# Clinico-pathological Features of Squamous Cell Carcinoma of **Urinary Bladder at South Egypt Cancer Institute** (Retrospective Study)

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## Abstract:

**Objectives:** The objective of this research is to determine the clinicopathological characteristics of bladder squamous cell carcinoma encountered over a ten year period in Radiation Oncology Department, South Egypt Cancer Institute, Assiut University.

Methods: the medical records of bladder cancer cases during the period from 2008 to 2018 were retrospectively reviewed and tabulated.

Results: A total of 62 urinary bladder cancer (UBC) cases were recorded. The mean age was  $57.21 \pm 7.44$  years (range; 40-70) years. The male-to-female ratio was 3.4:1. The main clinical presentation was burning micturition in 46.8%, followed by hematuria in 37.1%, dysuria in 9.7%, and cystitis in 6.5%. The ECOG performance status of the study cases was also assessed and showed that; 85.5 % have PS I, 11.3% have PS II, and 3.2% have PS III. Regarding tumor grade; almost all study cases (90.3%) have tumor grade II, while 9.7% have tumor grade III. Regarding tumor stage; 19.4%, 45.2%, 29.0%, and 6.5% had T1, T2, T3, and T4 respectively, and only one case suffered from positive nodal metastasis. Regarding treatment; 64.5% underwent radical cystectomy with uretero-cutaneous shunt, 22.6% underwent anterior pelvic excentration, 6.5% underwent partial cystectomy, and another 6.5% have bladder preservation. Patients who underwent radical cystectomy and partial cystectomy received neoadjuvant chemotherapy then underwent surgery and patients who underwent anterior pelvic excentration receive postoperative radiotherapy and patients refusing surgery underwent maximal TURBT then received concurrent chemoradiation. The median duration of follow up was 50 months (range; 5-171 months). According to Kaplan-Meier analysis, at five year the rate of OS was 79.2%. By the end of the study, 17.7% of patients had died of their cancer. A total of 6/62 patients (9.7%) developed disease recurrence. The median time to locoregional recurrence was 49 months (range, 4 to 171 months). According to Kaplan-Meier analysis, at five year the rate of DFS was 91.1%. There were 900 cases of bladder cancer attending to South Egypt Cancer Institute in the period from the 1st of January 2008 up to the end of December 2018; 62 of these patients met the criteria in our study.

**Conclusion:** Bladder cancer is fairly common in our locality. SCC is generally, decreasing compared with TCC. This trend may be the outcome of improved bilharziasis control in rural Egyptian populations due to the use of potent oral antibilharzial medications.

Keywords: Bladder cancer, Squamous Cell Carcinoma, South Egypt Cancer Institute.

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# **Introduction:**

Bladder cancer is a worldwide health issue. It is the ninth most common cancer in the world. The situation in Egypt is critical. Bladder cancer is one of the most common cancers, accounting for 12.22% of all cancers and accounting for the majority of urinary system malignancies [1].

Schistosomiasis-associated bladder cancer is an aggressive variant of this type of cancer that has been seen in bladder cancer patients. Certain alterations in

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the features of bladder cancer related with schistosomiasis (bilharziasis) have been noticed in Egypt during the last decade, with a drop in the frequency of squamous cell carcinoma (SCC) cases and an increase in the incidence of transitional cell carcinoma (TCC) cases [2].

The grading and pathological staging of urinary bladder cancer are based on histo-pathological tissue evaluation, which also defines the treatment plan and predicts the clinical result. However, there is a lack of reliable prognostic data about the biological behaviour of these tumours [3]. Additionally, bladder cancer has significantly diverse behavioural traits, although patients with the same disease stage may experience variable clinical outcomes after the same course of treatment [4].

Numerous researches showed that Egypt has a greater prevalence of SCC subtype and a different histological pattern than other nations in terms of bladder cancer. However, among the nations where schistosomiasis is endemic, only Egypt demonstrated a high frequency of SCC [5].

In South Egypt Cancer Institute the squamous cell carcinoma of urinary bladder is about 20%. Over 90% of bladder tumours in the US are transitional cell carcinomas (TCCs). Adenocarcinoma, squamous cell carcinomas (SCCs), and small cell carcinomas are the less frequent histological kinds of bladder cancer, making up to 6%, 2%, and less than 1% of cases, respectively [6].

