

Prevalence of Low-Grade and High-Grade Squamous Intraepithelial Lesions in Cervical Biopsies

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Abstract

Background: Squamous intraepithelial lesions (SIL) of the cervix represent premalignant epithelial abnormalities strongly associated with persistent high-risk human papillomavirus (HPV) infection. Based on the Bethesda system and WHO classification, cervical squamous intraepithelial lesions are categorized into low-grade squamous intraepithelial lesion (LSIL) and high-grade squamous intraepithelial lesion (HSIL). Early detection and accurate histopathological grading of these lesions are essential for preventing progression to invasive cervical carcinoma. The aim is to determine the prevalence and histopathological spectrum of LSIL and HSIL in cervical biopsy specimens and to evaluate associated demographic and clinical factors. **Material and Methods:** This hospital-based observational cross-sectional study was conducted in the Department of Pathology, Acharya Shri Chander College of Medical Sciences and Hospital (ASCOMS), Jammu, over a period of one year. A total of 100 cervical biopsy specimens from women with clinically suspected cervical lesions were included in the study. Histopathological examination was performed for diagnosis and classification of lesions into LSIL and HSIL according to WHO/Bethesda criteria. Data were analyzed using SPSS version 27.0 and GraphPad Prism version 5. Statistical significance was considered at $p < 0.05$. **Results:** The majority of patients belonged to the 41–50 years age group (34%). LSIL was the most common lesion observed in 46% cases, while HSIL accounted for 54% cases. Multiparity showed a significant association with increasing severity of cervical squamous intraepithelial lesions. White discharge per vaginum was the most common presenting symptom (38%). HPV positivity was observed in 76% cases and showed a significant association with HSIL lesions ($p = 0.001$). **Conclusion:** Squamous intraepithelial lesions of the cervix are common among middle-aged women and are strongly associated with persistent HPV infection and multiparity. Histopathological evaluation of cervical biopsy specimens plays a crucial role in early diagnosis, accurate grading, and timely management of premalignant cervical lesions, thereby reducing the burden of invasive cervical carcinoma.

Keywords: LSIL, HSIL, Squamous intraepithelial lesion, Cervical biopsy, Human papillomavirus, Cervical dysplasia, Histopathology, Cervical cancer screening.

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INTRODUCTION

Cervical cancer is one of the most frequently occurring cancers in women globally and a significant public health problem, especially in low-resource countries. It is curable and a malignancy with a long premalignant phase, allowing for a great opportunity for early detection and therapeutic intervention. High-risk human papillomavirus (HPV), particularly HPV types 16 and 18 has been proven as the major etiological agent in the occurrence of cervical squamous intraepithelial lesions and invasive cervical carcinoma.

A premalignant cervical epithelial lesion was traditionally classified under the cervical intraepithelial neoplasia (CIN) system into either CIN I, CIN II or CIN III depending on how dysplastic the cervical epithelium is. Since the understanding of HPV biology and the behavior of the lesions, the Bethesda system and WHO Classification had been shaped to a two-tiered system, with low-grade squamous intraepithelial lesion (LSIL) corresponding to productive HPV infection and high-grade squamous intraepithelial lesion (HSIL) being

associated with transforming HPV infection and lesions, which have much higher malignant potential when compared to the low grade ones.^[1-3]

Limited availability of screening programs, poor access to health services, poor socioeconomic conditions and lack of awareness and delayed clinical presentation contribute to the higher burden of cervical cancer in LMCs compared to high- and middle-income countries. India has significant role in the burden of cervical cancer morbidity and mortality associated with various risk factors such as early age at marriage, multiparity, poor

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genital hygiene, immunosuppression, smoking, prolonged oral contraceptive use and multiple sexual partners in the pathogenesis of cervical squamous intraepithelial lesions.^[4,5] Cervical cytology and HPV testing are excellent prevention and screening tools; however, histopathological evaluation of samples from cervical biopsy is the gold standard for definitive diagnosis and grading of cervical squamous intraepithelial lesion, and is the essential tool for diagnosis and early detection of LSIL, HSIL, and invasive carcinoma.^[7,6]

Histomorphologically, LSIL shows koilocytic atypia, mild nuclear abnormalities, and dysplastic changes that are mostly in the basal third of the squamous epithelium. However, there are significant differences between the two categories, between LSIL and HSIL, that make it important to distinguish the two categories in order to make appropriate management decisions, follow up appropriate, and make appropriate prognosis.

