# REVIEW Open Access

# The trend of schistosomiasis related bladder cancer in the lake zone, Tanzania: a retrospective review over 10 years period

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#### **Abstract**

**Introduction** Bladder cancer is a possible outcome of chronic urinary schistosomiasis in many endemic countries. In Tanzania, the Lake Victoria area is one of the areas with the highest prevalence of urinary schistosomiasis and higher incidences of squamous cell carcinoma (SCC) of the urinary bladder. A previous study in the area over one decade (2001–2010) showed SCC to be common in patients aged below 50 years. With various prevention and intervention programs there are likely to be notable changes in schistosomiasis-related urinary bladder cancer, which is currently unknown. Updated information on the status of SCC in this area will be useful for giving an insights into efficacy of control interventions implemented and help guide the initiation of new ones. Therefore, this study was done to determine the current trend of schistosomiasis-related bladder cancer in lake zone. Tanzania.

**Methods** This was a descriptive retrospective study of histologically confirmed urinary bladder cancer cases diagnosed at the Pathology Department of Bugando Medical Centre over 10 years period. The patient files and histopathology reports were retrieved and information was extracted. Data were analyzed using Chi-square and student t-test.

**Results** A total of 481 patients were diagnosed with urinary bladder cancer during the study period whereby, 52.6% were males and 47.4% were females. The mean age regardless of histological type of cancer was  $55 \pm 14.2$  years. The SCC was the commonest histological type accounting for 57.0%, followed by transitional cell carcinoma 37.6%, and 5.4% were adenocarcinomas. The *Schistosoma haematobium* eggs were observed in 25.2% and were commonly associated with SCC (p = 0.001). Poorly differentiated cancers were observed mostly in females (58.6%) compared to males (41.4%) (p = 0.003). Muscular invasion of the urinary bladder by cancer was observed in 11.4% of the patients, and this was significantly higher in non-squamous than in squamous cancers (p = 0.034).

**Conclusion** Schistosomiasis-related cancers of the urinary bladder in the Lake zone of Tanzania is still a problem. *Schistosoma haematobium* eggs were associated with SCC type indicating the persistence of infection in the area. This calls for more efforts on preventive and intervention programs to reduce the burden of urinary bladder cancer in the lake zone.

**Keywords** Urinary schistosomiasis, Bladder cancer, Lake zone, Tanzania

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#### Introduction

Human schistosomiasis is one of the 21 neglected tropical diseases [16]. It is endemic in 78 countries affecting about 240 million people worldwide and 700 million people are at risk of infection [24, 50]. The disease is caused by a parasitic worm of the genus *Schistosoma* with six major species namely *Schistosoma haematobium*, *S. mansoni*, *S. japonicum*, *S. mekongi*, *S. intercalatum* and *S. guineensis*. While *S. haematobium* affects the urogenital system, the remaining 5 species affect the gastrointestinal tract [34, 41, 71]. Schistosomiasis is endemic in Sub-Saharan Africa, the Middle East, the Islands of Madagascar, and Mauritius [50, 71].

Chronic urinary schistosomiasis due to S. haematobium is commonly associated with SCC, a type of cancer affecting the urinary bladder [52, 55]. The association comes as a result of adult S. haematobium male and female partners living in the venous plexus of the urinary bladder in pairs. While there they mate and the female releases eggs in blood vessels, the eggs then find their way to the bladder lumen to be expelled with urine [8, 46]. However, not all eggs are expelled outside the body as some are trapped in the urinary bladder tissues [9, 12, 59]. The eggs retained in the bladder wall tissues act as a mechanical irritants releasing their antigens and provoking a strong chronic inflammatory reaction leading to the surrounding of the eggs by host immune cells contributing to granulomatous formation [9, 43, 59]. This process is also associated with the fibrotic reaction resulting in the death of Schistosoma eggs at the core of the fibrosis as well as the conversion of the transitional epithelium to squamous epithelium (squamous metaplasia) [9, 43]. The bladder fibrosis may further lead to bacterial infection that converts nitrite and dietary nitrates into nitrosamines which are carcinogenic [8, 51]. Thereafter, nitrosamines act on metaplastic squamous epithelium with subsequent development of SCC [8]. The SCC of the bladder is one of the most severe complications caused by chronic S. haematobium infection and has been reported in many parts of Africa [12, 22, 34, 41, 55, 64].

The known risk factors for urinary bladder cancer worldwide are aging, the use of tobacco products, and working with industrial chemicals [20, 21, 55]. Other reported risk factors include prolonged catheter indwelling, birth defect, diabetic medicines, obesity, chronic bladder inflammation, and inherited gene mutations [3, 60]. The aforementioned risk factors are common in developed countries causing prevalence of TCC of the bladder ranging between 90 and 95% [5, 14]. On the other hand, schistosomiasis-related SCC of the bladder is more commonly diagnosed among people with schistosomiasis in developing countries with prevalence varying from 53 to 85% [13, 53, 64]. The variation in the prevalence

between SCC and TCC depend largely on the risk factors prevailing in a particular area [20, 21]. In African countries, the prevalence of *Schistosoma*-related SCC among people infected with schistosomiasis has been reported from Zimbabwe 28% and Zambia at 65% [14], Angola at 71.2% [13], South Africa at 85% [30], Ethiopia at 72.4% [62], and North-Western Nigeria at 50% [17]. The SCC incidence has been reported to decrease with the reduced prevalence of schistosomiasis [38, 42, 64]. For instance, in Egypt, SCC prevalence decreased from 75.9% in 1980 to 28.4% in 2005 which was related to control initiatives undertaken to eliminate schistosomiasis in the country [8, 27, 42, 53].

