

## Histopathologic Patterns of Urological Malignancies in Calabar, South-Southern Nigeria: A Ten-Year Review

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### Authors' contributions

This work was carried out in collaboration between all authors. Authors EMI and IAEB designed the study and performed the statistical analysis. Author EMI wrote the protocol and the first draft of the manuscript. Authors EEI, GEE and FOO managed the analyses of the study. Authors EMI, AE and PDE managed the literature searches. All authors read and approved the final manuscript.

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### ABSTRACT

**Background:** Malignant diseases have become more prominent in Nigeria over the past years with urological malignancies contributing significantly to cancer related morbidity and mortality. Cancers of the prostate, bladder, kidney, testis and penis are documented as the most common group of non-cutaneous cancers. This study was carried out to document the pattern and distribution of urological malignancies seen in a tertiary hospital in Calabar, South-southern Nigeria over a 10-year period.

**Materials and Methods:** This was a retrospective study carried out in the Department of Urology, University of Calabar Teaching Hospital, Nigeria. Cases of all pathologically proven urological malignancies managed between January 2006 and December 2015 were included. Data were retrieved from patients' case notes, operation registers and histopathology records. The histological slides of all cases were retrieved and reviewed. Patients' demographic data, tumour

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site, histologic diagnoses as well as pathologic grades of malignancies were extracted and analysed.

**Results:** A total of 617 cases of urological malignancies were included in the study over the 10 years under review, comprising of 598 (96.9%) males and 19 (3.1%) females giving a male: female ratio of 31.5:1. There were 600 adults (97.2%) and 17 children (2.8%). The median age was 43 years with range of 1-100 years. The frequency of urological cancers showed prostate cancer to be the most common urologic cancer as follows: Prostate cancer constituted 564 (91.4%), Kidneys 27 (4.4%), Urinary bladder 9 (1.5%), Testis 8 (1.3%), Scrotum 5 (0.8%), Penis 2 (0.3%) and Urethra 2 (0.3%). The most common histologic type of prostate cancer was adenocarcinoma with Gleason Grade III being the commonest grade. Out of the 17 childhood urological malignancies recorded, 13(76.47%) were kidney malignancies, 3 (17.65%) were testicular malignancies and 1 (5.88%) was bladder malignancy.

**Conclusion:** Prostate cancer is by far the commonest urological malignancy, with renal cancer being a distant second in Calabar, ahead of bladder cancers. Childhood urological malignancies in Calabar are predominantly nephroblastomas. The need for increased effort in creating awareness about prostate cancer and for routine screening is reiterated.

*Keywords: Calabar; histopathologic patterns; urological malignancies.*

## 1. INTRODUCTION

Urological malignancies contribute significantly to cancer related morbidity and mortality in Nigeria and worldwide. Several studies carried out in Nigeria have shown urological malignancies to be on the increase in various parts of the country with prostate cancer being the commonest cancer affecting men [1–4]. Cancers of the prostate, bladder, kidney, testis and penis are documented to be the most common group of non-cutaneous cancers in the UK with more than 58000 new cases being diagnosed in 2008 alone. Urological malignancies also have one of the highest mortality rates of any cancer accounting for nearly 20000 deaths in 2009 [5]. Data from the office of National Statistics, England and Wales documented in 2000 and 2001 revealed that these cancers account for 16.5% of all new cases of cancer and 11.7% of cancer deaths [6,7].

Prostate cancer is the most common cancer among men, accounting for 29% of all cancers in men and is the second highest cause of cancer death among men of all races [8,9]. The specific cause of prostate cancer is not known, but several risk factors have been identified. These include advancing age, the male hormone-testosterone and its derivatives, race, family history and diet (low vegetable, high fat and red meat intake) [10,11]. Kidney cancer is the seventh most common cancer in men and the ninth most common in women [12]. Several risk factors have been well-established for renal cancer, including tobacco use, obesity, and hypertension, however the associations and

mechanisms are not well elucidated [13–17]. The incidence of bladder cancers has continued to rise worldwide with 53,000 new cases diagnosed in the USA in 1996 and claims approximately 5000 lives in the UK annually [5,18]. Aetiological factors associated with its development include cigarette smoking, occupational exposures to chemicals like benzene and 4-aminobiphenyl and Schistosomal infection [18–20]. This study was carried out to document the pattern and distribution of urological malignancies seen at the University of Calabar Teaching Hospital, Calabar, South-southern Nigeria over a 10-year period. Several studies from Calabar have been published on individual urological malignancies but this is a comprehensive study of all urological malignancies seen over this period.

