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Original Research Article

Prevalence of cervical intraepithelial neoplasia and cervical carcinoma in a tertiary care hospital at Rajshahi

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ABSTRACT

Background: Cervical intraepithelial neoplasia (CIN) is a precancerous cervical condition with the potential to develop into cervical carcinoma if untreated. While research on CIN and cervical carcinoma exists in various regions, the Rajshahi area lacks such investigations. Examining the prevalence of CIN and cervical carcinoma in this region is essential. This study aimed to assess the prevalence of CIN and cervical carcinoma in a tertiary care hospital at Rajshahi in Bangladesh.
Methods: This cross-sectional descriptive study was conducted at the department of pathology, Rajshahi medical college, and the department of gynaecology and obstetrics, Rajshahi medical college hospital, Rajshahi, Bangladesh from July 2019 to June 2022. A total of 1000 VIA test-positive cases of cervical lesions were enrolled as study subjects purposively. Data were processed and analyzed by the MS office tools.
Results: Cervical carcinoma was identified through cytological analysis in 4.6% of cases, with 7.6% exhibiting high-grade squamous intraepithelial lesions (HSIL) and 13.1% showing low-grade squamous intraepithelial lesions (LSIL). Through histopathological analysis, cervical carcinoma found in 5.3% of cases, CIN-grade III (CIN-III) in 7.1%, and CIN-II and CIN-I in 2.2%, 16.4% of cases, respectively. Human papillomavirus (HPV) vaccination rate was 0.70%.
Conclusions: The prevalence of CIN and cervical carcinoma in the Rajshahi region of Bangladesh is alarmingly high. These findings underscore the pressing need for the immediate implementation of a comprehensive vaccination and awareness development program for cervical carcinoma.

Keywords: Prevalence, CIN, Cervical carcinoma, HPV

INTRODUCTION

Cervical cancer ranks as the third most common cancer among women worldwide, following breast and colorectal cancer. Most cases, over 85%, are concentrated in developing countries.[1] Persistent infection with HPV can cause high-grade CIN, which can progress to invasive cervical cancer if left untreated.[2] Cervical cancer, responsible for 274,000 annual deaths worldwide, remains a significant health challenge despite effective screening and treatment for high-grade CIN precursor lesions. It is primarily caused by high-risk HPV types, notably HPV 16 and 18, which account for 70% of cases. In 2018, Bangladesh recorded 8,068 new cases (10.6 per 100,000 women) and 5,214 deaths (7.1 per 100,000 women).[3] Cervical cancer contributes to more than 2.7 million years of life lost among women aged 25 to 64 globally.[4] It claims the lives of over 288,000 women annually worldwide and has a particularly significant impact on the most disadvantaged and vulnerable women.[5] In India, an estimated 134,420 new cases of cervical cancer and 72,825 deaths were reported in 2008,

constituting approximately 25% of the worldwide burden. The age-standardized incidence rate (ASR) for cervical cancer in 2008 was 27.0 per 100,000 women across various regions of India.[1] In Bangladesh, cervical cancer ranks as the second most common cancer among women, with ASRs for both incidence and mortality considerably exceeding the global average figures. The incidence rate in Bangladesh is 19.3 per 100,000 women, compared to the global average of 14.0, while the mortality rate is 11.5 per 100,000 women, in contrast to global average of 6.8.[6]

Cervical cancer screening coverage in developing countries is generally low, with an average of 19%, in stark contrast to the 63% coverage reported in developed countries. In Bangladesh, specifically, the reported screening coverage has been as low as 1%, highlighting a significant disparity in access to cervical cancer screening services in this region.[7] According to the WHO regional policy framework, cervical cancer screening policies should be organized as part of a comprehensive cancer screening program.[8] Therefore, since June 2018, the government of Bangladesh (GOB) and BSMMU initiated a development project called the "electronic data tracking with population-based cervical and breast cancer screening program (2018-2021).[9] In a study it was reported that the challenges of introducing cytological screening in low and middle-income countries like Bangladesh have led to the development of alternative screening strategies that need to be adapted to meet the specific needs of each individual country.[10] Cancer screening should be a component of public health programs in developing countries.[11]

There are several types of HPV therapeutic vaccines evaluated in preclinical and clinical trials: live vector, protein or peptide, nucleic acid, and cell-based vaccines.[12] However, 3 types of HPV vaccines are currently available in the vaccination programs in several countries: cervarix (bivalent vaccine for HPV 16, 18), Gardasil (quadrivalent vaccine for HPV 6, 11, 16, 18), and nine-valent vaccine (for HPV 6, 11, 16, 18, 31, 33, 45, 52, 58). These vaccines can target between 2 and 7 oncogenic HPV serotypes.[13] They promise, in the long-term (30-50 years), to reduce the incidence of disease associated with HPV vaccine types.[14] Some studies have proved that HPV vaccination is a secure and efficient method to prevent cancer.

