Original Article

Characteristics of bladder neoplasms in the young population of Saudi Arabia

Abdulrahman I. Alabdulkareem, Fares H. Al-Jahdali, Ahmed I. Nazers[1], Sultan S. Alkhateeb[1]

College of Medicine, King Saud bin Abdulaziz University for Health Sciences, [1]Department of Urology, King Abdulaziz Medical City, Riyadh, Saudi Arabia

Abstract

Context: Bladder neoplasms are a well-studied subject in medicine. However, the evidence of bladder neoplasms in children and the young adult population (≤40 years), particularly in Saudi Arabia, is lacking.

Aims: The aims of this study were to identify histopathological characteristics as well as clinical features, prognosis, and treatment of bladder neoplasms in this age group in a single tertiary referral center, Riyadh, Saudi Arabia.

Settings and Design: A retrospective cohort study.

Materials and Methods: Children and young adults (≤40 years) diagnosed with epithelial and mesenchymal bladder neoplasms from 1994 to 2017.

Statistical Analysis Used: Descriptive data are presented as mean (standard deviation) or median (interquartile range) for continuous variables and *n* (%) for categorical variables. Statistical Package for Social Sciences version 23 was used.

Results: Thirty-eight cases were identified. The majority, 71.1% ($n = 27$) were male. The median age of diagnosis was 33 years ranging from 1 to 40 years. Nearly 45% ($n = 17$) were smokers. Macroscopic hematuria was present in 57.8% ($n = 22$). The most common histopathology was papillary urothelial carcinoma ($n = 18$, 58%). All mesenchymal neoplasms accounted for 18.4% ($n = 7$). Of all malignancies, 63.2% ($n = 24$) and 44.7% ($n = 17$) were low stage and low grade, respectively. Transurethral resection of bladder tumor (TURBT) was conducted for 81.6% ($n = 31$). The mean length of follow-up was 36.05 months (±39.4 months). Recurrence occurred in 15.8% ($n = 6$) and 7.9% ($n = 3$) had progression. Distant metastasis was reported in 5.3% ($n = 2$). Nearly 8% ($n = 3$) died during their follow-up.

Conclusions: Bladder malignancies at the early fourth decade of life tend to be a low stage and low grade. The most common histopathology was papillary urothelial carcinoma. Management should be based on the clinical and histopathological features. However, most of the patient underwent TURBT.

Keywords: Bladder, cancer, neoplasm, Saudi Arabia, young

Address for correspondence: Dr. Abdulrahman I. Alabdulkareem, 7575 Al Laymun, Al Mughrizat, Riyadh, P.O: 11564, Saudi Arabia.
E-mail: 3bdlrahman@gmail.com
Received: 10.08.2017, **Accepted:** 04.09.2017

INTRODUCTION

According to the International Agency for Research on Cancer (IARC), bladder cancer (BC) is the ninth most common cancer globally.[1,2] The IARC states that the worldwide incidence and 5-year-period prevalence of BC in both genders among all cancers are 3.1% (5.3 per 100,000)

Access this article online	
Quick Response Code:	Website: www.urologyannals.com
	DOI: 10.4103/UA.UA_122_17

How to cite this article: Alabdulkareem AI, Al-Jahdali FH, Nazers AI, Alkhateeb SS. Characteristics of bladder neoplasms in the young population of Saudi Arabia. Urol Ann 2017;9:343-7.

and 4.1% (25.4 per 100,000), respectively. BC ranks 13 among the most common cancer diagnosis in Saudi Arabia, affecting 3.8/100,000 men and 0.9/100,000 women.[3] It is a disease of the elderly and peaks at the sixth decade of life.[4] Nevertheless, BC could also affect children, adolescents, and young adults with a prevalence of <1% in the first 4 decades of life.[5]

Although BC is a well-studied subject in the elderly, its clinicopathological characteristics in the young adult population are conflicting. Some studies have stated that BC at young ages has a better outcome than those in the elderly,[6-8] whereas others reported that it has similar clinical behavior and outcomes.[5-9] In addition, mesenchymal tumors of the bladder are rare and there is a huge gap in the global and local literature. The overall prevalence of such neoplasms is <5% of all bladder tumors.[10]

Despite the increased focus on the subject in the literature, to the best of our knowledge, there has been no local data reporting the clinicopathological features of BC in the children and young adult population (≤40 years). The primary aim of this study is to review the clinical presentation, histopathological features, staging and grading, treatment as well as the recurrence, progression, and survival rate of BC in patients aged 40 and below in a tertiary referral center in Riyadh, the capital of Saudi Arabia.

