

Original Research Article

Histological pattern of bladder cancer at a tertiary hospital in North Western Nigeria: an update

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ABSTRACT

Background: An update on the histopathological patterns of bladder cancer in our environment is pertinent to determine the current prevalent histological type and if there is worsening schistosomal infestation as these can guide the management of bladder cancer.

Methods: This is a prospective study of patients managed for bladder cancer at the urology unit, department of surgery, Usmanu Danfodiyo University Teaching Hospital, Sokoto, Nigeria between 02 February 2018 and 01 February 2019. Histology of biopsy specimens were done at the histopathology department of Usmanu Danfodiyo University Teaching Hospital, Sokoto. Data was collected using a structured proforma and analyzed using statistical package for the social sciences (SPSS) version 20.0.

Results: A total of 65 patients were recruited into the study with mean age of 51.9 years and standard deviation of ± 14.7 . The male to female ratio was 6:1 and the commonest occupation of the patients was farming (41.5%). A total of 46 patients (70.8%) had squamous cell carcinoma following histology, followed by transitional cell carcinoma seen in 9.2% of patients and adenocarcinoma seen in 3.1% of patients. Schistosoma ova was seen in 13.8% of the patients while 3.1% of the patients had cystitis cystica.

Conclusions: The commonest histological type of bladder cancer in our environment is squamous cell carcinoma. In this current study, the percentage of patients with squamous cell carcinoma is higher than the previously reported percentages while the percentage of patients with transitional cell carcinoma is lower than the previously reported percentages thus revealing worsening schistosomal infestation in our environment.

Keywords: Bladder cancer, Histology, Schistosomiasis

INTRODUCTION

Bladder cancer is the 9th most common cancer worldwide and the 13th most common cause of death, accounting for 145,000 deaths worldwide.¹ It accounts for 6% of all cancers in men and 2% of all cancers in women globally.^{2,3} In North America and Europe, 95% to 97% of cases of bladder cancer are of urothelial variety. However, in

Africa, 60% to 90% are urothelial and 10% to 40% are squamous cell carcinoma with Egypt having the highest rate of squamous cell carcinoma in 2008 because of the endemic infestation with schistosoma haematobium.¹

Males are 3 to 4 times more likely to develop bladder cancer worldwide presumably because of an increased prevalence of smoking and exposure to environmental

toxins.¹ Adolescents and young adults tend to develop well differentiated non-invasive rather than invasive bladder cancer.⁴

The incidence and prevalence of urothelial cancer increase with age, with exposure to environmental toxins as part of the risk factors. Histologically, 90% of bladder cancers are of urothelial origin, 5% are squamous cell carcinoma and less than 2% are adenocarcinoma or other variants.⁵

In Sokoto, bladder cancer is the most common male cancer and the incidence is rising.^{6,7} Patients come predominantly from rural and agricultural areas of the region known to be endemic for urinary schistosomiasis.⁷ The male to female ratio is 11.1:1, this is higher than the reported ratio from other Nigerian Centers.^{5,8-10} The mean age was 46 years with a range of 20-82 years.⁷ The histological types were mostly differentiated squamous cell carcinoma which comprised 65.1% of cases and these demonstrated histological evidence of chronic schistosomiasis in 50% of squamous cell carcinoma variant.⁷

Study of the histological patterns of bladder cancer in our environment is thus pertinent to determine the current histological pattern as this can affect the management of patients with bladder cancer.

METHODS

This is a prospective study of patients presenting at the urology out-patient clinic of Usmanu Danfodiyo University Teaching Hospital (UDUTH) between 02 February 2018 and 01 February 2019 with clinical and radiological features of bladder cancer, who met the inclusion criteria and gave informed consent.

Inclusion criteria

Patients with clinical and radiological features of bladder cancer (haematuria, necroturia, and ultrasound finding of bladder mass) were included in the study.

Exclusion criteria

Patients with haematuria from other genito-urinary malignancies – prostate, urethra, ureter, and kidney; patients too ill to withstand anaesthesia; and patients who refused consent were excluded.