The population prevalence of CIN is an important indicator to assess the disease burden in the community. However, information about the prevalence of CIN in Bangladesh was not available. It is noteworthy that the research programs for the Rajshahi region of Bangladesh may not be sufficient, given the prevalence of CIN and cervical carcinoma in the area.[15]

Therefore, this study aimed to assess the prevalence of CIN and cervical carcinoma in a tertiary care hospital at Rajshahi in Bangladesh.

METHODS

This cross-sectional descriptive study was conducted at the department of pathology, Rajshahi medical college, and the department of gynecology and obstetrics, Rajshahi medical college hospital, Rajshahi, Bangladesh, from July 2019 to June 2022. The study enrolled 1000 VIA tests (visual inspection with acetic acid) positive cases of cervical lesions using purposive sampling. VIA test-negative patients and already histo-pathologically proven cases of cervical carcinoma were excluded from this study. After taking written consent, data were collected from patients by face-to-face interview through a questionnaire. Socio-demographic information and reproductive health characteristics were collected and recorded in the data collection sheet. After examining the cervix by Cusco's speculum, the condition of the cervix was noted and samples were collected using cervical cyto-brush for a Pap smear and colposcopically guided punched biopsies were taken for histopathological examination. hematoxylin and eosin (H and E) stain was used for both Pap's smear and histopathological examination. Results were analyzed using the SPSS software program. Chi-square tests were performed where $p<0.05$ was considered as the level of significance.

RESULT

The histopathological findings among the 1000 participants in this study revealed a diverse spectrum of diagnosis. Figure 1 and 2 showing microscopic data of biopsy specimen, followed by histopathological findings where carcinoma was detected in 5.3%, CIN-I was 16.4%, CIN-II was 2.2% and CIN-III was 7.1%. As per the cytological findings Figure 3 showing carcinoma was detected in 4.6%, HSIL 7.6%, low grade squamous intraepithelial lesion (LSIL) was 13.1%.

In Table 1, the relationship between various predictive factors and histopathological findings was disseminated. Here the highest number of carcinomas was detected in 45-64 years age group (9.1%) followed by 35-44 years age group (8.2%). Different grades of CIN also found most frequently in the same age groups. According to the questionnaire, among poor population, carcinoma was detected higher (6.4%) than the average social status (5.0%). Different grades of CIN also seen most frequently in the same social status. Both carcinoma and all CIN grades were most prevalent in those, who stopped their education in primary level (Carcinoma 12.2%, CIN-III 37.6%, CIN-II 3.7% and CIN-I 15.9%). Furthermore, marital age was a significant factor, with individuals marrying before the age of 18, demonstrating higher rates of both carcinoma 7.3% and different grades of CIN (CIN-III 17.2%, CIN-II 2.9%, CIN-I 8.5%) compared to those marrying between 18-30 years or more. Oral contraceptive pill users exhibited a higher carcinoma rate at 9.4% than the non-users. Regarding parity, carcinoma revealed mostly in the group with more than 2 children (8.9%). Different grades of CIN also seen higher in this

group. Notably, carcinoma was exclusively observed in the cytological diagnosis category (100%) and HSIL displayed a remarkable high carcinoma prevalence at 86.8%. In evaluating the relationship between different predictive factors and histopathological findings in every comparison, we found significant correlations and the p<0.05. Among the total participants only 0.7% were vaccinated (Table 2).

