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ORIGINAL RESEARCH

HISTOMORPHOLOGICAL STUDY OF PREMALIGNANT AND MALIGNANT EPITHELIAL LESIONS OF THE UTERINE CERVIX

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ABSTRACT

Background: Cervical cancer is the most common type of carcinoma in Indian women, and it develops after years of morphologically defined precancerous lesions. The diagnostic criteria for intraepithelial neoplasia and microinvasion vary greatly. In addition, in cases of frank malignancy, histomorphological studies aid in lesion typing, establishing stages of development and determining the extent of involvement, this is critical for prognosis and clinical management. The present study is undertaken to examine the histomorphological characteristics of premalignant and malignant lesions of the uterine cervix and to characterize them based on microscopy.

Materials and Methods: The present study was a prospective study done from June 2021 to May 2022. All histologically verified premalignant and malignant epithelial lesions of the uterine cervix received at the Department of Pathology at Kamineni Institute of Medical Sciences Narketpally were studied and classifed them using the WHO classification, examined accompanying morphological changes, and graded these lesions.

Results: There were 30 premalignant and 35 malignant uterine cervix lesions. The most common premalignant lesion was high grade squamous intraepithelial lesion (HSIL) constituting 16(53.34%) cases followed by 14 (46.66%) cases of low grade squamous intraepithelial lesion (LSIL). IHC analysis reveals p16 positivity in 7 (23.3%) cases of premalignant condition and 6 (20%) cases showed koilocytic change. Among the 35 malignant tumors, all were epithelial carcinomas. 30(85.72%) cases were Squamous Cell carcinoma, 3 (8.58%) were Adenocarcinoma and 1 (2.85%) each were neuroendocrine carcinoma and adenosquamous carcinoma.

Conclusion: Cervical cancer remains the most frequent malignancy in women in underdeveloped countries. Most of the factors associated with invasive cervical cancer in previous epidemiological studies were discovered to be connected to carcinoma in situ and dysplasia of the cervix, such as early age at first intercourse, multiple sexual partners, and pregnancy outside marriage. Histopathological examination is considered

the gold standard for the identification of intraepithelial neoplasia and cervical cancer, and it should be undertaken as early as possible to provide a better prognosis, treatment, and protection against invasive cervical carcinoma.
Keywords: Uterine cervix, cervical intraepithelial neoplasia, carcinoma, squamous cell carcinoma, microinvasive carcinoma adenocarcinoma, neuroendocrine carcinoma.

INTRODUCTION

Cervical cancer is the world's second most frequent malignancy among women. This disease claims the lives of over 2,500 women each year. The incidence of cervix carcinoma in India is estimated to be 1,30,000 new cases per year, accounting for 86-90 % of all genital cancers.[1-3] The cervix's transformation zone, notably the squamocolumnar junction, is sensitive to human papillomavirus. Persistence infection with high-risk human papillomavirus is a required cause of cervical cancer. It is, nevertheless, insufficient, as several factors influence the development of cervical cancer.[3-5] In the transformation zone, certain host target epithelial cells play a significant role in the development of cervical neoplasia.[4] Cervical intraepithelial neoplasia diagnosis must be accurate and dependable to prevent cervical cancer. However, reproducing its histologic diagnosis can be problematic.[5] Grading cervical intraepithelial lesions based on whether basaloid growth occupies less than or more than half of the epithelium may be simpler, more reproducible, and more biologically valuable.[6-8] Invasive cervical carcinomas can be squamous, columnar, or neuroendocrine in naturuamous, glassy cell, sarcomatoid, lymphoepithelial like, transitional, and undifferentiated patterns have also been described. This neoplastic differentiation spectrum represents either specific cell types infected by human papillomavirus or differentiation pathways chosen following neoplastic cell transformation.[9-11] Pathologic markers such as the amount of invasion, the margin status, and the presence of lymphovascular invasion are crucial for patient care. The purpose of this study was to investigate the spectrum of cervical carcinomas and their precursor lesions, classify them using the WHO classification, examine accompanying morphological changes, and grade these lesions.[12]

MATERIALS & METHODS

The present study was conducted at Kamineni Institute of Medical Sciences Narketpally with cases taken of one year duration from June 2021 to May 2022. The detailed clinical history and results of relevant investigations were recorded form the case sheets. A total of 65 samples were studied which included 30 cervical biopsies and 35 hysterectomies. The study covered all histologically proven premalignant and primary malignant epithelial lesions of the uterine cervix. Non neoplastic lesions, benign tumours and secondary cervical tumours were excluded. The cervical biopsies and hysterectomy specimen were fixed in 10% Neutral buffered formalin. The cervical biopsies were entirely submitted for processing. Hystrectomy specimen was grossed according to standard surgical grossing procedure and representative sections were submitted for tissue processing. The processed tissue were embedded in paraffin blocks and multiple sections of four micron sections obtained from paraffin block, stained with haematoxylin and eosin stain and studied under microscope. Wherever possible, special stains such as PAS and Mucicarmine, as well as immunohistochemistry markers such as p16 and Chromogranin were used. Cervical lesions were diagnosed as premalignant or

malignant and were further classified using the World Health Organization's histological classification for uterine cervix tumours. Characteristics of the tumour-stromal border or mechanism of invasion, degree of stromal inflammatory cell infiltration, and presence or absence of lymphovascular invasion were evaluated histopathologically. Mitotic index and tumour differentiation degree were studied. The mode of invasion was classified as either diffuse with an ill- defined border or diffuse with infiltrating growth. The grading score index ranged from 8 to 24 points.The index was categorised into three categories: low (8 to 13), middle (14 to 16), and high (17 to 24). If tumour cells were discovered in an endothelium-lined area, it was said to be present. The Mitotic figures were counted in ten high power fields (HPF) at 400x magnification, and the mitotic index was computed. Malignant lesions were characterised as having few (0-1), moderate (2-4), or many (>=5) mitosis based on the number of mitosis/HPF. The degree of infiltration in the majority of the fields of evaluation, lymphoplasmacytic stromal infiltration was classified as mild, moderate, or significant.The degree of stromal eosinophilic leucocytic infiltration in malignant tumours was rated using Jansen FW 54 criteria. Mild :< 10 eosinophils in 3 HPF 10-50 eosinophils/HPF or a series of hot patches between infiltrates are considered moderate. >50 eosinophils/HPF is considered severe. The modified Broder approach, which has poor clinical correlation and is rarely used today, was used to grade squamous cell carcinomas. It consists of three levels: well-differentiated (grade 1), moderately differentiated (grade 2), and poorly differentiated (Grade 3). (Grade-3). Cervical adenocarcinomas were classified into poorly differentiated, moderately differentiated, and well-differentiated tumours, as well as nuclear atypia in nuclear Grades 1-3. All LSIL were immunostained with p16 to confirm koilocytic atypia and HSIL with invasive carcinoma and neuroendocrine markers such as chromogranin to confirm small cell neuroendocrine tumour. IBM SPSS version 22 for Windows was used to analyse the data. Categorical data were analysed using frequency and percentages, and the Chi-Squaree test was used to determine the correlation.

