

ORIGINAL PAPER

Pattern of Bladder Cancer at University Teaching Hospital, Lusaka, Zambia in the era of HIV Epidemic

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ABSTRACT

Background: Human Immunodeficiency Virus (HIV) is endemic to Zambia and is associated with changes in the patterns of both AIDS and non- AIDS defining cancers. Bladder cancer is one malignancy that has been noted to increase in the era of HIV/ AIDS epidemic. This study sought to describe the pattern of cancer of the bladder at UTH in the era of HIV/AIDS epidemic in respect with the epidemiological characteristics, prevalence of HIV infection and the histological types of bladder cancer in patients with cancer of the bladder.

Patients and Methods: A prospective cross sectional, hospital based study was performed at the University Teaching Hospital (UTH), Lusaka, Zambia, between November 2009 and November 2010. Patients with bladder cancer who presented to the hospital during this period were recruited and parameters studied included patients demographics, HIV status and pathology of cancer. Data collected was analyzed using SPSS 17.

Results: A total of 53 patients with median age of 57.49 years who had histological confirmed bladder cancer were recruited during this one year period. The male to female ratio was 1.3 to 1. Of the 53 patients, HIV infection was found in six patients (11.3 %). Squamous cell carcinoma was the most common histological type (60.4%) followed by Transitional cell carcinoma (30.2%) and adenocarcinoma was least common type (9.4%). Schistosoma infection was found in 14 patients all had SCC. The study found a statistically significant reduction in the mean age of bladder cancer in HIV infected patients.

Conclusions: Squamous cell carcinoma is still the most common histological type of bladder cancer in Zambia and it's strongly associated with schistosomia infection. Haematuria remains to be the most common presenting symptom in bladder cancer patients.

INTRODUCTION

The United Nations joint programme on AIDS estimated that by the end of 2008, there were 33 million people who were infected with HIV worldwide of which 24.5 million people are in sub-Sahara Africa, making the region the most affected by the epidemic.¹ Despite pioneering efforts to control the epidemic, Zambia in southern Africa has one of the highest HIV/AIDS epidemic with an estimation of 1100000 people living with HIV infection and a prevalence rate of 14.3%.² The number will quite likely increase as access to life extending antiretroviral therapies increases.

The HIV epidemic provides an opportunity to study the risk of cancers in immunosuppressed populations and thus make conclusions on the association of cancer and HIV. Cancer of the urinary bladder is one such cancer which has been noted to have increased in prevalence in the era of HIV epidemic. According to the audit reports of the department of surgery at the University Teaching Hospital, for the year 2007, cancer of the bladder was the leading cause of death among urology patients³. Of the 32 mortalities recorded that year, 20 patients died of cancer of the bladder. Other reports from the same audit show that cancer of the bladder is the most common cause of non elective hospital admission in urology units.

In Zambia, relatively few studies have been done on patterns of cancer among HIV infected patients because both the cancer registry and the histopathological records do not capture the HIV status of patients. Patil et al reviewed histopathological records of cancer at the University Teaching Hospital, Lusaka, Zambia for the

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period of 1980 to 1989 and showed that bladder cancer accounted for 6.3% of adult malignancies ⁴. Bowa et al later reviewed histopathological reports for the period of 1990 to 2005, and noted that although cancer of the bladder was one of the top ten, it accounted for 3.2% of all malignancies ⁵. The Zambia cancer registry on the other hand reports that for the year 2007, cancer of the bladder accounted for 3% of the cancers. This is an underestimation since not all cancers are captured and certain provinces did not report. The above data shows conflicting results on the trends of cancer of the bladder in the light of HIV infection despite the hospital departmental audits reporting an increase in the number of bladder cancers admission and deaths.

Changes have been seen in other parts of Africa that had the same pattern of cancer of the bladder as Zambia. A study in Egypt from the National Cancer Institute of Cairo University, showed a change in pattern over 26 years period from 1980 to 2005 where transitional cell carcinoma was more common than Squamous cell carcinoma in the second half of the study period that corresponded to the HIV era ⁶.

It's therefore imperative that a study was conducted to determine the pattern of bladder cancer in the era of HIV in Zambia a country that initially shared the same histopathological distribution of bladder cancer type as Egypt.