The main objective of the current study is to determine the clinic-pathological characteristics of bladder squamous cell carcinoma diagnosed on cystoscopic bladder biopsies or resections in the local population at Radiation Oncology Department, South Egypt Cancer Institute, Assiut University during the period from (2008-2018).

## **Patients and Methods:**

Patients:

This is a retrospective study in which all cases of bladder cancer diagnosed between 2008 till 2018 years were included. The study group consisted only of incident cases of adult patients with non-metastatic isolated urinary bladder squamous cell carcinoma.

The files were thoroughly examined for patient age, sex, histopathological subtype, grade, pathological stage, involvement of pelvic lymph nodes and the presence of bilharzial eggs or other manifestation of bilharzial infection in the pathological specimens. The tumors were graded histologically, and staged pathologically according to World Health Organization (WHO). Also, different lines of therapy, presentation and radiological data were also, recorded. Overall survival and disease-free survival were also, determined in those patients. We performed subgroup analysis based on different characteristics of patients and the tumours.

End points of the study

The primary endpoint was the detection of distribution of clinico-pathological features of squamous cell carcinoma of urinary bladder. Secondary end point was the treatment outcome (overall survival OS, and disease free survival, DFS).

Statistical analysis:

SPSS (statistical package for the social sciences; SPSS Inc., Chicago, IL, USA) version 22 was used for all statistics. When applicable, percentages (number of instances) and frequency distributions (percentages) were used to statistically describe the data along with means, standard deviations (SD), medians, and ranges when the data were not normally dispersed. An analysis using the Chi square ( $\chi 2$ ) analysis was done to compare categorical variables, Fisher Exact test was used instead when the expected frequency was less than 5. Kaplan-Meier's method with log rank test was used for overall and disease free survival analysis. P-value set significant at 0.05 level.

### **Results:**

Clinico-pathological characteristics:

The clinico-pathological data of the studied participants was summarized in Table 1. The mean age was  $57.21 \pm 7.44$  years (range; 40-70 years), 12 patients (19.4%) aged less than 50 years old, 20 patients (32.3%) with age ranged 50 - 59 years, and 30 patients (48%) aged  $\geq$  60 years old, with male to female ratio of 3.4:1. The majority of the studied cases (82.3%) were rural residents. About half of the study cases (58.1%) workers, 25.8% not workers, and 16.1% were housewives. 8.1% were active smokers, and 25.8% have positive history of bilharzial infestation. Burning micturition was the most common clinical presentation documented in 46.8%, followed by hematuria in 37.1%, dysuria 9.7%, and cystitis in 6.5%. The ECOG Performance Status revealed that; 85.5 % have PS I, 11.3% have PS II, and 3.2% have PS III.

Regarding tumor grade; almost all study cases (90.3%) have tumor grade II, while six cases (9.7%) have tumor grade III. Tumor stage; 19.4%, 45.2%, 29.0%, and 6.5% had T1, T2, T3, and T4 respectively. Only case have positive nodal metastasis. For treatment; 64.5% received radical cystectomy with ureterocutaneous shunt, 22.6% received anterior pelvic excentration, 6.5% received partial cystectomy, and 6.5% have bladder preservation. Patients who underwent radical cystectomy and partial cystectomy received neoadjuvant chemotherapy then underwent surgery and patients who underwent anterior pelvic excentration received postoperative radiotherapy and patients refusing surgery underwent maximal TURBT then received concurrent chemoradiation.

During the follow up period; six cases (9.7%) developed disease locoregional recurrence, 11 cases died giving an overall mortality percentage among our study cases of 17.7%.