RESULTS

During the study period, a total of 200 cervical biopsies and hysterectomy specimens were received at the department of Pathology. Out of which 65 cases were included in the study. Out of 65 cases, 35 were malignant cases and 30 cases were of premalignant conditions. Among the 35 patients, majority of the were having high grade squamous intraepithelial lesion constituting 16(53.34%) cases and remaining 14(46.66%) cases were low grade squamous intraepithelial lesion. Majority of cases with premalignant condition were in the age group of 31-40 years constituting 5 (35.71%) cases and majority of cases with malignancy were in the age group of 41-50 constituting 14(39%) cases. The age and malignant group have statistically significant ($p<0.05$) correlation. The larger the age, the higher the chances of getting malignancy

Table 1: Age Distribution of Cases

Age group	LSIL		HSIL		Carcinoma	
	Cases	%	Cases	%	Cases	%
21 – 30	4	28.57	0	0	0	0
31 – 40	5	35.71	9	56.25	4	14.6
41 – 50	4	28.57	4	25	14	39.0
51 – 60	1	7.15	2	12.5	9	26.8
> 60	0	0	1	6.25	8	19.5
Total	14	100	16	100	35	100

Table 2: Correlation between age and malignancy

Age group	Pre Malignant group (N=30)	Malignant group (N=35)	Chi-Square test
21 – 30	4	4	25.12, df=3, P<0.05
31 – 40	14	14	
41 – 50	9	9	
≥ 51	4	17	

In the present study, we observed that none of the cases were nulliparous. Majority of cases with premalignant lesion were having 3-4 children, constituting 17(56.3%), followed by 10 (33.3%) cases having parity of 1-2. Parity of more than or equal to5 were observed in 3(10%) cases. The mean parity was 3.2. Similar observation was observed in malignant cases where majority 20(57.14%) cases were having parity of 3-4, followed by 12(34.3%) cases with parity of more than or equal to 5 and least number of cases 3(85.7%) cases were having parity of 1-2. There was a significant relation between parity and malignancy. Higher the parity, more were the chances of malignancy.

Table 3: Distribution of cases according to parity and correlation with malignancy

Parity group	Pre Malignant group (N=30)	Malignant group (N=35)	Chi- Square test
1 – 2	10	3	8.48, df=2, P<0.05
3 – 4	17	20	
5+	3	12	

The majority of patients with premalignant lesion had presented with complaints of white discharge per vaginum seen in 20(66.67%) cases followed by abnormal vaginal bleeding in 5 (16.66%) cases, 2 (6.67%) cases each presented with post coital bleed and blood stained discharge. One (3.33%) case presented with pain abdomen. In patients with malignancy, majority of them presented with white discharge per vaginum, constituting 23(65.72%) cases followed by abnormal vaginal bleeding in 12 (34.28%) cases. The clinical diagnosis in majority of patients with premalignant condition was chronic cervicitis in 22 cases (76.68 %), followed by fibroid, dysfunctional uterine bleeding and prolapsed uterus in two cases each (6.66%) and carcinoma cervix in one case (3.34%) In the present study, 17(56.67%) cervical

biopsies and 13(43.33%) hysterectomy specimen were diagnosed as premalignant condition. Gross examination of all specimens with premalignant condition was unremarkable. In LSIL cases, dysplasia was seen in the basal one third of the thickness of epithelium and maturation was present in the upper two-thirds of the epithelium in all cases. Mild nuclear pleomorphism and mitotic figures were confined to the basal third of the epithelium. 4(13.33%) cases showed koilocytic atypia. In HSIL cases, dysplasia was seen in more than basal one third of the epithelium and can cover full thickness without invasion. Koilocytic atypia was seen in (6.66%) cases. Mild lymphoplasmacytic infiltrate was seen in 13(43.34%) cases, moderate was seen in 7(23.33%) cases and severe was seen in 10(33.33%) cases. IHC with p16 was performed in all the 30 cases, out of which 5(16.66%) cases were positive and 25 (83.37%) cases were negative. Among the 5 cases, 3 were LSIL and 2 were HSIL.

Table 4: Immunohistochemistry of P16 in Premalignant Cases

Type	**IHC p16 Positive**	**IHC p16 Negative**	**Total**
LSIL	3(21.43%)	11(78.57%)	14(100%)
HSIL	2 (12.5%)	14 (87.5%)	16 (100%)
Total	5(16.66%)	25(83.37%)	35 (100%)

In majority 32 (91.42%) of cases with carcinoma, clinical diagnosis of carcinoma was made. In 2 (5.72%) cases, clinical diagnosis of chronic cervicitis was made and in 1(2.86%) case, clinical diagnosis of fibroid uterus was made. This discrepancy is due to microinvasion of the carcinoma which was not detected clinically as there were no gross changes. Cervical biopsies were obtained in 13(37.15%) cases and hysterectomy specimens in 22 (62.85%) cases. On cut section of 22 hysterectomy specimens, greyish white friable growth was seen in 20 (90.9%) specimens. The cut section of two specimens was unremarkable. The size of the growth ranged from 1x1x0.7 cm to 6.2x5.4x1.5 cm. All the growths showed areas of haemorrhage and necrosis. Extension of tumour into the uterine corpus was seen in 5(14.28%) cases. All the 35 malignant tumours were epithelial in origin. 3(8.58%) cases were microinvasive squamous cell carcinoma and the other 32(91.42%) cases were invasive. Invasive squamous cell carcinoma was diagnosed in the majority of cases 27(77.1%), among which 20(57.14%) cases were non-keratinizing type, 7 (20%) cases were keratinizing type. Remaining 3(8.58%) cases of adenocarcinoma and 1 (2.85%) case each of adenosquamous carcinoma and neuroendocrine carcinoma was seen.

Table 5: Histological type of invasive carcinoma

Malignant group		
Tumour type	Number of cases	Percentage
Microinvasive Squamous cell carcinoma	3	8.58
Keratinizing squamous cell carcinoma	7	20
Non keratinizing Squamous	20	57.14
Adenocarcinoma	3	8.58
Adenosquamous	1	2.85
Neuroendocrine	1	2.85
Total	35	100