Sample size estimation

The sample size estimation calculation was done using the formula for calculating sample size for validity assessment of a screening test as all the patients did urine cytology as well.¹¹ It is as follows.

$$n = \frac{[Z_{1-\alpha/2}\sqrt{P_0(1-P_0)} + Z_\beta\sqrt{P_1(1-P_1)}]^2}{(P_1 - P_0)^2}$$

Here, $Z_{1-\alpha/2}$ is percentage point of the normal distribution corresponding to the required (two-sided) significance level (α) of 0.05=1.96; Z_β is one sided percentage point of the normal distribution corresponding to 100% minus the power.

$$Z_\beta = 100\% - power$$

For example, if power = 80% (100% – power) = 20% (i.e. p value of 0.2) = 0.84

P_0 is null hypothesis proportion (i.e. no increase is expected, which means that the proportion will remain as previously obtained i.e. sensitivity of minichromosome maintenance deficiency 5 (MCM5).

P_1 is alternative hypothesis proportion.

$$P_1 = 87\% \text{ baseline} + 10\% \text{ increase} = 97\% = 0.97$$

$P_1 - P_0$ is the difference (i.e. expected increase in the proportion of MCM5, new biomarker in diagnosis of bladder cancer).

$$P_1 - P_0 = 0.97 - 0.87 = 0.1$$

$$n = 64.38 \approx 64 \text{ patients or subjects}$$

Approval to carry out the study was obtained from the research and ethics committee of UDUTH, Sokoto prior to the commencement of the study. Urethrocystoscopy with biopsy was done under regional (spinal) or general anaesthesia only in patients with negative urine culture after giving prophylactic antibiotics using 1 gram of ceftriazone given intravenously at induction of anaesthesia.

Histological analysis of the cystoscopy and biopsy samples were done at the histopathology department of UDUTH, Sokoto.

A structured proforma was used to collect data on the relevant clinical details from the patients involved in the study including history to identify risks and classical presentation, investigations and cystoscopy with biopsy. The IBM statistical package for the social sciences (SPSS) version 20.0 (SPSS Inc; Chicago, IL, USA) computer software was used for the data analysis. Frequencies and proportions of socio-demographic variables were reported.

RESULTS

A total number of 65 patients participated in the study. The age range of the patients was 16-80 years with mean age of 51.9 years and standard deviation of 14.7.

There were 56 males and 9 females with male to female ratio of 6:1.

The commonest occupation of the patients was farming seen in 27 patients (41.5%). Details of the socio-demographic characteristics are shown in Table 1.

Table 1: Socio-demographic characteristics of patients.

Variables	Frequency (percentage), n=65
Mean age±SD	51.86±14.7
Sex	
Male	56 (86.2)
Female	9 (13.8)
Marital status	
Single	3 (4.7)
Married	62 (95.3)
Occupation	
Student	2 (3.1)
Housewife	7 (10.8)
Farmer	27 (41.5)
Civil servant	11 (16.9)
Businessman	16 (24.6)
Fisherman	2 (3.1)

Following urethrocystoscopy, 4 patients (6.2%) had features of cystitis (hyperaemic bladder mucosa), 4 patients (6.2%) had features of schistosomiasis (sandy patches, tubercles, nodules), 4 patients (6.2%) had features of early bladder carcinoma (solitary papillary lesions) while 53 patients (81.5%) had features of advanced bladder carcinoma (extensive sessile and papillary lesions). None of the patients had clinical stage 1 following bimanual palpation. Figure 1 shows comparison between urethrocystoscopy findings and staging after bimanual palpation.

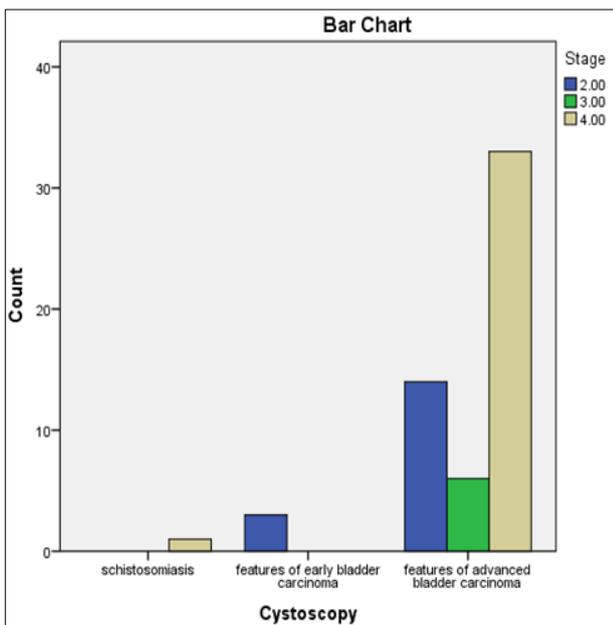


Figure 1: Comparison between urethrocystoscopy findings and staging following bimanual palpation.