Several studies have reported different prevalence of LSIL and HSIL in various populations based on demographic characteristics, HPV prevalence, sexual behaviour and implementing cervical cancer screening programmes, with higher proportion of women presenting late in the developing region as a result of social stigma and lack of awareness.^[8-10] The knowledge of the histopathological spectrum and prevalence of LSIL and HSIL is valuable to assess the burden of the disease, optimize cervical cancer screening programs, and implement preventive health care measures. Early diagnosis and timely intervention to deal with the premalignant conditions of the cervix greatly minimises morbidity and mortality rates of cervical carcinoma.

Thus, the current study was conducted to assess the prevalence and histopathology spectrum of LSIL and HSIL in cervical biopsy samples and to investigate associated demographic and clinicopathological parameters that play role in progression and development of squamous intraepithelial lesion in the cervix.

MATERIALS AND METHODS

Study Design: Hospital-based observational cross-sectional study.

Study Population: Female patients undergoing cervical biopsy for suspected cervical lesions and whose biopsy specimens were received in the Department of Pathology.

Sample Size: A total of 100 patients were included in the study.

Study Duration: The study was conducted over a period of 1 year.

RESULTS

Study Place: Department of Pathology, Acharya Shri Chander College of Medical Sciences and Hospital (ASCOMS), Jammu.

Inclusion Criteria:

- Women of all age groups undergoing cervical biopsy.
- Patients with clinically suspected cervical lesions.
- Adequately preserved cervical biopsy specimens received for histopathological examination.
- Patients who provided informed consent for participation in the study.

Exclusion Criteria:

- Inadequate or poorly preserved biopsy specimens.
- Previously diagnosed and treated cases of cervical malignancy.
- Patients unwilling to participate in the study.
- Repeat biopsy specimens from the same patient during the study period.

Statistical Analysis: The collected data were entered into Microsoft Excel and analyzed using IBM SPSS Statistics version 27.0 (SPSS Inc., Chicago, IL, USA) and GraphPad Prism version 5. Continuous variables were expressed as mean \pm standard deviation (SD), while categorical variables were presented as frequencies and percentages. Comparisons of continuous variables between independent groups were performed using the unpaired t-test, whereas the paired t-test was used for within-group comparisons. Categorical variables were analyzed using the Chi-square test or Fisher's exact test, as appropriate. A p-value of <0.05 was considered statistically significant.