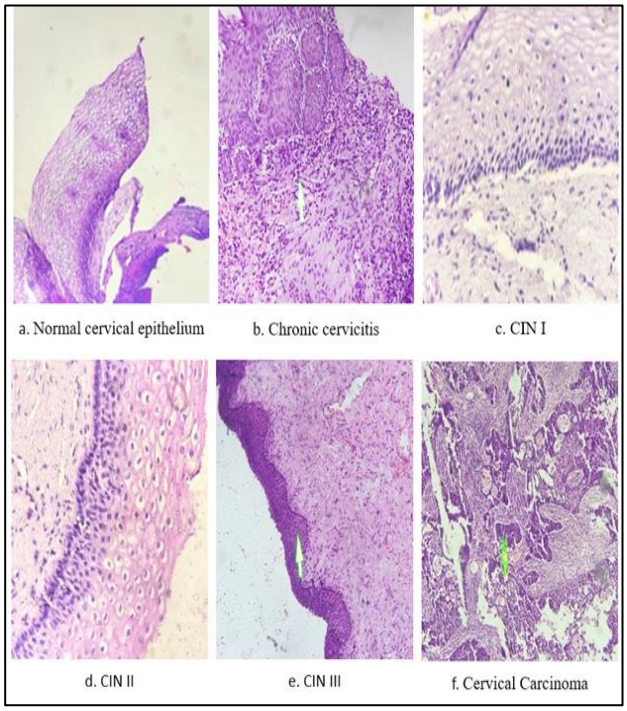

Figure 1 (A-F): Histopathological findings (Normal cervical epithelium, H and E stain X100. Chronic cervicitis case no-968 H and E stain X400, CIN I case no-371 H and E stain X400. CIN II case no-91 H and E stain X400, CIN III case no-223 H and E stain X100 and cervical carcinoma case no-72 H and E stain X400).

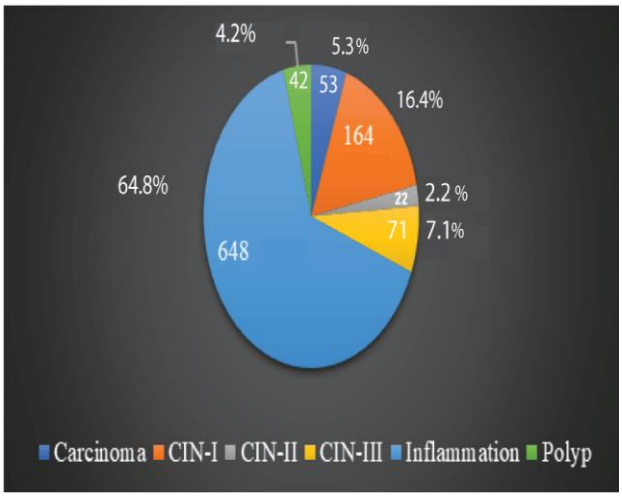

Figure 2: Distribution of histopathological findings, (n=1000).

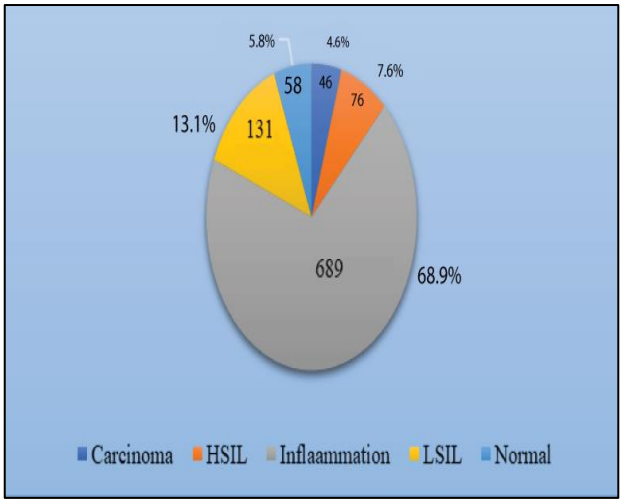

Figure 3: Distribution of the respondents by cytological diagnosis, (n=1000).

Table 1: Relation between different predictive factors and histopathological findings, (n=1000).

