Uro-Genital Cancers in Nigerians: Clinical Patterns and Challenges of Management

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ABSTRACT

Clinical patterns of urogenital cancers and management challenges in a tertiary hospital over ten years are presented. This study aims to highlight the incidence, relative ratio frequencies, management difficulties and outcomes with urogenital cancers. Three hundred and ninety-eight patients (M: F=1:1.1), were analysed for age, sex, site, types of tumours, histopathological stages, management challenges and outcomes. Carcinomas of cervix uteri (39.2%) and prostate (36.4%), constituted (75.6%) of urogenital cancers in the series. Others included cancers of uterine body (4.5%), nephroblastoma (4.0%), bladder (3.8), renal cells, testicles and ovaries (3.3% respectively), vulva (2.0%) and penis (0.3%). Of 13 testicular tumours, 8 were GCT (61.5%) and 3 were non-GCT (23%)]. Histology reports of two patients (15.4%) were missing. Only 11 of 15 (73.3%) bladder tumours (M: F=14:1), were biopsied, returning 6 TCC (54.5%), 4 SCC (36.4%) and 1 rhabdomyosarcoma (9%). All presented with advanced disease and refused surgery. Late presentations (80%), inoperability and non-availability of appropriate chemotherapy presented major challenges. Uterine carcinomas were treated mostly by radical hystero-salpingectomy, prostate cancer by medical and surgical hormonal palliation, renal cancers by surgery and pre and post-operative anti-neoplastic and hormonal therapies. Most survived for less than twelve months. Addition of medroxyprogesterone after radical nephrectomy for adult clear-cell carcinoma though now obsolete, produced arguably favourable results. One patient with stage three disease inexplicably survived for 4 years after radical nephrectomy without additional therapy. Apart from cervical, prostatic, and renal cancers (in children), we did not see enough of the other cancers to establish a regular pattern of treatment.

Keywords: Uro-genital Cancers, Nigerians, Clinical Patterns, Management

INTRODUCTION

As the causes of severe morbidity and mortality in Nigeria are shifting from infections and poor nutrition, neoplastic and other chronic diseases are gaining prominence.[1] The incidence of certain cancers is reportedly rising worldwide. Racial and ethnic variations and geographic epidemiology are important determinants of the incidence and prevalence of cancer worldwide.[2] It is conceivable that some regional differences in cancer indices may exist in Nigeria with its large and diverse population of more than 200 million and over 350 ethnic nationalities. In the past, institutions of South-Western Nigeria blazed the trail in studies on cancer in Nigeria.[1,3-7] Inevitably, the emphasis in those studies was on the populations close to those institutions and their results reflected largely the patterns within those populations. Studies from higher health institutions in other zones in Nigeria are essential to highlight inevitable variations, thus updating the data for the whole country. Such studies of significance have been undertaken in other zones of the country in recent years but the emphasis has weighed heavily in favour of prostate cancer.[8-14] Several of these studies have also been undertaken from this centre in the past, but none has specifically addressed urogenital cancers as a group.[9,10,14]

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The sparse published cancer statistics in Nigeria and particularly the Niger Delta region of Southern Nigeria, with over 12 million population, is further motivation for carrying out this hospital-based retrospective study, the results from which are expected to form the baseline for similar studies in future. Until recently our institution was the only tertiary healthcare institution in our locality, to which most patients were referred. With a functioning Urology unit for more than twenty years and the only cancer registry in operation, it is expected that figures obtained in this study, will be representative, informative and reflect, to a large extent, the pattern of malignant urogenital conditions in the South-South zone of Nigeria. It is therefore expedient to document our local experiences with urogenital cancers in our part of Nigeria. We hereby report the first part of our experience with urogenital cancers and the problems associated with their management in our institution.

MATERIALS AND METHODS

This study is a retrospective, descriptive clinical study of urogenital malignancies seen at the University of Calabar Teaching Hospital (UCTH), Calabar, Nigeria, over ten years (1984-1993). It involved a review of all clinical files and histology reports of patients with clinical cancers of the urogenital system in both sexes. The malignant conditions targeted include those of the prostate gland, cervix uteri, kidneys, urinary bladder, vulva, body of uterus, ovaries, testicles, and penis, at all ages.