METHODS

The study was a cross sectional survey conducted at the University Teaching Hospital in Lusaka, Zambia. All patients with a diagnosis of cancer of the bladder referred from all the districts of the country during the study period of November 2009 and November 2010 were recruited into the study. Cases were defined as those patients with a histological proven primary cancer of the urinary bladder regardless of the stage of presentation. Convenient sampling was employed were all patients with cancer of the bladder who presented to the urology units during the study period were recruited. The sample size was determined by how many participants presented during the 12 months study duration.

The study used personal interview to collect social-demographic data (age, sex, residence) and presenting symptoms of the patients. Physical findings, laboratory results including HIV test results, cystoscopic findings and histopathological report were entered into the data collection sheet.

Data collected was entered into Excel programme and exported to SPSS version 17 where variable were named recoded and measures and values were assigned. Data analysis was done which included descriptive analysis, cross tabulation, independent sample T test and Fishers test. Chi-square could not be computed because the sample size could not produce five and more figures in all the cells.

ETHICAL CONSIDERATION

Approval was obtained from the University of Zambia Biomedical and Research Ethics committee (UNZAREC). An informed consent was obtained from all the participants, security and confidentiality of all the information obtained was guaranteed and maintained throughout the study duration and after. The study made sure that the participation of participants in the study was purely voluntary and participants were assured that they could withdraw from the study at any time if they felt injured or inconvenienced with no consequence of their treatment.

RESULTS

A total of 53 patients with cancer of the bladder were recruited over the period of one year from November 2009 to November 2010. The youngest was 25 years and the oldest was 80 years. The mean age was found to be 57.49 years. The study showed that cancer of the bladder was more in males than in females with the male to female ratio of 1.3: 1. Of the total of 53 patients, 23 were females and 30 were males. Participants residence was collapsed from the districts into provinces for easy of presentation and analysis. Table 1 shows participants characteristics.

Table 1: Patient social and demographic characteristics

<u>Gender</u>	Mean age	number	Percentage
Total	(57.49)	53	100
Male	(58.93)	30	56.6
Female	(55.61)	23	43.4
<u>Age distribution</u>			
25 -30years		3	5.6
31 -40years		7	13.2
41 -50years		7	13.2
51 -60years		10	18.9
61 -70years		18	34.0
71 years and above		8	15.1
<u>Provincial residence</u>			
Lusaka		18	34
Central		3	5.6
Copperbelt		3	5.6
Southern		6	11.4
Eastern		15	28.3
Western		1	1.9
North - Western		1	1.9
Northern		2	3.8
Luapula		4	7.5

Table 2 shows the prevalence of HIV infection, distribution of different histological subtypes and the prevalence of schistosomia infection isolated in malignant tissues.

Table 2: Distribution of variables among patients

Variable	Mean age	Number of female (%)	Number of Males (%)
HIV status			
Positive (n=6)	50.33	3 (5.7)	3 (5.7)
Negative (n=47)	59.57	20 (37.7)	27(50.9)
Histological subtype			
Adenocarcinoma (n=5)	64.40	2 (3.8)	(5.7)
Transitional cell carcinoma (n=16)	54.47	8 (15.1)	8 (15.1)
Squamous cell carcinoma (n=32)	62.63	13(24.5)	19 (35.8)
Schistosomia infection in SCC (n=32)			
SCC with infection (n=14)	48.14	10	4
SCC without infection (n=18)	59.39	3	15

Table 3 shows the relationship between the histological subtype and HIV infection

Table 3: histological type vs. HIV sero status

HIV sero status	histological type of cancer			Total
	Adenocarcinoma	Squamous cell carcinoma	Transitional cell carcinoma	
Negative	5	27	15	47
Positive	0	5	1	6
Total	5	32	16	53

DISCUSSION

Age distribution of patients

The mean age of patients with bladder cancer in this study was 57.49 years which agrees with a study from Egypt that found that the mean age of bladder cancer cases was 58.34years.⁷ This mean age is less than what is reported in the literature for other parts of the world where Lynch and Cohen reported that the mean age of urothelial carcinoma in USA is 67years for males and 71 years for females.⁸ In this study the mean age in male patients was 58.93 years and for females was 55.61 years. This shows that there is no statistical difference between males to females (t = 0.778, df= 41.184, P = 0.441) The findings

are in contrast to earlier studies in USA where there is a statistical difference in gender for the mean age at the time of diagnosis of bladder cancer.⁸ However the study agrees with another study in Zambia which showed that the peak age of bladder cancer was found to be in the age range of 56 and 65 years.⁵ In this study the peak age for bladder cancer was found to be age ranges of 61 and 70years.

