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ABSTRACT

Background: Urinary bladder cancer is the ninth leading cause of morbidity and mortality globally, necessitating characterization of clinical and pathological features for early detection and improved management.

Objective: To profile and document the clinicopathological features of urinary bladder cancer at Moi Teaching and Referral Hospital (MTRH).

Materials and methods: A prospective assessment of patients diagnosed with urinary bladder cancer. Patient characteristics and associated causal factors obtained from full clinical evaluation and review of clinical records. Tumour characterization was based on examination and review of radiological imaging and histopathology findings and documented in structured questionnaires. Descriptive statistics and tests of association used Fisher's exact tests for socio-demographic characteristics, causal factors, histological type, and Tumor, Node, Metastasis (TNM) stage of bladder cancer.

Results: Forty-five patients aged between 21 to 85 (mean: 61.84 ± 14.46) years with urinary bladder cancer were evaluated. Males were 68.9% and painless hematuria was most common symptom. Exposure to agrochemicals (60%) and cigarettes smoking (mean pack years = 9.43 ± 6.198) in 31%. Clinical staging showed 71.1% with T₁, while 6.7% had metastatic disease. 55.6% had TNM stage I, while 91.1% had low-grade tumors. Transitional cell carcinoma (51.1%) was the most common histological type. Agrochemicals exposure was associated with low-grade tumors ($p=0.013$), TNM clinical stage I ($p=0.021$), and adenocarcinoma ($p=0.029$).

Conclusions: Urinary bladder cancer affected males over 60 years old with a history of smoking and agrochemical exposure. Majority presented with classical symptoms of early disease and low-grade tumors. History of exposure to agrochemicals was a significant risk factor.

INTRODUCTION

Urinary bladder cancers are among the common malignant neoplasms that involve the urinary tract system (1). Urinary bladder cancer has been ranked the ninth prevalent malignant diseases and thirteenth among the causes of cancer-related deaths globally (2). Its overall prevalence has been estimated at 3% of all cancer diagnoses globally while in North America the prevalence is 1.2% (3). Its incidence in the Eastern Africa region is estimated at 2.8% with the male and female incidence at 3.2% and 2.4% respectively. In Kenya, bladder cancer is the ninth among the urological cancers (4). Despite this high disease burden and mortality risk, urinary bladder cancer receives limited attention from both healthcare policymakers and healthcare practitioners in comparison to prostate cancer among men and breast and cervical cancer among women. Majority of the patients diagnosed with bladder cancer are males in the sixth decade of life while those at-risk are often bread winners whose quality of life and socioeconomic activities are interrupted by the disease.

Studies have often associated urinary bladder cancer with smoking or occupational exposure to carcinogens, chronic cystitis particularly with schistosomiasis, first-degree relatives (parent, sibling, or child) with a family history of urinary bladder cancer or those who have undergone previous cancer treatment. In Kenya, local hospital records indicate that patients younger than 30 years with no associated familial history and identifiable exposure to carcinogens have been diagnosed with various types of urinary bladder cancer (5). There are several histological bladder types of urinary bladder cancer with varying prevalence and prognosis depending on the predisposing factors. This necessitates further better understanding of clinical pathological features, mode, and stage at presentation as well as treatment approaches.

Although there is the possibility of clinical management of the disease, treatment resistance risks abound enabling a combined approach that integrates surgery. The preferred mode of management of muscle-invasive bladder cancer is surgical, however, empirical data indicate several challenges that are not limited to high rates of recurrence and surgical complications that directly impact the patient's quality of life. Published studies (5,6) have reported late presentation among patients with advanced bladder cancer in developing countries. With the foregoing, there is a need for local contextualized data that describes the patient characteristics of those diagnosed with urinary bladder cancer, predisposing factors, clinical as well as histological variants, and stage at presentation. Anecdotal reports show that there could be high prevalence of squamous cell carcinoma in countries around the Nile Basin of which parts of the Western Kenya belongs.

This is because clinicopathological characteristics have a direct influence on surgical management approaches and treatment outcomes.

MATERIALS AND METHODS

Design: This was a prospective descriptive hospital-based study among patients diagnosed with bladder cancer.

Duration: Between April 2022 to May 2023.

Site: The data was collected at the urology clinic and surgical wards of Moi Teaching and Referral Hospital in Eldoret, Kenya. The facility is the second largest teaching hospital in Kenya that serves the greater Western Kenya and North Rift regions. Majority of the patients suspected of having urinary bladder cancer are referred to MTRH for both surgical and clinical management. Furthermore, this hospital has urologists, consultants and residents in general surgery who participate in management of urinary system management. In addition, the Chandaria cancer center, a comprehensive cancer care

facility provides both immediate and follow-up cancer management.