The data retrieved included the age of patients, sex, site and type of tumour and histopathology report for each patient, where this was retrievable. Details of treatment methods adopted and the outcomes were also analysed. All multiple specimens from the same patient were regarded as one specimen except where the patient had a different type of cancer on a subsequent visit. The various clinical data and bio-data of the patients as well as the number of cases involved were tabulated per site or organ involved. The relative ratio frequencies (RRF) of the tumours were calculated and management methods and outcomes were highlighted, including the associated challenges encountered.

In children, we adopted a policy of neoadjuvant pre-nephrectomy combination chemotherapy in the management of nephroblastoma, using actinomycin-D and vincristine in appropriate dosages four weeks before surgery. This is said to have the effect of shrinking the tumour size (and downstaging it) making it more manageable during surgery and reducing the chances of tumour rupture/spillage, a practice most appropriate to our circumstances in which tumours are so advanced they often crossed the midline. The same combination of chemotherapy was continued after surgery for up to six months in these patients who often had stages III and IV disease. Where there was a recurrence, cyclophosphamide was added to vincristine and actinomycin-D. We had no access to platinum-based chemotherapy at this time. Appropriate data obtained from the study were subjected to simple statistical analyses.

RESULTS

There were 409 urogenital cancers of which 11 were excluded due to incomplete data, leaving 398 for analysis. Of these, 203(51%) were purely urological while 195(49%) were purely genital cancers. Figure 1 shows the yearly incidence of urogenital cancers. Table 1 shows the size distribution and their relative ratio frequencies. Males accounted for 191(48%) and females 207(52%), a ratio of 1:1.1. Cancers of cervix uteri (RRF 39.2), and prostate (RRF 36.4%) (Fig. 2), together accounted for 75.6%. Less than 25% were from other sites of the urogenital system.

Figure 3 shows a low peak below ten years of age and a second peak at 60-79 years, followed by a sharp drop above 80 years. The mean age of all patients was 60.1 ± 17.2 years (range 5 months to 88 years); for the males, this was 60.75 ± 10.9 years and for the females 58.38 ± 8.7 years. This apparent difference in mean ages between the male and female populations was not statistically significant (P>0.50). The age group 40-79 years accounted for 331 patients (83%), the bulk of which was due to prostate and cervical cancers. Only 6% of urogenital cancers were found in patients above 79 years of age; 10.8% in those below 40 years and 5% (20 patients) were under 20 years of ageindicating that urogenital cancers in our environment are largely adult disease. The peak incidence of prostate cancer of 70% was in the age group 60-79 years.

Cancer of cervix uteri and most other female genital cancers were managed by Gynaecologists alone or jointly with the Urologists; the urological cancers in both sexes were managed by the Urologist, prostate cancer by surgical or medical endocrine manipulation or androgen deprivation therapy (ADT). Robotic radical prostatectomy, a minimally invasive means of carrying out radical prostatectomy, and other modalities of treating early prostate cancer such as radical external beam radiotherapy (EBRT), brachytherapy, or high-frequency focused ultrasound (HIFU) treatment, to mention a few, are not available in our centre. So, they did not feature as treatment optionsamong less than 20% of our patients with early prostate cancer. Only two of our patients could afford robotic radical prostatectomy (RRP) offshore, with good results.

Overall, there were 29 renal cancers (RRF 7.3%) in the series, 16 males and 13 females. Childhood renal cancers slightly outnumbered adult renal cancers by 16 cases to 13 or 1.2:1. All the adult renal cancers were adenocarcinomas (renal cell carcinoma); the childhood ones were nephroblastomas, most presenting late, having crossed the midline in about 68.75%. The peak incidence of nephroblastomas was in the age group 0-3 years (9), followed by the age group 4-6 years (4) and three in the age group 7-9 years. There were 10 females to 6 males (1:1.7) among the childhood renal cancers; the reverse was the case in adult renal cancers (9 males to 4 females (2.25:1). Nine (56.25%) patients presented with stage 4 disease, three (18.75%) with stage 3, two (12.5%) with stage 1, and one each with stages 2 and 5 diseases respectively. One of the stage 1 cases of Wilms tumour was associated with ipsilateral hemihypertrophy. The tumour in a two-year-old boy measured 15cm x 18cm x 7cm at excision, and the renal capsule was intact at the surgery. The para-aortic nodes were free of tumours. He was our longest survivor, remaining healthy for 6 years before he was lost to follow-up. The others with stage 1 disease were lost to follow-up early after radical nephrectomy. Bilateral disease in a three-year-old female was confirmed by exfoliative cytology of the ascitic fluid and needle aspiration biopsy of both tumours. She was never seen again after a discussion of her condition with her parents.

