ORIGINAL ARTICLE

Efficacy of Urine Cytology in the Diagnosis of Bladder Cancer in Aminu Kano Teaching Hospital: Comparism of Cytology and Histological Findings.

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Abstract

Background: Bladder cancer is a common urologic malignancy worldwide and second most common genitourinary malignancy after prostate cancer. Diagnosis of bladder cancer in developing countries is challenging. Despite the varying results in detection rate of bladder cancer by using the urine cytology, the method can be used in developing countries such as Nigeria, where there are limited diagnostic facilities. **Objective:** The general objective of the study was to determine the efficacy of urine cytology in the diagnosis of bladder cancer, in Aminu Kano Teaching Hospital. The specific objectives were; to determine the sensitivity, specificity and accuracy of urine cytology in the diagnosis of bladder cancer in Aminu Kano Teaching Hospital. **Methodology:** It was a prospective descriptive study of 52 patients who consecutively presented with suspected bladder cancer and were recruited via the Urology outpatient unit and casualty unit of Aminu Kano teaching hospital over a period of one year. On presentation patients with emergencies were resuscitated and evaluated clinically to establish the diagnosis of bladder cancer. Patient who had met the inclusion criteria and consented to the study had urinalysis and urine microscopy culture and sensitivity, abdominopelvic ultrasound scan, electrolyte urea and creatinine and full blood count. All the patients subsequently had fresh voided or catheter urine sample taken immediately for cytological analysis. Cystoscopy was done in the urology theatre under local anaesthesia in most patients with exception of few who had general anaesthesia. The cystoscopic findings were noted and multiple biopsies were taken and sent for histological analysis. **Results:** Of the Fifty two patients reviewed, the mean age was 55.6± 16.3 with male to female ratio of M: F 4.2:1. The overall Sensitivity, Specificity and Accuracy of Urine cytology were 60.4%, 100% and 63.5% respectively. The False negative rate was 39%. Urine cytology was found to be effective in detecting bladder cancer, $p<0.05$). **Conclusion:** Based on the findings from this study, Urine cytology is an effective method for evaluation of patients presenting with features suggestive of bladder cancer. Routine use of urine cytology as the initial test for evaluating patient with suspected bladder cancer is recommended.

Key Words: Efficacy, Urine cytology, Bladder cancer, Diagnosis.

Introduction

Cancer of the urinary bladder is a common urologic malignancy worldwide. It is the 4th to 5th most common cancer in men, and the 8th in women.[1] It is the second most common genitourinary malignancy worldwide after prostate cancer with 260,000 new cases occurring each year in men and 76,000 in women. It affects about 1 in 2,500 people per year throughout the western world. Incidence of bladder cancer is increasing worldwide, estimated to be the 13th cause of cancer related death.[2] It accounts for 5% of all diagnosed cancer in human worldwide and between 5 to 10% in Europe.[1-3]

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Bladder cancer is commonest in the 50 – 70 year age group with mean age of 54.6±16 year.[1,3,4] In the western world, transitional cell carcinoma (TCC) is the commonest, while in developing countries squamous cell carcinoma (SCC) is the most prevalent especially in Egypt where schistosomiasis is endemic.[2,5] Malignant tumours of the bladder have been observed to be quite common in Nigeria, especially in the northern part where schistosomiasis is common.[3,5,16] In Kano, it constituted about 6.4% of all cancers with squamous (53%) and transitional (35%) carcinomas being the most common histological types. Males outnumbered females more than five times (M: F = 5.2:1) presumably because of an increased contact with stagnant water and exposure to smoking and environmental toxins. Cancer of the bladder was most prevalent in the 5th and 6th decades (range of 20 – 82) with a mean age of 48.8 years.[3,7] The prevalence is lower in Zaria with about 3.1%.[6] However in Lagos University Teaching Hospital (LUTH), the south-western part of Nigeria

bladder cancer constitutes about 0.86% of all diagnosed cancers, which is much lower with transitional cell carcinoma being commonest (61.5%).[7] In Enugu the south eastern Nigeria also the commonest type of bladder cancer is Transitional cell carcinoma with about 56.3% and 38.8% Squamous cell carcinoma.[8]

It has been shown that 80-90% of patients with bladder tumours, present with painless hematuria, particularly in people with TCC. Patients with SCC usually present with irritative lower urinary tract symptoms; hematuria comes at later stages of the illness.[9,10]

