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A Study on Clinical Status of Urothelial Carcinoma in Bangladesh

Dr. Sharmin Haque[1*], Dr. Suporna Saleh[2], Dr. MST Rommana Akter[3], Dr. Syeda Sadia Afrin[4], Dr. Nazma Shaheen[5]

[1]Associate Professor (cc), Department of Pathology, Bangladesh Medical College, Dhaka, Bangladesh
[2]Associate Professor (cc), Department of Pathology, Dhaka National Medical College, Dhaka, Bangladesh
[3]Assistant Professor, Department of Dermatology and Venereology, Monowara Sikder Medical College and Hospital, Shariatpur, Bangladesh
[4]Lecturer, Department of Pathology, Dhaka Medical College, Dhaka, Bangladesh
[5]Assistant Professor, Department of Pathology, Monowara Sikder Medical College and Hospital, Shariatpur, Bangladesh

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***Corresponding author:** Dr. Sharmin Haque
Associate Professor (cc), Department of Pathology, Bangladesh Medical College, Dhaka, Bangladesh

Abstract **Original Research Article**

Background: Urothelial carcinoma, a predominant malignancy of the bladder, represents a growing public health concern in Bangladesh due to environmental and lifestyle factors, including tobacco use and arsenic exposure. Limited healthcare infrastructure and delayed diagnosis exacerbate the burden, emphasizing the need for region-specific research. ***Objective:*** To evaluate the demographic, clinical, and pathological characteristics of urothelial carcinoma in a Bangladeshi population. ***Methods:*** This descriptive cross-sectional study was conducted at Dhaka Medical College from January 2016 to December 2017. Fifty histologically confirmed bladder cancer cases were analyzed based on clinical and demographic profiles, tumor grading, and pathological extent. Data were collected systematically using a pre-designed pro forma, and histopathological and immunohistochemical analyses were performed. Statistical analysis was conducted using SPSS. ***Results:*** The majority (58.0%) of patients were ≤60 years, with a mean age of 60.9 ± 13.1 years, and males constituted 80.0% of cases. Most patients (72.0%) had a history of smoking and betel nut chewing, with hematuria (100.0%) and anemia (100.0%) being the most common clinical features. Tumors were predominantly confined to PT1 (68.0%), with high-grade tumors showing a greater likelihood of PT2 extension (38.9%). Smoking and tumor grade were not statistically significantly associated ($p = 0.517$). ***Conclusion:*** The study highlights the high prevalence of urothelial carcinoma in males, its association with modifiable risk factors, and the predominance of non-muscle-invasive tumors. These findings underscore the urgent need for public health interventions targeting risk factors, early detection, and accessible treatment options tailored to the Bangladeshi context.

Keywords: Urothelial Carcinoma, Bladder Cancer, Tumor Grade, Hematuria.

INTRODUCTION

Urothelial carcinoma, primarily affecting the bladder, ureters, and renal pelvis, is a significant public health concern globally and in Bangladesh. As one of the most common urinary tract malignancies, it contributes substantially to cancer-related morbidity and mortality. The disease primarily manifests in the bladder and accounts for the majority of cases within this group. In Bangladesh, bladder cancer is emerging as a growing concern due to lifestyle factors, environmental exposures, and limited healthcare access, which delay early diagnosis and effective treatment [1-3].

One of the major risk factors for urothelial carcinoma in Bangladesh is tobacco use, which remains prevalent in both rural and urban areas. Tobacco smoking and smokeless tobacco consumption are well-documented contributors to carcinogenesis in the urothelium. Furthermore, the presence of arsenic in drinking water, particularly in certain regions of Bangladesh, exacerbates the risk, as chronic arsenic exposure has been directly linked to urothelial malignancies. These environmental and lifestyle risk factors uniquely position the Bangladeshi population at a higher vulnerability to this cancer [4-6].

Additionally, occupational exposures to industrial chemicals, including aromatic amines found in dye, rubber, and leather industries, significantly increase the risk of urothelial carcinoma. As Bangladesh continues to develop its industrial sector, the lack of stringent occupational safety regulations further heightens the potential for carcinogenic exposure [7-9]. Despite this, awareness of occupational risks and

preventive measures remains minimal among workers, leading to late-stage diagnosis and poor outcomes.