Population: The study targeted 45 adult patients suspected of having bladder cancer at the time of visiting the study site.

Eligibility Criteria: We enrolled treatment-naïve adult patients presenting with features of bladder cancer who were scheduled for cystoscopy.

Study Procedure of data accrual: Required for the study were socio-demographic characteristics of; age, sex, level of education, and employment status. In addition; patient history data; history of smoking cigarettes, exposure to agrochemicals and paint, familial history of bladder cancer) were collected using a structured questionnaire while clinical characteristics were haematuria, abdominal pain, irritating and obstructive voiding symptoms as well as constitutional symptoms were obtained through reviewing medical records. Each patient had diagnostic CT-scan performed for; the abdomen, pelvis and chest to correctly stage the urinary bladder cancer. Cystoscopies performed by qualified urologist and sample biopsies taken for histopathological analysis at the histopathology laboratory where they were analyzed by a qualified anatomical pathologist. The diagnostic histopathological report consisted of type of bladder cancer, its stage and grade. The pathological stage was defined according to the TNM classification system (7) while the tumor grade was classified as per the World Health Organization (WHO) system (8).

Data management and analysis: Continuous variables such as age were summarized as mean (with corresponding standard deviations) as well as median (with corresponding interquartile range). Categorical data such as predisposing factors to urinary bladder cancer, histological types, clinical stage at presentation as well as surgical and clinical interventions offered were descriptively summarized as frequencies (with corresponding

proportions). Tests of association using Pearson chi-square and Fisher's exact test were conducted to establish any statistically significant association between socio-demographic characteristics, predisposing factors as well as histological type or tumor, node and metastasis (TNM) staging of urinary bladder cancer.

Ethical Considerations: Ethical approval (Approval number:0004130) was obtained from the Institutional Research and Ethics Committee (IREC) of Moi Teaching and Referral Hospital (MTRH) and Moi University School of Medicine and a research license (NACOSTI/P/22/18168) sought from the National Commission for Science, Technology and Innovation (NACOSTI). A written informed consent was also obtained from each participant prior to enrollment.

RESULTS

This study enrolled 45 individuals diagnosed with urinary bladder cancer aged between 21 to 85 years with a mean of 61.84 ± 14.46 years. Males were 68.9%; $n=31$ and females 31.1%; $n=14$. Of the studied, 55.6%; $n=25$ had attained primary, 33.3%; $n=15$ secondary and tertiary 11.1%; $n=5$ tertiary level of formal education. When participants' occupation was assessed, 57.8%; $n=26$ reported that they were unemployed at the time of data collection while the rest 42.2%; $n=19$ employed in various ways. We obtained history of smoking in 31.1%; $n=14$, an average of 9.43 ± 6.198 pack years while exposure to agricultural chemicals was in 60.0%; $n=27$. All the participants presented complaints of hematuria, while other commonly noted clinical features were lower abdominal pain 93.3%; $n=42$, irritating 95.6%; $n=43$ and obstructive voiding symptoms 91.1%; $n=41$. The constitutional symptoms noted were weight loss 93.3%; $n=42$, fatigue 95.6%; $n=43$, anorexia 91.1%; $n=41$, night sweats 86.7%; $n=39$. On physical examination, 55.6%; $n=25$ participants had a pelvic mass (Table 1).

Table 1
Demographic, Social and Clinical features

Sociodemographic Characteristics		n (%) / Mean (SD)
Age (years)	Less than 30	2 (4.4)
	30-39	1 (2.2)
	40-49	7 (15.6)
	50-59	5 (11.1)
	60-69	16 (35.6)
	Above 70	14 (31.1)
Sex	Male	31 (68.9)
	Female	14 (31.1)
Level of formal Education	Primary	25 (55.6)
	Secondary	15 (33.3)
	Tertiary	5 (11.1)
Employment status	Employed	19 (42.2)
	Unemployed	26 (57.8)
Predisposing Factors	Smoking History (n=14; 31.1%)	Pack years (9.43±6.198)
	Exposure to Agrochemicals	27 (60.0)
Haematuria	Yes	45 (100.0)
Abdominal Pain	Yes	42 (93.3)
Irritating /painful voiding Symptoms	Dysuria	42 (93.3)
	Increased frequency of urination	41 (91.1)
	Urge incontinence.	39 (86.7)
	Nocturia	41 (91.1)
Obstructed Voiding Symptoms	Straining	37 (82.2)
	Intermittent stream	39 (86.7)
	Poor stream of urine	35 (77.8)
	Feeling of incomplete voiding	41 (91.1)

Cystoscopy findings

All the study participants had multiple lesions which appeared intraoperatively as fragments (20%), papillary fronds (57.8%), patches (17.8%), polypoid masses (2.2%) and spiral necrotic (2.2%).