In Tanzania, bladder cancer (both SCC and TCC) has been reported from the northern and north-western parts of the country with the former being more common in both areas [37, 51]. It was observed during the studies that SCC was commonly associated with S. haematobium eggs detection in 46.9% and 73.5% of biopsies, respectively. This prevalence level exceeded the World Health Organization (WHO) determined threshold value [70]. Since then schistosomiasis control interventions have been undertaken at various levels aimed at reducing the prevalence and intensity of the disease [18, 54]. It is important to understand the current status of schistosomiasis-associated bladder cancer especially in the north-western part of the country. Therefore, this study was done to assess the current trend of schistosomiasisrelated bladder cancer in the lake zone area of Tanzania.

## **Methods**

This was a descriptive retrospective study on cases of urinary bladder cancer diagnosed at the Pathology Department, Bugando Medical Centre (BMC) over 10 years period from January 2011 to May 2021. BMC is a private consultant, tertiary care facility, and teaching hospital for the Catholic University of Health and Allied Sciences Bugando (CUHAS-Bugando). It is situated along the shores of Lake Victoria in Mwanza city with a capacity of over 950 beds and serving a catchment's population of over 15 million people. This study included all histologically confirmed cancers cases of the urinary bladder diagnosed during the study period. Data were retrieved from records in the Pathology Department. Patient files kept in the medical records were also used for clinical and demographic information such as sex, age, and place of origin. Retrieved pathological information included histological type of cancer, degree of differentiation, presence of Schistosoma eggs, and the involvement of urinary bladder muscularis propria by cancer. Patients with incomplete data and benign confirmed cases were excluded from the study. Ethical approval for the study (No. NIMR/HQR.8a/ Vol. IX/3546) was issued by the National Institute for

Medical Research (NIMR) before the commencement of the study. Data were entered and analyzed using SPSS computer software version 20.0. Chi-square test was used to test for the association between categorical data while Student t-test was used for categorical and continuous data. A p value of  $\leq$  0.05 was considered to be statistically significant.

#### Results

A total number of 481 patients were diagnosed with urinary bladder cancer during the study period whereby 52.6% (n=253) were males and 47.4% (n=228) were females, and the variation was statistically significant ( $c^2$ =28.142, p=0.002). The patient's age ranged from 8 to 95 years with a mean age of  $55\pm14.20$  years. The mean age for males was  $57.6\pm14.941$  years while for females was  $53.7\pm13.048$  and the difference was statistically significant (95% CI 1.413–6.464, t (479)=3.064, p=0.002). In addition, 33.9% (n=163) of the patients diagnosed with bladder cancer were aged below 50 years. The number of patients diagnosed with bladder cancer increased significantly (p=0.002) from 2011 to 2021 (Fig. 1).

Patients whose records were studied came from different areas of Tanzania. Mwanza Region had the highest number of patients diagnosed with bladder cancer at 39.9% (n=192), followed by Simiyu region at 17.5% (n=84). Other regions include Shinyanga 14.8% (n=71), Mara 8.9% (n=43), and Geita 8.9% (n=43). The occurrence of different types of bladder cancer varied from one region to another and the difference was statistically significant ( $c^2$ =52.575, p<0.001) (see Table 1).

For all histologically diagnosed urinary bladder cancers, SCC was the most common constituting 57.0% (n=274) of all cancer cases. Of these 44.5% (n=122)

of cancer-infected patients were males while 55.5% (n=152) were females. SCC was significantly common in females than males ( $c^2 = 17.703$ , p < 0.001). TCC was the second most common histological cancer being present in 37.6% (n = 181) of the patients and mostly males 64.6% (n=117) compared to 35.4% (n=64) in females displaying statistically significant difference ( $c^2 = 17.706$ , p < 0.001). A total number of 26 (5.4%) patients were diagnosed with adenocarcinoma, 53.8% (n = 14) of them being males and 46.2% (n = 12) females. Among all cancers diagnosed 6.0% (n = 29) were poorly differentiated cancer, 20.8% (n = 100) were moderately differentiated and 29.3% (n = 141) were well-differentiated while 43.9% (n=211) were not graded. Most females 58.6% (n = 17) had poorly differentiated cancer compared to males 41.4% (n = 12), and the difference was statistically significant ( $c^2 = 14.148$ , p = 0.003). Only 11.4% (n = 55) of confirmed cancer cases had already invaded the bladder muscle. The difference in muscle invasion between males and females was not statistically significant ( $c^2 = 0.353$ , p = 0.552) (see Table 2).

S. haematobium eggs were detected in 121 (25.2%) of all confirmed cancer cases. Among them 79.3% (n=96) were squamous cancers and 20.7% (n=25) non-squamous cancers ( $c^2=33.014$ , p<0.001). The presence of S. haematobium eggs was not statistically different between males and females ( $c^2=0.120$ , p=0.729) (Table 2). Muscle invasion of the urinary bladder was significantly lower in S. haematobium-related cancers compared to those not related to the parasite ( $c^2=7.268$ , p=0.007). The mean age for patients who had S. haematobium eggs in cancer was  $50.93\pm15.612$  while for those without S. haematobium eggs in cancers was  $57.40\pm13.323$  and the

