

## Pathological Pattern of Urinary Bladder Cancer: Data from a Single Egyptian Institute

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**Background:** The control of schistosomiasis in Egypt was associated with changes in the prevalence and histopathology of urinary bladder cancer.

**Aim:** To investigate the histological pattern among patients treated for bladder cancer at our institution over a 5-year period.

**Methods:** This retrospective study was conducted by reviewing the medical records of 632 patients treated for urinary bladder cancer at the departments of Urology and Clinical Oncology, Al Azhar Faculty of Medicine, between January 2011 and December 2015.

**Results:** The study included 632 patients. Their age ranged from 27-87 years old with a median of 62 years. Male to female ratio was about 6:1. Fifty-nine percent of the patients had Non-Muscle Invasive Bladder Cancer (NMIBC) versus 41% had Muscle Invasive Bladder Cancer (MIBC). Patients with history of schistosomiasis were 46.5%; besides, 67.9% of the patients were smokers. Transitional Cell Carcinoma (TCC) was the predominant histological type (87.5%), followed by Squamous Cell Carcinoma (SCC) 9.1%, mixed SCC and TCC (2.8%), and other subtypes 0.6%.

**Conclusion:** Our study confirms that the histopathological pattern of urinary bladder cancer in Egypt is still changing. Over the last decades, the incidence of bladder SCC is declining and bladder TCC is rising. Yet the incidence of bladder SCC is the lowest compared to previous reports.

**Keywords:** Urinary Bladder Cancer, Schistosomiasis, Egypt

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### INTRODUCTION

According to the first published national population based study for the period between 2008 and 2011, bladder cancer is the 3rd most common malignancy (6.9%) in Egypt. It comes after breast cancer (41 % and hepatocellular carcinoma (23.8%), with more predominance in males 78 % than females 22%<sup>1</sup>.

Squamous Cell Carcinoma (SCC) of the bladder is a rare histological type in the Western countries and North America, representing around 5% of all urinary bladder carcinomas<sup>2, 3</sup>. In Africa, the incidence is different especially in the countries located on the Nile River; because of the high incidence of schistosomal infection that leads to chronic irritation and squamous metaplasia<sup>4</sup>.

Historically, the incidence of bladder SCC was known to be high in Egypt<sup>5</sup>; however, recent data from Egypt show significant decrease in this incidence along the last decades<sup>6</sup>.

In this study, we aimed to analyze the histological pattern of patients treated for urinary bladder carcinoma at our institution over a 5-year period.

### METHODS

This retrospective study was conducted by reviewing the medical records of patients admitted and treated for

urinary bladder cancer at the Urology and Clinical Oncology Departments, Faculty of Medicine, Al-Azhar University from January 2011 to December 2015. A total of 632 patients were diagnosed and treated for bladder cancer.

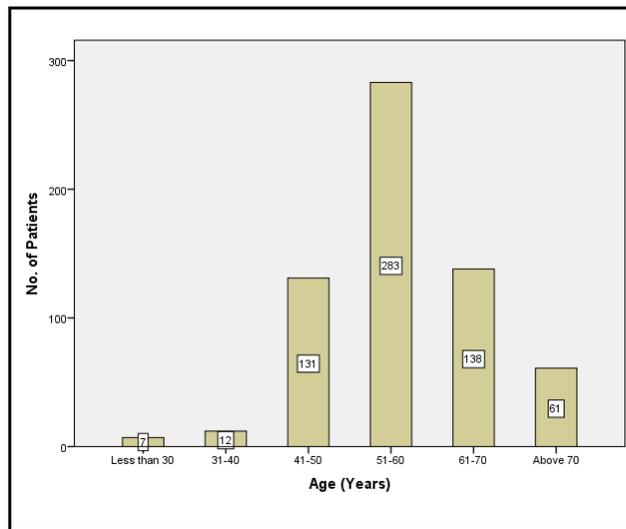
Patients' demographic data, risk factors for urinary bladder cancer and tumor characteristics were collected. Patients diagnosed and/or received treatment for schistosomiasis (*S. haematobium*), in addition to those whereas schistosomal ovum was detected in histopathology specimen were considered of positive history of schistosomiasis.

We have used SPSS version 20 to analyze the data. Quantitative data was presented as mean  $\pm$  standard deviation, while qualitative data was presented as frequency distribution. The Chi Square test was used to compare nominal variables and Student t-test was used to compare numerical values. For all statistical tests,  $P < 0.05$  was considered significant.

### RESULTS

The total number of patient included in this study was 632 patients with median age of 62 years (range 27- 87). The age of the majority (87.2%) was between 40 and 70 years old with peak between 51 and 60 years (44.7%) as

shown in Fig. 1. Only 3% of patients were under the age of 40 years.



**Figure 1: Distribution of patients according to age groups**

Male to female ratio was about 6:1 for all patients, clinical and pathological characteristics are presented in Table 1.