Diagnosis of bladder cancer in developing countries is challenging, because of lack of modern diagnostic medical equipment in most hospitals. In an ideal setting the diagnosis of bladder cancer involves the use of urine cytology, abdominopelvic ultrasound and urethrocystoscopy and biopsy for histology. In urine cytology, malignant cells can be detected in patients commonly with urothelial cancer. This may be supplemented by the detection of tumour makers in the urine. Ultrasound scan is used as an initial test prior to urethrocystoscopy. Abdominopelvic ultrasound can predict the presence of the lesion, its site and number. It can also detect obstruction along the upper urinary tract and presence of metastatic deposits. Urethrocystoscopy is the cornerstone for the confirmation of the presence of tumour and for a biopsy to be taken for histology. Further radiological investigations such as computed tomography scanning (CT scan) and magnetic resonance imaging (MRI) can be done to evaluate the extent of the disease.

In developing countries however, all of these investigations are not readily available and where available they are expensive and many patients cannot afford them. The accuracy of urine cytology in the diagnosis of bladder cancer depends on the grade of the cancer; it has high sensitivity and specificity in high grade urothelial cancer and low in low grade lesions.[11,12] Other factors that determine the accuracy of urine cytology in diagnosis of bladder cancer are the nature of the urine sample and collection method. Urine cytology is an essential modality for the detection of urothelial neoplasia. It has various indications that generally fall into 3 principal groups: in the evaluation of Patients with genitourinary symptoms, especially hematuria, screening of high risk patients and as a surveillance tool for patients with a history of bladder cancer.[13]

The accuracy of urine cytology in the diagnosis of high-grade urothelial carcinoma (HGUCA) with cytohistologic correlation has been reported to be as high as 98%.[14,15] In contrast, low-grade urothelial neoplastic lesions such as papillary neoplasm of low malignant potential (PUNLMP) and low-grade papillary urothelial carcinoma (LGUCA), has sensitivity and specificity values as low as 8.5% and 50%, respectively.[16] Despite the varying results in detection rate of bladder cancer by using the urine cytology, it is clear that the method can be used in developing countries such as Nigeria, where there are limited diagnostic facilities. It is in this context that this study was carried out to assess the efficacy of urine cytology in diagnosis of bladder cancer at Aminu Kano Teaching Hospital in Kano.

Materials and Methods

It was a descriptive prospective study of fifty two patients conducted at Aminu Kano Teaching Hospital, which is a tertiary health institution situated in the ancient city of Kano, North-western Nigeria.

The inclusion criteria were all new patients with suspected bladder cancer (i.e. presenting with features suggestive of bladder cancer) who presented to the Urology outpatient Clinic and accident and emergency Department within the period of the study, and who consented. The exclusion criteria were all patients who presented with histologically confirmed bladder cancer that had surgery or are on chemotherapy/chemoradiation and all patients who did not consent. Ethical approval was obtained from the research ethics committee of Aminu Kano Teaching Hospital before commencing the study. All patients with suspected bladder cancer that meet the inclusion criteria at presentation to the Urology outpatient clinic were recruited into the study. On presentation, biodata including age, sex, tribe, address, and occupation were obtained. Also a detailed history including symptoms of bladder cancer such as hematuria, necroturia, lower urinary tracts symptoms were obtained. History of risk factors such as childhood terminal hematuria, exposure to chemicals and drugs (cyclophosphomide and phenacetin) and cigarette smoking were obtained. Others were general features of malignancy such as anorexia weight loss and complications of bladder cancer such as uraemia etc. All other aspects of the history were covered appropriately. All patients were also examined generally looking for features of malignancy and complications of bladder cancer such as wasting, pallor, facial puffiness, pedal oedema and scratch marks. The pulse rate, respiratory rate, body temperature and blood pressure were obtained. Abdomen was examined for suprapubic or loin

swelling, and masses. Other aspects of abdominal examination including rectal examination to look for mass at the region of the bladder were done. Other systems such as chest and central nervous systems were examined for extent of the malignancy. Patients who presented with emergency such as anemia, uraemia, clot retention, and urosepsis were admitted for resuscitation. Urgent pack cell volume, full blood count and serum electrolyte urea and creatinine were done. Patients were resuscitated with blood transfusion, haemodialysis, and urethral catheterization with irrigation, rehydration and antibiotics depending on patient's emergency condition. Following stabilization of patients, fresh urine sample was collected for cytology, and immediately taken to Histopathology department.