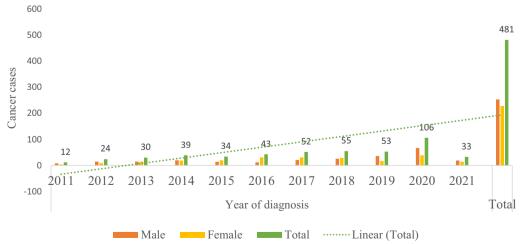


Fig. 1 Variation of histologically confirmed cancer cases in 2011–2021

**Table 1** Variation of bladder cancer with patients' place of residence in Tanzania

Place of origin	Histological type			Total N (%)	p value at 95% CI
	SCC N (%)	TCC N (%)	Adenocarcinoma N (%)		
Mwanza	102 (53.1)	77 (40.1)	13 (6.8)	192 (39.9)	
Simiyu	64 (76.2)	20 (23.8)	0 (0.00)	84 (17.5)	
Shinyanga	43 (60.6)	26 (36.6)	2 (2.8)	71 (14.8)	
Mara	19 (44.2)	21 (48.8)	3 (6.98)	43 (8.9)	
Tabora	16 (64.0)	8 (32.0)	1 (4.0)	25 (5.2)	
Geita	24 (55.8)	16 (37.2)	3 (6.98)	43 (8.9)	< 0.001
Kagera	4 (26.7)	8 (53.3)	3 (20.0)	15 (3.1)	
Rukwa	2 (50.0)	2 (50.0)	0 (0.00)	4 (0.8)	
Singida	0 (0.00)	0 (0.00)	1 (100)	1 (0.2)	
Kigoma	0 (0.00)	2 (100)	0 (0.00)	2 (0.4)	
Manyara	0 (0.00)	1 (100)	0 (0.00)	1 (0.2)	
Total	274 (56.96)	181 (37.6)	26 (5.4)	481 (100)	

**Table 2** Patient's sex concerning demographic characteristics and pathological features

	Sex		p value at 95% C	
	Male	Female		
	N (%)	N (%)		
Age group				
Below 50 years	77 (47.2)	86 (52.8)	0.092	
Above 50 years	176 (55.3)	142 (44.7)		
Histological type				
Squamous cell carcinoma	122 (44.5)	152 (55.5)	< 0.001	
Transitional cell carcinoma	117 (64.6)	64 (35.4)		
Adenocarcinoma	14 (53.8)	12 (46.1)		
Presence of Schistosoma eggs				
Yes	62 (51.2)	59 (48.8)	0.729	
No	191 (53.1)	169 (46.9)		
Muscle invasion				
Yes	31 (56.4)	24 (43.6)	0.552	
No	222 (52.1)	204 (47.9)		
Tumour differentiation				
Well-differentiated	60 (42.6)	81 (57.4)	0.003	
Moderately differentiated	51 (51)	49 (49)		
Poorly differentiated	12 (41.4)	17 (58.6)		
No differentiation	130 (61.6)	81 (38.4)		

difference was statistically significant (95% CI - 9.343 to - 3.589, t (479) = - 4.417, p < 0.001) (see Table 3).

The mean age was significantly lower for squamous cancer patients (53.6 years) compared to that in non-squamous cancer patients 58.7 years (95% CI-7.577 to -2.514, t (479)=-3.916, p<0.001). SCC prevalence was 68.1% (n=111) and 51.3% (n=161) for patients below and above 50 years respectively. Muscular invasion of the urinary bladder cancer was significantly higher in non-squamous cancers than in squamous cancer ( $c^2=4.500$ , p=0.034). Poorly differentiated cancer 68.9% (n=20) was significantly higher in patients with SCC compared to 31% (n=9) in those with non-squamous cancers ( $c^2=273.374$ , p<0.001) (see Table 4).

# Discussion

In this study, the number of patients diagnosed with bladder cancer has dramatically increased compared to the past decade with male individuals being more affected compared to their female counterparts. This is contrary to the findings reported previously in the same area [51], whereby female were diagnosed more with bladder cancer compared to male. It is not clear if this reflects an increase in incidence or just awareness of bladder cancer with a rise in detection rate. For the observed high

**Table 3** Histological type of urinary bladder cancer and the presence of *Schistosoma haematobium* eggs

Schistosoma eggs	Histological type			c²-value	p value at 95% CI
	SCC N (%)	TCC N (%)	Adenocarcinoma N (%)		
Present	96 (79.3)	21 (17.4)	4 (3.3)	28.402	< 0.001
Absent	180 (50.0)	158 (43.9)	22 (6.1)		
Total	274 (57.0)	181 (37.6)	26 (5.4)		

Table 4 Variation of patients socio-demographic characteristics with squamous and non-squamous cancers

	Type of cancer		c²-value	<i>p</i> value
	Squamous N (%)	Non-squamous N (%)		
Age group				
Below fifty	111 (68.1)	52 (31.9)	12.466	0.000
Fifty and above	161 (51.3)	157 (48.7)		
Presence of Schistosoma eggs				
Yes	96 (79.3)	25 (20.7)	33.014	0.000
No	178 (49.4)	182 (50.6)		
Muscle invasion				
Yes	24 (43.6)	31 (56.4)	4.500	0.034
No	250 (58.7)	176 (41.3)		
Tumour differentiation				
Well-differentiated	128 (90.8)	13 (9.2)		< 0.001
Moderately differentiated	88 (88.0)	12 (12.0)	237.374	
Poorly differentiated	20 (69.0)	9 (31.0)		
No differentiation	38 (18.0)	173 (82.0)		

infection in males than females, the findings concur with those reported from other areas [28, 38, 53, 73] who also found more men being infected with bladder cancer compared to females.

In the present study, bladder cancer was diagnosed in patients with more than 50 years whereby the mean age was similar to that reported by the previous study in the same study area [51]. It was found that females were likely to be diagnosed with bladder cancer at an earlier age compared to males, similar to those reported by other studies [38]. The findings are, however, different from the results reported by Rambau et al. [51], who found no difference between the sexes. However, it was observed that all bladder cancer regardless of histological types was diagnosed in 33.9% of patients with less than 50 years, indicating that in the area people of all age groups are at risk of urinary bladder cancer, and this finding corroborate with those reported in other studies in the same area [51] and from other study area [13].