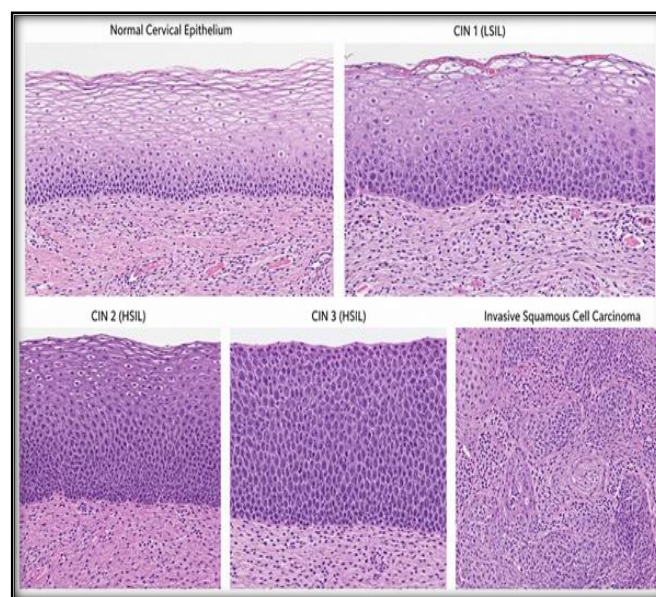


Table 1: Age-wise Distribution of Cervical Intraepithelial Lesions

Age Group (Years)	LSIL (CIN I) n (%)	HSIL (CIN II/III) n (%)	Total n (%)	P value
<30	12 (24.0)	3 (6.0)	15 (15.0)	0.012
31-40	18 (36.0)	12 (24.0)	30 (30.0)	
41-50	11 (22.0)	19 (38.0)	30 (30.0)	
51-60	6 (12.0)	11 (22.0)	17 (17.0)	
>60	3 (6.0)	5 (10.0)	8 (8.0)	
Total	50 (50.0)	50 (50.0)	100 (100)	

Table 2: Distribution of Histopathological Grading of Cervical Intraepithelial Neoplasia

Histopathological Grade	Number of Cases	Percentage (%)	P value
CIN I (LSIL)	50	50	0.001
CIN II	28	28	
CIN III	22	22	
Total	100	100	

Table 3: Association Between Parity and Cervical Intraepithelial Lesions

Parity	LSIL n (%)	HSIL n (%)	Total	P value
Nulliparous	8 (16.0)	2 (4.0)	10	0.007
1–2 Children	22 (44.0)	14 (28.0)	36	
≥3 Children	20 (40.0)	34 (68.0)	54	
Total	50	50	100	

Table 4: Association Between Presenting Symptoms and Histopathological Grade

Presenting Symptom	LSIL n (%)	HSIL n (%)	Total	P value
White vaginal discharge	24 (48.0)	11 (22.0)	35	0.035
Intermenstrual bleeding	10 (20.0)	13 (26.0)	23	
Postcoital bleeding	8 (16.0)	18 (36.0)	26	
Postmenopausal bleeding	3 (6.0)	6 (12.0)	9	
Asymptomatic	5 (10.0)	2 (4.0)	7	
Total	50	50	100	

Table 5: Distribution of Cervical Lesions According to Transformation Zone Involvement

Transformation Zone Involvement	LSIL n (%)	HSIL n (%)	Total	P value
Present	32 (64.0)	45 (90.0)	77	0.002
Absent	18 (36.0)	5 (10.0)	23	
Total	50	50	100	

Table 6: Age Group and Severity of CIN (CIN I, CIN II, CIN III)

Age Group (Years)	CIN I	CIN II	CIN III	Total	P value
<30	12	2	1	15	0.018
31–40	18	8	4	30	
41–50	11	10	9	30	
51–60	6	5	6	17	
>60	3	3	2	8	
Total	50	28	22	100	

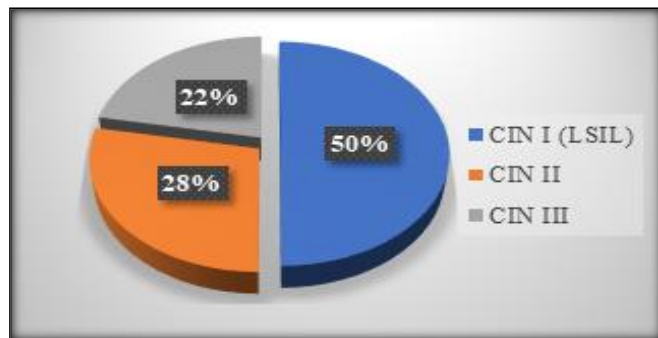


Figure 1: Distribution of Histopathological Grading of Cervical Intraepithelial Neoplasia

