of Papillary squamous cell carcinoma and 1 (1.56%) case of Basaloid Squamous cell carcinoma. Krishnappa C et al[9] and Fatima Qadir et al[23] reported 6 (3.75%) cases and 1 (0.58%) case of Papillary squamous cell carcinoma respectively.(Figure 8,9,10,11)

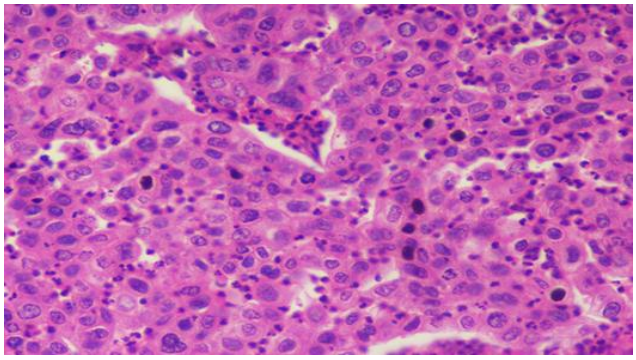


Figure 7:-Non –Keratinizing Squamous cell carcinoma of cervix. (H&E 1000)

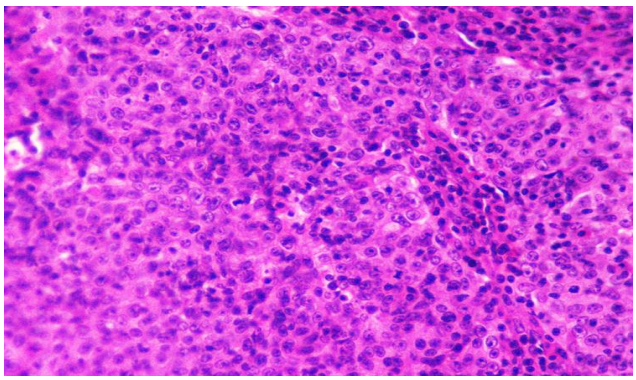


Figure 8:- Lymphoepithelioma like carcinoma of cervix. (H&E X 400)

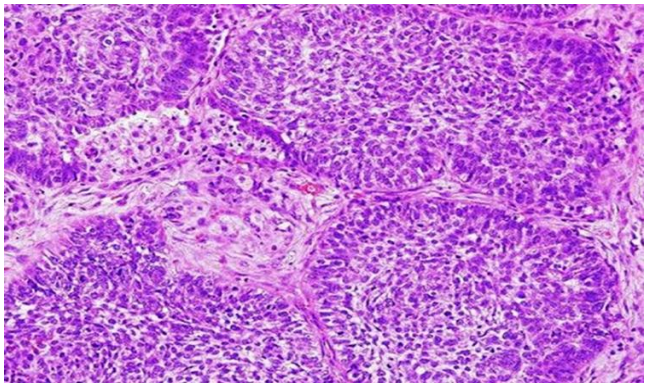


Figure 9:-Basaloid Squamous cell carcinoma of cervix. (H&E X 400)

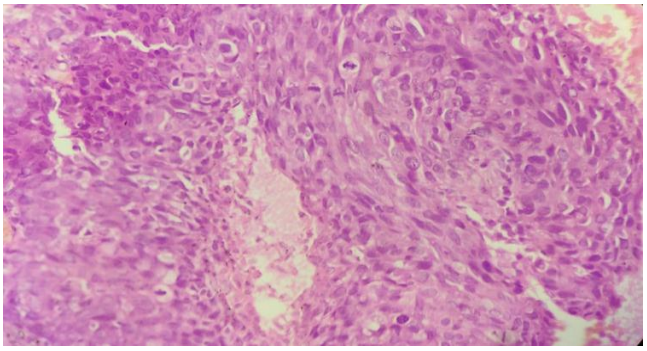


Figure 10:-Papillary squamous carcinoma of cervix with fibrovascular core. (H&E X 400)

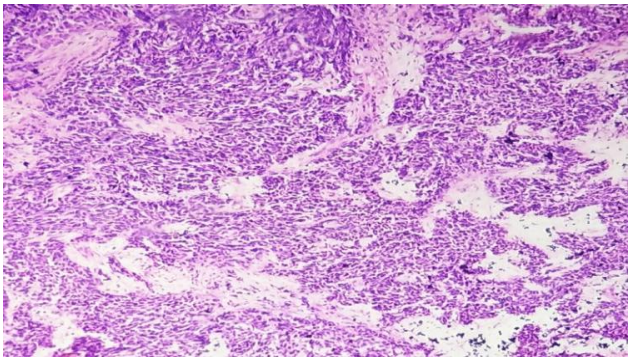


Figure 11:-Small cell carcinoma of cervix. (H&E X 100)

Table 4:-Comparison of subtypes of squamous cell carcinoma in various studies.

Author (year)	Non keratinizing Squamous cell carcinoma	Keratinizing Squamous cell carcinoma
Jedpiyawongse A et al[21] (2008)	15 (93.75%)	1 (6.25%)
Jain A et al[8] (2014)	13 (61.9%)	8 (38. 01%)
Poste P et al[10] (2015)	109 (69.43%)	48 (30.57%)
Krishnappa C et al[9] (2016)	88 (55%)	65 (40.63%)
Present Study	48 (75%)	10 (15.62%)

CONCLUSION

Cervical lesions constitute a major source of mortality and morbidity if they are not detected early. The present study provides valuable information to clinicians and pathologists about frequency, clinical presentation, and histopathological types of cervical cancer in this Sub‑Himalayan region which can further be used to chalk out management strategies for these preneoplastic and neoplastic cervical lesions.

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Conflicts of interest - There are no conflicts of interest.

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