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HISTOPATHOLOGICAL FEATURES AND THERAPEUTIC OUTCOMES IN CERVICAL INTRAEPITHELIAL NEOPLASIA: A CROSS-SPECIALTY CLINICAL INVESTIGATION

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Abstract

Background: Cervical Intraepithelial Neoplasia (CIN) is a pre-cancerous condition associated with persistent infection by high-risk human papillomavirus (HPV). CIN is graded into three levels (CIN 1, CIN 2, CIN 3) based on histopathological features, with treatment strategies varying depending on the severity of the lesion. This study aims to assess the histopathological characteristics of CIN and evaluate therapeutic outcomes in a cohort of 75 patients.

Methods: This retrospective study analyzed 75 patients diagnosed with CIN between January 2020 and December 2020. Patients were classified by CIN grade and underwent different treatments, including conservative management, ablative therapies (cryotherapy, laser ablation), or excisional therapies (LEEP, conization), based on lesion severity. Therapeutic outcomes, including lesion resolution, recurrence, and progression, were tracked over a two-year follow-up period. Factors such as patient age, HPV type, immune status, and excision margin status were also analyzed for their impact on outcomes.

Results: Of the 75 patients, 42.7% had CIN 1, 29.3% had CIN 2, and 28% had CIN 3. Lesion regression was observed in 71.9% of CIN 1 patients managed conservatively. Recurrence was most frequent in CIN 3 (14.3%), followed by CIN 2 (18.2%) and CIN 1 (9.4%). Positive excision margins, high-risk HPV infection, and compromised immune status were significant predictors of recurrence. Patients with high-risk HPV strains had a 27% recurrence rate compared to 9% for other HPV types. Immune-compromised patients had a 60% recurrence rate compared to 15% for immunocompetent patients.

Conclusions: Histopathological features and therapeutic outcomes in CIN are strongly influenced by lesion severity, HPV type, immune status, and excision margins. While low-grade CIN often regresses, higher-grade lesions require aggressive intervention and close monitoring. Personalized treatment strategies based on patient characteristics and lesion factors are essential to optimize

therapeutic success and minimize recurrence. The findings support the need for ongoing HPV vaccination and effective screening programs to prevent CIN progression to cervical cancer.

Keywords: Histopathological Features, Therapeutic Outcomes, Cervical Intraepithelial Neoplasia, Clinical Investigation.

Introduction

Cervical Intraepithelial Neoplasia (CIN) is a pre-cancerous condition characterized by abnormal cellular changes in the squamous epithelium of the cervix. It is commonly detected through routine cervical cancer screening methods, such as Pap smears or HPV testing, and is closely associated with persistent infections of high-risk human papillomavirus (HPV) strains, particularly HPV 16 and 18 [1]. CIN is classified into three grades—CIN 1, CIN 2, and CIN 3—based on the extent and severity of abnormal cellular changes observed histologically. CIN 1 is indicative of mild dysplasia and typically involves the lower third of the cervical epithelium, with a high likelihood of spontaneous regression. CIN 2, or moderate dysplasia, extends into the middle third of the epithelium and has a greater potential for progression to higher-grade lesions. CIN 3, or severe dysplasia, represents the most advanced pre-cancerous stage, affecting the full thickness of the epithelium, and poses the greatest risk for progression to invasive cervical cancer if untreated [2]. Histopathological examination of cervical tissue remains the gold standard for diagnosing and grading CIN.

The microscopic features of CIN include nuclear enlargement, hyperchromasia, irregular nuclear contours, and an increase in mitotic figures, with the severity of these features corresponding to the grade of the lesion. Additionally, histopathology can reveal koilocytosis, a hallmark of HPV infection [3]. Accurate grading is critical for determining the most appropriate therapeutic approach and predicting patient outcomes. Treatment options for CIN vary based on the severity of the lesion, with conservative management recommended for CIN 1, as most low-grade lesions regress spontaneously, particularly in younger women. In contrast, higher-grade lesions, such as CIN 2 and CIN 3, typically require intervention to prevent progression to invasive carcinoma [4]. Therapeutic interventions include ablative procedures, such as cryotherapy and laser ablation, which destroy abnormal tissue, and excisional procedures, such as Loop Electrosurgical Excision Procedure (LEEP) and cone biopsy, which physically remove the affected tissue [5]. The success of CIN treatment depends on several factors, including the patient's age, immune status, and HPV type.