**Table (1):** Clinico-pathological data of the studied Bladder Cancer Cases

Variable da	ıta	N	(%)
Age (years			
• N	Mean ± SD	57.21	± 7.44
• F	Range	40	-70
Age group	•		
• 4	0 - 49	12	(19.4)
• 5	60 - 59	20	(32.3)
• ≥	<u>≥</u> 60	30	(48.4)
Sex			
• N	Male	48	(77.4)
• F	Female	14	(22.6)
Residence			,
	Jrban	11	(17.7)
• F	Rural	51	(82.3)
Occupation			( /
	Vorker	36	(58.1)
	Not worker	16	(25.8)
	Housewife	10	(16.1)
Smoking s		5	(8.1)
Bilharziasi		16	(25.8)
Clinical pre		10	(20.0)
_	Burning micturition	29	(46.8)
	Hematuria	23	(37.1)
	Dysuria (1971)	6	(9.7)
	Cystitis	4	(6.5)
Performan	•	•	(0.0)
• I		53	(85.5)
• I		7	(11.3)
	П	2	(3.2)
Tumor grad		_	(= :=)
	Grade II	56	(90.3)
	Grade III	6	(9.7)
Tumor sta		Ü	().1)
	51 1	12	(19.4)
	Γ2	28	(45.2)
	73	18	(29.0)
	74	4	(6.5)
	de metastasis	7	(0.5)
	Negative	61	(98.4)
	Positive	1	(1.6)
Treatment		1	(1.0)
	Radical cystectomy with urtero-		
	cutanous shunt	40	(64.5)
		14	(22.6)
	Anterior pelvic excentration Partial cystectomy	4	(6.5)
		4	
	Bladder preservation	4	(6.5)
Outcome	)		(0.7)
	Recurrence	6	(9.7)
	Death e data are presented as mean + SD	11	(17.7)

Quantitative data are presented as mean  $\pm$  SD and range; qualitative data are presented as number (percentage).

Clinico-pathological features, complications, and outcome of the study bladder cancer cases according to age:

The study bladder cancer cases were stratified according to their age into three groups; group 1 aged (40 - 49 years, n=12), group 2 aged (50 - 59 years, n=20), and group 3 aged  $(\ge 60 \text{ years, n=30})$ . No significant difference was observed between the clinic-pathological features, complications, and outcome of the studied bladder cancer cases according to their age (P>0.05, for all), as shown in Table 2.

Clinico-pathological features, complications, and outcome of the study bladder cancer cases according to gender:

Table 3 shows that there was no significant difference between the clinic-pathological features, complications, and outcome of the studied bladder cancer cases and their gender (P>0.05, for all).

Clinico-pathological features, complications, and outcome of the study bladder cancer cases according to the smoking status:

By comparing the clinical features of the study cases according to their smoking status we observed no significant difference between the clinic-pathological features, complications, and outcome of the studied bladder cancer cases and their smoking status (P>0.05, for all), as shown in Table 4.

Clinico-pathological features, complications, and outcome of the study bladder cancer cases according to the presence of Bilharzial infestation:

presentation. The distribution of clinical performance status, and tumor grade were comparable among patients with and without Bilharzial infestation with no significant difference between them (P=0.134, 0.093, and 0.172) respectively. However, patients with Bilharzial infestation were more likely to be presented with early tumor stage (56.5% vs. 87.5%, P=0.026) in patients with and without Bilharzial infestation respectively, meanwhile the development of nodal metastasis show no significant difference between those with and without Bilharzial infestation (P=1). Also, complications, and outcome of the studied bladder cancer cases were comparable between those with and without Bilharzial infestation (P>0.05, for all), as shown in Table 5.

Overall and disease free survival of the studied bladder cancer cases:

After 5 years of follow-up, either patient's age, sex, smoking status, bilharzial infestation, tumor size (T), treatment received, and tumor grade have an effect on the overall or the disease free survival among the study cases (P>0.05, for all), as shown in Table 6.

Outcome analysis (Figures 1, 2):

The median follow-up duration of the 62 bladder cancer patients was 50 months (range, 5 to 171 months). During follow-up, 11/62 patients (17.7%) died. According to Kaplan-Meier analysis, at 171 month the OS rate was 52.0%. At five year the rate of OS was 79.2% (figure11). A total of 6/62 patients (9.7%) developed disease recurrence. The median time to locoregional recurrence was 49 months (range, 4 to 171 months). According to Kaplan-Meier analysis, the DFS rate at 171 months was 75.9%. At five year the rate of DFS was 91.1%.