## 2. MATERIALS AND METHODS

This was a single institutional retrospective analysis of all pathologically proven urological malignancies seen at the University of Calabar Teaching Hospital, Nigeria from January 2006 to December 2015. Records of all patients with histological diagnosis of urological cancers were retrieved from patients' case notes, operation registers and histopathology records. The histological slides of all cases were retrieved and reviewed. All specimen had previously been fixed in 10% formalin and embedded in paraffin wax. Five-micrometer thick sections were cut using a rotary microtome and slides prepared therefrom. The prepared slides were subsequently stained with haematoxylin and eosin (H&E), covered with a glass coverslip and viewed under light

microscopy. Classification of malignancies was based on the World Health Organization (WHO) classification of tumours. Patients' demographic data, tumour site and histologic diagnoses were extracted and data obtained were analysed using SPSS (Statistical Package for Social Sciences) version 20.0.

### 3. RESULTS

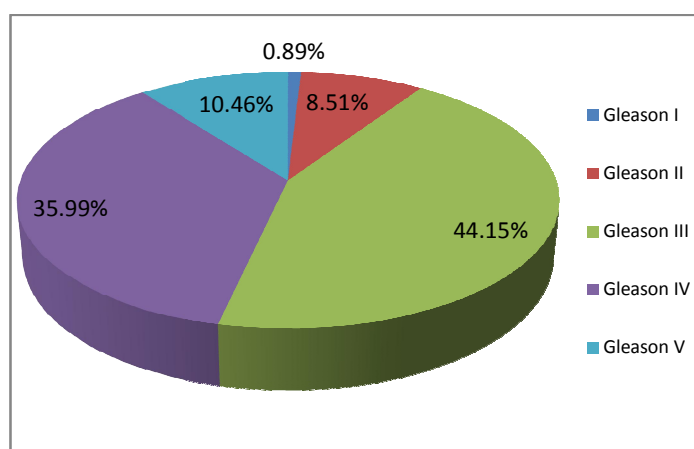
A total of 617 cases of urological malignancies were included in the study over the 10 years under review. It comprised of 598 (96.9%) males and 19 (3.1%) females giving a male: female ratio of 31.5:1. There were 600 adults (97.2%) and 17 children (2.8%). The median age was 43

years with range of 1 to 100 years. Prostate cancer was seen in 564 patients (91.41%), renal malignancies in 27 (4.38%), cancer of the urinary bladder in 9 (1.46%), testicular cancers in 8 (1.30%), scrotal cancer in 5 (0.81%), cancer of the penis in 2 (0.32%) and urethral cancers in 2 patients (0.32%) (Table 1).

Adenocarcinoma was the most common histologic type of prostate cancer (99.1%) with only one case of urothelial cancer recorded. The kidney cancers were mostly renal carcinoma, seen mostly in the adult population closely followed by nephroblastoma, which were all seen in children. Bladder cancers were mostly of the urothelial variety (Details in Table 2).

**Table 1. Distribution of urological malignancies according to anatomic site, sex and maturity**

Anatomic Site	Male	Female	Total	Adult	Children	Total
<b>Prostate</b>	564	0	564	564	0	<b>564</b>
%	91.41	0.00		91.41	0.00	<b>91.41</b>
<b>Kidney</b>	13	14	27	14	13	<b>27</b>
%	2.11	2.34		2.27	2.11	<b>4.38</b>
<b>Testis</b>	8	0	8	5	3	<b>8</b>
%	1.30	0.00		0.81	0.49	<b>1.30</b>
<b>Scrotum</b>	5	0	5	5	0	<b>5</b>
%	0.81	0.00		0.81	0.00	<b>0.81</b>
<b>Urinary Bladder</b>	5	4	9	8	1	<b>9</b>
%	0.81	0.67		1.30	0.16	<b>1.46</b>
<b>Urethra</b>	1	1	2	2	0	<b>2</b>
%	0.16	0.17		0.32	0.00	<b>0.32</b>
<b>Penis</b>	2	0	2	2	0	<b>2</b>
%	0.32	0.00		0.32	0.00	<b>0.32</b>
<b>Total</b>	598	19	617	600	17	<b>617</b>
<b>% Total</b>	<b>96.92</b>	<b>3.08</b>	<b>100.00</b>	<b>97.24</b>	<b>2.76</b>	<b>100.00</b>