Schistosomiasis-related bladder cancer is reported to occur in people of younger age compared to cancers caused by other risk factors like chemical exposure, bladder stones, and chronic indwelling catheters [3, 13, 21]. In the present study, the mean age for patients with *Schistosoma*-related cancer was statistically lower than the patients with non-*Schistosoma*-induced cancers. In addition, the mean age of patients with SCC was significantly lower than the mean age for other types of cancer, and this has previously been reported by other studies [37, 38, 51]. Furthermore, the confirmed *Schistosoma* cystitis in a patient with 8 years old has shown

that schistosomiasis is acquired early in life and that *Schistosoma*-related bladder cancer develop earlier compared to non-*Schistosoma*-linked cancers as also reported by other studies [11, 72, 73].

The present study has also shown that the majority of patients diagnosed at BMC originated from Mwanza, Simiyu and Shinyanga Regions. This might have been contributed by various reasons including; firstly the fact that the three regions have been reported to be endemic for urinary schistosomiasis [6, 40], which is the known risk factor for urinary bladder cancer in developing countries including Tanzania. Another reason maybe the higher accessibility of patients to BMC for diagnosis and management.

It was observed that the number of bladder cancer patients increased significantly from 2011 to 2021 over the last decade which can be explained by various factors; firstly, the rise in the life expectancy from 47.19 years in 1971 to 65.82 years in 2020 growing at an average annual rate of 0.68% [32] has led to an increase in older patients aged 60 and above. It should be appreciated that people aged 60 and above are more at risk of bladder cancer compared to other age groups as reported previously [53]. Secondly, an increase of population in Tanzania from 35 million in 2002 to 45 million in 2012 [63], has resulted in a large number of patients suffering from various diseases including bladder cancer. Thirdly, the rise of public awareness on health issues may have resulted in increased hospital attendance for diagnosis leading to large number of bladder cancer patients observed in the present study. Fourth, the improvement of health facilities in terms

of personnel and diagnostic facilities can explain the increased number of patients with bladder cancer.

The trend of urinary bladder cancer observed in this study is higher compared to that reported in the past 10 years (57% Vs 55.1%) and SCC being the predominant, similar findings have been reported in the same study area [51]. However, this is lower than those reported in Zimbabwe [64, 67], Angola [13], Yemen [2], South Africa [30] and Ethiopia [17]. Furthermore, the current SCC prevalence findings were slightly higher than those reported in north-western Nigeria [62]. Nonetheless, the trend in the present study is also above the WHO determined threshold value, suggesting that bladder cancer is still contributing to the negative health impact in Lake zone Tanzania. The observed variation in SCC prevalence between countries is contributed by various factors including; ecological variations from country to country that influences the distribution of intermediate host snails responsible for *S. haematobium* transmission [6, 46, 61, 74]. Secondly, people engaging in economic activities which involve infested freshwater contacts such as fishing, agriculture, washing and other recreational activities including swimming, wading and bathing may result in high schistosomiasis infection and eventually high SCC incidences. In addition, the implementation of schistosomiasis control programs which may result in the reduction of the disease prevalence varies from one country to another thus the observed variations in SCC incidences. Therefore, control of schistosomiasis will significantly reduce the burden of bladder cancer, especially SCC type in this area as also alluded in other reports [35].

In this study, the diagnosis of SCC was significantly higher in females than in males as also reported previously in the same study area [51]. However, the findings are different from those reported by other studies in Zimbabwe [67] and Egypt [38] where SCC prevalence was higher in males than females. This can be explained by different water contact activities performed by particular genders in respective areas. Furthermore, the differences in cultural practices influence the variation in schistosomiasis prevalence between males and females in different locations [26, 49]. The involvement of females in domestic chores and water contact increases the risk of acquiring schistosomiasis and SCC compared to males [13]. In addition, haematuria may be confused with menses in female thus delay in schistosomiasis-related SCC diagnosis and managements, leading to variation in prevalence between males and female in different countries. On the other hand, in some communities, males are working more in the rice field and fishing which may lead to high SCC incidences in males compared to females [26, 29, 38]. However, in the present study, the difference in presence of S. haematobium eggs between males and females was not statistically significant, signifying that both males and females are at the same risk of contracting schistosomiasis-related SCC in the Lake-zone Tanzania.

The TCC was the second most prevalent histological type observed (Table 1). This is slightly lower than the prevalence reported previously in the same area [51], as well as in Egypt [38]. Furthermore, the observed prevalence is lower than that reported in developed countries [14, 20, 53]. This suggests that there are prevailing risk factors for TCC in the country and the incidences may arise in the future due to the increase of industries and other occupational exposures [48]. The risk factors for TCC, include; the use of tobacco and occupational exposure to carcinogenic chemicals such as aromatic amines and aniline dyes [15, 20, 21]. Such risk factors are commonly reported in western countries than in developing countries, which is in line with low TCC incidences in developing countries including the one for lake zone Tanzania.

The TCC diagnosis was common in males than in female patients, this is because males are more at risk of TCC due to smoking behavior and other industrial activities compared to females [38, 53], similar findings was observed in other studies [3, 5, 25, 36, 55, 67, 68] who also reported the TCC to be the most common bladder cancer in men. However, information on patients' occupation history was missing during the present study making it difficult to make a strong argument. Furthermore, in the present study, TCC was observed to be common in patients older than 50 years indicating that exposure to TCC causing risk factors occurs late in life compared to S. haematobium infection which starts at young ages [3, 38, 48]. The prevalence of urinary bladder cancer has been reported to decrease in developed countries since the 1960s after the banning of tobacco use and its products [1, 53]. However, in developing countries such as Tanzania industrialization and tobacco use are now increasing which could lead to a rise in the number of patients with TCC as reported by other studies [1, 9, 48].

Histologically, a bladder cancer invading the muscularis propria is an indicator of the advanced stage which is associated with poor diagnosis [25, 53]. In this study, few cancer cases (11.4%) had invaded the bladder muscles at the time of diagnosis, contrary to previous study Rambau et al. [51] where more than half (67%) of cancers had invaded the bladder muscles. The current findings are likely a result of good accessibility to the health facility, availability of modern medical equipment such as cystoscopes and trained personnel.

