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Pathology

Invasive Cervical Carcinoma and CIN: A Histological Grade-Based Analysis in Bangladesh

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Abstract **Original Research Article**

Background: Cervical cancer remains a significant public health concern in low- and middle-income countries like Bangladesh, where limited access to screening programs leads to late-stage diagnoses. Invasive cervical carcinoma, characterized by aggressive behavior and high mortality, requires precise histological grading to guide treatment strategies effectively. This study aims to provide a comprehensive histopathological analysis of invasive cervical carcinoma cases in Bangladesh to enhance diagnostic accuracy and treatment outcomes. ***Objective:*** To assess the histological grade distribution of invasive cervical carcinoma and cervical intraepithelial neoplasia (CIN) in Bangladesh, identifying prevalent histopathological patterns and their potential implications for clinical management. ***Methodology:*** A cross-sectional descriptive study was conducted at the Department of Pathology, Rajshahi Medical College, from March 2020 to February 2022. A purposive sampling method was used to select 100 cases diagnosed histopathologically as CIN or invasive cervical carcinoma. Histological sections were stained with Hematoxylin and Eosin (H&E) and Periodic Acid-Schiff/Alcian Blue (PAS/AB) and examined microscopically. Invasive tumors were categorized based on the World Health Organization (WHO) grading system into well-differentiated (grade 1), moderately differentiated (grade 2), and poorly differentiated (grade 3). CIN cases were classified as CIN-I, CIN-II and CIN-III. Data were analyzed using SPSS version 28, with Chi-square tests to assess associations. ***Results:*** Among the 100 cases analyzed, 75% were aged 40–60 years, with a mean age of 51.42 ± 8.75 years. Squamous cell carcinoma was the most common type (45%), followed by adenocarcinoma (15%) and adenosquamous carcinoma (10%). Of the 70 invasive carcinoma cases, 61.43% were well-differentiated (grade 1), 24.29% were poorly differentiated (grade 3), and 14.29% were moderately differentiated (grade 2). Regarding CIN cases, 36.67% were CIN-II, 33.33% were CIN-III, and 30% were CIN-I. Notably, all adenocarcinomas and adenosquamous carcinomas were well-differentiated. ***Conclusion:*** The findings indicate a high prevalence of well-differentiated squamous cell carcinoma and high-grade CIN (CIN-II and CIN-III) in Bangladesh, underscoring the urgent need for enhanced screening programs and early intervention strategies. Strengthening diagnostic capabilities and expanding access to preventive services could significantly reduce the burden of cervical cancer in this population.

Keywords: Cervical cancer, invasive cervical carcinoma, histological grading, cervical intraepithelial neoplasia (CIN).

INTRODUCTION

Cervical cancer remains a significant public health concern worldwide, particularly in low- and middle-income countries, where healthcare infrastructure and cancer screening programs are limited. Among the various types of cervical cancers, invasive cervical carcinoma stands out due to its aggressive nature and high mortality rates if not detected early [1-2]. Histological grading, which assesses the degree of tumor differentiation, plays a crucial role in determining prognosis and guiding treatment strategies for affected women. Understanding the histological characteristics of invasive cervical carcinoma within the Bangladeshi population can provide valuable insights for clinicians and public health experts aiming to improve diagnostic accuracy and treatment outcomes [3].

The burden of cervical cancer is exacerbated by socio-economic challenges, limited access to healthcare, and low participation in screening programs such as Pap smears and HPV testing. A significant proportion of

cases are diagnosed at advanced stages, where invasive carcinoma has already developed [4]. In this context, histological grade-based analysis becomes essential for categorizing the aggressiveness of the tumor, thereby facilitating appropriate treatment decisions. Given the diversity in tumor biology, a detailed histopathological evaluation can reveal patterns that might be unique to the population, aiding in the formulation of targeted therapeutic approaches [5-6].