Histological findings

The histological types noted were transitional cell carcinoma (51.1%), adenocarcinoma (28.9%) and squamous cell carcinoma (20.0%). Of all the participants enrolled, 91.1%; n=41 had low grade and 8.9%; n=4 had high grade tumors (Figure 1).

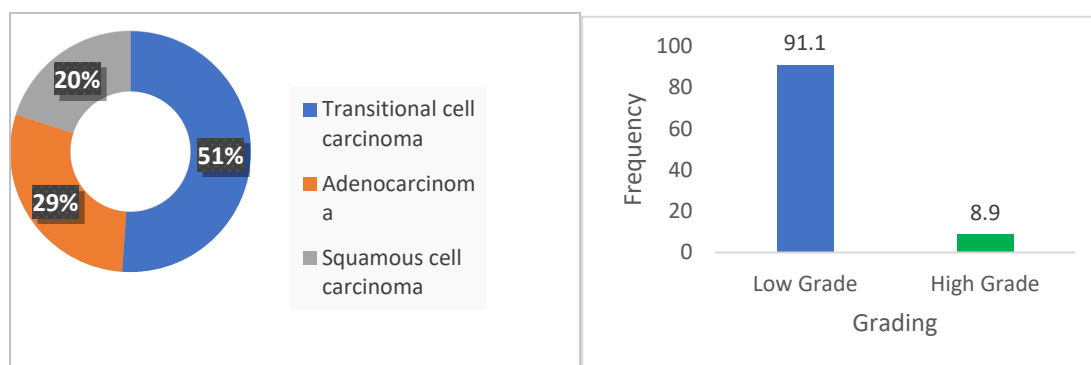


Figure 1: Histological types and grade of urinary bladder cancer

Clinical Staging results

Participants common clinical stages were T₁ (71.1%), T_{2a} (17.8%), T₃ (8.9%) and T_{4a} (2.2%). Of the participants 15.6%; n=7 had extra vesical extensions, 11.1%; n=5 had nodal

involvement of the disease, 6.7%; n =3 had metastatic disease. As per TNM staging criteria, Stage I (55.6%) was the most prevalent, followed by Stage II (31.1%) and Stage III at 6.7% (Table 2).

Table 2
Clinical Findings: Cystoscopy, Histology and Clinical Staging

Variable	Sub-category	n (%)
Multiple Lesions		45 (100)
Intraoperative Findings (Appearance)	Fragments	9 (20.0)
	papillary fronds	26 (57.8)
	Patches	8 (17.8)
	Polypoid masses	1 (2.2)
	spiral necrotic	1 (2.2)
Clinical Staging	T ₁	32 (71.1)
	T _{2a}	8 (17.8)
	T ₃	4 (8.9)
	T _{4a}	1 (2.2)
Imaging Findings	Extravesical extensions	7 (15.6)
	Nodal involvement	5 (11.1)
	metastases	3 (6.7)
TNM Staging Criteria	Stage 0 _{is}	1 (2.2)
	Stage I	25 (55.6)
	Stage II	14 (31.1)
	Stage III	3 (6.7)
	Stage IV _a	1 (2.2)
	Stage IV _b	1 (2.2)

Chi-square test results: Association between participants' exposure to agrochemicals (independent variable) and bladder cancer histopathological variants (dependent variable). Participants who were exposed to agrochemicals had a two-fold significantly

increased likelihood of low-grade tumors (AOR = 2.276; 95% CI: 1.366, 9.935) and adenocarcinoma (AOR =2.100; 95% CI: 1.436, 9.000). Furthermore, they were significantly (p=0.021) more likely to present with TNM stage I of urinary bladder cancer (Table 3).

Table 3
Histopathological variants and associated factors

Exposure	Histopathological variants of Urinary Bladder Cancer	p-value	AOR (95% CI:)
Exposure to Agrochemicals	Low grade Tumor	0.013	2.276 (1.366, 9.935)
	Adenocarcinoma	0.029	2.100 (1.436, 9.000)
	TNM Stage I	0.021	1.737 (1.407, 7.658)

Legend: AOR- Adjusted Odds Ratio; TNM- Tumor, Node, Metastases

DISCUSSION

The proportion of males (68.9%) and females (31.1%) in this study showed remarkable similarities with other published results. This could be attributed to the fact that impaired emptying of the bladder in males increases with advancement of age compared to females. In addition, higher exposure to risk factors such as smoking and agrochemicals appear more in the males than females. These findings match that reported in Turkey (9) where 62% of the participants were male and Germany (10) at 85.7%. Furthermore, when the participants' age was assessed, majority of them were older adults with a mean age at presentation of 61.84 (± 14.46) years. This mean age corroborates our attribution that urinary bladder cancer incidence rises with advancement of age, despite the fact that younger adults are also being diagnosed with the disease. The high mean age could also be attributed to the latent effects of the risk factors for bladder cancer such as environmental or dietary exposures, when the symptoms are noticed as was also noted in other studies under comparison.