Gender distribution among patients

The study shows there is a male predominance in bladder cancer with a male to female ratio of 1.3: 1. This agrees with other studies within the country and outside the country that the disease is more common in males. Bowa et al found that the male to female ratio among patients with bladder cancer was 2: 1.⁵ Other studies outside the country reports a wide disproportion of 4: 1 ratio.^{6,8} The narrow ratio in this study can be attributed to the fact that in Zambia males and females are equally exposed to the risk factors like schistosomia where both males and females do participate equally in farming although boys are slightly more exposed to swimming in schistosoma infected streams and males smoke more than females. This is in contrast to other countries such as Egypt were males engage in farming in dam areas much more than females hence the ratio is as wide as 4: 1 with male predominance.⁶

Residential distribution of patients

The patients in this study came from all the nine provinces of Zambia although some provinces such as North-Western and Western had only one patient each. Lusaka province had the most patients followed by Eastern province. The high figure recorded from Lusaka and Eastern provinces can be attributed to the accessibility to the main referral hospital, UTH which is located within Lusaka province, while Eastern province has a strongest referral system where patients are provided with transport to reach their referral destination. The presence of St. Francis mission hospital with specialists who are able to diagnose bladder cancer and refer patients makes may contribute to high figures from that province. However the risk factor for most patients which is schistosomia infection was isolated in most patients from Eastern province. Of the total 15 patients from this province, schistosomia infection was isolated in 7 patients. On the other had Lusaka province which had a total of 18 patients, schistosomia infection was only isolated in 4 patients. This agrees with geographical distribution that Eastern province is largely a rural settlement and people are more likely to be engaged in fishing, swimming and other activities that bring them into contact with schistosomia infected water bodies.

HIV prevalence among bladder cancer patients

The prevalence of HIV infection in the patients studied was 11.3% where only six patients out of the 53 were HIV positive. Of the 6 who were HIV positive, only two were diagnosed during the study while the other four were already on HAART. This prevalence of HIV infection is lower than the national prevalence of HIV in Zambia which currently is reported to be 14.3%.² This may suggest that bladder cancer may not be an AIDS defining malignancy. A recent 2008 epidemiologic study using HIV/AIDS Cancer Match Study data reported a lower incidence of bladder cancer in the HIV population as compared to the general population⁹. This low level of HIV prevalence rate agrees with previous studies in the country that bladder cancer was not among the top five cancers at UTH.⁵ In a retrospective study of the pattern of malignancies at UTH from January 1997 to December 2005, it was found that the five most common cancers in males were Kaposi's sarcoma, cancer of the eye, soft tissue sarcoma, prostate cancer and non-Hodgkin's lymphoma. In females the most common cancers were cancer of the cervix, cancer of the eye, breast cancer, Kaposi's sarcoma and non-Hodgkin's lymphoma.

Histological types of bladder cancer

Histopathological examination in this study showed that 60.4% of the cases had SCC, 30.2% had TCC and adenocarcinoma constituted 9.4%. (Table 2). This agrees with the previous studies done in Zambia which showed that SCC is most predominant type of bladder cancer.⁵ Bowa et al found that the histological type of bladder cancer was mainly SCC (46.2%), TCC constituted 23.4% and adenocarcinoma had 22.2%. However this study showed that 2/3 of the cases was SCC as contrasted with the above study of SCC constituting less than half of the cases. The study agrees with some studies in Africa which shows that SCC is the most predominant in Africa.¹⁰ Zarzour et al in a study of muscle invasive bladder cancer in Upper Egypt showed that 67.6% of cases had SCC, 15.4% had TCC.¹⁰ This agrees with the traditional pattern of bladder cancer in Egypt. However a study on the changing patterns of bladder cancer in Egypt over the past 26 years showed that from period of 1990 to 2005 the most common type of bladder cancer was TCC constituting about 73% while SCC decreased from 78% in 1980 to 27% in 2005.⁶ This change in pattern has been attributed to the decline in schistosoma infection in Egypt. This is as a result of control of the parasite in the water bodies and treatment of patients with active schistosoma infection. Zambia is however still paying

