Original Article

Urine Cytology as Seen in Uyo, Nigeria: How Relevant Is It to Medical Practice?

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Abstract

Aim: The aim of this study is to know the pattern of urine cytology (UC) requests seen in Uyo and how relevant they were to the management of the patients. **Materials and Methods:** This retrospective study was carried out in the Department of Pathology, University of Uyo Teaching Hospital. The extracted data from the cytology registers were analyzed using the Statistical Package for the Social Sciences version 17. **Results:** A total of 46 patients did UC during the period. The patients were aged between 21 years and 90 years, with a mean age of 56.89 ± 14.65. Thirty (67.4%) were male. The age group of 60–69 years accounted for most cases (37.8%). Suspicion of bladder cancer was the most common indication as it was seen in 28.9% (n = 13) of cases. Thirty-eight cases (84.4%) were referred from urology clinic, 2 each (4.4%) from general outpatient clinic, general surgery clinic, and from gynecology clinic. In 44.4% (n = 20) of cases, the cytological diagnosis was inflammatory smear, while the UC was normal in 24.4% (n = 11) cases. Malignant cells were seen in 11.1% of (n = 5) cases. Of the 13 cases that the indication was suspected bladder cancer, only four were positive for malignant cells and one was suspicious on UC. No malignant cell or suspicious cell was seen in any of the UC specimens from patients that had prostate cancer, lower urinary tract outlet obstruction with hematuria due to prostatic enlargement. **Conclusion:** UC should not be requested for in prostatic diseases since the reports are always negative or at most inflammatory. The department should start using The Paris System of UC reporting to assist the managing physician/surgeon to take the best decision.

Keywords: *Bladder cancer, malignant cells, urine cytology, urology clinic*

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Introduction

Urine cytology (UC) is the microscopic evaluation of the shed transitional (urothelial) epithelial lining of the urinary tract either in voided urine or following bladder washing (irrigation). Although an old procedure with doubts on its specificity and sensitivity, some surgeons and physicians routinely request and make the use of UC in the diagnosis, workup, and follow-up of patients.[1] UC is requested for in the following conditions: detection of bladder tumors associated with extensive chronic inflammation, in which the biopsy may be negative because of sampling errors, carcinomas *in situ* of the bladder, carcinomas hidden in bladder diverticulum, and in situations when cystoscopy is equivocal for cancer. Other indications for UC are during the evaluation of patients for hematuria and other genitourinary symptoms and as a surveillance tool for patients with a history of cancer.[1-3] The advantages of UC are its minimal invasiveness or noninvasiveness of the procedure (which makes it safe), quick (rapid) reports, affordability, and its role as an adjunct to radiographic and endoscopic evaluation.[3] Its major limitation is the varied sensitivity and specificity which fluctuates between 15% and 90% for sensitivity and

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80%–100% for specificity and depends on the urine collection method and tumor grade.[4-6] Other limitations are the lack of standardized diagnostic criteria and wide interobserver variability (which is dependent on the experience of the cytopathologist). Furthermore, in some situations, the microscopic images may not be a perfect reflection of the biologic behavior of the tumor due to factors such as inflammation, degenerative changes, instrumentation, and lithiasis. UC does not give information about cancer location.[3-8] Following a literature search, only one study on UC has been done in Nigeria, while numerous studies on UC has been done in various countries.[1,3-11]

The aim of this study is to review all the UC seen in our institution, to know the pattern and how relevant (if any) it is to the patient management.

Materials and Methods

This retrospective study was carried out in the Department of Pathology, University of Uyo Teaching Hospital (UUTH) from January 1, 2006, to December 31, 2017. The patients were mainly referred from urology clinic, general outpatient's clinic and from gynecology clinic of UUTH. Early morning urine specimens were collected, centrifuged, and four slides were prepared for each case from the sediments. Two of the slides were stained with May-Grünwald-Giemsa stain and the other two stained with Papanicolaou stain. All the stained slides were evaluated and correlated with their corresponding request cards. Information derived from the request cards includes age, sex, clinical history, and clinical diagnosis. Cytological diagnosis was made by consultants and consultants' peer group review based on cytopathological details of slides. The extracted data from the cytology registers were analyzed using the Statistical Package for the Social Sciences version 17 incorporated Chicago, Illionois, USA.