A total of 46 patients (70.8%) had squamous cell carcinoma following histopathology and this was the commonest histopathological type of bladder cancer seen. This was followed by transitional cell carcinoma seen in 6 patients (9.2%) and adenocarcinoma seen in 2 patients (3.1%). A total of 9 patients (13.8%) had schistosoma ova following histopathology while 2 patients (3.1%) had cystitis cystica.

Figure 2 shows comparison between the various histopathological types of bladder cancer and their Gleason's grades.

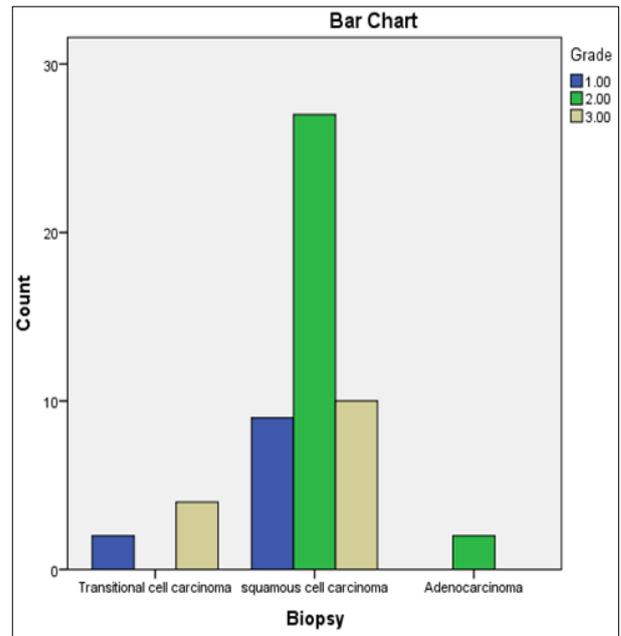


Figure 2: Comparison between histological types of bladder cancer and Gleason's grade.

DISCUSSION

The mean age of the patients in the study is similar to the mean age of patients in studies done at schistosomiasis endemic areas of Sokoto and Plateau states.^{7,9} The earlier age of onset of bladder cancer noticed in these patients when compared with the global mean age of onset of bladder cancer was due to childhood exposure to schistosomiasis. The late onset of bladder cancer globally may be attributed to occupational exposure to aromatic hydrocarbons and cigarette smoking, as these risk factors occur in adults.

The male to female ratio in this study was lower than the ratio reported in the study done in this environment where they reported 11.1:1.⁷ This however was higher than the ratio reported in some Nigerian centers (2.5:1) as well as the worldwide reported ratio of 4:1.^{1,9} The higher prevalence in males was due to their increased involvement in farming which was reported as the commonest occupation from a study done in this environment.⁷

The commonest occupation of the patients was farming which is in keeping with the study done in this environment.⁷ This was believed to be due to the fact that these rural farming communities' dwell at riverside areas so are more predisposed to schistosomal infestation and re-infestation even when treated, this thus may progress to bladder cancer which is one of the complications of schistosomiasis.

Following urethroscopy, majority of the patients had features of advanced bladder cancer which could also be due to the late presentation of the patients in our environment. Some of these features were extensive sessile and papillary lesions in the bladder. The correlation of bimanual palpation findings with the clinical stage of the bladder cancer revealed that most of these patients found to have features of advanced bladder cancer on urethroscopy had stage 4 bladder cancer thus still supporting the fact that most of the patients with bladder cancer in our environment are seen at the advanced stage of bladder cancer. It was also found that the patients with features of early bladder cancer such as solitary papillary lesions on urethroscopy had clinical stage 2 bladder cancer, this synchrony between the urethroscopy findings and clinical staging amongst these group of patients supported these urethroscopy findings, the few number of patients with these features supported the fact that very few patients present with features of early bladder cancer in our environment and some of them were incidental findings diagnosed during evaluation of symptoms of other urinary tract diseases such as benign prostatic hyperplasia. It was also found that some of the patients with urethroscopy features of schistosomiasis such as sandy patches, nodules and papilloma had clinical stage 4 bladder cancer. This may be due to the fact that some of these features of schistosomiasis seen such as papilloma may actually be papillary lesions of bladder cancer.