SUBJECTS AND METHODS

We identified and retrospectively reviewed the medical records of 38 cases aged ≤ 40 years diagnosed with primary BC at a tertiary center in Riyadh, Saudi Arabia. The period was from 1994 to 2017. The primary data recorded were as follows: (1) clinical presentation, (2) histopathology, (3) anatomical topography, (4) staging, (5) grading, (6) treatment, (7) risk factors, (8) cancer recurrence, (9) cancer progression, and (10) mean length of follow-up. Patients with both benign and malignant pathologies were included in the study. Patients with primary bladder neoplasm and aged ≤40 were included in the study. Patients with a non-diagnostic histopathology and no subsequent diagnostic work-up were excluded from the study.

Tumors were staged and graded according to the tumor node metastasis system and the World Health Organization system, respectively. Histopathology was based on biopsy obtained after performing transurethral resection of bladder tumor (TURBT) or by other means of surgical intervention. Recurrence was defined as a new neoplastic growth at the same or different site of the bladder after complete remission. Disease progression was defined as an increase in the tumor stage and/or grade on recurrence.

The research proposal has been reviewed and approved by the International Review Board committee (Reference number: RC17/045/R) at King Abdullah International Medical Research Center, Riyadh, Saudi Arabia.

Statistical analysis

Descriptive data are presented as mean (standard deviation) or median (interquartile range) for continuous variables and *n* (%) for categorical variables. Statistical Package for Social Sciences version 23 was used.

RESULTS

A total number of 38 patients were included in the study. The median age of diagnosis was 33 ranging from 1 to 40 years of age. The majority of patients, 71.1% were male and of Saudi nationality (76.3%) [Table 1]. The prevalence of bladder neoplasms in children and young adults over the period of 1994 to 2017 was 11.4%.

Most patients presented initially with macroscopic haematuria (57.8%) [Table 1]. Cigarette smoking was reported by 42.1% with 2.6% reporting heavy use of shisha (water pipe). One patient reported a personal history of the renal tumor, whereas another patient had neurogenic bladder with a history of recurrent self-catheterization and multiple urinary tract infections (UTIs). One patient was found with an EWSR1 (22q12) Gene Rearrangement and developed extra-skeletal myxoid chondrosarcoma of the urinary bladder.

All patients underwent cystoscopy. Tumors were most frequently located on the left lateral wall (23%). The main histopathological findings were papillary urothelial carcinoma (58%), followed by flat carcinoma *in situ* (19.3%) [Table 2]. All mesenchymal neoplasms accounted for 18.4% (*n* = 7) [Table 2]. The majority of tumors were low grade (44.7%) [Table 1]. Nearly 81.2% of tumors were non-muscle invasive. Only 2 patients with high grade papillary urothelial carcinoma had distant metastasis to "lung and liver" and "lung and brain."

Most tumors were excised through TURBT (81.6%). Three patients (7.8%) had radical cystectomy (2 ileal conduit urinary diversion and 1 orthotopic neobladder) in which 1 had squamous cell carcinoma, and 2 had high grade papillary urothelial carcinoma. One had laparoscopic excision of urinary leiomyoma, 1 robotic partial cystectomy for a fibroepithelial tumor of the bladder, 1 fulguration for papillary urothelial carcinoma and only 1 underwent

Table 1: Demographics and clinical features of bladder cancer patients ≤40 years of age in a single tertiary referral center from 1994 to 2017