The lone child with stage 2 disease in the series had his tumour probably at birth in that it was reportedly palpable by the mother at six weeks of age. Medical opinion was not sought until he was 5 months of age. He had a right nephrectomy with adjuvant vincristine and actinomycin-D. This child was prone to frequent drastic drops of his haemoglobin which necessitated blood transfusion, after each course of chemotherapy. He responded well to treatment for 6 months but unfortunately died of sudden onset of fulminating hepatitis at the age of 11 months.

All thirteen adult renal cell carcinoma (9 males and 4 females) presented late. Success with their management was also

worse than with the children. Of these, five were technically inoperable at presentation despite attempts at downstaging, responding poorly to chemotherapy with methotrexate and 5-fluorouracil. Due to technical difficulties, residual tumour had to be left behind in one of the remaining eight patients, with lymph node metastasis. The first six patients were treated with a combination of methotrexate and 5-fluorouracil which were started just before surgery. There was no appreciable success, the longest survival being only five months after initiation of treatment. When we introduced medroxyprogesterone (Depo-provera) as adjuvant therapy in five of the remaining eight patients after radical nephrectomy, we noticed dramatic survival for 17 and 23 months respectively, in two (25%). One of these, a 28-year-old woman survived for 23 months. She lived for 20 months with good quality of life following total nephrectomy for advanced renal clear cell carcinoma before deterioration set in and she died three months later. The other, also a female, survived for 17 months with good quality of life. One patient with stage three disease survived for 4 years after radical nephrectomy without additional therapy. The rest died within nine months following radical surgery. Medroxyprogesterone was continued post-operatively for the duration of their survival. Overall, our impression is that the patients treated with additional medroxyprogesterone survived for longer periods than those without this additional therapy.

There were 13 cases of testicular cancer in the series (RRF 3.2%) consisting of 8 germ-cell tumours [four embryonal carcinomas and four seminomas (Fig.4), (one spermocytic), and three non-germ-cell tumours - two high-grade non-Hodgkin's lymphomas and one adenomatoid tumour. The histology reports of two patients (15.4%) were not found. Among the 15 cases of bladder cancer encountered (RRF 3.8%), only one was female. There was only one case of penile cancer in the series (0.3%) (Fig. 5).

Table 1: Site Frequency and RRF of Uro-Genital Cancers by Gender

S/No.	Site of Tumours	Male	Female	Total	Relative Ratio Frequency (RRF%)
1	Cervix	-	156	156	39.2
2	Prostate	145	-	145	36.4
3	Uterine Body	-	18	18	4.5
4	Wilmss tumour (Nephroblastoma)	9	7	16	4.0
5	Bladder	14	1	15	3.8
6	Renal Cell	9	4	13	3.3
7	Ovarian	-	13	13	3.3
8	Testicular	13	-	13	3.3
9	Vulva	-	8	8	2.0
10	Penis	1	-	1	0.3
	Total	191	207	398	100