Micro invasive squamous cell carcinoma was seen in three cases. The ages were 48, 52 and 53 years. All of them presented with white discharge per vagina. The gross examination was uneventful in all. A big cell non-keratinizing squamous cell carcinoma was observed under microscopy. Tumour cells were grouped in nests, and the depth of invasion was less than 5 mm. There was a moderate to severe lymphocytic infiltration in the cervical stroma. Lympho vascular invasion was not present. In seven (20%) cases, a histological diagnosis of invasive keratinizing squamous cell carcinoma was made. Four were cervical biopsies and three were hysterectomy specimens. The age of patients varied from 35 to 70 years, with mean age of 48.5 years. The majority of patients had ulceroproliferative growth on gross examination (63.8%). The majority of tumour cells were distributed in nests and sheets on microscopic examination (90.2%). Prominent epithelial pearl formation was observed in 6 cases (85.72%) and attempted pearl formation with individual cell keratinization in 1 case (14.28%). Tumor cells were found to have spread into the endometrium in two cases and into the myometrium in one. Lymphovascular infiltration was found in two (28.56%) of the cases. Non-keratinizing squamous cell carcinoma diagnosis was made in 20 patients (57.14%). There were 7 cervical biopsies and 13 hysterectomy specimens. The age varied from 35 to 70 years, with a mean of 46.8 years. In the majority of patients, gross examination revealed ulceroproliferative growth in (75%). Tumor cells were organised in nests and sheets on microscopic examination in the majority of instances. Individual cell keratinization was observed in four cases, although epithelial pearl formation was not observed. In one case, tumour cells extended into the endometrium, and in another, both endometrial and myometrial extension was observed. One case had lymphovascular invasion (5%). Lymph node metastases were not observed in any of the seven cases where lymph node excision was performed. Two cervical biopsies and one hysterectomy in patients with age of 48, 52 and 56 were received. All three presented with history of discharge per vagina. Grossly they had cauliflower like lesion with size ranging from 3.2cm as largest to 1.5cm as smallest size. Microscopy revealed tumour cells arranged in glandular arrangement, with moderate pleomorphism, back to back arrangement of glands with no stroma. Nucleus is round to oval with fine chromatin conspicuous nucleoli and scant cytoplasm. Areas of necrosis were seen. The diagnosis was given as adenocarcinoma of cervix. Adenosquamous carcinoma was discovered in a hysterectomy specimen from a 46- year-oldwomann. Microscopy revealed that the tumour was made up of both moderately differentiated adenocarcinoma and keratinizing squamous cell carcinoma. Atypical mitosis and stroma with significant inflammatory cell infiltrate were seen. There was no vascular or lymphatic invasion. On hysterectomy specimens, a histologic diagnosis of small cell carcinoma was made in one case (2.8%). Patients were 50 years old and had reported polymenorrhea for four months and postmenopausal haemorrhage for six months. Gross revealed a small grey-white exophytic growth. Tumour cells demonstrated neuroendocrine development under microscopy. The cells were organised into cords, trabeculae, and layers of cells with inconspicuous cytoplasm and spherical to spindly nuclei. Nuclear moulding and rosette- like structures were seen. Keratinization was missing in both cases. There were foci of glandular differentiation and lymphovascular invasion visible. There were no metastatic deposits in the lymph node.

Immunohistochemistry with synaptophysin was negative, whereas chromogranin was focally positive.

Table 6: Chi-Square Test Correlation between Histopathological & Clinical Diagnosis

Diagnoses	**Kappa**
Histopathological diagnosis Vs Clinical Diagnoses	0.91
Histopathological diagnosis Vs Gross Morphological findings	0.44
Clinical Diagnoses Vs Gross Morphological findings	0.45

There is a strong agreement between Histopathological diagnosis & Clinical Diagnosis. The age of the patients with invasive carcinoma ranged from 35 years to 70 years with a mean age of 49.9 years. The majority of the patients were in the 4^{th} and 5^{th} decade of life.

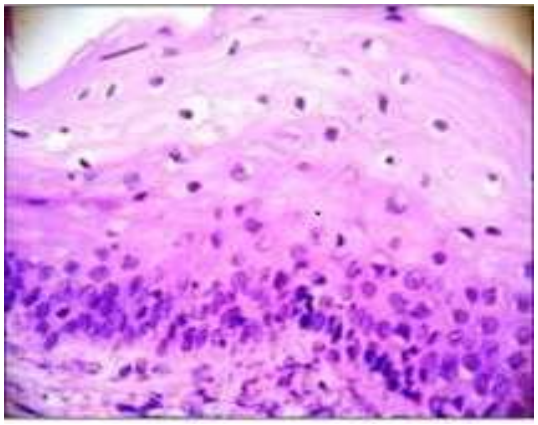


Figure 1: Cervical Intraepithelial neoplasia 1 – Mild nuclear atypia in the basal one third of the epithelium. The upper two thirds of the epithelium show maturation with focal koilocytosis. (H & E x 400)

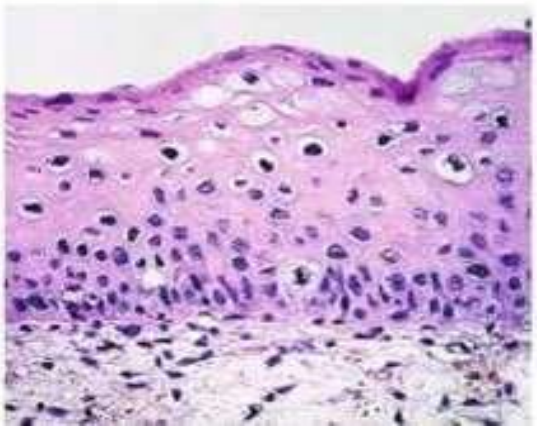


Figure 2: Cervical Intraepithelial neoplasia 1 – Squamous cell differentiation, koilocytic.(H&E x400)

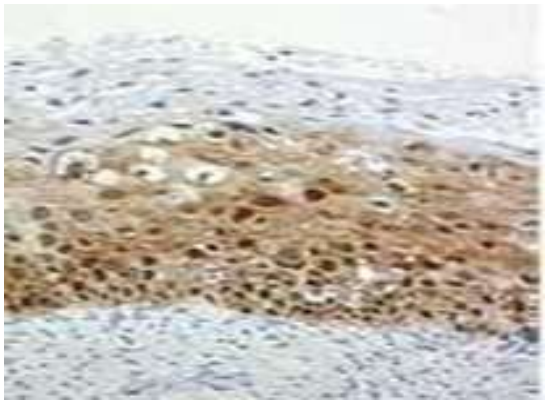


Figure 3: Cervical Intraepithelial neoplasia 1- following HPV infection. Immunostaining with p16 shows koilocytic atypia in the lower 2/3rd of the epithelium.(H&E x 100)

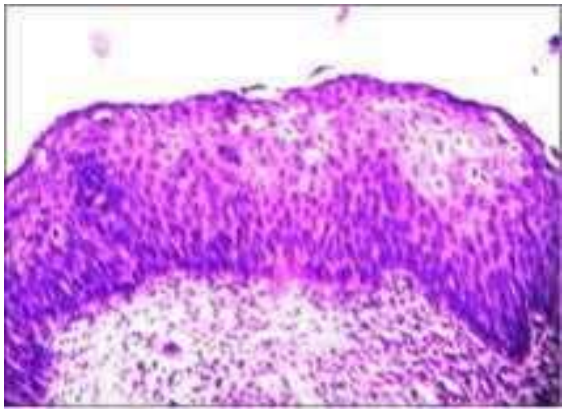


Figure 4: Cervical intraepithelial neoplasia
2 – Nuclear atypia in the basal two third of the epithelium. The upper one thirds show maturation with focal koilocytosis.