**Table (2):** Clinico-pathological features of the study bladder cancer cases according to age

Variable data	Age groups			
variable data	40 – 49 (n=12)	50 – 59 (n=20)	≥ 60 (n=30)	P value
Clinical presentation				0.346
<ul> <li>Burning micturition</li> </ul>	9 (75.0)	6 (30.0)	14 (46.7)	
<ul> <li>Hematuria</li> </ul>	2 (16.7)	10 (50.0)	11 (36.7)	
<ul> <li>Dysuria</li> </ul>	1 (8.3)	2 (10.0)	3 (10.0)	
<ul> <li>Cystitis</li> </ul>	0 (0.0)	2 (10.0)	2 (6.7)	
Performance status				0.088
• 1	11 (91.7)	20 (100.0)	22 (73.3)	
• 2	1 (8.3)	0 (0.0)	6 (20.0)	
• 3	0 (0.0)	0 (0.0)	2 (6.7)	
Tumor grade				1
• Grade 2	11 (91.7)	18 (90.0)	27 (90.0)	
<ul> <li>Grade 3</li> </ul>	1 (8.3)	2 (10.0)	3 (10.0)	
T staging				0.877
<ul> <li>Early</li> </ul>	7 (58.3)	13 (65.0)	20 (66.7)	
<ul> <li>Advanced</li> </ul>	5 (41.7)	7 (35.0)	10 (33.3)	
Lymph node metastasis				0.194
<ul> <li>Negative</li> </ul>	11 (91.7)	20 (100.0)	30 (100.0)	
<ul> <li>Positive</li> </ul>	1 (8.3)	0 (0.0)	0 (0.0)	
Renal impairment				0.729
• No	9 (75.0)	16 (80.0)	21 (70.0)	
<ul> <li>Yes</li> </ul>	3 (25.0)	4 (20.0)	9 (30.0)	
Recurrence				1
• No	11 (91.7)	18 (90.0)	27 (90.0)	
<ul> <li>Yes</li> </ul>	1 (8.3)	2 (10.0)	3 (10.0)	
Death status				0.752
<ul> <li>Survived</li> </ul>	11 (91.7)	16 (80.0)	24 (80.0)	
<ul> <li>Non-survived</li> </ul>	1 (8.3)	4 (20.0)	6 (20.0)	

Qualitative data are presented as number (percentage). Significance defined by p < 0.05.

**Table (3):** Clinico-pathological features of the study bladder cancer cases according to gender

Variable name	Male (n=48)	Female (n=14)	P value
Clinical presentation			0.391
<ul> <li>Burning micturition</li> </ul>	20 (41.7)	9 (64.3)	
<ul> <li>Hematuria</li> </ul>	19 (39.6)	4 (28.6)	
<ul> <li>Dysuria</li> </ul>	6 (12.5)	0 (0.0)	
<ul> <li>Cystitis</li> </ul>	3 (6.3)	1 (7.1)	
Performance status			0.797
• 1	41 (85.4)	12 (85.7)	
• 2	5 (10.4)	2 (14.3)	
• 3	2 (4.2)	0 (0.0)	
Tumor grade			1
• Grade 2	43 (89.6)	13 (92.9)	
<ul> <li>Grade 3</li> </ul>	5 (10.4)	1 (7.1)	
T staging			0.539
<ul> <li>Early</li> </ul>	32 (66.7)	8 (57.1)	
<ul> <li>Advanced</li> </ul>	16 (33.3)	6 (42.9)	
Lymph node metastasis			1
<ul> <li>Negative</li> </ul>	47 (97.9)	14 (100.0)	
<ul> <li>Positive</li> </ul>	1 (2.1)	0 (0.0)	
Renal impairment			0.162
<ul> <li>No</li> </ul>	38 (79.2)	8 (57.1)	
• Yes	10 (20.8)	6 (42.9)	
Recurrence			0.610
• No	44 (91.7)	12 (85.7)	
<ul><li>Yes</li></ul>	4 (8.3)	2 (14.3)	
Death status			0.429
<ul> <li>Survived</li> </ul>	38 (79.2)	13 (92.9)	
<ul> <li>Non-survived</li> </ul>	10 (20.8)	1 (7.1)	

Qualitative data are presented as number (percentage). Significance defined by p < 0.05.