Each of the patients had abdominopelvic ultrasound scan, CT urography, chest x-ray, and liver function test, depending on the patient's presentation. Then urinalysis and urine microscopy culture and sensitivity was done to rule out infection, and subsequently urethrocystoscopy and biopsy for histological diagnosis was done.

The urethrocystoscopy was done under local anaesthesia in most of the patients with exception of few who had general anaesthesia due to low pain threshold. The cystoscopic findings were noted and any suspected bladder lesions were biopsied. Data collected was entered into the proforma and analysed.

Results

Sociodemographic Characteristics of the Patients

In the 52 patients reviewed, the age range was 25 to 90 years with mean age of 55.6± 16.3. The commonest age group was 51 – 60years accounting for about 30.8% (n=16). Male patients predominate with male to female ratio of M: F 4.2:1. Islam and Hausa were the predominant religion and tribe among the patients respectively. Most of the patients were from Kano state. Farming is the predominant occupation among the respondents, and most of them were irrigation farmers.

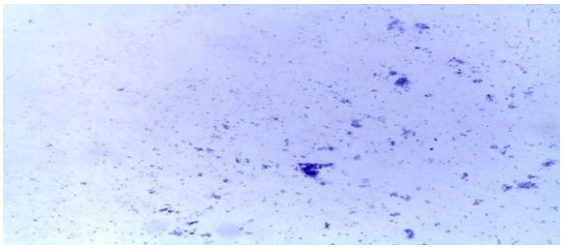

Figure 1: Cytological smear from one of the urine sample, (Diff quick stain, x4)

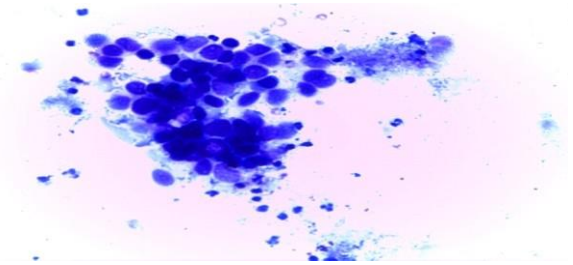

Figure 2: Cytological smear from one of the urine samples, (Diff quick stain, x40) .

Pathological Characteristics of the Tumour

Out of the 52 patients studied 92.3% (n = 48) were confirmed to have malignancy by histology, the remaining 7.7% (n = 4) were non-malignant, and were found to be schistosomiasis on histology. Majority of the patients 27 (56%) had positive urine cytology while the rest were negative The histological types of cancer recorded were transitional cell carcinoma in 23 (47.9%) Squamous cell carcinoma 22 (45.8%) and adenocarcinoma in 3 (6.3%).

The predominant grade was high grade tumours in 33 (69%) while the rest 15 (34%) were of low grade type.

Bivariate Analyses

Relationship between urine cytology and histology

The Sensitivity and specificity of Urine cytology in detecting malignant cells in patients with Bladder cancer were determined using a contingency table. The positive predictive value, negative predictive value, false negative rate and accuracy of urine cytology in detecting malignant cells in patients with bladder cancer were also determined. The correlation obtained (r = 0.324), using Pearson two tailed correlation analysis was linear. See table 6.3 below.

Sensitivity of Urine Cytology = 60.4%
Specificity of Urine Cytology = 100%
Positive predictive value of Urine Cytology = 100%
Negative predictive value of Urine Cytology = 17.4%
False Negative rate of Urine Cytology = 39.0%
Accuracy of Urine Cytology = 64%.

Relationship between urine cytology and high grade bladder cancer.

The Sensitivity and specificity of Urine cytology in detecting malignant cells in a high grade tumour were determined using a contingency table. The positive predictive value, negative predictive value, false negative rate and accuracy of urine cytology in detecting high grade bladder cancer were also obtained.

Sensitivity of Urine Cytology for high grade Cancer = 88%
Specificity of Urine Cytology for high grade Cancer = 100%
Positive predictive value of Urine Cytology for high grade Cancer = 100%
Negative predictive value of Urine Cytology for high grade Cancer = 79%
False Negative rate of Urine Cytology for high grade Cancer = 12%
Accuracy of Urine Cytology for high grade Cancer = 92%.