Histological grading of cervical carcinoma typically involves examining cellular differentiation, mitotic activity, and architectural disruption of the tissue [7]. The World Health Organization (WHO) classifies cervical carcinomas into different grades, ranging from well-differentiated (low-grade) to poorly differentiated (high-grade) forms, with higher grades being associated with more aggressive behavior and poorer prognosis. In Bangladesh, however, there is a scarcity of comprehensive studies that focus on the histopathological profiles of invasive cervical carcinoma. Addressing this gap is essential to enhance the effectiveness of clinical management and to tailor treatment protocols to the needs of local patients.

In addition to histological grading, various risk factors contribute to the prevalence and progression of cervical carcinoma in Bangladesh, including early marriage, multiple pregnancies, and limited awareness of preventive measures like HPV vaccination. The interplay between these risk factors and histopathological findings can provide a deeper understanding of the disease's etiology and progression in the Bangladeshi context. Therefore, a histological grade-based analysis not only aids in prognosis but also helps in identifying potential correlations between tumor characteristics and patient demographics.

Objective

This study aims to conduct a comprehensive histological grade-based analysis of invasive cervical carcinoma cases in Bangladesh, focusing on identifying prevalent histopathological patterns and their associations with clinical outcomes.

METHODOLOGY

Type of Study: This research was designed as a cross-sectional descriptive study to assess the histological characteristics of cervical precancerous lesions and invasive cervical carcinomas.

Study Period: The study was conducted over a span of two years, from March 2020 to February 2022.

Place of Study: All samples and data were collected and analyzed at the Department of Pathology, Rajshahi Medical College.

Study Population: The study included paraffin blocks of patients who were histopathologically diagnosed with cervical precancerous lesions and cervical carcinomas at the Department of Pathology, Rajshahi Medical College.

Sampling Method: A purposive sampling method was employed to select the required sample size of 100 cases for analysis.

Inclusion Criteria: The study included cases diagnosed histopathologically as Cervical Intraepithelial Neoplasia (CIN) grades I, II, and III, squamous cell carcinoma, adenocarcinoma, and adenosquamous carcinoma.

Exclusion Criteria:

- Samples that were poorly fixed.
- Patients who had undergone previous chemotherapy, radiotherapy, or hormonal therapy.

Sample Size Determination:

The sample size was determined using Cochran's formula, considering a 95% confidence interval (Z = 1.96), a prevalence rate of cervical cancer of 22.27% (based on Globocan Bangladesh, 2020), and a 5% margin of error. The initial estimated sample size was 350, which included both carcinoma and CIN cases. However, considering the finite population correction for the study period (N = 168), the corrected sample size was calculated to be 100 cases.

Data Collection Procedure: Clinical information was obtained by interviewing patients or their attendants and recorded on data collection sheets. Informed written consent was obtained from each participant prior to sample collection.

Sample Processing: Histological sections were prepared and stained using Hematoxylin and Eosin (H&E) and Periodic Acid-Schiff/Alcian Blue (PAS/AB) stains following the standard protocols of the Department of Pathology, Rajshahi Medical College.

Microscopic Evaluation: All microscopic examinations were conducted using an Olympus multi-headed microscope (Model: u-MDO10R3, Olympus Corporation, Tokyo, Japan). Photomicrographs were captured for further analysis.

Tumor Categorization under H&E Stain:

Histological slides were reviewed to classify tumors based on their differentiation: well-differentiated (Grade I), moderately differentiated (Grade II), and poorly differentiated (Grade III) for invasive carcinomas. Precancerous lesions were categorized as CIN-I, CIN-II, and CIN-III.

Statistical Analysis:

Data were entered into Microsoft Excel and analyzed using SPSS version 28. Categorical variables were expressed as frequencies and percentages, and comparisons were made using the Chi-square test. Continuous variables were presented as mean ± standard deviation. A p-value of less than 0.05 was considered statistically significant. The relationship between mucin type, content, and tumor grade was also examined using the Chi-square test.