**Table (4):** Clinico-pathological features of the study bladder cancer cases according to smoking status

Variable name	Non-smoker (n=57)	Smoker (n=5)	P value
Clinical presentation			1
Burning micturition	26 (45.6)	3 (60.0)	
<ul> <li>Hematuria</li> </ul>	21 (36.8)	2 (40.0)	
<ul> <li>Dysuria</li> </ul>	6 (10.5)	0 (0.0)	
<ul> <li>Cystitis</li> </ul>	4 (7.0)	0 (0.0)	
Performance status			1
• 1	48 (84.2)	5 (100.0)	
• 2	7 (12.3)	0 (0.0)	
• 3	2 (3.5)	0 (0.0)	
Tumor grade			1
• Grade 2	51 (89.5)	5 (100.0)	
<ul> <li>Grade 3</li> </ul>	6 (10.5)	0 (0.0)	
T staging			0.337
• Early	38 (66.7)	2 (40.0)	
<ul> <li>Advanced</li> </ul>	19 (33.3)	3 (60.0)	
Lymph node metastasis			1
<ul> <li>Negative</li> </ul>	56 (98.2)	5 (100.0)	
<ul> <li>Positive</li> </ul>	1 (1.8)	0 (0.0)	
Renal impairment			1
• No	42 (73.7)	4 (80.0)	
<ul> <li>Yes</li> </ul>	15 (26.3)	1 (20.0)	
Recurrence			1
<ul> <li>No</li> </ul>	51 (89.5)	5 (100.0)	
<ul> <li>Yes</li> </ul>	6 (10.5)	0 (0.0)	
Death status			0.575
<ul> <li>Survived</li> </ul>	46 (80.7)	5 (100.0)	
<ul> <li>Non-survived</li> </ul>	11 (19.3)	0 (0.0)	

Qualitative data are presented as number (percentage). Significance defined by p < 0.05.

**Table (5):** Clinico-pathological features of the study bladder cancer cases according to the presence of Bilharzial infestation

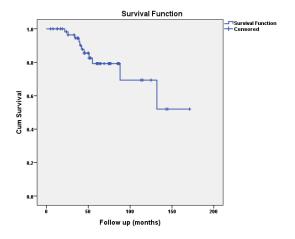
V	Bilharzial i	D l	
Variable name -	No (n=46)	Yes (n=16)	P value
Clinical presentation			0.134
<ul> <li>Burning micturition</li> </ul>	23 (50.0)	6 (37.5)	
<ul> <li>Hematuria</li> </ul>	18 (39.1)	5 (31.3)	
<ul> <li>Dysuria</li> </ul>	2 (4.3)	4 (25.0)	
<ul> <li>Cystitis</li> </ul>	3 (6.5)	1 (6.3)	
Performance status			0.093
• 1	40 (87.0)	13 (81.3)	
• 2	6 (13.0)	1 (6.3)	
• 3	0 (0.0)	2 (12.5)	
Tumor grade			0.172
• Grade 2	43 (93.5)	13 (81.3)	
<ul> <li>Grade 3</li> </ul>	3 (6.5)	3 (18.8)	
T staging			0.026*
Early	26 (56.5)	14 (87.5)	
<ul> <li>Advanced</li> </ul>	20 (43.5)	2 (12.5)	
Lymph node metastasis			1
Negative	45 (97.8)	16 (100.0)	
<ul> <li>Positive</li> </ul>	1 (2.2)	0 (0.0)	
Renal impairment			0.528
• No	33 (71.7)	13 (81.3)	
• Yes	13 (28.3)	3 (18.8)	
Recurrence			1
• No	41 (89.1)	15 (93.8)	
• Yes	5 (10.9)	1 (6.3)	
Death status			1
<ul> <li>Survived</li> </ul>	38 (82.6)	13 (81.3)	
<ul> <li>Non-survived</li> </ul>	8 (17.4)	3 (18.8)	

 $\label{eq:Qualitative} Qualitative \ data \ are \ presented \ as \ number \ (percentage). \ Significance \ defined \ by \ p < 0.05.$ 