The clinical diagnosis and management of urothelial carcinoma in Bangladesh face numerous challenges, particularly due to limited access to advanced diagnostic tools such as cystoscopy, imaging studies, and histopathological analysis. Most patients present with hematuria, a hallmark symptom of the disease, often at an advanced stage when the prognosis is poor [10, 11]. This delay in diagnosis reflects the gaps in public health education, healthcare infrastructure, and regular screening programs, especially in rural and underprivileged areas.

Treatment options for urothelial carcinoma, including transurethral resection of bladder tumors (TURBT), chemotherapy, and immunotherapy, are available in some tertiary hospitals but remain inaccessible to a large portion of the population [12, 13]. The financial burden of these treatments further complicates the situation, with many patients opting for incomplete or alternative therapies. As a result, survival rates for urothelial carcinoma in Bangladesh are often lower than those reported in high-resource countries, highlighting the urgent need for interventions.

Given the growing burden of urothelial carcinoma in Bangladesh, it is imperative to focus on prevention, early diagnosis, and accessible treatment strategies. Public health initiatives aimed at reducing tobacco use, mitigating arsenic contamination, and raising awareness about occupational risks can significantly impact disease prevention. Furthermore, the development of cost-effective diagnostic protocols and improved healthcare delivery systems is crucial to addressing this pressing public health challenge. Research tailored to the genetic and environmental factors specific to the Bangladeshi population may pave the way for more effective prevention and management of urothelial carcinoma in the region.

Objective: To assess clinical status of urothelial carcinoma In Bangladesh.

MATERIALS AND METHODS

Study Design

This research was conducted as a descriptive cross-sectional study to assess specific parameters within a defined population.

Place and Period of Study

The study was carried out in the Department of Pathology at Dhaka Medical College over a span of two years, from January 2016 to December 2017.

Ethical Considerations

Prior to commencing the study, the research protocol was submitted to and approved by the Ethical Review Committee (ERC) of Dhaka Medical College (DMC).

Sample Size: A total of 50 cases were enrolled in the study, as detailed in Appendix II.

Sampling Method: Nonrandom purposive sampling was employed to select the study population.

Sample Selection Criteria:

- **Inclusion Criteria:** Patients of any age group with histologically diagnosed bladder cancer were included.

- **Exclusion Criteria:**

Patients who had undergone neo-adjuvant or adjuvant chemotherapy for bladder carcinoma were excluded, along with tissue samples exhibiting extensive necrosis or cautery effects.

Data Collection and Recording

During specimen collection, all relevant data were systematically recorded in a pre-designed pro forma. Each case was assigned a unique number, which was consistently used for histological and immunohistochemical analyses.

Sample Collection

Clinically suspected bladder tumor cases were identified among patients admitted to the Urology Department at DMC. These patients, presenting symptoms such as macroscopic hematuria or dysuria, underwent radiological evaluations. Among 73 suspected cases, 50 were histologically confirmed as bladder tumors through cystoscopy and transurethral resection (TUR) or biopsies. The remaining 23 cases were excluded due to necrosis, inadequate samples, or cautery effects.

Histopathological Examination:

- **Sample Processing:**

Bladder tumor specimens were collected via biopsy and fixed in 10% buffered formalin for 6–48 hours to ensure accurate hematoxylin and eosin (H&E) and immunostaining results.

- **Gross Examination:** Specimens were evaluated for number and consistency at the Department of Pathology, DMC.

- **Tissue Processing and Staining:** Routine tissue processing and H&E staining were conducted on all 50 cases following standard protocols.

- **Microscopic Analysis**

Histopathological evaluations included tumor grade, configuration (papillary or solid), depth of invasion, presence of muscle, lymphatic and vascular invasion, and changes in adjacent mucosa, if present.

- **Immunohistochemical Analysis:**

Immunohistochemistry for HER2/neu and Ki67 was performed at the Armed Forces Institute of Pathology (AFIP), Dhaka. Four-micrometer-thick tissue sections from paraffin blocks were prepared on poly-L-lysine-coated slides.

Primary Antibodies

- HER2/neu: Polyclonal Rabbit Anti-Human cerbB-2 oncoprotein (DAKO, Code-A0485, Glostrup, Denmark).
- Ki67: Monoclonal Mouse Anti-Human Ki-67 Antigen (1:100, MIB-1, DAKO, Code-M7240, Glostrup, Denmark).