	Age (year)		
	≤30	31-40	Total
Patients, *n* (%)	15 (39.5)	23 (60.5)	38 (100)
Median age in years (IQR)	24 (1-30)	36 (33–40)	33 (1–40)
Gender, *n* (%)			
Male	11 (40.7)	16 (59.2)	27 (71)
Female	4 (63.6)	7 (63.6)	11 (29)
Nationality, *n* (%)			
Saudi	14 (43.7)	18 (56.2)	32 (84.2)
Non-Saudi	1 (16.7)	5 (83.3)	6 (15.8%)
Marital status, *n* (%)			
Single	10 (62.5)	3 (13.6)	13 (34.2)
Married	2 (12.5)	17 (77.3)	19 (50)
Smoker, *n* (%)	6 (35.2)	11 (64.7)	17 (44.7)
Clinical presentation, *n* (%)			
Macroscopic hematuria	7 (31.8)	15 (68.1)	22 (57.8)
LUTS	6 (75)	2 (25)	8 (21)
Asymptomatic	1 (25)	3 (75)	4 (10.5)
Microscopic hematuria	1 (50)	1 (50)	2 (5.2)
Recurrent UTIs	1 (50)	1 (50)	2 (5.2)
Mean length of follow-up (months)	12	25.9	36.05
Tumor stage, *n* (%)			
Nonmuscle invasive	8 (30.7)	18 (69.2)	26 (81.2)
Muscle invasive	3 (50)	3 (50)	6 (18.7)
Tumor grade, *n* (%)			
Low grade	2 (12.5)	15 (68.2)	17 (44.7)
High grade	2 (12.5)	5 (22.7)	7 (18.5)
Tumor type, *n* (%)			
Malignant	13 (38.2)	21 (61.7)	34 (89.4)
Benign	2 (50)	2 (50)	4 (10.5)
Topography, *n* (%)			
Left lateral wall	3 (33.3)	6 (66.6)	9 (23.7)
Left ureteric orifice	2 (66.6)	1 (33.3)	3 (7.9)
Posterior wall	2 (100)	0	2 (5.3)
Dome of the bladder	0	2 (100)	2 (5.3)
Recurrence rate, *n* (%)	0 (0)	6 (100)	6 (15.7)
Progression rate, *n* (%)	0 (0)	3 (100)	3 (100)
TURBT, *n* (%)	13 (40.6)	19 (59.3)	32 (84.2)
Cystectomy, *n* (%)	1 (25)	3 (75)	4 (10.5)
Intravesical therapy, *n* (%)	2 (18.1)	9 (81.8)	11 (28.9)
Chemoradiotherapy, *n* (%)	1 (100)	0 (0)	1 (2.6)

LUTS: Lower urinary tract symptoms, UTIs: Urinary tract infections, TURBT: Transurethral resection of bladder tumor, IQR: Interquartile range

Table 2: Summary of histopathological findings of bladder cancer patients ≤40 years of age in a single tertiary referral center from 1994 to 2017

Histopathology	*n* (%)
Urothelial carcinoma	31 (81.5)
Papillary urothelial carcinoma	18 (58)
Flat carcinoma *in situ*	6 (19.3)
Urothelial carcinoma, NOS	4 (12.9)
Mucinous adenocarcinoma	1 (3.2)
Squamous cell carcinoma	1 (3.2)
Inverted urothelial papilloma	1 (3.2)
Mesenchymal neoplasm	7 (18.4)
Bladder leiomyoma	2 (28.5)
Rhabdomyosarcoma, NOS	1 (14.2)
Embryonal rhabdomyosarcoma	1 (14.2)
Extra-skeletal myxoid chondrosarcoma	1 (14.2)
Inflammatory myofibroblastic tumor (fibroepithelial tumor)	1 (14.2)
Malignant rhabdoid tumor	1 (14.2)

NOS: Not otherwise specified

chemoradiotherapy for rhabdomyosarcoma (RMS). One patient with malignant rhabdoid tumor had preoperative chemotherapy. Five patients (13.2%) had postoperative chemotherapy (2 urothelial carcinoma, 2 RMS, 1 mucinous adenocarcinoma), where one of the RMS was embryonal and underwent further transurethral resection of the base of bladder tumor. Two patients underwent postoperative radiotherapy (2 RMS). Eleven patients (28.9%) received an installation of intravesical therapy; 4 (36.3%) had Bacillus Calmette-Guérin (BCG) and 7 (63.6%) had mitomycin.

The mean length of follow-up was 36.05 months (1096.81 days) (±39.4 months). Overall, 6 patients (15.8%) had recurrences (5 papillary urothelial carcinoma, 1 mucinous adenocarcinoma). Only 1 patient had 2 recurrences with a low grade papillary urothelial carcinoma. In addition, 3 patients (7.8%) had progressions, in which 1 had a higher grade and underwent TURBT and received intravesical BCG and 2 progressed into a higher stage. The average length of time when recurrence occurred was 47.68 months. Three patients (7.9%) died during their follow-up, 2 due to urothelial carcinoma and 1 RMS.