Table 6 Overall and disease free survival of the studied bladder cancer cases

	OS (5 years)		DFS (5 years)	
	Estimate ± SE	P value	Estimate ± SE	P value
Age groups		0.643		0.967
• 40 - 49	$57.5\% \pm 11.7$		$91.7\% \pm 8.0$	
• 55 - 59	$79.4\% \pm 10.6$		$94.4\% \pm 5.4$	
<ul> <li>≥ 60</li> </ul>	$74.9\% \pm 10.3$		$88.7\% \pm 6.2$	
Sex		0.245		0.476
• Male	$76.7\% \pm 7.5$		$93.2\% \pm 3.8$	
<ul> <li>Female</li> </ul>	$88.9\% \pm 10.5$		$83.9\% \pm 10.4$	
Smoking status		0.301		0.417
<ul> <li>Non smoker</li> </ul>	$77.3\% \pm 6.9$		$90.3\% \pm 4.1$	
<ul> <li>Smoker</li> </ul>	$100.0\% \pm 0.0$		$100.0\% \pm 0.0$	
Bilharzias		0.955		0.640
<ul> <li>No</li> </ul>	$80.1\% \pm 7.5$		$90.5\% \pm 4.5$	
<ul><li>Yes</li></ul>	$77.8\% \pm 11.4$		$92.9\% \pm 6.9$	
T staging		0.293		0.344
<ul> <li>Early</li> </ul>	$85.1\% \pm 6.2$		$94.4\% \pm 3.8$	
<ul> <li>Advanced</li> </ul>	$70.0\% \pm 12.9$		$85.4\% \pm 7.8$	
Treatment received		0.450		0.360
<ul> <li>R.C.U.C.S.</li> </ul>	$82.7\% \pm 7.3$		$92.0\% \pm 4.4$	
<ul> <li>APE</li> </ul>	$75.0\% \pm 15.8$		$92.3\% \pm 7.4$	
<ul> <li>PC</li> </ul>	$75.0\% \pm 21.7$		$100.0\% \pm 35.4$	
<ul> <li>BP</li> </ul>	$66.7\% \pm 27.2$		50.0% ± 35.4#	
Tumor grade		0.834		0.754
• Grade 2	$79.0\% \pm 6.8$		$90.3\% \pm 4.1$	
• Grade 3	$80.0\% \pm 17.9$		$100.0\% \pm 35.4$	

R.C.U.C.S: Radical cystectomy with urtero-cutanous shunt; APE: Anterior pelvic excentration; PC: Partial cystectomy; BP: Bladder preservation. # the last follow up end at 36 months.



**Figure 1** Overall survival curve of the study bladder cancer cases.

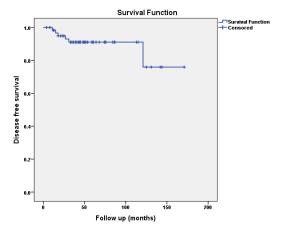


Figure 2 Disease free survival curve of the study bladder cancer cases

# **Discussion:**

The present study was a retrospective study aimed to determine the clinic-pathological characteristics of bladder squamous cell carcinoma diagnosed on cystoscopic bladder biopsies or resections among patients with non-metastatic bladder cancer who attended to South Egypt Cancer Institute, Assiut

Universality, Assiut, Egypt. This study included 62 patients with non metastatic bladder cancer (TNM0) in the period from the 1st of January 2008 up to the end of December 2018.

The mean age of the study cases was  $57.21 \pm 7.44$  years and ranged from 40 up to 70 years old, 12 patients (19.4%) aged less than 50 years old, 20 patients

(32.3%) with age ranged 50-59 years, and 30 patients (4.4%) aged  $\geq 60$  years. The majority of the study cases (77.4%) were males versus 14 cases (22.6%) were female with male to female ratio of 3.4:1. Fifty-one cases (82.3%) were rural residents, and 11 cases (17.7%) were urban residents.

Regarding occupation; about half of the study cases (58.1%) workers, 16 cases (25.8%) not workers, and ten cases (16.1%) were housewives. Five cases (8.1%) were active smokers, and 16 cases (25.8%) have positive history of bilharzial infestation

In line with these findings, the study of Abd El-Rehim et al. on 125 patients (106 men and 19 women) with bladder tumours who were sent to the El-Minia University Hospital in Minia, Egypt between January 2009 and July 2011. The median age of the patient was 56 years, with a range of 45 to 70 years (mean 56.97±6.38 years) [7]. Many previous studies were consistent to these findings [8-10].

Also, another study enrolled a total of 5071 patients were treated with radical cystectomy or anterior pelvic exenteration during the time period from 1988 to 2004. Their mean age was 54.3 years and the standard deviation was 10.2 years (range, 19-80 years). They were 3990 males and 1081 females with a ratio of 3.7:1 [5]. It's known that World widely, the lifetime risk of getting UBC is 1.1% in men, and 0.27% in women [11].

The male predominance in our study is a reflection of the different lifestyles that exist for men and women in our nation, with men being more exposed to schistosomal infection, smoking, and workplace dangers known to induce bladder cancer (such as those associated to the rubber, dye, paint, tobacco, and bezidine) [1, 12].

