Short Communication

Clinicopathological Study of Bladder Cancer in the South of Iraq and the Impact of Age, Gender, and Smoking

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Abstract

Background: Bladder cancer is among the most common malignancies globally. **Objectives:** This study aimed to investigate the influence of age, gender, and smoking habits on urinary bladder carcinoma, along with their associated clinicopathological correlations. **Material and Methods:** A total of 67 cases of urinary bladder cancer attended Almawaddah Private Hospital from April to November 2023 were included in the study. Data of patients were recorded in questionnaire form and evaluated for age, sex, history of smoking, cystoscopic findings, and histopathological characteristics. Biopsies collected from urothelial bladder cancer (UBC) patients were sent for histopathological examination. **Results:**The median age of incidence of the lesions was 65 years (range: 36–89 years). The incidence was highest among men (95.5%). Transitional cell carcinoma (TCC) emerged as the predominant variant observed in all patients included in this study. At the time of presentation, 24.4% of patients displayed muscle-invasive disease, while the remaining 71.6% of patients exhibited non-muscle-invasive bladder carcinoma, with 26.9% classified as pTa and 44.8% as pT1. Overall, 46.3% of patients were diagnosed with high-grade disease. No significant disparities were noted in tumor grade, muscle invasiveness, or recurrence between patients aged 60 years and older and those younger. A total of 46 (71.9%) males with bladder cancer are smokers, while 18 (28.1%) are non-smokers. This difference was found to be statistically significant. **Conclusion:** The most prevalent histological type of UBC is TCC. Males are more likely to develop bladder tumors, and most occurrences happen in the sixth decade of life. In this study, TCC in stages (PT1) and (PTa) was comparatively common patterns.

Keywords: Bladder cancer, smoking, transitional cell carcinoma, urothelial carcinoma

Introduction

Bladder cancer is among the most common malignancies globally, with 549,393 new cases recorded in 2018. It is the 12th most common cancer worldwide; it accounts for 2.1% of cancer-related deaths and 3% of cancer cases diagnosed annually.[1] The prevalence of bladder cancer increases with progressive age, predominantly affecting individuals aged 65 years and older, comprising the majority (80%) of diagnosed cases.[2] Bladder cancer predominantly affects males. It is three times more common in men than in women,[3] and 90% of bladder tumors are transitional cell carcinoma (TCC).[4,5] Other types of non-UBCs that can occur include adenocarcinoma, squamous cell carcinoma (SCC), small cell carcinoma, and other tumors with a combination of different cell types.[4,6,7] Various factors such as age, sex, smoking, chemical and gas exposure, certain medications, radiation, and genetic predisposition have been recognized as contributors to the onset and advancement of bladder cancer. Additionally, there are indications pointing toward the potential influence of other environmental aspects like dietary habits, nutrition, and metabolic syndrome.[8] Even though the majority of patients (75%–80%) present with non-muscle-invasive

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bladder cancer (NMIBC), it is estimated that up to 80% of these patients will experience recurrence and up to 44% will progress to muscle-invasive bladder cancer MIBC.[9,10]

To the best of our knowledge, there are limited studies available that delineate the demographic profile of bladder cancer in Iraq, especially in the southern region. The aim of this study was to provide an analysis of the clinicopathological features of bladder cancer, focusing on the influence of age, gender, and smoking habits on tumor biology.

Materials and Methods

Study design and patients

A cross-sectional study was conducted from the April 1, 2023, to November 30, 2023. The study included 67 subjects who attended the Urology Unit at Almawaddah Private Hospital in Basra, aged between 36 and 89 years.

During the sample collection process, all medical information for all patients involved in the study was recorded in a questionnaire form that included names, ages, gender, occupation, family history, smoking, symptoms, and other findings. Tissue samples were collected from newly diagnosed and already diagnosed patients (recurrence and advanced stage).

Biopsies were obtained from patients diagnosed with urothelial bladder cancer (UBC) who underwent transurethral resection of bladder tissue (TURBT) and radical cystectomy surgery. These biopsies were subsequently subjected to histopathological examination, and a CT scan was performed for staging.

The tumors were categorized as either low or high grade according to the WHO classification criteria. Additionally, based on the American Joint Committee on Cancer guidelines, the TNM stage was delineated into non-invasive (Ta–T1) and invasive (T2–T4) stages.

Statistical analysis

The data were analyzed utilizing Statistical Package for the Social Sciences (SPSS) version 26.0 (SPSS, IBM Company, Chicago, IL 60606, USA), with the chi-square test employed for comparing variables. A significance level of $P < 0.05$ was considered statistically significant.

Ethical approval

All investigations and procedures adhered to ethical standards, and the study protocols received approval from the Ethics Committee (Institutional Review Board) at the College of Medicine, Al-Nahrain University, according to document number 20221171 on April 17, 2023, to obtain this approval.