DISCUSSION

Bladder neoplasms are rare in the early four decades of life.[5] As per our analysis, the prevalence of bladder neoplasms at our institute from 1994 to 2017 was 11.4%. Diagnosis of BC in the young adult is quite the dilemma. The presentation of macroscopic hematuria and LUTS in these age groups leads to suspicion of a less malignant cause, such as UTIs, nephrolithiasis, and/or nephropathies. Physicians should attain a lower threshold of suspicion to exclude the possibility of cancers. Clinical features and histopathological findings of BC in patients at their young adulthood (≤40 years) are insufficient and local Saudi data are missing.

Macroscopic haematuria was the initial presenting symptom in 57.8%, which required further work-up and cystoscopy for the diagnosis to be made. Nomikos *et al*. and Gunlusoy *et al*. reported similarly. The diagnosis of BC below the age of 40 is usually delayed. The delay could be attributed mainly to higher incidences of benign causes. Nomikos *et al*. stated that the reason for the delay is the reluctance for diagnostic cystoscopy.

Our analysis showed that patients with bladder malignancy aged ≤40-year-old often have a low-stage (63.2%) and low-grade (44.7%) tumor, which supports the previous evidence that patients at this age group had low stage

and grade.[6-11] Tumor stage and grade is important in determining the natural history of the disease as well as the risk of recurrence. Compérat *et al.* stated that the most crucial elements in affecting disease prognosis were tumor's stage and grade.[12] Disease prognosis, quality of life, risk of recurrence, and life expectancy are the patients' and their families' utmost important information. This fact is much more evident if the patient is diagnosed early in life. Even though, these tumors are low stage and grade, vigilant follow-up and early identification of recurrence are necessary through regular urine cytology and cystoscopy.

Our cohort also reports mesenchymal tumors. These neoplasms are a rare entity, accounting for <5% of all bladder tumors.[10] Approximately 250 bladder leiomyoma has been reported in the English literature, and it generally affects females in their fourth and fifth decade of life.[13] We presented two cases of bladder leiomyoma in male patients aged 35 and 25. In regard to patient's age, gender, and the pathology itself, this is a rare finding as the prevalence of bladder leiomyoma is <0.4% of all bladder neoplasms.[13] Embryonal RMS is another rare neoplasm, with only 15 published case reports in the literature.[14] It is a disease of childhood and accounts for 3% of all childhood cancers (29% are genitourinary).[15,16] There has been to the best of our knowledge, no report in Saudi Arabia describing embryonal RMS. Our patient was a female who presented at the age of 15 years. Inflammatory myofibroblastic tumor (IMT) was another case of a 33-year-old female. The largest series with 46 cases of IMT was published by Montgomery *et al.*[17] with a reported mean age at diagnosis of 53.6 years. Another mesenchymal bladder neoplasm was extraskeletal myxoid chondrosarcoma in a 1 year old male who also had EWSR1 gene mutation. There have been 10 case reports of this disease, and only 1 of them affecting the bladder.[18] This is the first reported case of extraskeletal myxoid chondrosarcoma affecting the bladder in Saudi Arabia. Last but not least, malignant rhabdoid tumor of a 1 year old female was found. This is aggressive cancer affecting mainly central nervous system and kidneys. However, it can affect different sites of the body, including the bladder.

The limitation of the present study is it was a retrospective cohort in one center with a small number of patients. Further long-term multi-center prospective studies are recommended to explore the long-term complications and recurrences of the diseases. Another limitation is that we lost to follow up with some of the mesenchymal cases. On the other hand, the strength of this study is that it is the first to report on both epithelial and mesenchymal bladder neoplasms in Saudi Arabia. In addition, some of the reported diseases are quite rare, with only a handful of global reports.