Younger women, particularly those under the age of 30, are more likely to experience spontaneous regression of CIN lesions due to a more robust immune response, while immunocompromised individuals, such as those with HIV, are at greater risk for persistent HPV infection and treatment failure [6]. The type of HPV present also plays a role in prognosis, as infections with high-risk strains like HPV 16 and 18 are more likely to persist and progress to higher-grade lesions. Another important factor in therapeutic outcomes is the status of excision margins in patients undergoing surgical treatment; positive margins (indicating the presence of abnormal cells at the edges of the excised tissue) are associated with a higher likelihood of recurrence and may necessitate additional intervention. Regular follow-up after treatment is crucial for detecting recurrence, particularly in the first two years post-treatment [7,8].

Objective

This study aims to explore the histopathological features of CIN and assess the outcomes of different therapeutic interventions to better understand the factors influencing treatment success. By evaluating the efficacy of various treatment modalities and identifying predictors of recurrence, this research seeks to contribute to the optimization of treatment strategies for CIN and improve patient prognosis. The findings are especially pertinent in light of advancements in cervical cancer prevention, such as

HPV vaccination and enhanced screening techniques, which have the potential to reduce the incidence of CIN and its progression to invasive cancer.

Methodology

This study is a retrospective analysis of histopathological features and therapeutic outcomes in 75 patients diagnosed with Cervical Intraepithelial Neoplasia (CIN) between January 2020 and December 2020. The study population includes women aged 21 to 50 years, who were referred to the gynecology department for abnormal Pap smear results and were subsequently diagnosed with CIN through colposcopy-guided biopsy. Patients with a previous history of cervical cancer or other gynecological malignancies were excluded from the study.

The study cohort was categorized based on the grade of CIN into three groups: CIN 1 (mild dysplasia), CIN 2 (moderate dysplasia), and CIN 3 (severe dysplasia or carcinoma in situ). Histopathological examination of the cervical biopsy samples was performed by experienced pathologists, focusing on key diagnostic features, including nuclear enlargement, pleomorphism, hyperchromasia, mitotic activity, and the presence of koilocytosis.

The grading of CIN was confirmed based on the extent of epithelial involvement by abnormal cells. Therapeutic interventions were selected based on the grade of CIN, patient age, reproductive preferences, and overall health status. Patients with CIN 1 were managed conservatively with regular follow-up and HPV testing, while those with CIN 2 and CIN 3 underwent either ablative or excisional therapies.

Ablative therapies included cryotherapy, which was performed in an outpatient setting, and laser ablation for selected cases. Excisional therapies included the Loop Electrosurgical Excision Procedure (LEEP) and cold knife conization, with the choice of procedure depending on the size and location of the lesion, as well as patient factors such as fertility considerations. Follow-up data were collected for all patients, including the recurrence of CIN and the presence of residual disease. Recurrence was defined as the reappearance of CIN at the same site or a new site within two years of treatment.

The primary outcome of the study was the rate of complete lesion resolution, while secondary outcomes included recurrence rates and the impact of factors such as age, immune status, HPV type, and excision margin status on treatment success.

Data were analyzed using SPSS v10 to determine correlations between histopathological features and therapeutic outcomes. Chi-square tests were used to assess the association between categorical variables, while logistic regression was performed to identify factors predicting treatment failure or recurrence. A p-value of less than 0.05 was considered statistically significant. Ethical approval for the study was obtained from the institutional review board, and all patients provided informed consent for the use of their medical records in the analysis.

Results

A total of 75 patients diagnosed with Cervical Intraepithelial Neoplasia (CIN) were included in this study. The age of the patients ranged from 21 to 50 years, with a mean age of 34.2 years. The distribution of CIN grades among the patients was as follows: 32 patients (42.7%) had CIN 1, 22 patients (29.3%) had CIN 2, and 21 patients (28%) had CIN 3. Histopathological evaluation confirmed the presence of characteristic features such as nuclear enlargement, hyperchromasia, and increased mitotic activity in all cases, with the severity of these features correlating with the CIN grade. Koilocytosis, indicative of HPV infection, was observed in 48 patients (64%).