As regard smoking and UBC, in line with the current, Babjuk et al examined data on 467,528 people and found that former and current smokers had a two-and fourfold increase in urothelial bladder cancer risk, respectively, compared to never smokers. For both men and women, the population risk of bladder cancer linked to smoking was almost 50% [13].

A putative tumor-suppressor gene on the Y chromosome that has been deleted may have played a role in this gender gap, which is another hypothesis that has been proposed. Using the fluorescence in situ hybridization (FISH) method, Khaled et al. (2000) found that 7 of the 17 (41%) Schistosomiasis-associated bladder cancer cases had lost the Y chromosome [14].

Here, we found that burning micturition was the most common clinical presentation among our study cases documented in 29 cases (46.8%), followed by hematuria in 23 cases (37.1%), dysuria in six cases (9.7%), and cystitis in four cases (6.5%). The performance status (PS) of the study cases was also done and showed that; 53 cases (85.5%) have PS I, seven cases (11.3%) have PS II, and three cases (3.2%) have PS III.

Microscopic or gross hematuria is the most typical bladder cancer presenting sign, though irritation-related urine frequency or a decreased bladder capacity can also appear. Urinary tract infections appear as less frequent symptoms. Patients with a more advanced lesion may experience pain or upper tract obstruction. Patients who exhibit these symptoms should undergo an office cystoscopy evaluation to see if a lesion is present [15]. However, this is not matching with the finding in our study and we don't have explanation for that.

Gender differences in pelvic morphology, lymphatic and vascular drainage, or the role of androgens in the development and progression of cancer have all been connected to the unequal stage distribution of UBC. Alternately, it is possible to hypothesize that the gender gaps in UBC are due to differential clinical symptoms, varying assessments made prior to a final diagnosis, or inconsistent referral practices [16].

Several investigations have found that women present with more advanced tumour stages. In a study of the Surveillance, Epidemiology, and End Results database, women were more likely than men to present with muscle-invasive disease (22% of men versus 25% of women in Caucasian patients and 30% of men versus 43% of women in African-American patients, P< 0.001) [17].

In the current study we found that those 40 patients (64.5%) received radical cystectomy with urterocutanous shunt, 14 cases (22.6%) received anterior pelvic excentration, four cases (6.5%) received partial cystectomy, and another four cases (6.5%) have bladder preservation. Regarding to the tumor size; 12 cases (19.4%) had T1, 28 cases (45.2%) had T2, 18 cases (29.0%) had T3, and four cases (6.5%) had T4. For nodal metastasis; only one case suffered from positive nodal metastasis.

Regarding the recurrence status among our study cases; six cases (9.7%) developed disease recurrence during the follow up period. The recurrence rate wasn't affected by the type of management. During the follow up period 11 cases died giving an overall mortality rate among our study cases of 17.7%.

The median follow-up duration of the 62 bladder cancer patients was 50 months (range, 5 to 171 months). During follow-up, 11/62 patients (17.7%) died. According to Kaplan-Meier analysis, at 171 month the OS rate was 52.0%. A total of 6/62 patients (9.7%) developed disease recurrence.

The median time to local disease recurrence was 49 months (range, 4 to 171 months). According to Kaplan-Meier analysis, the DFS rate at 171 months was 75.9%. Also, we found that 5-year survival rate was 79.2% and 5-year DFS was 91.1%. In line with this study, Visser et al. found that 5-year OS in such patients was 75% [18]. Another study reported 5-year OS was 60% [19].

Also, subgroup analysis in the current study based on age group, sex, smoking status and bilharzial infestation had insignificant differences as regard presentation of UBC, staging, type of therapy and overall survival and disease-free survival.

Regarding bilharzial infestation and SCC, the high schistosomal history infection did not correspond to a higher SCC incidence (9%) in the recent years, most likely due to the sharp decline in the rate of new schistosomal infestation, with a drop in the number of egg-positive specimens from 82.4% in 1970-1974 to 55.2% in 2003-2007 [20].

#### **Conclusion:**

Bladder cancer is fairly common in our locality. SCC is generally, decreasing compared with TCC. This trend may be the outcome of improved bilharzia infestation control in rural Egyptian populations due to the use of potent oral antibilharzial medications.

### **Competing interests:**

The authors declare that they have no competing interests.

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## Ethics approval and consent to participate:

The protocol was approved by the Institutional Review Board of Faculty of Medicine, Assiut University (approval number: 17101451, 13 January 2020 date of approval). Our study conformed to all requirements as governed by the declaration of Helsinki.