Results

The study spanned a period of eight months, during which 67 lesions were assessed. Hematuria emerged as the predominant presenting symptom. The median age at which the lesions were diagnosed was 65 years (range: 36–89 years), with 63% of cases occurring in individuals in their sixth decade, representing the highest proportion. The incidence was highest among men (95.5%). Almost 74.6% of the sample is from TURBT, meanwhile 25.4% was from radical cystectomy.

TCC emerged as the predominant variant observed in all patients included in this study [Table 1]. At the time of presentation, 24.4% of the patients exhibited muscle-invasive disease, while the remaining 71.6% of the patients were diagnosed with non-muscle-invasive bladder carcinoma, among which 26.9% were classified as pTa and 44.8% as pT1. Overall, 46.3% of the patients were identified with high-grade disease.

Table 2 displays the pathological distribution of bladder cancers by age. Out of the total patients, only 37.3% (25 out of 67) were diagnosed with bladder cancer before the age of 60. It was observed that low-grade cancer was more prevalent among patients younger than 60 years compared to those aged 60 and above (60% vs. 50%), while high-grade represents 50% of participants in the older aged group (vs. 40%), although this difference was not statistically significant (P value = 0.472). There was a relatively higher occurrence of muscle-invasive bladder tumors in the older age group (31% vs. 24%), whereas non-muscle-invasive tumors were 76% among patients aged less than 60 years (P value = 0.541). A total of 15 patients (35.7%) had a recurrence in the older age group, this is comparable to other groups with 36% recurrent cases, and the difference was not statistically significant (P = 0.981).

Table 1: Patient demographics and clinical and pathologic findings in UBC

	Number	Total %
Age	Median (range)	65 (36–89)
Sex		
Male	64	95.5%
Female	3	4.5%
Histopathology		
TCC	67	100%
Pathologic stage		
PTa	18	26.9%
PT1	30	44.8%
PT2	10	14.9%
PT3a	5	7.5%
PT3b	2	3%
PT4	2	3%
Grade		
Low grade	36	53.7%
High grade	31	46.3%
Muscle		
Muscle non-invasive	48	71.6%
Muscle invasive	19	28.4%

Table 2: The clinicopathological distribution of bladder cancers according to age

	Age <60 years	Age >60 years	*P* value
Number of patients	25	42	
Smokers			
Smoker	18 (72%)	28 (66.7%)	0.649
Non-smoker	7 (28%)	14 (33.3%)	
Stage			
PTa	6 (24%)	12 (28.5%)	0.827
PT1	13 (52%)	17 (40.5%)	
PT2	2 (8%)	8 (19%)	
PT3a	2 (8%)	3 (7.14%)	
PT3b	1 (4%)	1 (2.38%)	
PT4	1	1 (2.38%)	
Grade			
Low grade	15 (60%)	21 (50%)	0.472
High grade	10 (40%)	21 (50%)	
Muscle invasive			
Muscle non-invasive	19 (76%)	29 (69%)	
Muscle invasive	6 (24%)	13 (31%)	0.541
Recurrence			
Yes	9 (36%)	15 (35.5%)	0.981
No	16 (64%)	27 (64.5%)	

†chi-square test. *P* value < 0.05

Table 3: The clinicopathological distribution of bladder tumors according to gender

	Male	Female	*P* value
Number of patients	64	3	
Smokers			
Smoker	46 (71.8%)	0 (0%)	0.009*
Non-smoker	18 (28.1%)	3 (100%)	
Stage			
PTa	16 (25%)	2 (66.7%)	0.726
PT1	29 (45.4%)	1 (33.3%)	
PT2	10 (15.6%)		
PT3a	5 (7.8%)		
PT3b	2 (3.2%)		
PT4	2 (3.2%)		
Grade			
Low grade	34 (53.1%)	2 (66.7%)	0.646
High grade	30 (46.9%)	1 (33.3%)	
Muscle invasive			
Muscle non-invasive	45 (70.3%)	3 (100%)	0.265
Muscle invasive	19 (29.7%)	0 (0%)	
Recurrence			
Yes	24 (37.5%)	0 (0%)	0.186
No	40 (62.5%)	3 (100%)	

*chi-square test. *P* value < 0.05

A total of 46 (71.9%) of the males with bladder cancer are smokers, while 18 (28.1%) are non-smokers. This difference was found to be statistically significant (*P* value = 0.009). Low-grade cancer was found less common in males than females (53.1% vs. 66.7%; *P* value = 0.646). The male group contained the majority of recurrent urothelial carcinomas in all 24 cases (37.5%) and no recurrent cases among female participants. Low-grade cancer was found more common in non-smokers compared to smokers (57.1% vs. 52.2%; *P* value = 0.705). Furthermore, 22 out of 31 high grades were smokers, and nine were non-smokers (47.8% vs. 42.9%), and there was no difference in terms of muscle invasiveness between smokers and non-smokers, at 14 (30.4%) and five (23.8%), respectively [Tables 3 and 4].