**Fig. 1. Histologic Grades of Prostate Adenocarcinoma in the patients**

**Table 2. Histologic types of the various malignancies**

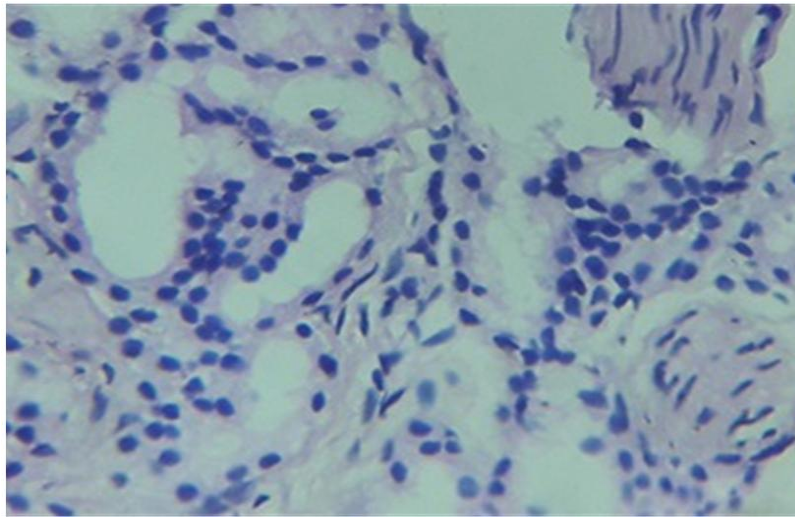
	<b>Histologic Type</b>	<b>Frequency</b>	<b>Percent</b>
<b>Prostate</b>	Adenocarcinoma	563	99.82
	Urothelial carcinoma	1	0.18
	<b>Total</b>	<b>564</b>	<b>100.00</b>
<b>Bladder</b>	Urothelial Carcinoma	6	66.67
	Nephroblastoma	1	11.11
	Pleomorphic Sarcoma	1	11.11
	Adenocarcinoma	1	11.11
	<b>Total</b>	<b>9</b>	<b>100.0</b>
<b>Renal</b>	Clear cell renal cell carcinoma	8	29.64
	Papillary renal cell carcinoma	6	22.22
	Nephroblastoma	11	40.74
	Urothelial Carcinoma	1	3.70
	Embryonal Tumor	1	3.70
	<b>Total</b>	<b>27</b>	<b>100.00</b>
<b>Testes</b>	Seminoma	5	62.50
	Sertoli cell	1	12.50
	Granulosa cell	1	12.50
	Rhabdomyosarcoma	1	12.50
	<b>Total</b>	<b>8</b>	<b>100.00</b>
<b>Scrotum</b>	Kaposi Sarcoma	2	40.00
	Squamous cell Carcinoma	1	20.00
	Angioleiomyoma	1	20.00
	Malignant melanoma	1	20.00
	<b>Total</b>	<b>5</b>	<b>100.00</b>
<b>Urethra</b>	Papillary transitional cell carcinoma	1	50.00
	Adenocarcinoma	1	50.00
	<b>Total</b>	<b>2</b>	<b>100.00</b>
<b>Penis</b>	Kaposi Sarcoma	1	50.00
	Condylomatous Squamous cell carcinoma	1	50.00
	<b>Total</b>	<b>2</b>	<b>100.00</b>