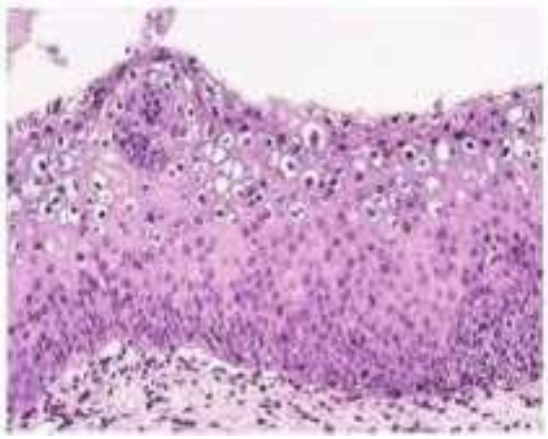


Figure 5 : Cervical intraepithelial neoplasia 2 – Squamous cell differentiation, koilocytic.(H&E x 400)

(H & Ex100)

Figure 6: Cervical intraepithelial neoplasia 2 – Diffuse p16 positivity for in dysplastic cells. Koilocytic change in upper epithelial cell layers. (H&E x100)

Figure 7: Cervical intraepithelial neoplasia 3 with koilocytes.(H&E x 400)

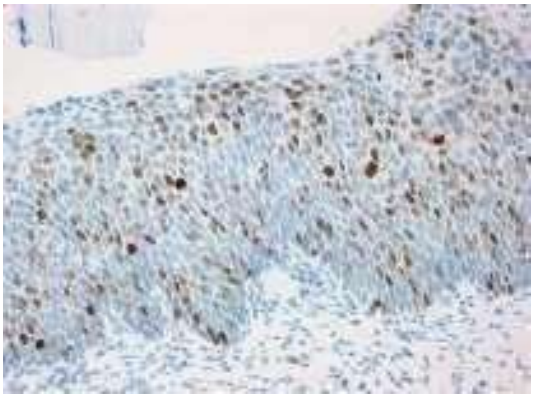


Figure 8: Cervical intraepithelial neoplasia 3. p16 Nuclear positivity dysplastic cells, koilocytic change in throughout epithelial cell layers (H&E x 100)

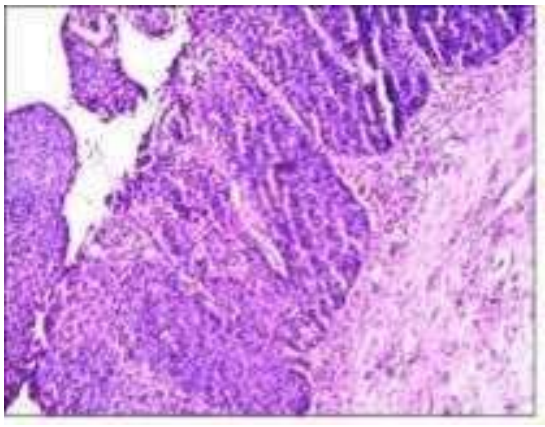


Figure 9: Cervical intraepithelial neoplasia

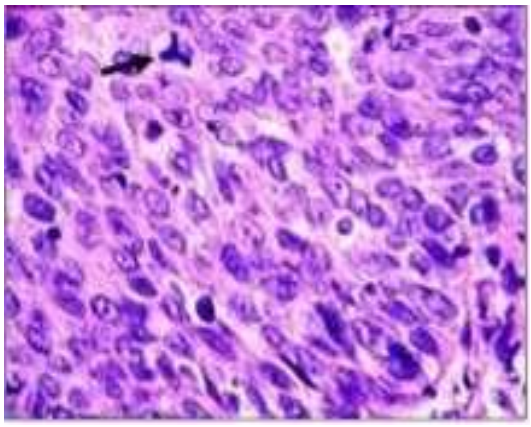


Figure 10: Cervical intraepithelial

3 – Atypical basaloid cells in entire squamous epithelium. (H&E x 100)

neoplasia 3 – Moderate to severe nuclear pleomorhism, coarse chromatin and atypical mitotic figure (□) in the upper half of epithelium. (H & E x 400)

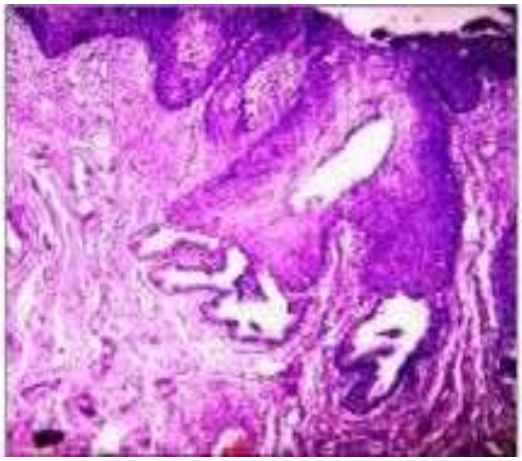


Figure 11: Cervical intraepithelial neoplasia 3 – with intraglandular extension. (H & E x 100)

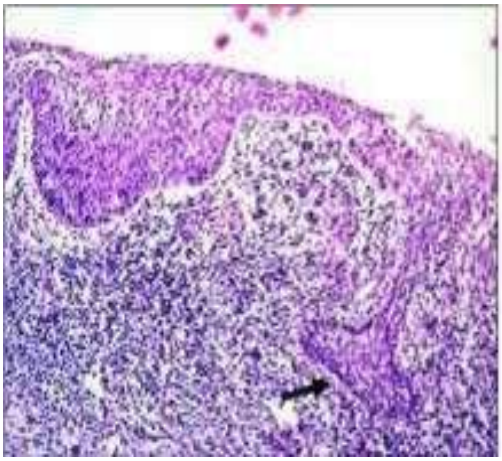


Figure 12: Microinvasive squamous cell carcinoma – prominent lymphotcytic infiltration around the tumour cells (□) that have breached through the basement membrane to invade the stroma. (H&E x 100)

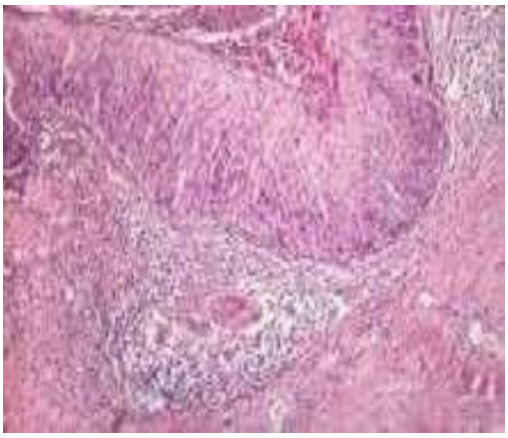


Figure 13. Microinvasive carcinoma, netlike spread of individual cells.(H&E x 100)