In this study, only a few patients (6.0%) presented with poorly differentiated carcinoma at the time of diagnosis, and this was more common in SCC type compared to non-squamous cancers. This probably is because SCC is

more aggressive than non-squamous cancers [10]. Poorly differentiated cancers were observed mostly in females than males. The poorly differentiated cancers tend to be in an advanced stage which is associated with a lower survival rate during treatment [4, 53]. Several factors are contributing to the observed differences of the advanced stage of bladder cancer between sexes; Firstly, it has been reported that most women with visible haematuria which is the common sign for urinary bladder cancer delay in seeking medical care for diagnosis, possibly due to confusion with menses [23, 57, 69]. Secondly, the thinner bladder wall in females and hormonal differences have been contributing to the variation in grades of urinary bladder cancer between sexes as discussed elsewhere [31, 36, 38, 53, 56].

Calcified S. haematobium eggs were seen in about a quarter of all cancer cases indicating chronic infection with the parasite, as reported by other studies [13, 19, 51, 58]. Most of the samples received for cancer diagnosis at BMC were small biopsy tissues, which could explain the observed low rate of S. haematobium eggs detected. The presence of S. haematobium eggs was highly associated with SCC type of cancer compared to non-squamous cancers implying that the former is associated with chronic urinary schistosomiasis than the latter. Similar findings have been reported by other studies [38, 51, 67]. The squamous cancer was diagnosed at equal rates in all age groups, suggesting that all residents in the Lake zone are at risk of schistosomiasis infection. On the other hand, the current study findings are contrary to the findings reported by other researchers whereby SCC was common in patients below 50 years [3, 65].

In Tanzania, only two hospital-based studies on bladder cancer have been reported [37, 51]. As also observed in the current study, both authors have reported SCC as being associated with the presence of *S. haematobium* eggs. The National Schistosomiasis and Soil-Transmitted Helminthes (STH) control program was established under the National School Health program in 2004 [33]. The program intended to control schistosomiasis and STH in school-aged children through mass distribution of praziquantel and other anti-helminthic drugs respectively. The pre-school-aged children and adults were not considered in the program which caused infected individuals to continue shedding *S. haematobium* eggs in the environment and thus perpetuates the existence of the disease [18, 24, 45].

Furthermore, in 2009 Tanzania, adopted the WHO's schistosomiasis control initiatives through preventive chemotherapy (PCT), and the NTDs control program began the same year [33]. However, among the 10.8 million people who required preventive treatment in Tanzania in 2014, only 27% were covered [66]. Schistosomiasis

control has however, contributed to reducing incidences of SCC in endemic areas [8, 27]. In Mwanza Region Tanzania for instance, some villages remained with high schistosomiasis prevalence after four rounds of MDA [45], while in Dodoma praziquantel uptake was below the WHO's minimum levels [18]. Variation in socioeconomic, cultural, and political factors influences the participation in MDA programs in communities [24, 45]. Therefore, the factors should always be considered for successful schistosomiasis elimination in communities as recommended [24, 45, 47].

The persistence of the high prevalence of schistosomiasis-associated bladder cancer for more than two decades in Lake-Zone Tanzania shows that disease control initiatives are not successful. This could be explained several factors including; lack of health education, motivation, and commitment of the community in controlling the disease. Secondly, the consideration that the disease is of low priority caused many people not turning-up to the arranged MDA program causing the infection to remain high especially among untreated individuals in the population [7, 45, 47]. Thirdly, there is a widespread misconception that the anti-helminthic drugs are disguised birth control agents making some people avoid them [39, 44]. It is important therefore that schistosomiasis control programs are accompanied by health education for maximum impact. Early medical care-seeking behavior should be promoted to enhance the prevention of late-stage complications of urinary schistosomiasis. However, this will be possible if people are aware of the signs and symptoms of urinary schistosomiasis and its sequelae such as anemia and bladder cancer.

#### **Conclusion and recommendations**

The number of patients infected with schistosomiasis-related urinary bladder cancer in the Lake Zone area of Tanzania has increased, with squamous cell carcinoma being predominant. This trend of schistosomiasis-related squamous cell carcinoma demand a better surveillance systems which can be implemented for control of disease and eventually elimination of health impacts caused thereof. Testing of SCC for patients presenting with schistosomiasis infection signs and symptoms should be mandatory to enable the early detection of lesions in the urinary tract system.

#### Abbreviations

BMC Bugando Medical Centre
LAP Lower abdominal pain
LUTS Lower urinary tract symptoms
MDA Mass drug administration
NTD Neglected tropical diseases
NIMR National Institute for Medical Research

PCT Preventive chemotherapy

SCC Squamous cell carcinoma STH Soil-transmitted helminths

SPSS Statistical package for social sciences

TCC Transitional cell carcinoma
UTI Urinary tract infection
WHO World Health Organization

#### Acknowledgements

Dr. Esther R. Bugumba and Dr. Aaron pathology department for their assistance during the review of patients files for data collection.

#### **Author contributions**

CY main author of the study, involved in proposal writing, study design, data collection, data processing and analysis, and preparation of the manuscript. JSB was involved in the development of proposal and study design and manuscript preparation. SMK was involved in the preparation of study design and preparation of the manuscript. BAN was involved in the preparation of the proposal and study design. PFR was involved in data collection, pathological review, data processing, analysis, and preparation of the manuscript. All authors read and approved the final manuscript.

#### **Funding**

The study was funded by Mbeya University of Science and Technology (MUST).