**Table 3. Distribution of childhood urological cancers**

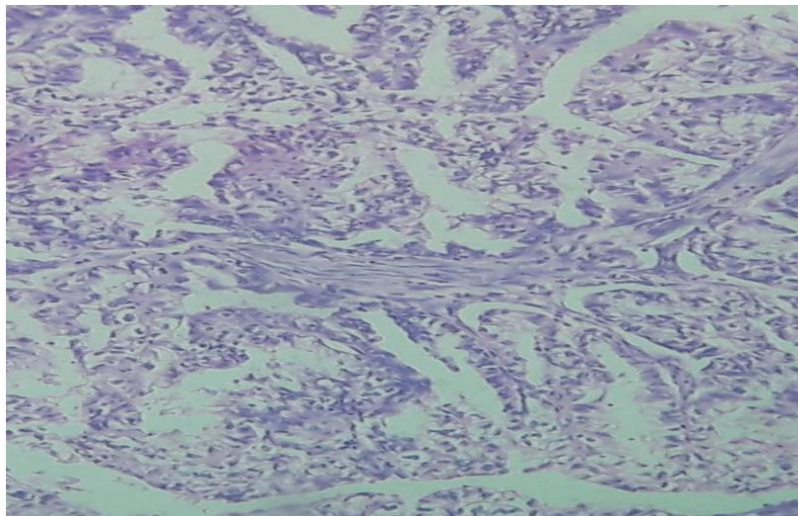
<b>Malignancy</b>	<b>Gender</b>		<b>Total</b>
	<b>Male</b>	<b>Female</b>	
<b>Kidney</b>			
Nephroblastoma	6	5	<b>11</b>
Adenocarcinoma	1	0	<b>1</b>
Embryonal	1	0	<b>1</b>
<b>Testes</b>			
Rhabdomyosarcoma	1	0	<b>1</b>
Seminoma	2	0	<b>2</b>
<b>Bladder</b>			
Nephroblastoma	0	1	<b>1</b>
<b>Total</b>	<b>11</b>	<b>6</b>	<b>17</b>

**Table 4. Relationship between Age and Gleason Grades in patients with Prostate Adenocarcinoma**

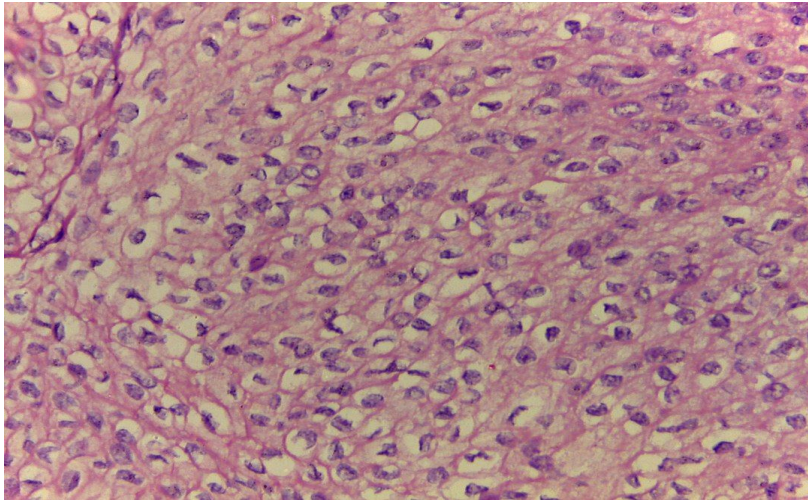
Age range (Years)	Number of patients					Total
	Gleason Grade 1	Gleason Grade 2	Gleason Grade 3	Gleason Grade 4	Gleason Grade 5	
30-39	0	0	0	0	1	1
40-49	0	0	5	5	1	11
50-59	0	8	37	42	17	104
60-69	2	16	99	78	18	213
70-79	2	17	67	51	16	153
80-89	1	3	25	24	6	59
90-99	0	4	16	1	0	21
≥ 100	0	0	0	1	0	1
<b>Total</b>	<b>5</b>	<b>48</b>	<b>249</b>	<b>202</b>	<b>59</b>	<b>563</b>



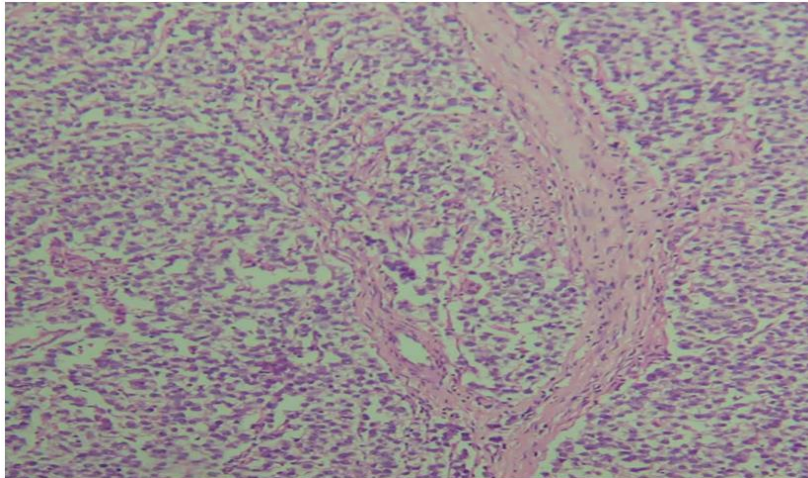
**Fig. 2. Adenocarcinoma of the prostate (H&E x100)**