Ethical Considerations: The study protocol was reviewed and approved by the Institutional Review Board (IRB) of Rajshahi Medical College. Written informed consent was obtained from all participants prior to sample collection.

RESULTS

Among the 100 cases analyzed, the majority, 75 (75%), were within the age range of 40–60 years. A smaller proportion, 7 (7%), were below 40 years of age, while 18 (18%) were above 60 years. The mean age of the patients was 51.42 ± 8.75 years.

Table I: Distribution of the study subjects by their age (n = 100)

Age (years)	Frequency	(%)
<40	7	7.0%
40-60	75	75.0%
>60	18	18.0%
Mean ± SD 51.42 ± 8.75 years Range (Min-Max) (29-74)		

Out of total 100 cases, 45 (45%) cases were invasive cervical squamous cell carcinoma, 15 (15%) cases were invasive adenocarcinoma, 10 (10%) cases were invasive adenosquamous carcinoma and 30 (30%) cases were cervical intraepithelial neoplasia (Figure 16).

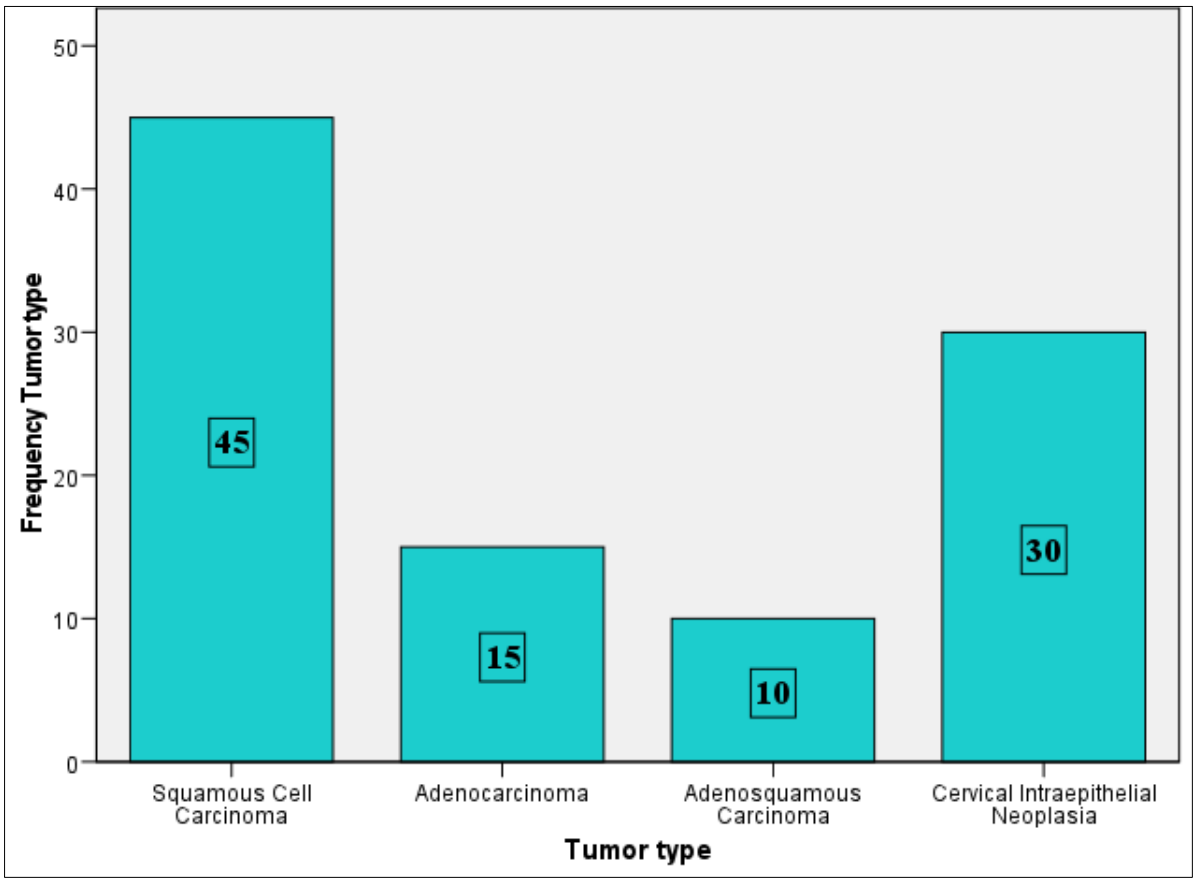

Figure-1: Bar Diagram Showing Tumor Type

Out of 70 invasive cervical cancers, most cases were grade-1 43(61.43%), followed by 17(24.29%) grade-3 and 10(14.29%) grade-2 tumors.

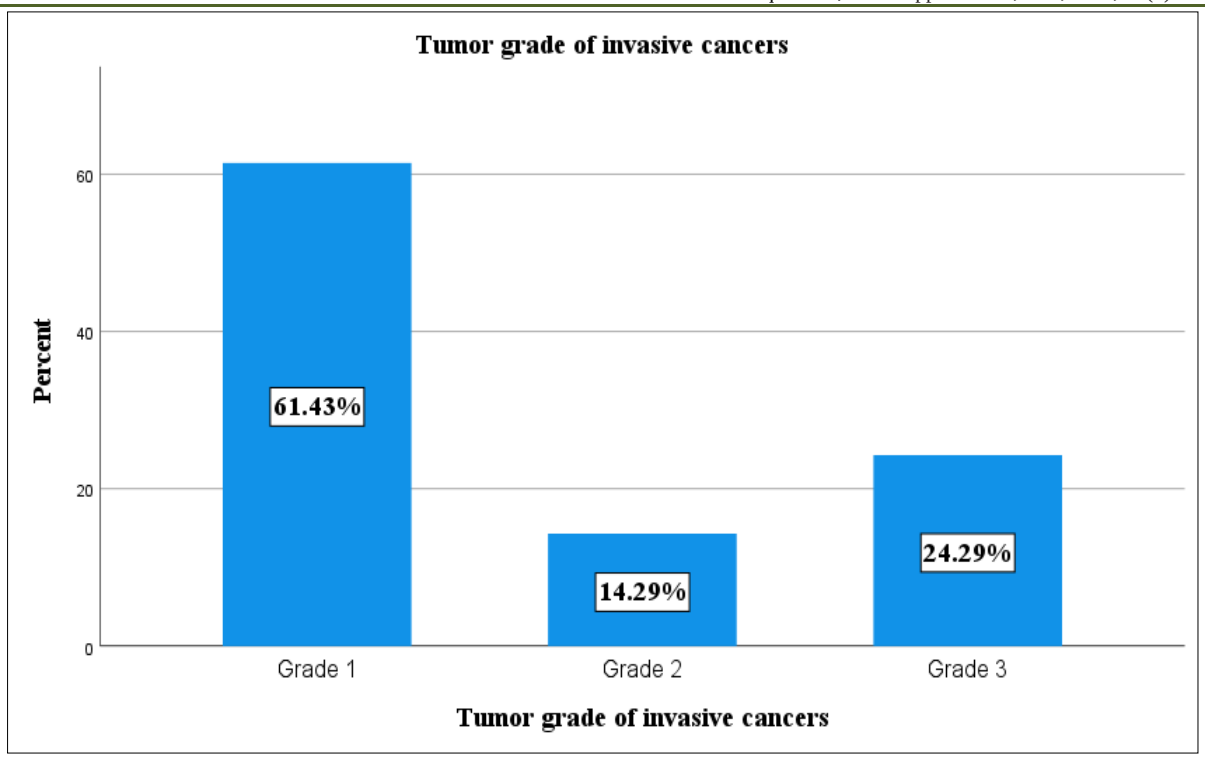

Figure-2: Bar Diagram Showing Grade of Invasive Cervical Cancers

Out of total 30 cases of cervical intraepithelial neoplasia, 11(36.67%) cases were CIN-II, followed by 10(33.33%) cases of CIN-III and 9(30%). cases of CIN-I (Figure 18).