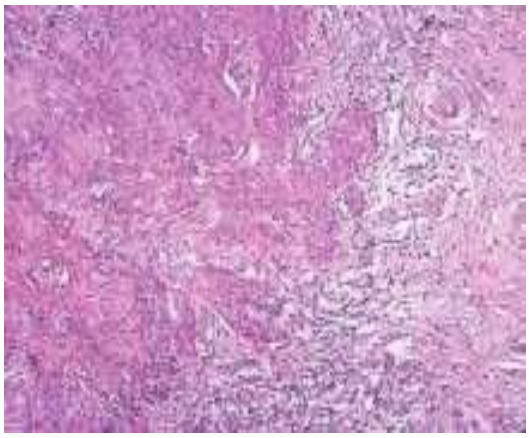


Figure 14. Microinvasive carcinoma, netlike spread.(H&E x 100)

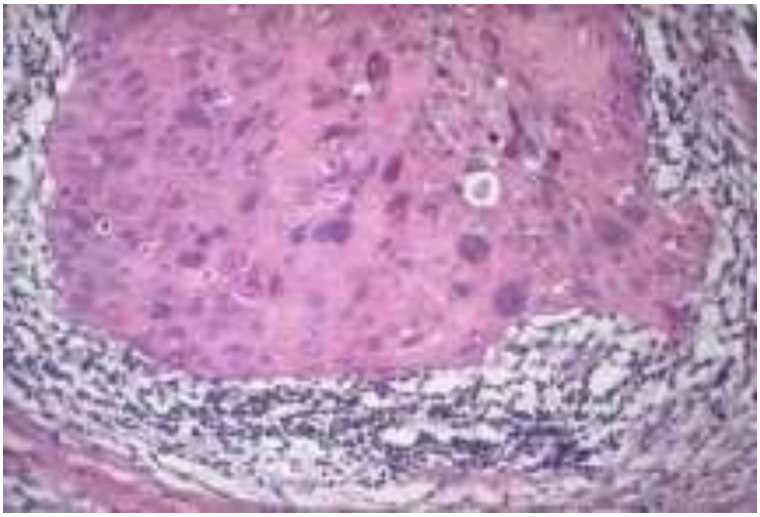


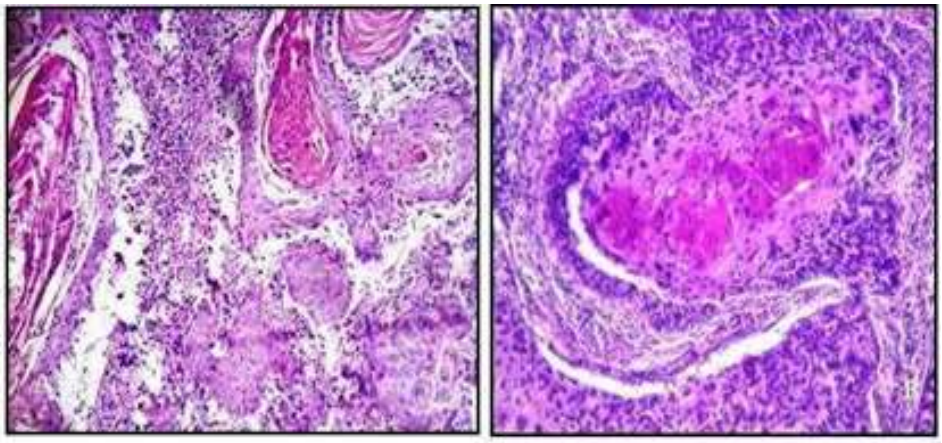
Figure 15. Microinvasive carcinoma, plump infiltration. (H&E x 400)

(A) (B)

Figure 16: Growth patterns in Squamous cell carcinoma A) Exophytic Mass protruding through the external OS (B) Ulcerative growth at external os

(A) **(B)**

Figure 17: Well differentiated grey white large endo phytic growth present at both the lips of cervix.



(A) **(B)**

Figure 18: Squamous cell carcinoma – Keratinizing type
(A) Nests of squamous cells with irregular contours and keratin pearls. (H&E x 100) Keratin pearls within tumour nests (H&E x400)

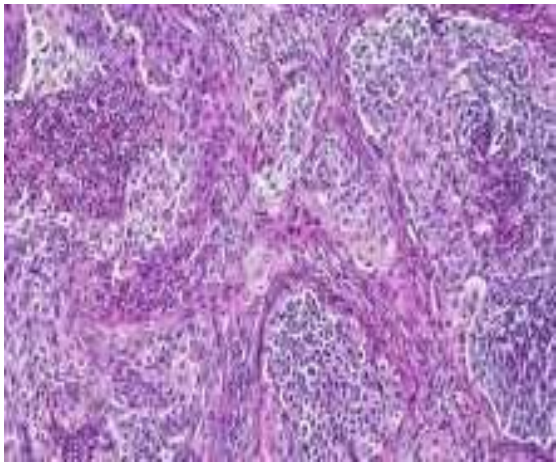


Figure 19. Large cell keratinizing carcinoma. (H&E x 400)

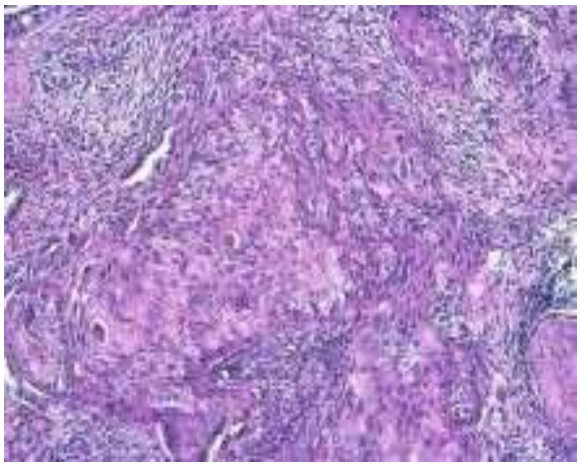


Figure 20. Large cell keratinizing carcinoma. (H&E x 400)

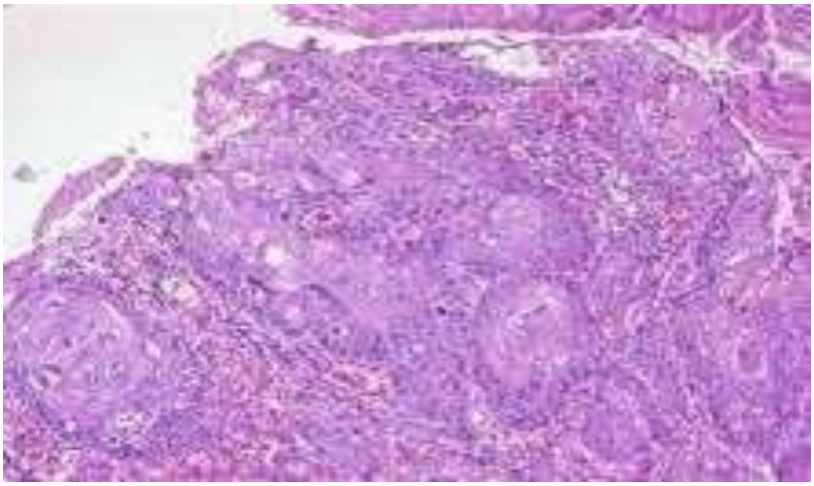


Figure 21. Large cell keratinizing carcinoma. (H&E x 100)