**Fig. 3. Papillary renal cell carcinoma of the kidney (H&E x40)**



**Fig. 4. Urothelial carcinoma of the bladder (H&E x100)**



**Fig. 5. Seminoma of the testis (H&E x 40)**

Out of the 17 childhood urological malignancies recorded, 13(76.47%) were kidney malignancies, 11 of which were nephroblastomas. Three cases (17.65%) of testicular and 1 case (5.88%) of bladder malignancy respectively were recorded (Details in Table 3).

Gleason grade III (44.15%) was the most common grade of prostate adenocarcinoma recorded followed by Gleason IV (35.99%) and distantly followed by Gleason V (10.46%). In relating age with Gleason Grade, the single patient diagnosed within the age group 30-39 years had Gleason grade of V, 44 out of 104 patients in the age group 50-59 years had Gleason Grade IV while 99 out of 213 patients within the age group 60-69 years had Gleason Grade III (Details in Fig. 1 and Table 4).

Figs. 2 - 5 show photomicrographs of prostate adenocarcinoma, papillary renal cell carcinoma of the kidney, urothelial carcinoma of the bladder and seminoma of the testis respectively.

#### **4. DISCUSSION**

The frequency of urological cancers in this study has shown that prostate cancer is by far the commonest urological malignancy in Calabar with 564 patients (91.41%). This has further reiterated the findings from an earlier study by Ekwere and Egbe [21] in this institution 16 years earlier. Previous studies carried out in different parts of the country as well as other countries have demonstrated prostate cancer to be the most common among the urological malignancies. This is not surprising as it is

currently the commonest malignancy affecting males worldwide [4,22–24]. However the reason for its overwhelming dominance (Over 91%) in our study is not readily available. The role of environmental factors and lifestyle including diet is noted to be important in the development of this disease. Diet is a modifiable risk factor in the development of this disease. The diet of the average Calabar man is based on sea foods and vegetables which are previously known to be protective. There may be need to reassess the impact of lifestyle including diet in the development of prostate cancer in subsequent research in order to ascertain the possible reason(s) for this trend. Adenocarcinoma was the most common histologic type of prostate cancer seen in this study with over 99% of cases and only one case (0.18%) being urothelial cancer. Obiorah and Nwosu [25] reported that all the cases of prostate cancer in their study were adenocarcinoma while Klufio [24] reported 99% of their cases in a Ghana study to be adenocarcinoma and indeed other studies have reported adenocarcinoma as the most common histologic type [2,26]. Gleason III was the most common grade of prostate adenocarcinoma with 44.5% of patients, showing the tumours to be predominantly well differentiated. This was followed by Gleason IV seen in 35.99% of patients. A similar finding was recorded in Zaria by Oluwole et al. [2] where the predominant Gleason grade was III. Higher Gleason grades were noted to be more common in the younger age groups in our study. The single case in the 30-39 year group was Grade V. Six out of 11 patients and 59 out of 104 patients had Grades greater than III in the 40-49 and 50-59 years age groups. On the other hand, 20 out of 21 patients in the 90-99 years age group had Gleason grades III or less. Gleason grades greater than III are associated with more aggressive disease as has been documented in earlier studies, and indeed Gleason and colleagues [27] had noted Gleason score to be the strongest clinical predictor of prostate cancer progression. The development of prostate cancer at a younger age is associated with more aggressive disease as has been previously documented by Basse and colleagues [28] in Calabar. Thus the finding of higher Gleason grades in the younger age group in our study further reiterates these previous findings.