the toll of the previously high prevalence of schistosoma infection. The bilharzia control programme was just launched less than six years ago and is still far from controlling the infection in the endemic areas.

This study also showed that there were no statistical association between gender and histological type of bladder cancer ($F=0.525$, $P=0.842$). Of the 30 male patients: 19 had SCC and 8 were TCC. The total of 23 female patients, 13 had SCC and 8 had TCC. This agrees with other report that suggests that there is no association between the type of bladder cancer and gender⁸.

Mean age at first presentation in different histological types

The study showed that among bladder cancer patients that there was no statistical significance in mean age between SCC and TCC. From the study the mean age for SCC was 54.47 ± 15.73 years and for TCC the mean age was found to be 62.63 ± 10.83 years. There was no statistical difference between the two ($t=-1.861$, $df=46$, $P=0.069$). This contrast with a study in Egypt which showed there was a statistical difference between SCC and TCC mean age at the time of diagnosis (58.3 vs. 50.3 years, $P < 0.001$)⁷. The small sample size in our study may account for the difference in results.

The study found interesting results regarding the mean age in patient with SCC. Of the total 32 patients with SCC, the mean age in patients with positive schistosoma infection was 48.14 years and in schistosoma negative SCC the mean age was found to be 59.39 years. This shows that there was a statistical difference in mean age at first diagnosis between schistosoma positive and negative ($P < 0.05$). This shows that schistosoma positive patients presented at a younger age than schistosoma negative bladder cancer (48.14 vs. 59.39 years). This finding agrees with other reports that patients with schistosoma associated bladder cancer presents at a younger age than non schistosoma SCC bladder cancer.¹⁰ Shokeir et al reports that the mean age of patients with bilharzia bladder cancer was 10-20 years lower than in non bilharzia cancer.

Analysis of histological types of bladder cancer type with HIV status

A cross tabulation of histological type against HIV status showed that of the patients who had HIV infection 5/6 had Squamous cell carcinoma and only one had TCC. This may suggest that HIV infection may be associated with SCC which traditionally presents at an earlier age and at

more advanced stage than TCC. That would mean that, the most common diagnosis of hemorrhagic cystitis given to HIV infected patients with haematuria needs to have a cystoscopic evaluation to exclude malignancy before they are diagnosed to have hemorrhagic cystitis which is presumed to be benign as opposed to malignant bladder cancer. The findings in this study contrast with a small retrospective study involving HIV positive patients with bladder cancer. The study showed that the mean age was 55 years and most patients (10/11) had Transitional cell carcinoma and only one had SCC¹¹. However this study agrees with the younger mean age of patients with bladder cancer in HIV positive. In our study the six patients had a mean age of 50.3 years still a younger age compared to the overall mean in bladder cancer patients. However in this study there was no statistical association between sero status and histological type of the bladder cancer (F= 0.971, P=0.812).

The study found no significant existence of co infection of HIV and schistosoma infection. It was found that of the six patients who were HIV positive only 2 had schistosoma infection. These two had SCC type of bladder cancer.

CONCLUSIONS

The Pattern of bladder cancer in Zambia in an era of HIV epidemic has not changed significantly. The disease is still male predominant with a slightly reduced male to female sex ratio and disease peaking in the sixth decade an age younger than the developed countries.

Squamous cell carcinoma has continued to be the most predominant histological type in Zambian patients although there is noticeable increase in the cases of adenocarcinoma. Zambia is still paying the toll of the high prevalence of schistosoma infection especially in the rural areas of the country.

Studies to determine the exact histological features of bladder cancer in HIV infected patients are needed as more people with HIV infection continues to live longer as a result of national wide roll out of anti retroviral treatment in Zambia.

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