Table 1: Patient Distribution and Histopathological Features

CIN Grade	Number of Patients (n=75)	Percentage (%)	Koilocytosis Present (n=48)	Nuclear Enlargement (%)	Hyperchromasia (%)	Increased Mitotic Activity (%)
CIN 1	32	42.7	20 (62.5%)	62.5	56.3	40.6
CIN 2	22	29.3	16 (72.7%)	72.7	68.2	59.1
CIN 3	21	28.0	12 (57.1%)	81.0	85.7	76.2
Total	**75**	**100%**	**48 (64%)**	—	—	—

Therapeutic Outcomes

Of the 32 patients with CIN 1, 25 (78.1%) were managed conservatively with regular follow-up and HPV testing, while 7 (21.9%) underwent ablative therapy due to persistent lesions after 12 months. After one year of follow-up, spontaneous regression occurred in 23 patients (71.9%), while 6 patients (18.8%) experienced persistent CIN 1. Three patients (9.4%) progressed to CIN 2, and no cases progressed to CIN 3. None of the patients in the CIN 1 group developed invasive cervical cancer during the follow-up period. In the CIN 2 group, 15 patients (68.2%) underwent excisional therapy (LEEP or conization), and 7 patients (31.8%) were treated with ablative therapy. Complete resolution of the lesion was achieved in 16 patients (72.7%) after treatment, while 4 patients (18.2%) experienced recurrence of CIN 2 within two years of treatment. Two patients (9.1%) had residual CIN 3 on follow-up biopsy and required further excisional intervention.

Among the 21 patients with CIN 3, all underwent excisional therapy, with 14 patients (66.7%) treated by LEEP and 7 patients (33.3%) undergoing cold knife conization. Complete resolution was observed in 17 patients (81%). However, 3 patients (14.3%) had recurrent CIN 3 within two years, and 1 patient (4.8%) progressed to invasive cervical cancer despite treatment.

Table 2: Therapeutic Outcomes by CIN Grade

CIN Grade	Therapy Type	Patients Treated (n)	Complete Resolution (%)	Persistent Disease (%)	Recurrence (%)	Progression to CIN 3 or Cancer (%)
CIN 1	Observation	25	71.9	18.8	9.4	0
	Ablative Therapy (Cryotherapy)	7	85.7	14.3	0	0
CIN 2	Ablative Therapy (Laser)	7	71.4	14.3	14.3	0
	Excisional Therapy (LEEP)	15	73.3	13.3	13.3	0
CIN 3	Excisional Therapy (LEEP)	14	78.6	14.3	14.3	0
	Excisional Therapy (Conization)	7	85.7	14.3	0	14.3
Total	—	**75**	**76.0%**	**12.0%**	**13.3%**	**1.3%**

Factors Affecting Outcomes

When analyzing factors that influenced therapeutic success, it was found that age, immune status, HPV type, and margin status were significant predictors of recurrence and treatment failure. Patients under 30 years of age had a higher rate of lesion regression (82.6%) compared to those over 30 years (65.1%), with a statistically significant difference ($p = 0.03$). HPV type also influenced outcomes, as patients with high-risk HPV 16 or 18 had a higher recurrence rate (27%) compared to those with other HPV types (9%) ($p = 0.02$). Immune status was another significant factor. Among the 10 patients with compromised immune systems (due to HIV or other conditions), 6 (60%) experienced recurrence or persistent lesions, compared to 15% in immunocompetent patients ($p = 0.001$). Positive margins after excisional therapy were associated with a higher recurrence rate; 8 patients (33.3%) with positive margins had recurrent CIN, compared to 2 patients (6.1%) with negative margins ($p = 0.005$).

Recurrence Rates

Overall, the recurrence rate across all CIN grades was 13.3% (10 out of 75 patients). Recurrence was most common in patients with CIN 3 (14.3%), followed by CIN 2 (18.2%), and CIN 1 (9.4%). No recurrences were observed in patients who had negative excision margins and were HPV-negative at follow-up.

Table 3: Factors Affecting Recurrence and Therapeutic Outcomes

Factor	No Recurrence (%)	Recurrence (%)	p-value
Age < 30 years	82.6	17.4	0.03
Age ≥ 30 years	65.1	34.9	—
High-risk HPV (16, 18)	73.0	27.0	0.02
Other HPV Types	91.0	9.0	—
Immune Compromised	40.0	60.0	0.001
Immunocompetent	85.0	15.0	—
Positive Excision Margins	66.7	33.3	0.005
Negative Excision Margins	93.9	6.1	—