#### **References:**

- 1. Salem HK, Mahfouz S. Changing patterns (age, incidence, and pathologic types) of schistosoma-associated bladder cancer in Egypt in the past decade. Urology. 2012;79(2):379-83.
- 2. Aiad HA, Hanout HM. Immunohistochemical expression of CD10 in cutaneous basal and squamous cell carcinomas. J Egypt Natl Canc Inst. 2007;19(3):195-201.
- 3. Cheng L, Montironi R, Davidson DD, et al. Staging and reporting of urothelial carcinoma of the urinary bladder. Modern Pathology. 2009;22(3):S70-S95.
- 4. Als AB, Dyrskjøt L, von der Maase H, et al. Emmprin and survivin predict response and survival following cisplatin-containing chemotherapy in patients with advanced bladder cancer. Clinical Cancer Research. 2007;13(15):4407-14.
- Zaghloul MS, Nouh A, Moneer M, et al. Time-trend in epidemiological and pathological features of schistosoma-associated bladder cancer. J Egypt Natl Canc Inst. 2008;20(2):168-74.
- Zarzour AH, Selim M, Abd-Elsayed AA, et al. Muscle invasive bladder cancer in Upper Egypt: the shift in risk factors and tumor characteristics. BMC cancer. 2008;8(4):1-6.
- 7. Abd El-Rehim DM, Abd El-Maqsoud NMR, Abd El-Hamid AM, et al. Expression of extracellular matrix metalloproteinase inducer and fascin in urinary bladder cancer: Correlation with clinicopathological characteristics. Mol Clin Oncol.

- 2013;1(2):297-304.
- 8. Khaled HM. Systemic management of bladder cancer in Egypt: revisited. Journal of the Egyptian National Cancer Institute. 2005;17(3):127-31.
- 9. Parkin DM, Bray F, Ferlay J, et al. Global cancer statistics, 2002. CA: a cancer journal for clinicians. 2005;55(2):74-108.
- 10. Fedewa SA, Soliman AS, Ismail K, et al. Incidence analyses of bladder cancer in the Nile delta region of Egypt. Cancer Epidemiology. 2009;33(3):176-81.
- 11. Richters A, Aben KKH, Kiemeney LALM. The global burden of urinary bladder cancer: an update. World Journal of Urology. 2020;38(8):1895-904.
- 12. Dason S, Wong NC. Environmental and Genetic Factors Contributing to Bladder Carcinogenesis. Comprehensive Diagnostic Approach to Bladder Cancer: Molecular Imaging and Biomarkers. 2021;44(2):13-44.
- 13. Babjuk M, Burger M, Zigeuner R, et al. EAU guidelines on non–muscle-invasive urothelial carcinoma of the bladder: update 2013. European urology. 2013;64(4):639-53.
- 14. Khaled HM, Aly MS, Magrath IT. Loss of Y chromosome in bilharzial bladder cancer. Cancer Genetics and cytogenetics. 2000;117(1):32-6.
- 15. Flaig TW, Spiess PE, Agarwal N, et al. Bladder cancer, version 3.2020, NCCN clinical practice guidelines in oncology. Journal of the National Comprehensive Cancer Network. 2020;18(3):329-54.
- 16. Henning A, Wehrberger M, Madersbacher S, et al. Do differences in clinical symptoms and referral patterns contribute to the gender gap in bladder cancer? BJU International. 2013;112(1):68-73.
- 17. Scosyrev E, Noyes K, Feng C, et al. Sex and racial differences in bladder cancer presentation and mortality in the US. Cancer. 2009;115(1):68-74.
- 18. Visser O, Nieuwenhuijzen J, Horenblas S, et al. Local recurrence after cystectomy and survival of patients with bladder cancer: a population based study in greater Amsterdam. The Journal of urology. 2005;174(1):97-102.
- 19. Noon A, Albertsen P, Thomas F, et al. Competing mortality in patients diagnosed with bladder cancer: evidence of undertreatment in the elderly and female patients. British journal of cancer. 2013;108(7):1534-40.
- 20. Gouda I, Mokhtar N, Bilal D, et al. Bilharziasis and bladder cancer: a time trend analysis of 9843 patients. J Egypt Natl Canc Inst. 2007;19(2):158-62.