Twenty seven patients (4.38%) had renal malignancies, making it a distant second. Earlier studies carried out in various parts of the country have indicated bladder malignancies to be the

second commonest urological malignancy in Nigeria after prostate cancer [4,23] but in our study this was not the case. The male-female ratio for renal malignancies was 1:1.08. This female preponderance was also recorded by Akinfenwa et al. [29] in Kano with a male-female ratio of 1:1.9. More researchers have however reported it to be more common in males than females [28–30]. Renal cell carcinoma (RCC) was the most common histologic type of renal malignancy seen (51.86%) followed by nephroblastoma (40.74%). Badmus et al. [31] recorded RCC as most common in their study in Ife, while Isah et al. [32] noted nephroblastoma to be the most common renal malignancy in their study in Kano. Only two subtypes of renal cell cancer were recorded in this study. Clear Cell RCC was more common with 8 out of 14 cases than Papillary RCC with 6 cases. Muglia and Prando [33] had noted Clear cell RCC to constitute 70 - 75% of all RCC. We recorded it to constitute 57.14% of the cases of RCC seen. Of the 13 children affected, 11 had nephroblastoma, one had embryonal renal cancer (a rare histologic type) and the other had renal cell carcinoma. All other cases of RCC were seen in the adult patients. The single case of urothelial cancer recorded was that of a 59 year old male.

Nine cases (1.5%) of urinary bladder cancer were seen in our study. This is a small number compared with the 217 cases recorded by Takure et al. [34] over 17 years in Ibadan, 97 cases (31.7%) recorded by Mandong et al. [4] over 10 years in Jos, 33 cases (28.0%) by Dauda et al. [23] over 7 years in Gombe and 117 cases (21.3%) by Klufio [24] over 10 years in Ghana. This makes bladder cancer an uncommon cancer in our own environment. Most of these patients (66.67%) had urothelial cancers. Takure and colleagues [34] had demonstrated in their study in Ibadan that urothelial bladder tumours were the most common histological pattern seen in Nigerians and our study further went on to prove this. Only one child (11.11%), a 5 year old female, had bladder cancer in our study and the histology was nephroblastoma, which is a very rare histologic variant [35].

Testicular cancer was seen in 8 patients (1.3%) with 5 (62.50%) of them being seminomas. Out of 8 cases of testicular cancer recorded by Magoha [36] over 5 years in his study in Lagos, 50% were seminomas. Germ cell tumours have been recorded to be the commonest variety of testicular tumours worldwide [37] and our study reflected this pattern. Five cases of scrotal

cancer (0.8%) were recorded in our study. Not many scrotal cancers have been documented in Nigerian studies. Ofuru [26] et al. documented a single case of squamous cell carcinoma in their study. This makes scrotal cancer relatively common in our environment. Of the 5 cases recorded, 2 were Kaposi sarcoma with 1 case each of squamous cell carcinoma, angioleiomyoma and malignant melanoma. With two cases each, penile and urethral cancers were found to be the rarest of the urologic malignancies in Calabar.

Childhood urological malignancies in children in Calabar are predominantly of renal origin with 13 (86.67%) cases. Out of the 13 renal cancers, 11 (84.62%) were nephroblastomas. Swinson and McHugh [38] had noted nephroblastoma of the kidney to be the most common childhood urological cancer. It is also documented to constitute between 85-90% of childhood renal cancers [38,39]. The results of our research are in keeping with these previous findings. Testicular cancers were seen in 3 children (17.65%). The only bladder tumour recorded in childhood in our study incidentally was also nephroblastoma.

The results of our research have shown over 91% of patients to have prostate cancer, making it the most common urologic malignancy in Calabar. There, therefore, is the need to increase efforts at early diagnosis and management of prostate cancer, being the predominant urologic malignancy, in order to reduce the morbidity and mortality that could be associated with the disease. Part of this should include increased awareness campaigns so that the majority of the population is aware of the disease, its common symptoms, diagnosis and need for treatment. This is especially important, bearing in mind the poor healthcare seeking attitudes of Nigerian patients especially concerning lower urinary tract symptoms as earlier documented by Olaopa et al. [40] in Ibadan and Basse et al. [41] in Calabar. Secondly, routine screening for prostate cancer is recommended, which can bring about early diagnosis and treatment of the disease with subsequent reduction in its devastating effects.

## 5. CONCLUSION

The commonest urologic malignancy diagnosed in Calabar is prostate cancer. Renal malignancies are more common than bladder cancers in Calabar and are predominantly renal cell cancers. Scrotal cancers have been found to

be relatively common in our environment. Childhood urological malignancies in Calabar are predominantly nephroblastomas distantly followed by testicular malignancies.

## CONSENT

It is not applicable.

## ETHICAL APPROVAL

It is not applicable.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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