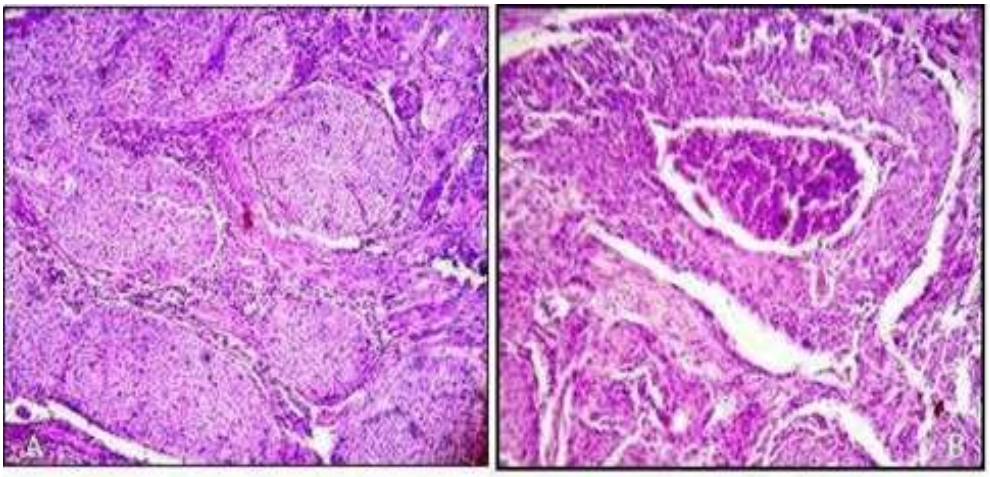


Figure 22: Squamous cell carcinoma – large cell non keratinizing type
A) Irregular nests of squamous cells invading into the stroma (H&E x 100)
Island of tumour cell with central necrotic debris (H&E x 400)

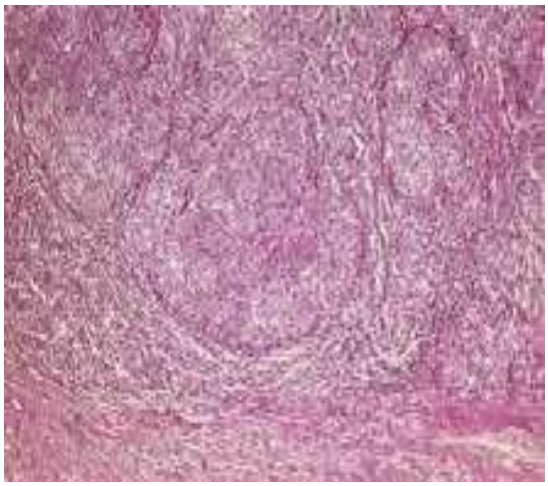


Figure 23: Large cell nonkeratinizing carcinoma. (H&E x100)

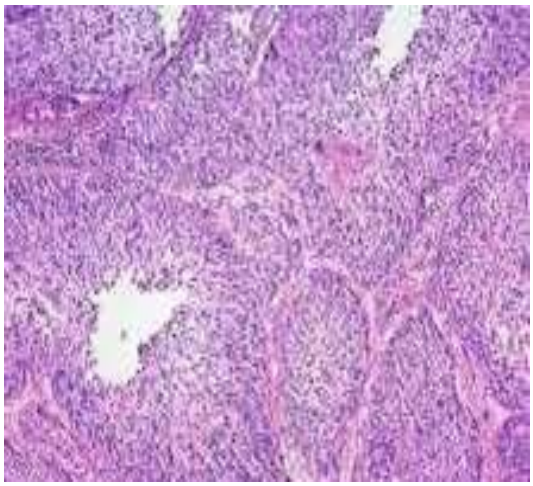


Figure 24: Large cell nonkeratinizing carcinoma, poorly differentiated, with spindle-shaped cellular appearance. (H&E x 400)

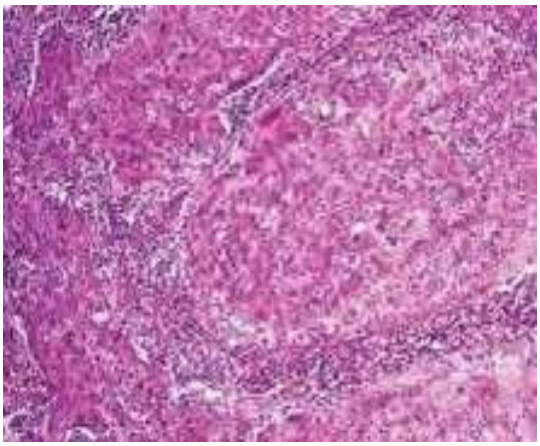


Figure 25: Large cell nonkeratinizing

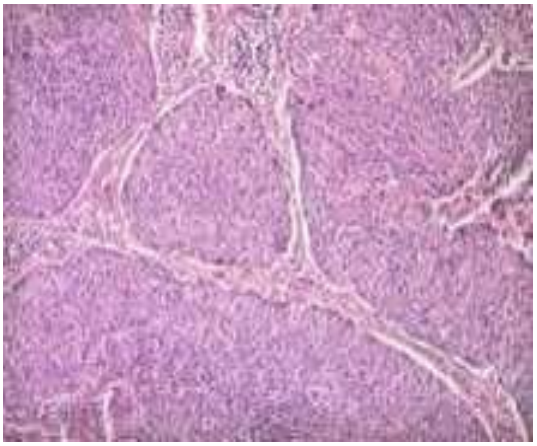


Figure 26: Large cell nonkeratinizing

carcinoma with slight nuclear polymorphism.(H&Ex400)

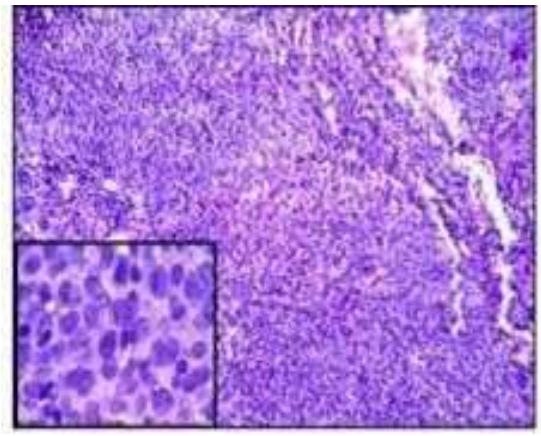


Figure 27: Squamous cell carcinoma – small cell non keratinizing type (H&E low power) Inset : Small round to oval basaloid cells with scant cytoplasm. (H&Ex 400)

carcinoma, moderately differentiated.(H&Ex400)