Results

A total of 46 patients did UC during the period. One was excluded from the study because of incomplete demographic information. The patients were aged between 21 and 90 years, with a mean age of 56.89 ± 14.65. Thirty (67.4%) males and 15 (32.6%) females were involved in a male-to-female ratio of 2:1. Age group of 60–69 years accounted for most cases (37.8%), distantly followed by the age group of 50–59 years and 40–49 years (each accounting for 15.6%), as shown in Table 1.

The minimum quantity of urine received was 4.2 ml and the maximum received was 120 ml with a mean quantity of 24.09 ± 24.90.

Table 2 shows the various indications of UC. Suspicion of bladder cancer was the most common indication as seen in 28.9% (n = 13) of cases.

Thirty-eight cases (84.4%) were referred from urology clinic, 2 each (4.4%) from general outpatient clinic, general surgery clinic, and from gynecology clinic. In a case, the referring clinic was not indicated, as shown in Table 3.

In 44.4% (n = 20) of cases, the cytological diagnosis was inflammatory smear, while the UC was normal in 24.4% (n = 11) cases. Malignant cells were seen in 11.1% (n = 5) cases, as shown in Table 4. Of the 13 cases that the indication was suspected bladder cancer, only 4 were positive for malignant cells and 1 was suspicious on UC, as shown in Table 5. There was no association between the clinical indication and UC diagnoses. No malignant cell or suspicious cell was seen in any of the UC specimens from patients that had prostate cancer or lower urinary outlet

Table 1: Age and sex distribution of cases

Age group	Male	Female	Total	Percentage
20-29	0	2	2	4.4
30-39	2	3	5	11.1
40-49	3	4	7	15.6
50-59	6	1	7	15.6
60-69	13	4	17	37.8
70-79	4	1	5	11.1
80-89	1	0	1	2.2
≥90	1	0	1	2.2
Total	30	15	45	100

Table 2: Indications for urine cytology

Indication	Frequency (%)
Bladder cancer	13 (28.9)
CAP	8 (17.8)
LUTO due to BPH with hematuria	8 (17.8)
Renal mass	2 (4.4)
Cancer of cervix	2 (4.4)
Others	6 (13.3)
Not indicated	6 (13.3)

Others include: A case each of cystitis, bladder stone, ovarian cancer, varicocele, urinary tract infection and lower urinary tract obstruction in a female. BPH: Benign prostatic hyperplasia, LUTO: Lower urinary tract obstruction, CAP: Prostate cancer

Table 3: Various referring clinics

Clinic	Frequency (%)
Urology out patient's clinic	38 (84.4)
General surgery out patient's clinic	2 (4.4)
Gynecology clinic	2 (4.4)
Medical out patients clinic	2 (4.4)
Not indicated	1 (2.2)

obstruction with hematuria due to benign prostatic enlargement.

Discussion

For proper diagnosis and management of urinary tract pathologies (especially bladder pathologies), a tripod of cystoscopy, biopsy and UC is needed, with UC being the quickest to do. Although previous studies have argued in favor of or against the usefulness of UC, especially in respect to its low sensitivity, nondefinitive nature of its diagnoses, high cost, and the need to always follow-up diagnosis with cystoscopy and biopsy, in our setting, it is still useful considering its affordability (less than 7 dollars), absence of general population health insurance coverage, and relative high cost of cystoscopy (100 dollars).[1,3-11]

The indications for UC in the index study are wide and nonspecific, similar to the study in Sokoto, Nigeria, and Bengal, India.[9,10] This is different from more specific bladder associated hematuria which was the main indication in Jeddah, Saudi Arabia, Midland, United Kingdom, and the Florida, United States of America.[1,6,11] The reason for the varied nonselective indications is due to the lack of other diagnostic aids. Suspicion or monitoring of bladder cancer is the main indication of UC, and however in Uyo, where this study was done, bladder cancer has been observed to be a rare tumor such that in a previous Uyo cancer study, it was not listed.[12] This may be the reason for the small sample size.

Globally, men are three to four times more likely to develop bladder cancer than women mainly as a result of differential exposure to carcinogens (i.e., tobacco and chemicals) as well due to reflecting genetic, anatomical, hormonal, societal, and environmental factors.[13] Males in the index study, twice outnumbered females, just like the observations in the studies by Alameddine and Nassir, Abdulwahab-Ahmed *et al*. and Manna *et al*.[1,9,10] The male preponderance in this study is also because a significant number of patients sent for UC by the surgeons were males suspected of having cancer of the prostate or lower urinary tract obstruction with hematuria due to benign prostatic enlargement.