CONCLUSIONS

The prevalence of bladder neoplasm in patients 40 years of age or below is 11.4%. Younger patients with epithelial neoplasms tend to have low stage, low-grade tumors, and lower recurrence rate. The majority of the histopathological findings were papillary urothelial carcinoma, and most of the neoplasms were surgically resected through TURBT.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, *et al.* GLOBOCAN 2012 Ver. 1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11. Lyon, France: International Agency for Research on Cancer; 2013. Available from: http://www.globocan.iarc.fr. [Last accessed on 2017 May 11].
2. Bray F, Ren JS, Masuyer E, Ferlay J. Global estimates of cancer prevalence for 27 sites in the adult population in 2008. Int J Cancer 2013;132:1133-45.
3. "Cancer Registry Reports". Saudi Health Council. N.p.; 2017. Available from: http://www.chs.gov.sa/Ar/HealthCenters/NCC/CancerRegistry/CancerRegistryReports/2013.pdf. [Last accessed on 2017 Jan, 26].
4. Howlader N, Noone AM, Krapcho M, Neyman N, Aminou R, Waldron W, *et al.* SEER Cancer Statistics Review, Bladder Section, 1975-2008. Bethesda, MD: National Cancer Institute; 1975-2008.
5. Wen YC, Kuo JY, Chen KK, Lin AT, Chang YH, Hsu YS, *et al.* Urothelial carcinoma of the urinary bladder in young adults – Clinical experience at Taipei Veterans General Hospital. J Chin Med Assoc 2005;68:272-5.
6. Nomikos M, Pappas A, Kopaka ME, Tzoulakis S, Volonakis I, Stavrakakis G, *et al.* Urothelial carcinoma of the urinary bladder in young adults: Presentation, clinical behavior and outcome. Adv Urol 2011;2011:480738.
7. Stanton ML, Xiao L, Czerniak BA, Guo CC. Urothelial tumors of the urinary bladder in young patients: A clinicopathologic study of 59 cases. Arch Pathol Lab Med 2013;137:1337-41.
8. Poletajew S, Walędziak M, Fus Ł, Pomada P, Ciechańska J, Wasiutyński A, *et al.* Urothelial bladder carcinoma in young patients is characterized by a relatively good prognosis. Ups J Med Sci 2012;117:47-51.
9. Yossepowitch O, Dalbagni G. Transitional cell carcinoma of the bladder in young adults: Presentation, natural history and outcome. J Urol 2002;168:61-6.
10. MurphyWM, Grignon DJ, Perlman EJ. Tumors of the Kidney, Bladder, and Related Urinary Structures. Washington, DC: American Registry of Pathology; 2004. p. 394.
11. Gunlusoy B, Ceylan Y, Degirmenci T, Kozacioglu Z, Yonguc T, Bozkurt H, *et al.* Urothelial bladder cancer in young adults: Diagnosis, treatment and clinical behaviour. Can Urol Assoc J 2015;9:E727-30.

12. Compérat E, Larré S, Roupret M, Neuzillet Y, Pignot G, Quintens H, *et al*. Clinicopathological characteristics of urothelial bladder cancer in patients less than 40 years old. Virchows Arch 2015;466:589-94.
13. Erdem H, Yildirim U, Tekin A, Kayikci A, Uzunlar AK, Sahiner C, *et al*. Leiomyoma of the urinary bladder in asymptomatic women. Urol Ann 2012;4:172-4.
14. Chen KW, Wu FM, Lee VK, Esuvaranathan K. Embryonal rhabdomyosarcoma of the adult urinary bladder: A rare case report of misclassification as inflammatory myofibroblastic tumor. Case Rep Surg 2015;2015:510508.
15. Jemal A, Siegel R, Xu J, Ward E. Cancer statistics, 2010. CA Cancer J Clin 2010;60:277-300.
16. Breitfeld PP, Meyer WH. Rhabdomyosarcoma: New windows of opportunity. Oncologist 2005;10:518-27.
17. Montgomery EA, Shuster DD, Burkart AL, Esteban JM, Sgrignoli A, Elwood L, *et al*. Inflammatory myofibroblastic tumors of the urinary tract: A clinicopathologic study of 46 cases, including a malignant example inflammatory fibrosarcoma and a subset associated with high-grade urothelial carcinoma. Am J Surg Pathol 2006;30:1502-12.
18. Mendez-Probst CE, Erdeljan P, Castonguay M, Gabril M, Wehrli B, Razvi H. Myxoid chondrosarcoma of the scrotum: a case report and review of the literature. Canadian Urological Association J 2010;4:E109-E111.