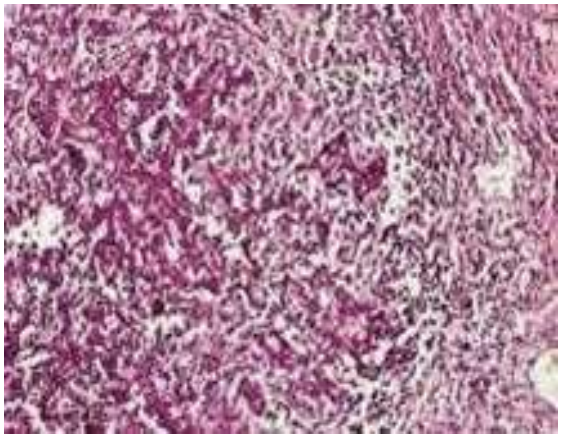


Figure 28: Small cell keratinizing type of squamous cell carcinoma.(H&E X 400)

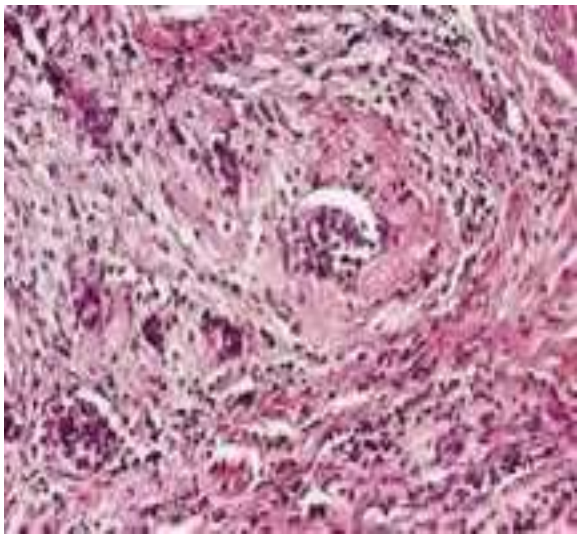


Figure 29 : Small cell keratinizing type of squamous cell carcinoma, extensive lymphatic invasion.(H&Ex400)

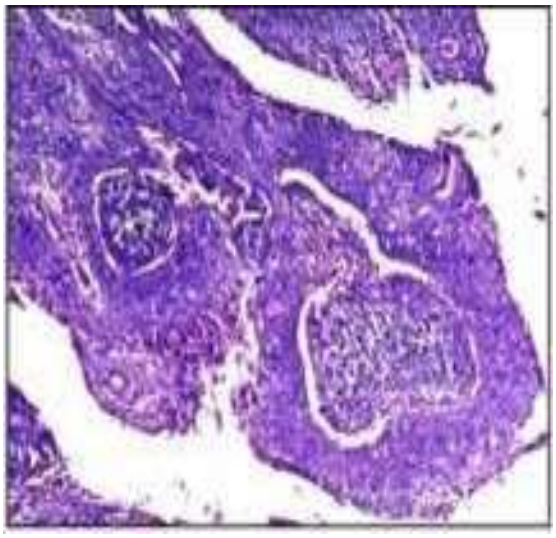


Figure 30: Papillary squamous cell carcinoma – broad papillae with connective tissue stroma are covered by epithelium showing features of CIN. (H&E x100)

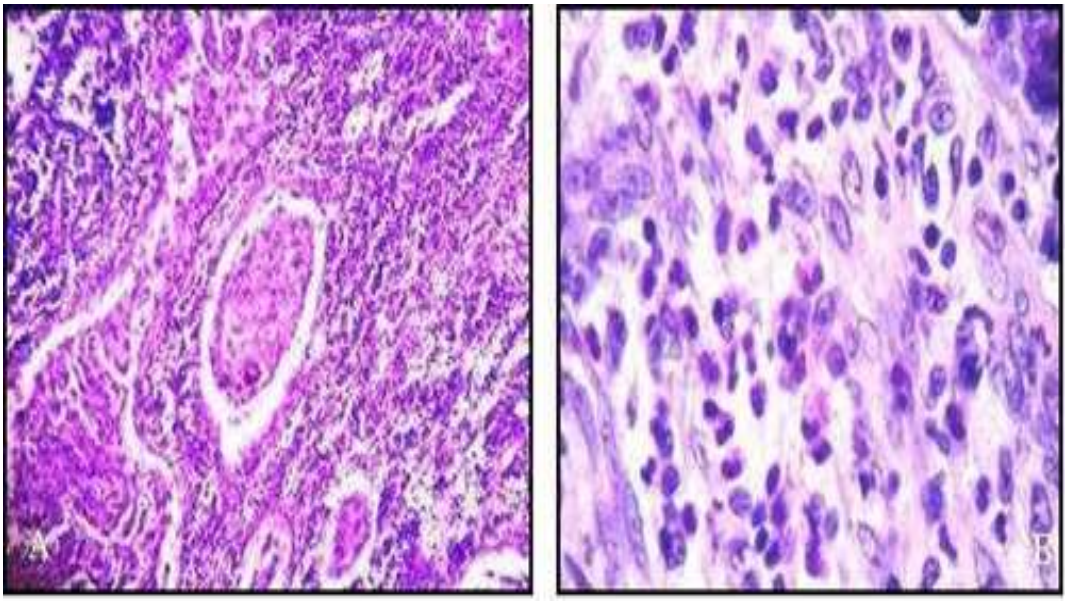


Figure 31: Squamous cell carcinoma – (A) Dense lymphoplamacytic infilitrate (H&E x 100)
(B) Moderate eosinophilic infiltrate (H&Ex 400)

DISCUSSION

Cervical carcinoma is the second most common malignancy in women worldwide.[11] Every year, an estimated 3,71,000 new instances of cervical cancer are detected, accounting for around 1,90,000 fatalities. Developing countries such as India account for 80% of these cases.[1] The most prevalent malignancy among Indian women is cervical carcinoma. It is the biggest cause of death in women around the world and is caused by cervical intraepithelial neoplasia. Histopathology continues to define cancer and precancer treatment by classifying them into particular kinds based on microscopic cell organisation patterns in tissue slices from biopsy or surgical materials. Although morphological conceptions of cervical cancer and precancer evolution are shifting to viral and molecular understanding, histopathology remains the most extensively used clinical endpoint for evaluating the effectiveness of new cervical cancer prevention, HPV vaccinations, and biomarkers.[2] Preneoplastic Cervical intraepithelial neoplasia has the potential to regress, persist, or develop into invasive cancer. As a result, the purpose of the cervical cancer prevention programme is to detect and treat all cancer precursors before they cause invasion.[2,3] The average mean age of patients in the current study for LSIL was 38.9 years, 46.4 years for HSIL, and 48.5 years for invasive cancer, which corresponded to the mean ages recorded by Fadare O et al.[5] According to the Momtahen et al,[6] study, the disease process begins roughly 10-12 years before the formation of invasive carcinoma. According to our findings, the most common age range for cervix cancer was 31 to 40 years. Patients with CIN ranged in age from 21 to 70 years. The majority of patients were in their third to the fourth decade of life.