Table 4: The pathological distribution of bladder tumors based on smoking habit

	Smoker	Non-smoker	*P* value
Number of patients	46	21	
Gender			
Male	46 (100%)	18 (85.7%)	0.009*
Female	0 (0%)	3 (14.3%)	
Stage			
PTa	12 (26%)	6 (28.6%)	0.897
PT1	20 (43.5%)	10 (47.62%)	
PT2	8 (17.4%)	2 (9.5%)	
PT3a	4 (8.7%)	1 (4.76%)	
PT3b	1 (2.2%)	1 (4.76%)	
PT4	1 (2.2%)	1 (4.76%)	
Grade			
Low grade	24 (52.2)	12 (57.1%)	0.705
High grade	22 (47.8%)	9 (42.9%)	
Muscle invasive			
Muscle non-invasive	32 (69.6%)	16 (76.2%)	0.577
Muscle invasive	14 (30.4%)	5 (23.8%)	
Recurrence			
Yes	17 (37%)	7 (33.3%)	0.774
No	29 (63%)	14 (66.7%)	

*chi-square test. *P* value < 0.05

Discussion

The heterogeneous nature of urinary bladder malignancies, characterized by different subtypes and behavioral characteristics, makes it difficult to make epidemiological and clinicopathological comparisons.[11] Cystoscopy and biopsy are the primary diagnostic procedures for bladder cancer, with transurethral resection of bladder tumors (TURBTs) being the most common method for obtaining specimens in our study.[12]

The clinicopathological characteristics of bladder tumors in patients undergoing TURBT and radical cystectomy were examined in this study. The majority of patients included in this analysis were in their sixth to seventh decades of life, with a median age of 65 years among those diagnosed with bladder cancer. This was in line with current research that indicates men between the ages of 50 and 70 years are most likely to develop bladder cancer.[13-17] Comparable research by Comperat

et al, however, found a somewhat lower mean age of occurrence of 33.2 years.[18] Compared to elderly individuals, younger participants are more likely to present with low-grade and low-stage malignancies.[11] This is similar to our findings in this study. It has been noted, meanwhile, that genetic changes that are common in elderly persons are incredibly uncommon in younger ones.[11] This may also be attributed to several years of exposure to environmental factors such as smoking,[19] aromatic amines, and chronic schistosomiasis infestation, which are risk factors for the development of bladder cancer.

Several studies indicate that age may play a role in the recurrence of bladder cancer.[20] According to the results of the current study, recurrence was slightly different in those aged 60 years and older. Woong *et al*. found that younger age patients have lower recurrence and progression rates compared to older patients.[20]

This study has revealed that men are more likely than women to develop bladder cancer. The current study's sex ratio was consistent with previous research showing a male-to-female predominance.[15,21,22] The observed male prevalence of bladder cancer can be explained by a number of factors. The notable gender disparity in bladder cancer incidence, with a disproportionately high prevalence among men, could potentially be attributed to elevated rates of tobacco smoking and occupational exposure to carcinogens in this demographic. Additionally, variances in biological and hormonal mechanisms between sexes have been proposed as contributing factors.[23-25]

In this study, it was found that TCC is the most common type of UBC in all of the studied cases. This result was in good agreement with findings from studies conducted by Laishram *et al*. and Raphael *et al*. which have shown that TCC is the most common malignant bladder tumor.[26,27]

However, the findings of our study contrast with those of other research, where SCC was identified as the most prevalent subtype of bladder cancer (10, 24). This disparity in results could be attributed to varying risk factors, and environmental influences implicated in the etiology of bladder malignancies. It could also be related to hereditary variables.[15]

Currently, tumor grading and staging of UBC are strongly associated with both recurrence and progression, carrying significant prognostic implications. According to our statistics, most of the UBC cases were low grade at 36 (53.7%) followed by high grade at 31(46.3%) cases. A similar result was also published, where 66 were low grade and 44 were high grade.[15]

In contrast, the findings of this study diverge from those of Shrestha EP *et al*., where 65.3% of cases were identified as high-grade urothelial carcinoma, with low-grade urothelial carcinoma accounting for 34.7% of cases.[28]

In this study, early pathological stages (PTa and PT1) were found to constitute 71.7% of cases, while late-stage cancer accounted for 28.4%. This is comparable to the results of Vaidya *et al*. who found that 73% of cases were early-stage malignancies (pTa and pT1).[29]

As per the pathology reports, the majority of the UBC cases examined—specifically, 48 patients (71.6%)—were diagnosed with NMIBC, while only 19 patients (28.4%) were identified with muscle-invasive bladder cancer (MIBC).

Conclusion

The most prevalent histological type of UBC is TCC. Males are more likely to develop bladder tumors, and most occurrences happen in the sixth decade of life. In this study, TCC in stages (PT1) and (PTa) was comparatively common patterns.

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Conflicts of interest

There are no conflicts of interest.

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