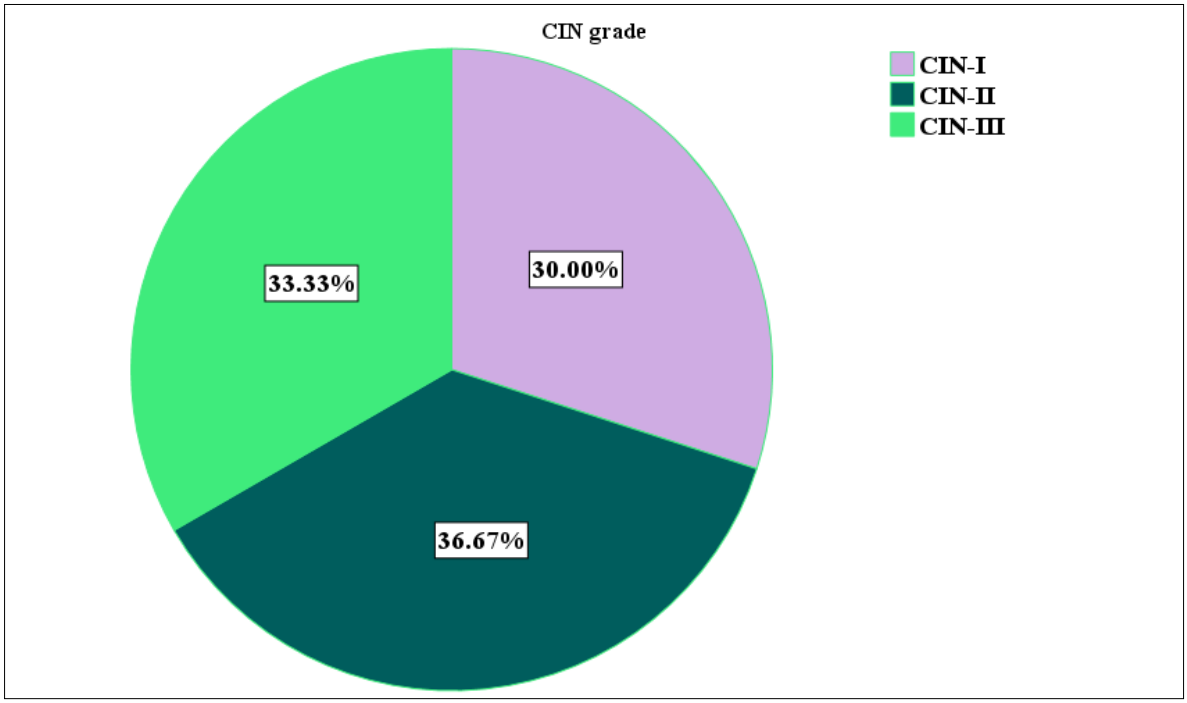

Figure-3: Pie Chart Showing Grades of Cervical Intra-Epithelial Neoplasia

Most grade 1 cancers (18) were squamous cell carcinomas. All other grade 2 (10 cases) and grade 3 (17 cases) invasive cervical cancers were squamous cell carcinoma. All adenocarcinoma and adenosquamous carcinoma were grade 1.