#### **Declarations**

#### Ethics approval and consent to participate

The research was approved by the Medical Research Coordination Committee (MRCC) of the National Institute for Medical Research (NIMR) certificate (No. NIMR/HQR.8a/Vol. IX/3546) and the University of Dar-es salaam higher degrees research and publication committee (HDRPC) approved the research before the commencement of study. This research was a retrospective study the patient's files were used to get the information, confidentiality of the patients was maintained by excluding the identifiers including names. Only file number and year of diagnosis were used, official permission was provided by joint of Bugando Medical Centre (BMC) and Catholic University of Health and Allied Sciences (CUHAS).

#### Consent for publication

Not applicable.

#### **Competing interests**

All authors declare that they have no competing interests.

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Received: 29 March 2022 Accepted: 28 September 2022 Published online: 19 February 2023

#### References

- Al-Husseini MJ, Kunbaz A, Saad AM, Santos JV, Salahia S, Iqbal M, Alahdab F. Trends in the incidence and mortality of transitional cell carcinoma of the bladder for the last four decades in the USA: a SEER-based analysis. BMC Cancer. 2019;19:46.
- Al-Samawi AS, Aulaqi SM. Urinary bladder cancer in Yemen. O Med J. 2013;28:337–40.
- 3. American Cancer Society: bladder cancer causes, risk factors, and prevention. *cancer.org* 2018 | 1.800.227.2345.

- Amiri M, Heshmatollah S, Esmaeilnasab N, Khoubi J, Ghaderi E, Roshani D. The survival rate of patients with bladder cancer and its related factors in Kurdistan Province (2013–2018): a population-based study. BMC Urol. 2020;20:195.
- Andreassen BK, Aagnes B, Gislefoss R, Andreassen M, Wahlqvist R. Incidence and survival of urothelial carcinoma of the urinary bladder in Norway 1981–2014. BMC Cancer. 2016;16:799.
- Angelo T, Buza J, Kinung'hi SM, Kariuki HC, Mwanga JR, Munisi DZ, Wilson S. Geographical and behavioral risks associated with Schistosoma haematobium infection in an area of complex transmission. Parasite Vectors. 2018:11:481.
- Angelo T, Kinung'hi SM, Buza J, Mwanga JR, Kariuki HC, Wilson S. Community knowledge, perceptions and water contact practices associated with transmission of urinary schistosomiasis in an endemic region: a qualitative cross-sectional study. BMC Public Health. 2019;19:703.
- 8. Barsoum RS. Urinary schistosomiasis: review. J Adv Res. 2013;4:453–9.
- 9. Barsoum RS, Esmat G, El-Baz T. Human schistosomiasis: clinical perspective review. J Adv Res. 2013;4:433–44.
- Badr KM, Nolen JDL, Derose PB, Cohen C. Muscle invasive schistosomal squamous cell carcinoma of the urinary bladder; frequency and prognostic significance of P53, BCL-2, HER2/neu, and proliferation (MIB-1). Hum Pathol. 2004;35(2):184–9.
- Bedwani R, Renganathan E, El Kwhsky F, Braga C, Seif HHA, Azm TA, Zaki A, Franceschi S, Boffettas P, La Vecchia C. Schistosomiasis and the risk of bladder cancer in Alexandria, Egypt. Br J Cancer. 1998;77(7):1186–9.
- Botelho MC, Machado JC, Brindley PJ, Correia-da-Costa JM. Targeting molecular signaling pathways of *Schistosoma haematobium* infection in bladder cancer. Virulence. 2011;2(4):267–79.
- 13. Botelho MC, Figueiredo J, Alves H. Bladder cancer and urinary Schistosomiasis in Angola. J Nephrol Res. 2015;1(1):22–4.
- Bowa K, Mulele C, Kachimba J, Manda E, Mapulanga V, Mukosai S. A review of bladder cancer in Sub-Saharan Africa: a different disease, with a distinct presentation, assessment, and treatment. Annals Afr Med. 2018;17:99–105.
- 15. Brown T, Slack R, Rushton L. Occupational cancer in Britain: urinary tract cancers: bladder and kidney. Br J Cancer. 2012;107(1):76–84.
- Casulli A. New global targets for NTDs in the WHO roadmap 2021–2030. PLoS Negl Trop Dis. 2021;15(5):e0009373.
- Chala B, Torben W. An epidemiological trend of urogenital schistosomiasis in Ethiopia. Front Public H. 2018;6:60.
- Chaula SA, Tarimo DS. Impact of praziquantel mass drug administration campaign on prevalence and intensity of *Schistosoma haema*tobium among schoolchildren in Bahi district, Tanzania. Tan J H Res. 2014;16(1):1–10.
- Cohen RA, Brown RS. Clinical practice. Microscopic Haematuria Nengl J Med. 2003;348:2330–8.
- Conti SL, Honeycutt J, Odegaard JI, Gonzalgo ML, Hsieh MH. Alterations in DNA methylation may be the key to early detection and treatment of schistosomal bladder cancer. PLoS Negl Trop Dis. 2015;9(6):e0003696.
- Cumberbatch MG, Rota M, Catto JWF, La Vecchia C. The role of tobacco smoke in bladder and kidney carcinogenesis: a comparison of exposures and meta-analysis of incidence and mortality risks. Eur Urol. 2016;70(3):458–66.
- Davis SM, Wiegand RE, Mulama F, Kareko El, Harris R, Ochola E, Samuels AM, Rawago F, Mwinzi PM, Fox LM, Odiere MR, Won KY. Morbidity associated with schistosomiasis before and after treatment in young children in Rusinga Island, Western Kenya. Am Soc Trop Med Hyg. 2015;92(5):952–8.
- Dobruch J, Daneshmand S, Fisch M, Lotan Y, Noon AP, Resnick MJ, Shariat SF, Zlotta A, Boorjian SA. Gender and bladder cancer: a collaborative review of etiology, biology, and outcomes. Eur Urol. 2016;69:300–10.
- Donohue RE, Mashoto KO, Mubyazi GM, Madon S, Malecela MN, Michael E. Biosocial determinants of persistent schistosomiasis among schoolchildren in Tanzania despite repeated treatment. Trop Med Inf Dis. 2017;2:61.
- 25. Dorak MT, Karpuzoglu E. Gender differences in cancer susceptibility: an inadequately addressed issue. Front Gene. 2012;3:268.
- Elmadani AE, Hamdoun AO, Monis A, Karamino NE, Gasmelseed N. Ultrasound findings in urinary schistosomiasis infection in school children in the Gezira State Central Sudan. S J Kid Dis Trans. 2013;24(1):162–7.
- 27. Felix AS, Soliman AS, Khaled H, Zaghloul MS, Banerjee M, El-Baradie M, El-Kalawy M, Abd-Elsayed AA, Ismail K, Hablas A, Seifeldin IA, Ramadan