For MIBC and NMIBC, the male to female ratio was about 8:1 and 4:1, respectively, whereas female patients tends to have MIBC cancer at presentation 50/92 (54%) more than male 209/540 (39%) as shown in Table 2.

History of smoking (either current or former) was recorded in 67.9% (429/632) of patients, with significantly higher incidence among males (78%) than females (10%), (P Value= 0.00). However, there was no significant correlation between smoking and tumor stage, grade or histological type.

History of schistosomiasis was observed in 294 patients (46.5 %), while 250 patients (39.6%) had no history, and data were not available for the rest 88 patients (13.9%). Transitional Cell Carcinoma was the dominant histopathological subtype 87.5 % (553/632), while SCC, mixed TCC and SCC and other subtype represented 9.1% (57/632), 2.8% (18/632) and 0.6% (4/632), respectively.

In the current research, the majority of patients developed NMIBC 59 % (373/632), while 41 % (259/632) had MIBC of which 21.2% (55/259) presented with metastatic disease (Table 2).

Grade I tumor has been identified only in 3 % (19/632) of patients, all had noninvasive TCC. In contrast, grade III tumor was reported for SCC, mixed TCC&SCC and other subtypes in 49.1% (28/57), 77.8% (14/18) and 75% (3/4), respectively. This was much higher than the reported for TCC 32.2% (178/553).

The rate of MIBC was significantly higher in female patients, non TCC histology, and high tumor grade (p value <0.01).

**Table 1: Clinical and pathological characteristics of our patients**

	No.	%
<b>Age</b>		
Median (range)	57	(22-89)
<b>Sex</b>		
Male	540	85.4
Female	92	14.6
<b>History of smoking</b>		
Yes	429	67.9
No	203	32.1
<b>History of Schistosomiasis</b>		
Yes	294	46.5
No	250	39.6
Unknown	88	13.9
<b>Histopathology</b>		
TCC	553	87.5
SCC	57	9.1
Mixed (TCC + SCC)	18	2.8
Other	4	0.6
<b>T stage</b>		
Ta	42	6.7
T1	331	52.4
T2	191	30.2
T3	47	7.4
T4	21	3.3
<b>Grade</b>		
GI	19	3
GII	390	61.7
GIII	223	35.3
<b>Distant metastases at presentation</b>		
Yes	55	8.7
No	577	91.3

TCC: Transitional cell carcinoma, SCC: Squamous cell carcinoma

On the other hand, patients with positive history of schistosomiasis tend to have higher T stage and MIBC of statistically significant p-values (0.02 and 0.04, respectively). Patients with non-TCC has significant tendency for higher T stage than TCC patients (p value = 0.03).

Out of the 57 patients with SCC, 33 patients (59.9%) had positive history of schistosomiasis versus 250 patients (46.9%) out of the 553 patients who have TCC. The difference was not significant (Table 3).

About 45% (251/552) of patients with TCC had history of schistosomiasis versus 57.9% (33/57) for patients with SCC. The difference was not statistically significant.

Noteworthy, in patients with NMIBC, Ta and T1 represent 11.3% (42/373), and 88.7 % (331/373)

respectively, while in patients with MIBC, T2, T3 and T4 represent 73.7% (191/259), 18.2% (47/259) and 8.1% (21/259), respectively.

**Table 2: Correlation between invasiveness of bladder cancer and different clinical and pathological characteristics**

Characteristic	Non-MIBC (n = 373)	MIBC (n = 259)	p value
	No. (%)	No. (%)	
<b>Age</b>			
Median (range)	55 (22-87)	58 (29-89)	0.01
<b>Sex</b>			
Male	331 (88.7)	209 (80.7)	0.01
Female	42 (11.3)	50 (19.3)	
<b>History of Smoking</b>			
Yes	251 (67.3)	178 (68.7)	0.7
No	122 (32.7)	81 (31.3)	
<b>History of Schistosomiasis</b>			
Yes	157 (42.1)	137 (53)	0.04
No	159 (42.6)	92 (35.5)	
Unknown	57 (15.3)	30 (11.7)	
<b>Histopathology</b>			
TCC	364 (65.8)	189 (73)	0.01
SCC	8 (14)	49 (18.9)	
Mixed	1 (5.6)	17 (6.6)	
Other	0	4 (1.5)	
<b>Grade</b>			
I	19 (5.1)	0	< 0.01
II	302 (81)	88 (34)	
III	52 (13.9)	171 (66)	
<b>Distant metastases at presentation</b>			
Yes	0	55 (21.2)	< 0.01
No	373 (100)	204 (78.8)	

Non-MIBC: Non-muscle invasive bladder cancer, MIBC: Muscle invasive bladder cancer, SCC: Squamous cell carcinoma, TCC: Transitional cell carcinoma.

**Table 3: Distribution of schistosomiasis history among different histopathological types**

Schistosomiasis history	Histopathological type (No.)				p value
	SCC	TCC	Mixed (TCC + SCC)	Other	
Yes	33	251	10	0	0.25
No	18	225	5	3	
Unknown	6	77	3	1	

SCC: Squamous cell carcinoma, TCC: Transitional cell carcinoma.