The common clinical features assessed in this study were painless gross hematuria, lower abdominal pain, irritating and obstructive voiding symptoms. All participants had painless gross hematuria, a major hallmark of urinary bladder cancer, as was also noted in a previous study reported at the University of Nairobi in Kenya (5) where nearly all (98%) of the participants had painless gross hematuria. Most patients presented with lower abdominal pain, a finding that could be attributed to the fact that most patients often present with a complaint of a painful lower abdomen, that on further investigations could be found to be a urinary bladder tumor. Additionally, this study reports that 93.3% had dysuria, a condition that is described as painful micturition. Because of the nature and location of urinary bladder tumors, the bladder is squeezed, and this increases

peripheral resistance during the passage of urine and the associated pain.

Several patient factors are known to increase the risk of an individual developing urinary bladder cancer. In this study, about one-third were found to have a history of smoking with an average of 9.43 (± 6.198) pack years. A higher proportion (73.4%) of reported smoking history was noted in India (11) where about three-quarters of the study participants reported a history of smoking. This proportionate difference could be attributed to sociocultural and demographic differences, as a higher proportion of smoking has been reported in countries with higher mean income located in the continents of America, Europe and Asia. Furthermore, this study noted that exposure to agrochemicals as a major risk factor for urinary bladder cancer. Because this study was conducted in Eldoret town, which is predominantly an agricultural area, as it is referred to as the breadbasket of Kenya, it could partly explain why nearly two-thirds (60%) of the participants diagnosed with urinary bladder cancer had an occupational exposure to agrochemicals (12). Exposure to agricultural chemicals causes cellular transformation which may interfere with the cell cycle especially the apoptotic process, making agrochemicals carcinogens. Just like agrochemicals, frequent exposure to the active ingredients of paints (such as lead) and its excipients have been noted to be carcinogens (13).

Common histological types of urinary bladder cancer seen were transitional cell carcinoma (51.1%), followed by adenocarcinoma (28.9%) and squamous cell carcinoma (20.0%). The high proportion of transitional cell carcinoma could be attributed to the fact that other than schistosomiasis, the risk factors (exposure to agrochemicals and smoking) identified in this study have also been associated with its occurrence (5). The trend of environmental and occupational exposure to carcinogens

may worsen in the near future in developing countries if measures to control cigarette smoking (or other nicotine derivatives) are not put in place (14). On the other hand, adenocarcinoma is associated with a family history of cancer, however, in this study, less than one-third of the participants acknowledged a family history of cancer.

The proportion of adenocarcinoma reported in this study is over three times higher than that previously reported in Kenya at 8% (5). While the current study adopted a one-year prospective design, the previous study under comparison which was conducted in Nairobi, adopted a ten-year retrospective design which explains proportionate variations on the factors of interest. Squamous cell carcinoma proportion in this study could be attributed to chronic urinary tract infections from either bacteria or *Schistosoma haematobium* parasite which are prevalent in Western Kenya that is within the Lake Victoria basin (15).

The current study observed that nearly, three quarters (71.1%) of the participants had non-muscle invasive tumors. On the other hand, muscle invasive tumors presented at Stage T2a (17.8%), Stage T3 (8.9%) and Stage T4a (2.2%). These findings closely match those presented in a histopathological study conducted in Nepal (16) where 64.18% of those enrolled had non-muscle invasive clinical stage of urinary bladder tumor identified. This can be described as a sign of early diagnosis with good prognosis if prompt treatment is offered to patients. When the TNM staging criteria were adopted in this study, the most prevalent stage was Stage I at 55.6%, followed by Stage II (31.1%), Stage IIIa (6.7%); with low proportions of Stage 0is, IVa and IVb at 2.2% each. The findings are comparable to that reported in Egypt (17) where 52.4% had Stage I, 30.2% with Stage II while 7.4% and 3.3% had Stages III and IV respectively. Metastatic tumors often spread to distant sites and may lead to

secondary tumors, further complicating patient outcomes.

This study was a hospital-based study, a situation that creates a limitation for heavy epidemiological derivations. However, the findings of this study should be viewed in light of this limitation.

CONCLUSION

Patients diagnosed with urinary bladder cancer are males of advanced age with a history of smoking and interaction with agrochemicals. Most of them presented with classical symptoms of early disease and low-grade tumors. Exposure to agrochemicals is a significant risk factor for low grade tumors and adenocarcinoma. We recommend that further studies be conducted to clearly describe the role of agrochemicals and cigarettes smoking in urinary bladder cancers in this population.

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