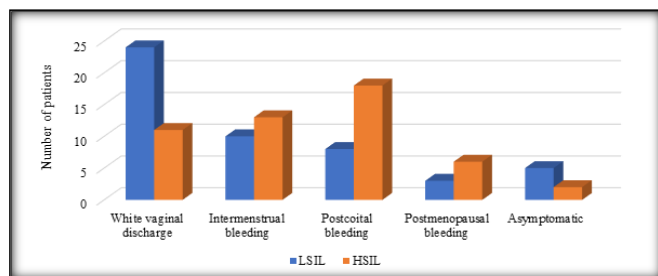


Figure 2: Association Between Presenting Symptoms and Histopathological Grade

A total of 100 cervical biopsy specimens diagnosed as cervical intraepithelial neoplasia were evaluated. The age of the patients ranged from less than 30 years to more than 60 years. The highest proportion of cases was observed in the 31–40 years and 41–50 years age groups, each accounting for 30.0% (30/100) of all cases, followed by the 51–60 years age group (17.0%), <30 years (15.0%), and >60 years (8.0%). LSIL (CIN I) was more frequent among younger women, whereas HSIL (CIN II/III) predominated in older age groups. This association between age and lesion grade was statistically significant ($p = 0.012$) [Table 1].

Histopathological grading revealed that CIN I (LSIL) was the most common lesion, observed in 50 cases (50.0%), followed by CIN II in 28 cases (28.0%) and CIN III in 22 cases (22.0%). The distribution of lesion grades showed a statistically significant difference ($p = 0.001$) [Table 2].

Assessment of parity demonstrated that the majority of patients were multiparous. Among women with one to two children, 36.0% (36/100) of cases were recorded, while 54.0% (54/100) had three or more children. HSIL was considerably more frequent among women with parity ≥ 3 (68.0%) compared to nulliparous women (4.0%). The association between parity and lesion severity was statistically significant ($p = 0.007$) [Table 3]. Regarding clinical presentation, white vaginal discharge was the

most common symptom, reported in 35.0% (35/100) of patients, followed by postcoital bleeding (26.0%), intermenstrual bleeding (23.0%), postmenopausal bleeding (9.0%), and asymptomatic presentation (7.0%). HSIL cases were more frequently associated with postcoital bleeding (36.0%) than LSIL cases (16.0%). A significant association was observed between presenting symptoms and histopathological grade ($p = 0.035$) [Table 4].

Evaluation of transformation zone involvement showed that 77.0% (77/100) of lesions involved the transformation zone, whereas 23.0% (23/100) did not. Transformation zone involvement was observed in 90.0% of HSIL cases compared with 64.0% of LSIL cases, indicating a strong relationship between transformation zone involvement and lesion severity. This association was statistically significant ($p = 0.002$) [Table 5].

Analysis of age-specific CIN severity demonstrated that CIN I predominated in younger age groups, particularly among women aged 31–40 years (18 cases) and <30 years (12 cases). In contrast, CIN II and CIN III lesions were more frequent in women aged 41–50 years and 51–60 years. The highest number of CIN III cases was observed in the 41–50 years age group (9 cases). The relationship between age and CIN severity was statistically significant ($p = 0.018$) [Table 6].

In all, the results suggest that the risk of developing high-grade cervical intraepithelial lesions was significantly associated with increasing age, higher parity, involvement of the transformation zone, as well as with certain clinical symptoms (postcoital bleeding). The association of younger women with LSIL and middle and older age with HSIL highlights the need for early screening and histopathological examinations for early detection and management of premalignant cervical lesions.

DISCUSSION

The present study aimed to assess the prevalence and histopathological spectrum of cervical intraepithelial lesions of cervical biopsy samples and showed significant associations between lesions grade and some of the demographic and clinical pathological parameters. The results reinforce the natural history of HPV related cervical carcinogenesis and offer an analysis of the distribution of LSIL and HSIL in the cohort studied.

Most patients were in the 31–40 years and 41–50 years age groups, representing 30.0% and 30.0% respectively, with the higher age groups in women more likely to have HSIL lesions as compared to men. There was a statistically significant correlation between age and severity of lesions ($p=0.012$). Similar observations were reported by Bukhari et al. who found that the peak incidence of cervical intraepithelial lesions occurred between 35 and 50 years of age, with HSIL predominating in women above 40 years.^[11] Likewise, Pimple and Mishra noted that advancing age was associated with a higher prevalence of high-grade lesions, likely reflecting prolonged persistence of oncogenic HPV infection and cumulative genetic alterations within cervical epithelial cells.^[12] The age-related increase in HSIL observed

in the present study supports the concept that progression from HPV infection to high-grade dysplasia is a gradual process requiring several years.