## DISCUSSION

Worldwide, bladder cancer is the ninth most common cancer with 430,000 new cases diagnosed in 2012<sup>7</sup>. It is more common in men than women and its incidence rates are highest in Europe, United States, and Egypt<sup>8</sup>.

According to the reported national incidence rates for Egypt, derived from a population-based cancer registry program, bladder cancer was the third most common cancer in both sexes with an incidence of 6.9%. Among men it was the second most common cancer with an incidence of 10.7%<sup>1</sup>. It is noted that earlier published research reported higher incidences of bladder cancer among Egyptians (27.6%)<sup>9</sup>, (11.7%)<sup>10</sup> and (13%)<sup>6</sup>.

Historically, Egypt known to be endemic with schistosomiasis, which was documented with radiologically-detected calcified schistosoma ova identified in mummies<sup>11</sup>. Scott was the first to describe the pattern of *S. haematobium* and *S. mansoni* infections throughout Egypt. In 1937, *S. haematobium* infection reached 60% all over Egypt, whereas Scott referred the high rates of *S. haematobium* infection in Upper Egypt to the change in the system of irrigation<sup>12</sup>.

Overall, the national and international efforts over the past 30 years have been remarkably effective in schistosomiasis control in Egypt<sup>6</sup>. The Egyptian National Schistosomiasis Control Project was closed in 2002, after declined rate of schistosomiasis infection. The prevalence of *S. Haematobium* among the general population in the Delta declined from 6.6% in 1993 to 1.9% in 2002, then to 1.2% in 2006<sup>13</sup>.

Positive history of schistosomiasis among patients included in this study was about 47%, which reflects the high incidence of infection up to the 80s of the last century. Such history doesn't affect the current status of schistosomiasis infection after the success of the schistosomiasis treatment campaign during the eighties and nineties and beginning of the current millennium. The high schistosomal history infection didn't translate into higher SCC incidence (9%) in the last few years, likely because of the sharp decrease in the rate of new schistosomal infection, with drop of the egg-positive specimens from 82.4% in 1970-1974 to 55.2% in 2003-2007<sup>10</sup>.

In 2011, Babjuk et al analyzed data of 467,528 individuals, whereas, former and current smokers had two and fourfold increase, respectively, in urothelial bladder cancer risk relative to never smokers. The population risk of bladder cancer attributable to smoking was approximately 50% for both men and women<sup>14</sup>.

According to the Global Adult Tobacco Survey for Egypt done by the WHO, 9.8 million Egyptians (19.7%) used some form of tobacco (9.6 million men and 157,000 women). Manufactured cigarettes smoked by 74.1% of men, followed by water pipe (the so called shisha) in 13.8%, and 7.4% who smoked cigarettes and used smokeless tobacco. About 35.2 million (70.8%) of the population live in homes where smoking is allowed. In

Egypt, over 25.5 million adults (51.2%) smoke at home<sup>15</sup>. The incidence of former and current smoker among patients included in this study was 62%, which clearly shows the higher risk of bladder cancer among Egyptian smokers and this is consistent with international published data that showed rate of smoking ranging between 69 and 77%<sup>16, 17</sup>. A higher incidence of smoking reported among urinary bladder cancer patients (85%) was because of false definition since the researchers defined positive smoking as active smoking, second-hand smoking, and even cigarette industry workers<sup>6</sup>.

Transitional Cell Carcinoma represents 90% to 95% of malignant bladder tumors. The remaining 5% to 10% comprises mesenchymal neoplasms and other types of epithelial tumors (such as; SCC and adenocarcinoma)<sup>18</sup>. However, in Egypt the malignant bladder tumors were histologically different because of schistosomal infestation. The schistosoma-associated bladder cancer has a distinctive clinico-pathological feature, quite different from that reported from Western countries. Schistosoma-associated bladder cancer affects patients at a younger age (mean 46.7 years) with a male to female ratio of 5.6:1<sup>5</sup>. The most common histological type is squamous cell carcinoma (76.6%) since it arises on top of squamous metaplasia resulting from chronic schistosomal cystitis<sup>5, 19</sup>.

After successful control of schistosomiasis, the histological pattern of malignant bladder tumors has changed. In our current work, pure SCC represented only 9% of malignant bladder tumors and if we add to this mixed TCC and SCC, the rate will be 12%. Previous reports revealed gradual decline in the incidence of bladder SCC. From all urinary bladder cancer, SCC represented 75.9% (1970-1974), 66% (1985-1989) and 33% (2003-2007)<sup>10</sup>. Between 2006 and 2010, Salem and Mahfouz reported an incidence of 25% for bladder SCC in Egypt<sup>6</sup>.

### Conclusion

The histopathological pattern of bladder cancer is changing among Egyptians. Over the last decades, the incidence of bladder SCC is declining, while bladder TCC is rising. Yet the incidence of bladder SCC is the lowest compared to previous reports.

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