- M, Wilson ML. The changing patterns of bladder cancer in Egypt over the past 26 years. Cancer Causes Control. 2008;19:421–9.
- 28. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray F. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2014.
- Frigerio S, Bert F, Clari M, DiFine G, Riva S, Bergese I, Diouf SG, Alvaro R, Buonomo E. Knowledge, attitudes, and practices related to Schistosomiasis among Children in Northern Senegal. Annals Global H. 2016;82(5):840–7
- Groeneveld AE, Marszalek WW, Heyns CF. Bladder cancer in various population groups in the greater Durban area of KwaZulu-Natal. South Africa Br J Urol. 1996;78(2):205–8.
- 31. Hakenberg OW, Linne C, Manseck A, Wirth MP. Bladder wall thickness in normal adults and men with mild lower urinary tract symptoms and benign prostatic enlargement. Neurolol Urodyn. 2000;19:585–93.
- 32. https://knoema.com/atlas/United-Republic-of-Tanzania. Accessed on 23 Sept 2021.
- 33. https://www.ntdcp.go.tz/ Accessed on 10 Oct 2021.
- Inobaya MT, Olveda RM, Chau TNP, Olveda DU, Ross AGP. Prevention and control of schistosomiasis: a current perspective. Res Rep Trop Med. 2014. https://doi.org/10.2147/RRTM.S44274.
- 35. Jin-Kyoung O, Weiderpass E. Infection and cancer: global distribution and burden of diseases. Ann Glob Health. 2014;80:384–92.
- Kim HI, Lim H, Moon A. Sex differences in cancer: epidemiology, genetics, and therapy. Biomol Ther. 2018;26(4):335–42.
- Kitinya JN, Laurèn PA, Eshleman EJ, Paljärvi L, Tanaka K. The incidence of squamous and transitional cell carcinomas of the urinary bladder in northern Tanzania in areas of high and low levels of endemic Schistosoma haematobium infection. Trans R Soc Trop Med Hyg. 1986;80:935–9.
- Kyritsi F, Loffredo CA, Zheng YL, Philips G, Amr S. Urinary bladder cancer in Egypt: are there gender differences in its histopathological presentation. Adv Urol. 2018. https://doi.org/10.1155/2018/3453808.
- Macharia JW, Ng'ang'a ZW, Njenga SM. Factors influencing community participation in control and related operational research for urogenital schistosomiasis and soil-transmitted helminths in rural villages of Kwale County, coastal Kenya. Pan Afr Med J. 2016;24:136.
- Mazigo HD, Nuwaha F, Kinunghi SM, Morona D, Pinot-de-Moira A, Wilson S, Heukelbach J, Dunne DW. Epidemiology and control of human schistosomiasis in Tanzania. Parasite Vectors. 2012;5:274.
- Meurs L, Mbow M, Vereecken K, Menten J, Mboup S, Polman K. Bladder morbidity and hepatic fibrosis in Mixed Schistosoma haematobium and Schistosoma mansoni Infections: a population-wide study in Northern Senegal. PLoS Negl Trop Dis. 2012;6(9):e1829.
- 42. Mohamed SZ. Bladder cancer and schistosomiasis. J Egy Natl Cancer Inst. 2012;24:151–9.
- Mostafa MH, Sheweita SA, O'connor PJ. Relationship between schistosomiasis and bladder cancer. Clin Microbiol Reviews. 1999;12(1):197–111.
- 44. Musuva RM, Awiti A, Omedo M, Ogutu M, Secor WE, Montgomery SP, Alaii J, Mwinzi PN. Community knowledge, attitudes, and practices on schistosomiasis in western Kenya–the SCORE project. Am J Trop Med Hyg. 2014;90:646–52.
- Mwanga JR, Kinung'hi SM, Mosha J, Angelo T, Maganga J, Campbel CH Jr. Village response to mass drug administration for schistosomiasis in Mwanza Region, Northwestern Tanzania: are we missing socioeconomic, cultural, and political dimensions? Am J Trop Med Hyg. 2020;103(5):1969–77.
- Ngasala B, Juma H, Mwaiswelo RO. The usefulness of indirect diagnostic tests for Schistosoma haematobium infection after repeated rounds of mass treatment with praziquantel in Mpwapwa and Chakechake districts in Tanzania. Inter J Inf Dis. 2019;90:132–7.
- Parisi S, Mazigo HD, Kreibich S, Puchner K, Kasang C, Mueller A. Factors associated with relevant knowledge of intestinal schistosomiasis and intention to participate in treatment campaigns: across sectional survey among school children at Ijinga Island on Lake Victoria. North-Western Tanzania BMC Public H. 2019;19:1762.
- 48. Parkin DM, Bray F, Ferlay J, Jemal A. Cancer in Africa. Cancer Epidemiol Biomarkers Prev. 2014;23(6):953–66.
- Person B, Ali SM, A'Kadir FM, Ali JN, Mohammed UA, Mohammed KA, Rollinson D. KnoppS: community knowledge, perceptions, and practices associated with urogenital schistosomiasis among school-aged