Table II: Distribution of invasive cancers by histolo-gical grades (N=70)

Tumor type	Tumor grade of invasive cancers						Total		P value
	Grade 1		Grade 2		Grade 3				
	N	%	N	%	N	%	N	%	
Squamous Cell Carcinoma	18	41.9%	10	100.0%	17	100.0%	45	64.3%	
Adenocarcinoma	15	34.9%	0	0.0%	0	0.0%	15	21.4%	<0.001
Adenosquamous Carcinoma	10	23.3%	0	0.0%	0	0.0%	10	14.3%	
Total	43	100.0%	10	100.0%	17	100.0%	70	100.0%	

*Data were analyzed using **Chi-Square (χ^2).**

DISCUSSION

n the present study, the majority of cervical cancer cases were observed in women aged 40–60 years, with a mean age of 51.42 ± 8.75 years. This age distribution aligns with findings from other studies conducted in South Asia, where the peak incidence of cervical cancer has been reported in women aged 45–55 years [8]. The relatively low percentage (7%) of cases observed in women under 40 suggests that cervical cancer remains predominantly a disease of middle-aged and older women in Bangladesh. This age trend might reflect delayed access to screening and healthcare services, emphasizing the need for targeted screening programs for women in their 40s and above.

Histopathological analysis revealed that squamous cell carcinoma was the most common type of invasive cervical cancer, accounting for 45% of cases, followed by adenocarcinoma (15%) and adenosquamous carcinoma (10%). These findings are consistent with global patterns, where squamous cell carcinoma remains the most prevalent histological subtype, particularly in regions with limited access to vaccination and regular screening [9-10]. However, the proportion of adenocarcinoma cases observed in our study appears higher compared to previous studies in South Asia, which reported a prevalence of around 10% [11]. This trend could suggest a gradual shift in histological patterns, potentially due to changing risk factors such as oral contraceptive use or variations in human papillomavirus (HPV) subtypes prevalent in Bangladesh.

Regarding tumor grade, a significant proportion of invasive cervical cancers were well-differentiated (grade 1, 61.43%), while grade 3 poorly differentiated tumors accounted for 24.29%. This distribution of tumor grades is somewhat similar to that report, who found that well-differentiated tumors were more common in early-stage cervical cancer cases [11]. The high proportion of well-differentiated tumors in our study might reflect an increased detection of early-stage cancers, possibly due to improved diagnostic capabilities at the study site. However, the notable percentage of poorly differentiated (grade 3) squamous cell carcinomas underscores the aggressive nature of a subset of these tumors, warranting further investigation into their molecular characteristics and treatment responses.

In the analysis of cervical intraepithelial neoplasia (CIN), CIN-II was the most frequently observed grade (36.67%), followed by CIN-III (33.33%) and CIN-I (30%). This distribution contrasts with studies conducted in developed countries where CIN-I is typically the most common grade detected, possibly reflecting differences in screening practices and the natural history of HPV infection [12]. The higher prevalence of CIN-II and CIN-III in our cohort suggests a considerable burden of high-grade lesions, which have a higher risk of progressing to invasive cancer if untreated. This finding highlights the need for effective management strategies for high-grade CIN lesions to prevent their progression to invasive disease.

Overall, the histopathological spectrum observed in this study emphasizes the importance of early detection and histological grading in managing cervical cancer. The predominance of squamous cell carcinoma and the significant proportion of high-grade CIN lesions suggest that expanding screening programs and enhancing diagnostic infrastructure could substantially impact cervical cancer outcomes in Bangladesh. Further multicenter studies with larger sample sizes are recommended to validate these findings and to explore the underlying causes of histological variations observed in this population.

CONCLUSION

In conclusion, the study highlights that the majority of cervical cancer cases in Bangladesh occur in women aged 40–60 years, with squamous cell carcinoma being the most prevalent histological type. A significant proportion of these cases were well-differentiated (grade 1), indicating a potential for early detection if effective screening programs are implemented. The high prevalence of high-grade cervical intraepithelial neoplasia (CIN-II and CIN-III) further emphasizes the urgent need for targeted prevention and management strategies. Enhancing diagnostic capabilities and expanding access to screening could substantially reduce the burden of cervical cancer in this population.

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