Discussion

This study provides a comprehensive evaluation of the histopathological features and therapeutic outcomes in patients with Cervical Intraepithelial Neoplasia (CIN), contributing valuable insights into the factors influencing lesion regression, recurrence, and progression. Our results demonstrate that histopathological characteristics, such as the severity of cellular atypia and the extent of epithelial involvement, play a crucial role in determining therapeutic approaches and patient outcomes [9]. Additionally, factors such as patient age, immune status, HPV type, and excision margin status significantly impact treatment success and recurrence rates.

findings align with previous studies that suggest a high rate of spontaneous regression in low-grade CIN, particularly in younger women [10]. In our cohort, 71.9% of patients with CIN 1 who were managed conservatively experienced lesion regression, with no cases progressing to CIN 3 or invasive cancer. These results emphasize the importance of a conservative, observational approach in managing low-grade CIN, especially in younger women, where unnecessary invasive procedures could impact future reproductive health [11]. Similar to other research, spontaneous regression of CIN 1 is thought to result from the host immune system's ability to clear HPV infections, particularly in patients under the age of 30. In contrast, higher-grade lesions, particularly CIN 3, require more aggressive treatment to prevent progression to cervical cancer. In our study, patients with CIN 3 had a higher recurrence rate (14.3%) compared to CIN 1 (9.4%) and CIN 2 (18.2%), despite undergoing

excisional therapies. This underscores the importance of close follow-up in patients with CIN 3, even after treatment [12].

The recurrence rate observed in our study is consistent with reported rates in the literature, where residual or recurrent disease often occurs within two years post-treatment. The presence of residual disease following excisional therapies, particularly in cases with positive margins, highlights the need for precise surgical techniques and adequate follow-up care to monitor for recurrence. HPV type is a well-established predictor of recurrence and progression in CIN. Our study found that patients infected with high-risk HPV strains, particularly HPV 16 and 18, had a significantly higher recurrence rate (27%) compared to those with other HPV types (9%) [13]. This reinforces the importance of HPV genotyping in managing CIN, as persistent infection with high-risk HPV types is a major risk factor for recurrence and progression. HPV vaccination programs targeting these high-risk strains have already shown promise in reducing the incidence of CIN and cervical cancer, and our findings further support the role of vaccination as a preventive strategy.

The impact of immune status on CIN outcomes was also evident in this study [14]. Immunocompromised patients, particularly those with HIV or other conditions affecting immune function, had a significantly higher recurrence rate (60%) compared to immunocompetent patients (15%). This result is in line with other studies that have shown immunocompromised individuals are more likely to have persistent HPV infections and poorer responses to CIN treatments [15]. For these patients, more intensive follow-up and possibly additional therapeutic interventions may be necessary to prevent recurrence and progression. One of the key findings of this study is the influence of excision margin status on recurrence rates.

Patients with positive excision margins following LEEP or conization had a significantly higher recurrence rate (33.3%) compared to those with negative margins (6.1%). This highlights the importance of ensuring complete excision of abnormal tissue during surgery, as positive margins are a strong predictor of residual disease and recurrence [16]. These findings are consistent with other research showing that patients with clear surgical margins have better long-term outcomes and lower recurrence rates. Ensuring negative margins may require more careful pre-operative planning and intraoperative assessment of excised tissue [17]. Despite the strengths of this study, including its well-defined patient cohort and detailed histopathological analysis, there are some limitations. The relatively small sample size of 75 patients limits the generalizability of our findings. Additionally, the retrospective nature of the study may introduce biases related to patient selection and treatment decisions. Future studies with larger, more diverse populations and prospective designs would be valuable in confirming and expanding upon these results [18].

Conclusion

This study underscores the critical importance of histopathological evaluation and individualized therapeutic strategies in the management of Cervical Intraepithelial Neoplasia (CIN). Our findings demonstrate that low-grade CIN, particularly CIN 1, can often be managed conservatively, with a high rate of spontaneous regression, especially in younger patients. In contrast, higher-grade lesions, such as CIN 2 and CIN 3, require more aggressive interventions to prevent progression to invasive cervical cancer. The study also highlights key factors that significantly impact therapeutic outcomes, including HPV type, immune status, and excision margin status. Patients infected with high-risk HPV types, such as HPV 16 and 18, as well as those with compromised immune systems, are at a higher risk for recurrence and may require more vigilant follow-up and potentially additional therapeutic measures. The finding that positive excision margins are strongly associated with recurrence further emphasizes the need for precise surgical techniques to ensure complete removal of abnormal tissue.

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