Characteristics			Histopathological findings					
			Carcinoma	CIN-I	CIN-II	CIN-III	Infl.	Polyp
Groups		**N**	**% within the groups**					
Age groups (In years)	15-24	76	0.0	14.5	0.0	0.0	80.3	5.3
	25-34	319	0.6	14.7	1.6	4.1	72.7	6.3
	35-44	473	8.2	12.9	3.2	7.2	65.8	2.7
	45-64	132	9.1	34.1	1.5	18.2	33.3	3.8
Social status	Average	361	5.0	15.2	1.7	7.5	64.8	5.8
	Good	127	1.6	9.4	2.4	0.0	82.7	3.9
	Poor	512	6.4	18.9	2.5	8.6	60.4	3.1
Education	Above HSC	36	0.0	2.8	2.8	2.8	88.9	2.8
	HSC (Higher secondary)	78	3.8	5.1	2.6	5.1	80.8	2.6
	SSC (Secondary)	102	2.0	10.8	3.9	3.9	79.4	0
	Class 5-10 (Secondary)	374	6.1	17.4	1.3	5.9	62	7.2
	<Class-5 (Primary)	410	6.1	20.2	2.4	10	58.5	2.9

Continued.

Characteristics			Histopathological findings					
			Carcinoma	CIN-I	CIN-II	CIN-III	Infl.	Polyp
Groups		**N**	**% within the groups**					
Marital age (In years)	<18	717	7.3	17.2	2.9	8.5	60	4.2
	>30	19	0.0	0.0	0.0	10.5	89.5	0.0
	18-30	264	0.4	15.5	0.4	3.0	76.1	4.5
Oral contraceptive	Non-user	520	1.5	21.7	2.3	0.2	70.2	4.0
	User	480	9.4	10.6	2.1	14.6	59.0	4.4
Parity	<2	94	0.0	10.6	2.1	2.1	80.9	4.3
	>2	584	8.9	18	2.2	8.7	59.1	3.1
	2	322	0.3	15.2	2.2	5.6	70.5	6.2
Mode of delivery	LUCS	328	0.0	2.4	4.3	1.8	88.7	2.7
	NVD	672	7.9	23.2	1.2	9.7	53.1	4.9
Vaginal discharge	Brownish	112	12.5	9.8	1.8	11.6	59.8	4.5
	Reddish	18	33.3	16.7	11.1	22.2	0.0	16.7
	Watery	32	12.5	6.3	9.4	12.5	53.1	6.3
	Whitish	838	3.5	17.7	1.8	6.0	67.3	3.8
Abnormal P/V bleeding	Absent	880	0.30	18.1	2.0	3.6	72.0	3.90
	Present	120	41.70	4.20	3.30	32.50	11.7	6.70
Post-coital bleeding	Absent	920	1.2	17.1	2.3	5.9	69.2	4.3
	Present	80	52.5	8.8	1.3	21.3	13.8	2.5
Lower abdominal pain	Absent	64	29.7	21.9	6.3	20.3	14.1	7.8
	Present	936	3.6	16	1.8	6.2	68.3	4.0
Backache	Absent	275	0.0	0.0	0.0	0.0	86.9	13.1
	Present	725	7.3	22.6	3.0	9.8	56.4	0.8
Clinical findings	Erosion	21	0.0	0.0	0.0	0.0	100	0.0
	Healthy	599	0.0	4.2	0.0	0.0	89.5	6.3
	Unhealthy	380	13.9	36.6	5.8	18.7	23.9	1.1
Cytological diagnosis	Carcinoma	46	100	0.0	0.0	0.0	0.0	0.0
	HSIL	76	9.2	0.0	3.9	86.8	0.0	0.0
	Inflammation	689	0.0	7.4	0.3	0.0	88.8	3.5
	LSIL	131	0.0	83.2	13	3.8	0.0	0.0
	Normal	58	0.0	6.9	0.0	0.0	62.1	31

Infl.: Inflammation $p<0.05$.

Table 2: Vaccination rate in Rajshahi, (n=1000).