Some patients that presented with clinical and radiological features of bladder cancer had no bladder mass following urethroscopy, some of them had hyperaemic areas following urethroscopy which was in keeping with cystitis, this finding was in keeping with the fact that vesical schistosomiasis is a good differential of bladder cancer and some of the bladder masses seen radiologically were actually blood clots or enlarged prostate seen at the region of the bladder base and not actually bladder mass. These differentials should be borne in mind during evaluation of patients with suspected features of bladder cancer.

The commonest histopathological type of bladder cancer from this study is squamous cell carcinoma. This is due to endemic infestation by schistosoma species. This finding is in keeping with similar studies done in environment with endemic infestation by schistosomiasis.^{2,7,9,12} This was followed by transitional cell carcinoma with findings from this study found to be lower than the previous study done in this environment where transitional cell carcinoma

accounted for 27.9% of cases thus showing worsening of infestation by schistosoma species in our environment.⁷ Adenocarcinoma accounted for the least number of cases which was comparable to 4.7% seen in the previous study done in this environment and 2% seen worldwide.^{2,7} Similar study done in this environment on urinary survival revealed that transitional cell carcinoma accounted for 38.1% of cases while adenocarcinoma accounted for 2.4% of cases, thus in keeping also with worsening infestation by schistosoma species while adenocarcinoma result was similar to the finding of the index study.¹²

Some of the patients had schistosoma ova following histology thus revealing the fact that some of the patients that presented with clinical or radiological features of bladder cancer actually had vesical schistosomiasis. Some of the patients that had strong suspicion of bladder cancer from urethroscopy and urine cytology results whom histology results revealed schistosoma ova had repeat urethroscopy and biopsy with confirmation of bladder cancer in patients with true diagnosis of bladder cancer. Thorough evaluation of patients with clinical and radiological features of bladder cancer are thus invaluable in ensuring right diagnosis, detailed and careful urethroscopy are all necessary to avoid missed bladder tumours with subsequent negative histology results.

A total of 58.7% of patients with histologically diagnosed squamous cell carcinoma had moderately differentiated carcinoma (G2) following histological grading while 19.6% of them had well differentiated carcinoma (G1) following histological grading. This is in contrast to the finding of a previous study done in this environment where 50% of the patients histologically diagnosed with squamous cell carcinoma had G1 histological grading while 42.9% had G2 histological grading.⁷ All the patients in this study histologically diagnosed with adenocarcinoma had moderately differentiated carcinoma (G2) following histological grading. These findings of predominantly moderately differentiated carcinoma for both the squamous cell carcinoma and adenocarcinoma in this study are contradictory to the previous knowledge known about these histological subtypes as they were known to be predominantly poorly differentiated carcinoma (G3). This difference in the current study may be due to inter-observer variation as noted by the international society of urological pathology, so most of these G2 tumours may be G3 tumours.²

Transitional cell carcinoma was found to have more of poorly differentiated carcinoma than well differentiated carcinoma from this study while none of the patients histologically diagnosed with transitional cell carcinoma from this study had moderately differentiated carcinoma, this was in contrast to what is known about this histological subtype of bladder cancer when compared with the other subtypes of bladder cancer and may reveal a changing trend in the biological behavior of this histological type of bladder cancer.

Limitations

The small sample size and the fact that the study was done in a single center were the limitations of this study. There is a need for large, multi-center study on this in the future to validate the findings of this study.

CONCLUSION

The commonest histological type of bladder cancer in our environment is squamous cell carcinoma seen in 70.8% of the patients, other histological types seen are transitional cell carcinoma and adenocarcinoma. The percentage of squamous cell carcinoma from this study is higher than the previously reported percentages while the percentage of transitional cell carcinoma is lower than the previously reported percentages thus revealing worsening schistosomiasis infestation in our environment.

Most of the patients with bladder cancer seen in our environment presented at the advanced stage of the disease and thus can only receive palliative form of treatment, there is thus need for increased awareness of this disease, improved screening in order to diagnose more patients early.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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