Before the publication of The Paris System (TPS) in 2016, there was no universally accepted and utilized system for reporting UC.[5] Different studies used different nomenclatures for their UC diagnosis and reporting, with the main emphasis being informing the requesting surgeon/physician if the UC result was normal (negative for malignant cell), atypical, suspicious, or malignant. Few other studies also used terminologies such as hemorrhagic smear, acellular smear, inflammatory nonspecific, suppurative inflammatory, and degenerative smear. This lack of uniformity and diagnostic criteria in reporting UC makes comparisons between studies on this same topic to be difficult or ambiguous.[14]

Inflammatory smear was the most common diagnosis made in this study and this may have contributed to the lower number of positive malignant smears because inflammation, degenerative changes, instrumentation effect, and lithiasis are known factors that limit the effectiveness and quality of UC reports.[15] Inflammation can also be a cause of false-positive UC report.[3]

Normal (negative for malignant cell) UC reports accounted for 24.4% of cases seen. This is less than observations in previous studies which reported a range 44.6%–72%.[3,9-11] Páez *et al*. in their study observed that negative for malignant cell smears does not exclude malignancy.[16] Hence, in situations where there is a strong suspicion of bladder cancer, other modalities should be used.

The malignant smears on UC in this study had increased nucleocytoplasmic ratios, hyperchromatic nuclei with irregular margins, coarse chromatin, and prominent

Table 4: Cytopathological diagnosis of urine cytology

Cytologic diagnosis	Frequency (%)
Inflammation	20 (44.4)
Normal (negative for malignancy)	5 (11.1)
Malignant	5 (11.1)
Suspicious	3 (6.7)
Accellular	3 (6.7)
Inadequate	3 (6.7)
Total	45 (100)

Table 5: Comparison of the indications to the cytologic diagnoses

Indications (n=39)	Cytologic diagnoses						
	Inflammation	Malignant	Inadequate	Acellular	Normal	Suspicious	Total, n (%)
Bladder cancer	4	4	-	1	3	1	13 (28.9)
CAP	4	-	-	1	3	-	8 (17.8)
LUTO due to BPH with hematuria	6	-	2	-	-	-	8 (17.8)
Others	5	-	-	1	3	1	10 (22.2)

P=0.661. BPH: Benign prostatic hyperplasia, LUTO: Lower urinary tract obstruction, CAP: Prostate cancer

nucleoli. These same features were seen on the cases reported as suspicious (only that they abnormal urothelial cells were very few in number). The index rate of 11.1% is slightly higher than 10.1% reported in Sokoto which has a similar study pattern to the current study.[9] The observed rates in Jeddah, Saudi Arabia (2.1%), Florida, USA (2%), South India (9.5%), and Bengal, India (25%) may be due to the fact that the patient selection, methodology, and aim of the authors were different from ours.[1,3,10,11] Studies have shown that a significant number of UC smears reported as normal (negative for malignant cell) in suspected bladder cancer cases were actually due to low-grade urothelial carcinoma (LGUC) which are by far the most common urothelial neoplasm. They are usually mistakenly reported as normal because they are well differentiated and look like normal urothelial cells (having cellular cohesiveness and lack of nuclear atypia/dysplasia) when shaded in the urine. Hence, this is why it is generally said that UC has low sensitivity (especially in identifying LGUC) and high specificity (ideal in recognizing high-grade urothelial carcinoma [HGUC]).[5-7,11,14] A diagnostic aid is the understanding that the higher the grade of the tumor, the more accurate the diagnosis will be.[17]

The limitations of this study include the small sample size, its retrospective nature and the non-availability of cystoscopic findings (in the very few patients that had it). Other limitations were lack of histologic correlation, lack of follow-up of the patients, and inability to grade the malignant smears into LGUC (associated with good prognosis) and HGUC (which has potential for recurrence, invasion, metastases, and high morbidity/mortality).

Conclusion

Since cystoscopy and biopsy combined are expensive compared to UC in our environment, we encourage urologists and other physicians to still send urine specimens for cytology using it as a screening test (for suspected bladder cancer cases) since its usefulness is known and proven. We equally advise them to request for UC in prostatic diseases with caution, since the reports are always negative or at most inflammatory. The department will henceforth use TPS of UC reporting to assist the managing physician/surgeon and by extension the patient.

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Conflicts of interest

There are no conflicts of interest.

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