Status	N	Percentages (%)
Vaccinated	7	0.70
Not vaccinated	993	99.30

DISCUSSION

This study aimed to assess the prevalence of CIN and cervical carcinoma in a tertiary care hospital at Rajshahi in Bangladesh. In this study, 5.30% of patients were diagnosed with cervical carcinoma, 16.40% with CIN I, 2.20% with CIN II, and 7.10% with CIN III. According to Daniyal et al cervical cancer incidence is high in Korea, Japan, and India, ranging from 32-40% while in Turkey, it is 4.4%. Prevalence of HPV is less in Muslim women that maybe due to religious practices and socio-economical cultures in Muslim societies, this reduction is attributed to male circumcision Garland et al noted that Asia carries 51.6% of the global burden of cervical cancer.[16,17] Lower vaccination rates and less awareness among the general population may have been the causes for such a higher prevalence in this region. According to the international agency for research on cancer, more than 50 million Bangladeshi women are at risk of cervical cancer, with 17,686 new cases and 10,362 deaths occurring annually.[18] Regarding vaccination, the majority (99.30%) of patients in our study were not vaccinated against HPV. In the study, 4.6% had cervical carcinoma, 7.6% had HSIL, and 13.1% had LSIL through cytological analysis. Histopathology confirmed these findings: 5.3% had cervical carcinoma, 7.1% had CIN-III, 2.2% had CIN-II, and 16.4% had CIN-I. But in a recent study, the rate of cervical carcinoma in Pakistan was found significantly lower (1.9%: 28/1450) than ours.[19] On the other hand, the findings regarding other lesions apart from cervical carcinoma were dissimilar to our findings, even though they also reported a lower rate of cervical carcinoma. Their study indicated that 35% had cervicitis, 12.5% had cervical polyps, 20% had CIN1, 3% had CIN2, 0.5% had CIN3, and 3.5% had cervical cancer.[20]

In this study, the majority of patients with carcinoma (3.9%), CIN I (6.1%), CIN II (1.5%) and CIN III (3.4%) were aged 35-44 years. Castle et al found a similar prevalence in the 25-35 age group.[21] However, we found some dissimilarity in another study conducted by Chowdhury et al where the majority (55.59%) were aged

21-25, which was younger than our findings.[22] Geographic location might have been the cause of such dissimilarity. Regarding social status, most patients with carcinoma (3.3%), CIN I (9.7%), CIN II (1.3%) and CIN III (4.4%) belonged to a poor socioeconomic status. Regarding educational status, the majority of patients with carcinoma (2.5%), CIN I (8.3%), CIN II (1.0%) and CIN III (4.0%) had low educational attainment, typically below primary level. Benard et al found that lower education and higher poverty correlated with increased incidence rates of penile, cervical, and vaginal invasive cancers.[23] Parikh et al also reported similar results.[24] The correlation between lower education and higher poverty with cervical carcinoma is a well-established fact. Additionally, in this study, most patients with carcinoma (98.1%), CIN I (75.0%), CIN II (95.5%) and CIN III (85.9%) were married before the age of 18. In a study conducted by Khalaf et al the mean age of women was 39.9±11.4 years, and the mean age of marriage was 19±5 years. They also reported that abnormal Pap results were found in 63.5% of them, and a significant association was observed between abnormal Pap smears and age 20-30 years, marrying at ≤18 years old, and a marriage duration of over 10 years.[25] In our study, most patients with carcinoma (4.5%) and CIN III (7.0%) used oral contraceptive pills (OCP) for contraception, while those with CIN I (5.1%), CIN II (1.0%), and inflammation (36.5%) did not use OCP. However, a study by Shields et al suggested that using barrier methods for contraception was protective against HPV which is also proven as a well-established fact.[26] HPV vaccination was only 0.70%. Low HPV vaccination rates highlight the urgent need for a nationwide vaccination program given the high cervical lesion prevalence in VIA test-positive cases. Countries with high HPV vaccination coverage have reported a significant reduction in HPV prevalence by 73-85% and a decline of 41-57% in high-grade cervical lesions.[27] Although the HPV vaccine has been available in the market in Bangladesh since 2006, the country has not been able to incorporate it into the national immunization program.[28] However, as of now, Bangladesh does not have any HPV vaccination coverage, making the country more susceptible to cervical carcinoma.[29]

CONCLUSION

The high prevalence of CIN and cervical carcinoma in the Rajshahi region of Bangladesh demands immediate and sustained action. The implementation of a comprehensive vaccination program, coupled with a targeted awareness campaign and improved healthcare infrastructure, is essential to combat this alarming health issue. For proper and effective vaccination, we have to know about the molecular pattern of HPV in this region, which is the established cause of cervical carcinoma and associated lesions. It is our moral obligation to prioritize the health and well-being of the women in this region and take proactive steps to reduce the burden of cervical carcinoma. Failure to act urgently would result in unnecessary suffering and loss of life, and it is imperative that these efforts be initiated without delay.

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