On histopathology grading the cases were grades: CIN I (50.0%), CIN II (28.0%) and CIN III (22.0%). The high prevalence of LSIL might be due to good detection of dysplastic cervical lesions prior to their advancement to higher-grade disease; however, the relatively high proportion of HSIL was found in the present study, reflecting the significant contribution of premalignant conditions in the cervical cancer burden.

In the present study, parity was found to be significantly associated with lesion severity ($p=0.007$), with women with three or more children having 54.0% of all cases and showing a very high prevalence of HSIL. These results corroborate the relevance of the reproductive history as a risk factor for the development of cervical neoplasia, as multinubility, hormonal changes, and chronic exposure of the transformation zone were shown to be independent risk factors for higher grade cervical lesions and cervical cancer by Muñoz et al,^[15] and Castellsagué & Muñoz.^[16] Vaginal discharge (pregnancy 35.0%) and postcoital bleeding and intermenstrual bleeding were the most common presenting symptoms. Interestingly, postcoital bleeding was more associated with HSIL lesions. The above results suggest the need for early detection of gynecological symptoms as possible markers for serious cervical disease, especially as they are more common in symptomatic women identified with cervical dysplasia as found by Sharma et al,^[17] and Sankaranarayanan et al,^[18] in women with high-grade lesions versus those with low-grade or none at all.

In the present study, its involvement in transformation zone was observed in 77.0% of the cases, while in case of LSIL cases, it is 64.0% ($p=0.002$). Biologically, this may be true because the HPV infection and subsequent neoplastic change is most likely to occur in the squamocolumnar junction and in the transformation zone. The results of this study corroborate earlier reports pointing to the importance of transformation zone epithelial cell involvement of lesions for the progression of lesions.

CIN severity by age revealed that the younger women were more likely to have CIN I, while women older than 41–60 years were more likely to have CIN II and III. The statistically significant increase in HPV severity associated with age ($p=0.018$) found in this study also supports previous studies suggesting a temporal progression model in cervical carcinogenesis in that older women with persistent infections are more likely to have a high-grade lesion than younger women with low-grade lesions, if they have any infection at all.

In summary, the results of the present study confirm that published reports have suggested that there is a significant association between the age of the older women, multiparity, transformation zone involvement and certain clinical symptoms with high-grade cervical intraepithelial lesions. The high percentage of HSIL detected highlights the importance of having a good cervical cancer screening program, timely histopathological diagnosis and consequent early therapeutic interventions to prevent malignant transformation to cervical carcinoma.

CONCLUSION

The present study emphasizes the high prevalence of CIN in women who had a cervical biopsy evaluated, in which the most prevalent histopathological diagnosis was LSIL (CIN I) and the least was CIN III lesions. The factors of transformation zone involvement, presenting symptoms, increasing age, and higher parity were significantly related to lesion severity. The distribution by age of women with LSIL showed that it was more common among younger women, while that of women with HSIL showed that this was more prevalent among middle age and older women, which is consistent with progression of persistent high-risk HPV infection. There is a high prevalence of HSIL, which highlights the importance of the implementation of adequate cervical cancer screening programs and timely histopathological diagnosis of suspicious lesions. Any clinical symptoms associated with abnormal vaginal discharge and postcoital bleeding should be taken as an indication of cervical evaluation and early detection of any premalignant changes in the cervix. Histopathological diagnosis and grading of cervical lesions is the standard; the most accurate method. Prompt diagnosis and treatment of LSIL and HSIL may significantly reduce the likelihood of progression to invasive cervical cancer and enhance women's reproductive health.

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Conflicts of interest

There are no conflicts of interest.

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