Discussion

Cytological examination of urine for malignant cells is a useful adjunct in the evaluation of bladder cancer. A positive urinary cytology is helpful in diagnosing bladder malignancies; however, a negative report does not exclude cancer, especially of a low-grade. This study was done to determine the efficacy of urine cytology in the diagnosis of bladder cancer. Fifty two patients with suspected bladder cancer had urine cytology and subsequently had cystoscopy and biopsy for histology. The age range of the patients in this study was 25-90 years with the mean age of 55.6±16.3 years. These findings were similar to that of Sule et al. In Kano with a mean of 51.2±11.74 years.[17] Similarly Mahmoud et al. in Saudi Arabia found mean age of 54.6±16 years, in their study.[4] In this study male patients accounted for 82% and a male to female ratio of M: F 4.2:1. It was similar to the findings of Alhassan et al.[18] in Kano, who also found a male preponderance with male to female ratio of M: F 5:1. Anunobi et al.[7] In Lagos found the sex distribution of male to female ratio M: F 4.6:1. The most common presenting symptom in our patients was hematuria which occurs in all the 52 patients, then followed by necroturia and lower urinary tracts symptoms especially irritative. Masumbuko et al.[9] and Desouza et al.[10] also observed hematuria as the commonest presenting symptom in their various studies. Waihenya et al.[19] found similar findings in their study with hematuria occurring in 51 out 52 patients (98.1%). The predominant histological type of the bladder cancer was transitional cell carcinoma, which accounted for 47.9%, followed by squamous cell carcinoma with 45.8% and adenocarcinoma with 6.3%. This is similar to recent studies by Sule et al [20] in Kano, Khalaf et al.[21] in Egypt and Ngowi et al.[22] in Tanzania, where gradual changing trend from Squamous to Transitional cell carcinoma were observed even in the schistosomiasis endemic area, unlike the earlier studies over a decade ago which revealed squamous cell carcinoma as the common histological type.[3,5] The relative decline of squamous carcinoma in these series is probably associated with a reduction in the proportion of bladder cancers with schistosoma ova, and early diagnosis and treatment of bladder schistosomiasis.[20]

n this study, the Sensitivity of urine cytology in detecting malignant cells in patients with Bladder cancer was 60.4% when compared to Histology, the Specificity was 100%. This is similar to a study by Bastacky et al.[14] in a multicenter study from United State which reported overall sensitivity of 64% and specificity of 95%; and Helmy et al.[23] in Egypt who reported Sensitivity of 53.4% and Specificity of 94.7%. However, Garcia et al.[15] revealed a higher

sensitivity of 97%, in their study which compared cytology with biopsy. This is probably because the study was purely on transitional cell carcinoma which has a higher sensitivity when compared with other histological types.Sanjay et al.[24] in United Kingdom had different findings, with lower sensitivity of 44% and specificity of 95%.The reason for the lower result was because their study was mainly on low grade and non-invasive cancers for which urine cytology has lower sensitivity. This study also revealed that urine cytology has high sensitivity in detecting high grade tumour, with sensitivity of 0 – 88% from the lowest to the highest grade. Hence the ability of urine cytology to detect bladder tumour increases with increasing grade of the tumour. Bolenz et al.[25] observed similar increasing sensitivity as the grade of the tumour increases; they found sensitivity of 16.7 – 62.2%.

In the same vein, Planz et al.[26] in their study to determine the role urinary cytology for detection of bladder cancer, observed overall sensitivity of 38.0% and specificity of 98.3% with positive predictive value and negative predictive value of 90.6% and 78.6% respectively. They also observed increasing sensitivity from 52.2 – 78.3% as the grade of the tumour increases. Karakiewics et al.[27] in a large multi-institutional cohort from four continents to assess the accuracy of urine cytology in predicting recurrence of transitional cell carcinoma of the bladder observed increasing sensitivity from 38 – 65% as the grade of the tumour increases. Niedworok et al.[28] in Germany conducted a three nationwide cytology survey and observed a very high sensitivity and specificity ranging from 81.34 – 87.08% and 83.5 – 89.15% respectively in high grade urothelial carcinoma.

Faysal et al.[29] and Tschirdewahn et al.[30] also observed a similar increasing sensitivity as the grade of the tumour increases, their findings are sensitivity of 48 – 84% and 85 – 95% respectively.

Conclusion

From this study, urine cytology was found to be effective in the diagnosis of bladder cancer among most patients presenting to Aminu Kano Teaching Hospital, with features suggestive of bladder cancer. Urine cytology was found to be more valuable in the diagnosis of TCC of the bladder and even more in those patients with high grade TCC of the bladder. Gradually changing pattern of bladder cancer histological variety was observed with TCC becoming more prevalent than SCC among our patients. However most patients with bladder cancer present with advance disease hence only palliative treatment could be offered.

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