Lowe D et al,[7] discovered that the frequency of various types of cervical malignancies in the current investigation is similar to previous research. M. Gupta et al,[2] discovered The big cell non- keratinizing form was seen in 32 cases out of the 62 invasive squamous cell carcinomas investigated, followed by the keratinizing type in 28 cases (44.1 %). Small cell non-

keratinizing SCC and papillary SCC were found in one case (1.5 %) each. Our findings on the major cell type of squamous cell carcinoma are consistent with the findings of Gupta M et al. There were two cases of micro-invasive squamous cell carcinoma and 34 cases of invasive squamous cell carcinoma, with 20 (57.14 %) cases being large cell non-keratinizing, 10 (28.57 %) cases being keratinizing, and one (2.4 %) case each of small cell non- keratinizing SCC and papillary SCC.

Gupta M et al,[8] discovered that the invasion mode of pushing with well-defined borders (69.4 %) was greater than diffuse with ill-defined borders (30.6 %); the majority of tumours showed a few to a moderate number of mitotic figures (85.5 %); and lymphovascular invasion was observed in five cases (8 %), which was less than other studies The stromal response ranged from moderate to severe (75.8 %). The current study's outcome was A clinical diagnosis of carcinoma cervix was made in 32 of the 35 cases of invasive cancer (91.4 %).

Gauthier P et al,[8] and van Nagell JR et al,[9] found similar results. Eosinophilic infiltration was found in 17 cases, with the majority of these being mild (64.7 %). Similarly, Van Driel WJ et al,[9] discovered comparable results, however, data on the prognostic significance of a high number of eosinophil granulocytes in the inflammatory infiltrate are contradictory. According to Gupta M et al,[2] the goal of assessing tumour grade (degree of differentiation) is to estimate biological behaviour and aid in patient management. The majority of tumours in this investigation were moderately differentiated (49.4 %).

Associated HSIL was found in 24 (38.7 %) of 62 invasive squamous cell carcinomas. Czernobilsky et al,[10] found similar findings in a study of 40 cases of invasive cancer, finding dysplasia in 23 (57.5 %) of the cases. Squamous cell carcinoma of the cervix with greater uterine involvement was thought to be a rare variation in anatomic involvement. The frequency of this sort of cancer growth has been observed to range between 4% and 17%. Squamous cell carcinoma expanded into the endometrium and/or myometrium in 9 of 25 hysterectomy specimens (36 %) in the current study. Wentz WB et al,[11] found uterine corpus involvement in 7 of 15 individuals (46.7 %). This observation draws attention to the importance of a more comprehensive biopsy process and pretreatment workup before starting therapy. The current investigation discovered. In seven cases, histology revealed invasive keratinizing squamous cell cancer (20%). There were four cervical biopsies and six hysterectomy specimens. The ages varied from 35 to 70 years old, with a mean of 48.5 years. In the majority of patients, gross examination revealed ulcer proliferative development (63.8 %). Radiotherapy causes nuclear and cytoplasmic modifications, as well as significant stromal changes. Features of partial pathogenic reaction were described in one such instance diagnosed in the current study. Cervical primary adenocarcinoma is a rare lesion. According to research conducted on a large population- based database by Chen J et al,[12] there has been a relative and absolute increase in the incidence of uterine cervix cancer in recent years.

In the Gupta M,[2] study, 8.1 % of the malignant tumours detected in the uterine cervix were produced. In the current study, uterine cervix malignant tumours accounted for 2.4 % of all malignant tumours detected. The current study's outcome was that 35 malignant tumours were all epithelial. Three cases (8.58%) were micro invasive carcinoma, whereas the remaining 32 cases (91.42 %) were invasive. Squamous cell carcinoma was found in 30 instances (85.71%), followed by 3 cases (8.57%) of adenocarcinoma, 1 case (2.85%) of

neuroendocrine carcinoma, and 1 case (2.85%) of adenosquamous carcinoma. According to the Gupta M et al,[2] study, neuroendocrine tumours accounted for 5.4 % of all malignant lesions. Wang T et al. reported 6% cases of big and small cell neuroendocrine tumours in his study of 250 malignant tumours, which is similar to the current findings. However, no substantial series of cervix neuroendocrine tumours with comparable behaviour has been documented.

R. Makaju et al,[13] discovered The sensitivity of clinical examination, particularly colposcopy, in distinguishing normal from abnormal cervical tissue ranged from 87 to 99 %, whereas the specificity ranged from 26 to 87 %. The positive predictive value ranged from 53% to 96%, and the negative predictive value ranged from 51% to 99 %. 23 Except for the lower sensitivity, this is consistent with our findings. When p53 grades were compared with premalignant and malignant tumours, as well as their histological subtypes, Yadav et al,[14] found no statistically significant correlation. In the current investigation, malignant lesions had a substantially higher percentage of p53 overexpression than premalignant lesions, with the difference being statistically significant (P = 0.009). Malignant lesions have a higher mean p53 expression (13.29 16.00) than premalignant lesions (1.12 2.23). The same effect was seen in the current investigation. There is a strong link between parity and cancer risk. The greater the parity of malignant instances. This relationship is statistically significant at the P0.05 level.

L Silfverdal et al,[15] Carcinoma cervix is more common in lower socioeconomic classes, when risk factors are less well understood and the disease is more advanced. National cervical screening and education programmes for women are desperately needed, particularly in rural areas. In women with low-grade squamous abnormalities, the histologic examination is strongly related to a lower risk of invasive cancer compared to recurrent cytology.

The current study's limitation was that follow-up was not available in cases of malignancy since they were referred to a higher centre for further therapy. Furthermore, we were unable to see progression or regression in instances classified as intraepithelial neoplasia on cervical biopsy. Further research and association with the coexistence of HPV infection may aid in disease management and prognosis.

CONCLUSION

Cervical cancer remains the most frequent malignancy in underdeveloped countries' women. The realisation that cervical intraepithelial lesions behave as increasing stages of a biologic continuum towards the development of invasive cancer has been one of the most significant advances in the management of cervical neoplasms. For the diagnosis of intraepithelial neoplasia and cervical cancer, the histopathological investigation is regarded as the gold standard. Light microscopy is suitable for almost all instances, with only a few histologic types requiring histochemical stains and immunohistochemistry, particularly in weakly differentiated carcinomas and neuroendocrine tumours. To provide a better prognosis, treatment, and protection against invasive cervical carcinoma, histologic examination of intraepithelial neoplasia and cervical carcinoma should be undertaken at an early stage of the disease. With recent advances in molecular techniques, more research comparing diverse histological features and biomarkers is needed to assure the implementation of targeted therapy and the prevention of invasive cancer.

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