Secondary Antibody: Ready-to-use Envision (DAKO) was applied for both HER2 and Ki67 staining.

Positive Controls: HER2-positive and Ki67-positive high-grade urothelial carcinoma samples were used as controls.

Scoring Systems

- HER2/neu scoring followed the American Society of Clinical Oncology/College of American Pathologists guidelines, categorizing scores from 0 (negative) to 3+ (positive).
- Ki67 immunohistochemical scoring was based on nuclear staining intensity and percentage of positive cells, with scores of 0–1 considered negative and scores of 2–3 positive.

Statistical Analysis of Data

The data were analyzed using SPSS software version 22. Results were presented in tables, figures, and diagrams to illustrate findings effectively.

RESULTS

The majority (58.0%) were aged 60 years or younger, while 42.0% were older than 60 years. The mean age was 60.9 ± 13.1 years. Males were predominant among the patients, most of whom came from low socioeconomic backgrounds and were engaged in various occupations. Only one patient was employed in a dye factory. The majority of the patients had a history of smoking and betel nut chewing.

Table I: Demographic profile of the patients (n=50)

	Frequency	Percentage
Age (years)		
≤60	29	58.0
>60	21	42.0
Mean ± SD (Min-Max)	60.9 ± 13.1 (20 - 88)	
Gender		
Male	40	80
Female	10	20
Socioeconomic status		
Middle	19	38.0
Low	31	62.0
Personal history		
Smoking	36	72.0
Betel nut chewing	36	72.0

The table outlines the clinical findings of the patients. Hematuria was observed in all cases, while the majority (82.0%) experienced dysuria, and 52.0% reported lower abdominal pain. Additionally, all patients presented with anemia.

Table II: Distribution of patients according to clinical findings (n=50)

Clinical findings	Frequency	Percentage
Hematuria	50	100.0
Dysuria	41	82.0
Lower abdominal pain	26	52.0
Anaemia		
Mild	18	36.0
Moderate	14	28.0
Severe	18	36.0

Table III presents the distribution of patients based on their smoking habits in relation to tumor grade. Among the 50 patients, 36 (72.0%) were smokers, while 14 (28.0%) were non-smokers. Within the smoker group, 11 (78.6%) had low-grade tumors, and 25 (69.4%) had high-grade tumors. Conversely, among non-smokers, 3

(21.4%) had low-grade tumors, and 11 (30.6%) had high-grade tumors. The observed differences between smokers and non-smokers regarding tumor grade were not statistically significant (p = 0.517).

Table III: Distribution of patients according to smoking habit (n=50)

Smoker	Low grade (n=14)	High grade (n=36)	Total	p-value
Yes	11 (78.6)	25 (69.4)	36 (72.0)	0.517
No	3 (21.4)	11 (30.6)	14 (28.0)	
Total	14 (100.0)	36 (100.0)	50 (100.0)	

Fisher's exact test was done to measure the level of significance.

Table shows that most (36.0%) of the tumors were found on the lateral wall of the urinary bladder. Rest were on anterior wall (24.0%), posterior wall (20%) and on base (20%).

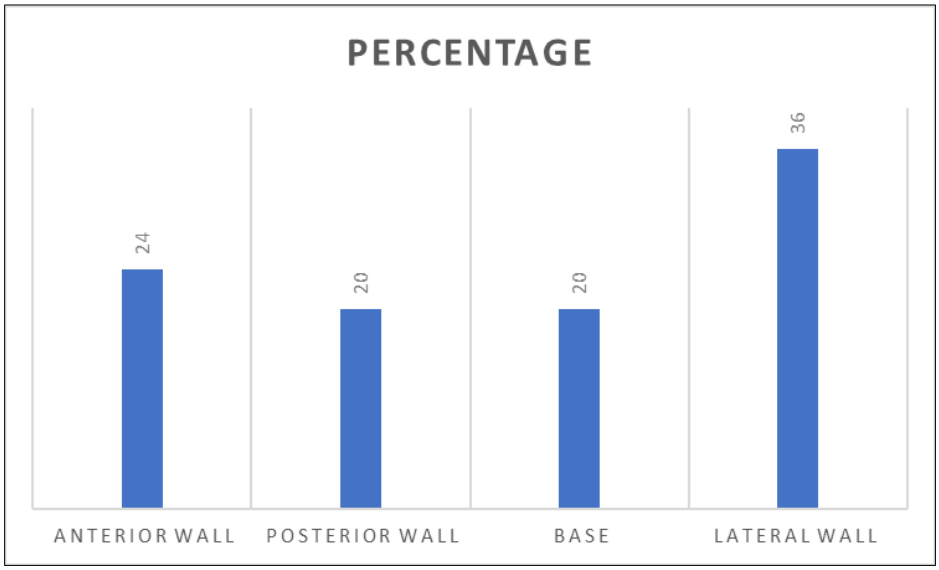

Figure 1: Distribution of patients according to site of tumor (n=50)