- children in Zanzibar, United Republic of Tanzania. PLoS Negl Trop Dis. 2016;10(7):e0004814.
- Poturalski MJ, Magi-Galluzzi C, Liu PS. Squamous cell carcinoma of the bladder complicating schistosomiasis. Published Online. 2017:37(2):500–4.
- Rambau PF, Chalya PL, Kahima J. Schistosomiasis and urinary bladder cancer in North-Western Tanzania: a retrospective review of 185 patients. Inf Ag Canc. 2013;8:19.
- 52. Remppis J, Verheydena A, Bustinduyd AL, Hellere T, García-Tardóna N, Manouana GP, Obianga R, Adegnika AA, Grobuscha MP, Ramhartera M, Joekes E, Bélard S. Focused assessment with sonography for urinary schistosomiasis (FASUS)-pilot evaluation of a simple point-of-care ultrasound protocol and short training program for detecting urinary tract morbidity in highly endemic settings. Trans Royal Soc Trop Med Hyg. 2019;00:1–11.
- 53. Richters A, Aben KKH, Kiemeney LALM. The global burden of urinary bladder cancer: an update. World J Urol. 2020;38:1895–904.
- Ruganuza DM, Mazigo HD, Waihenya R, Morona D, Mkoji G. Schistosoma mansoni among pre-school children in Musozi village, Ukerewe Island, North-Western-Tanzania: prevalence and associated risk factors. Parasite Vectors. 2015;8:377.
- Saginala K, Barsouk A, Aluru JS, Padala PRSA, Barsouk A. Epidemiology of bladder cancer. Med Sci. 2020. https://doi.org/10.3390/medsci8010015.
- Sarasqueta C, Zunzunegui MV, Navascues JME, Querejeta A, Placer C, Perales A, Gonzalez N, Aguirre U, Baré M, Escobar A, Quintana JM. on behalf of the REDISSEC-CARESS/CCR Group: gender differences in stage at diagnosis and preoperative radiotherapy in patients with rectal cancer. BMC Cancer. 2020;20:759.
- Shariat SF, Sfakianos JP, Droller MJ, Karakiewicz PI, Meryn S, Bochner BH.
   The effect of age and gender on bladder cancer: a critical review of the literature. BJU Int. 2010;105:300–8.
- Silva IM, Thiengo R, Conceição MJ, Rey L, Pereira FE, Ribeiro PC. Cystoscopy in the diagnosis and follow-up of urinary schistosomiasis in Brazilian soldiers returning from Mozambique, Africa Review. Inst Med trop S Paulo. 2006;48(1):39–42.
- Skelly P.The use of imaging to detect schistosomes and diagnose schistosomiasis. Parasite Immunol. 2013;35:295–301.
- Smith AB, Jaeger B, Pinheiro LC, Edwards LJ, Tan HJ, Nielsen ME, Reeve BB. Impact of bladder cancer on health-related quality of life. BJU Int. 2018;121(4):549–57.
- 61. Stothard JR, Loxton N, Rollinson D, Mgeni AF, Khamis S, Ameri H, Ramsan M, Savioli L. The transmission status of Bulinus on Zanzibar Island (Unguja) with implications for control of urinary schistosomiasis. Annals Trop Med Parasitol. 2000;94:87–94.
- Takure AO, Odubanjo MO, Olapade-Olaopa EO. Histopathologic pattern of bladder cancers in Ibadan southwest Nigeria: an update. J West Afr College Surg. 2015;5(2):17–42.
- Tanzania Population and Housing Census National Bureau of Statistics. Ministry of Planning, Economy and Empowerment 2012. http://www.nbs. go.tz/sensa/PDF. Accessed on 24th Mar 2020.
- Thomas JE, Bassett MT, Sigola LB, Taylor P. Relationship between bladder cancer incidence, *Schistosoma haematobium* infection, and geographical region in Zimbabwe. Trans R Soc Trop Med Hyg. 1990;84:551–3.
- 65. Thomas JO, Onyemenen NY. Bladder carcinoma in Ibadan, Nigeria; a changing trend? East Africa med J. 1995;72:49–50.
- The United Republic of Tanzania and neglected tropical. https://unitingtocombatntds.org/accessed on 22 Sept 2021.
- Vizcaino AP, Parkin DM, Boffetta P, Skinner MEG. Bladder cancer: epidemiology and risk factors in Bulawayo. Zimbabwe Cancer Causes Control. 1994;5(6):517–22.
- Waihenya CG, Mungai PN. Pattern of transitional cell carcinoma of the urinary bladder as seen at Kenyatta National Hospital. Nairobi East Afr Med J. 2004;81(3):114–9.
- Wolff I, Brookman- May S, May M. Sex difference in presentation and outcomes of bladder cancer: biological reality or statistical fluke? Curr Opin Urol. 2015;25:418–26.
- World Health Organization. Prevention and control of schistosomiasis and soil-transmitted helminthiasis: report of a WHO expert committee. Geneva: Bull World Health Organization; 2002.
- World Health Organization: Global health Estimates 2016, Death by cause, age, sex, by country and by region 2000–2016. Geneva, world health organization 2018.

- 72. Zepeda CM, Coffey KH. *Schistosoma haematobium* infection that mimics bladder cancer in a 66-year-old ethnic Egyptian man. Lab Med Fall. 2015;46:338–42.
- Zhong X, Isharwal S, Naples JM, Shiff C, Veltri RW, Shao C, Bosompem KM, Sidransky D, Hoque MO. Hypermethylation of genes detected in urine from ghanaian adults with bladder pathology associated with Schistosoma haematobium infection. PLoS ONE. 2013;8(3):e59089.
- 74. Zumstein A. A study of some factors influencing the epidemiology of urinary schistosomiasis at Ifakara (Kilombero District, Morogoro Region, Tanzania). Acta Trop. 1983;40:187–204.

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