Among the 50 patients, 34 (68.0%) had tumors confined to PT1, with 12 (85.7%) being low-grade and 22 (61.1%) being high-grade. The remaining 16 patients (32.0%) had tumors extending to PT2, of which 2 (14.3%) were low-grade and 14 (38.9%) were high-grade. Although there was a higher proportion of PT2 tumors in the high-grade group, the association between tumor extent and grade was not statistically significant (p = 0.175), as determined by Fisher's Exact Test.

Table IV: Distribution of patients according to its extent in low and high grade tumor (n=50)

Extent of tumor	Low grade (n=14)	High grade (n=36)	Total	p-value
PT1	12 (85.7)	22 (61.1)	34 (68.0)	0.175
PT2	2 (14.3)	14 (38.9)	16 (32.0)	

Fisher's exact test was done to measure the level of significance.

DISCUSSION

In our study, 58.0% of patients were aged 60 years or younger, and 42.0% were older than 60 years, with a mean age of 60.9 ± 13.1 years. Similar trends have been observed in other studies, where bladder cancer predominantly affects individuals aged over 60 years but increasingly presents in younger populations, particularly among those with specific environmental exposures or habits like smoking and betel nut chewing [13]. The predominance of males (80.0%) in our study aligns with findings from studies in neighboring regions, where male-to-female ratios of bladder cancer cases often range from 3:1 to 4:1, potentially linked to greater exposure to risk factors like smoking.

The majority of our patients (62.0%) belonged to the low socioeconomic group and were engaged in diverse occupations, with one patient working in a dye factory. Smoking and betel nut chewing were common habits among the patients, each reported in 72.0% of cases. The association of smoking with bladder cancer is well-documented, with studies indicating that smokers

are two to three times more likely to develop the disease compared to non-smokers. Our results align with findings from a study which reported a similar smoking prevalence among bladder cancer patients [14]. However, the observed association between smoking and tumor grade in our study was not statistically significant ($p = 0.517$), a result consistent with some reports but contrasting others that emphasize a stronger link between smoking and high-grade tumors.

The clinical profile of our patients demonstrated that hematuria was the most common symptom (100.0%), followed by dysuria (82.0%) and lower abdominal pain (52.0%). All patients presented with anemia, distributed across mild (36.0%), moderate (28.0%), and severe (36.0%) categories. These findings are comparable to those reported in studies where hematuria remains the most frequent presenting symptom, emphasizing the need for its early evaluation in suspected cases [15].

Most tumors in our study were located on the lateral wall of the urinary bladder (36.0%), with the remainder on the anterior (24.0%), posterior (20.0%), and base (20.0%). This distribution aligns with prior studies indicating that the lateral wall is a common site due to factors like urine pooling and exposure to carcinogens. Tumor extent was analyzed according to grade, revealing that 68.0% were confined to PT1, with the majority being low-grade (85.7%) and only 14.3% extending to PT2. High-grade tumors, however, showed a greater proportion of extension to PT2 (38.9%). These findings are similar to reports from studies which highlight a higher risk of invasion and progression in high-grade tumors, although our study did not find statistical significance in the association between tumor extent and grade ($p = 0.175$) [16].

CONCLUSION

In conclusion, this study highlights the demographic, clinical, and pathological features of urothelial carcinoma in a Bangladeshi population, revealing a predominance of cases among males, a significant association with smoking and betel nut chewing, and a higher prevalence of tumors confined to PT1. While hematuria was the most common presenting symptom, all patients exhibited anemia, reflecting advanced clinical presentations. The findings underscore the need for early detection, public health initiatives to address modifiable risk factors like smoking and betel nut chewing, and further research to explore the unique regional and environmental influences on the disease's progression and pathology.

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