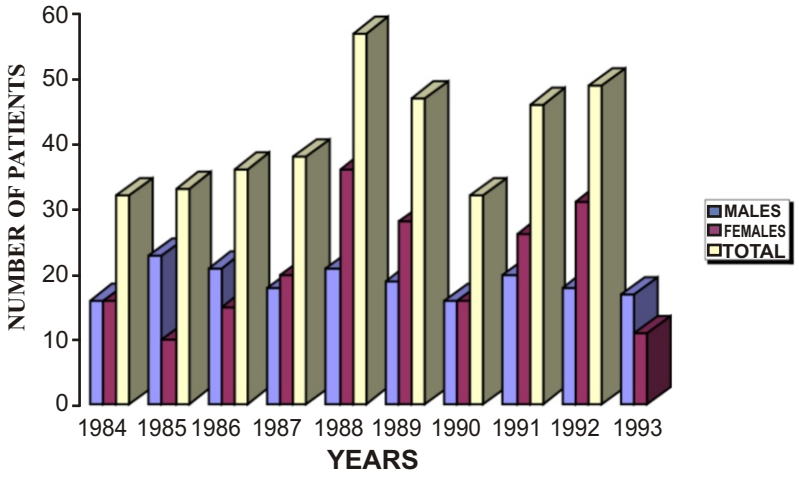

Figure 1: Yearly Distribution of Urogenital Cancers in Nigerians

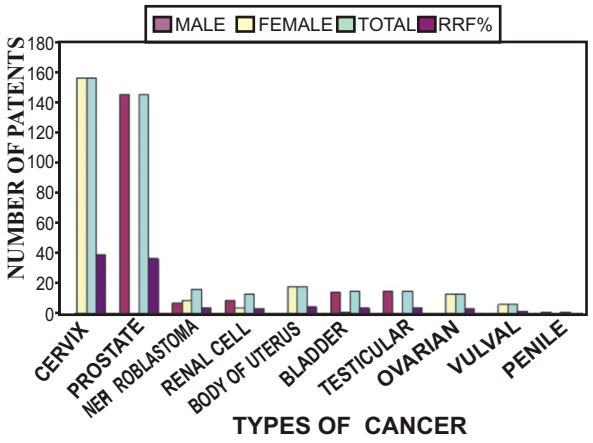

Figure 2: Site Distribution and Relative Ratio Frequencies (RRF) of Urogenital Cancers

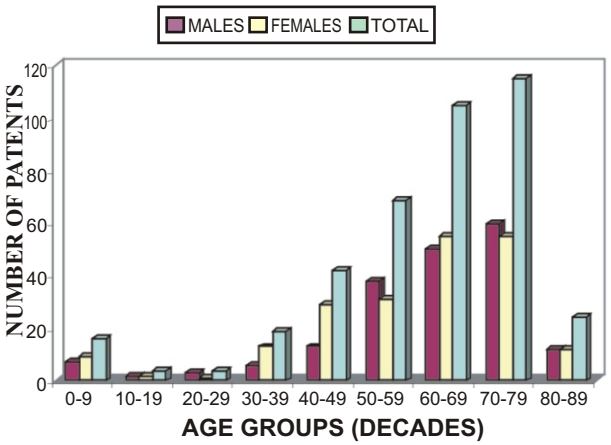

Figure 3: Age-Sex Distribution of Urogenital Cancers

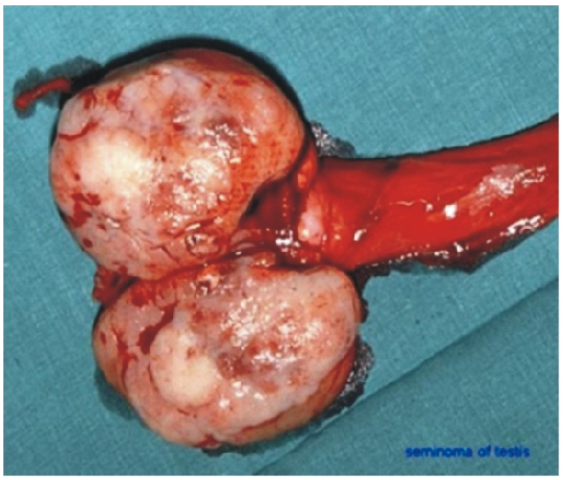

Figure 4: Freshly Excised Seminoma of the Testis

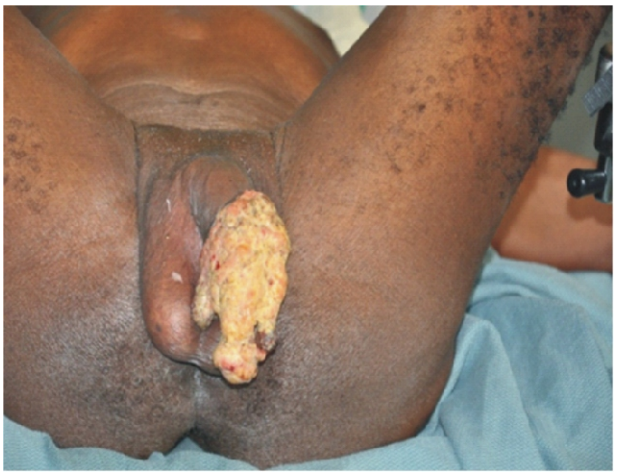

Figure 5: Cancer of the Penis

DISCUSSION

Uro-genital cancers, particularly cervical and prostatic cancers, are a major cause of morbidity and mortality in our environment, together constituting 75.6% of all urogenital cancers seen in our centre. With an incidence of 61.3 per 100, 000 males, cancer of the prostate has become the most common male cancer in our environment, accounting for 81% of all male urogenital cancers.[14] It is also the commonest cause of cancer deaths in Nigerian men.[8,12,14] Prostate

cancer is often presented initially with urinary retention in 26.7% of patients, an aspect of late presentation (unpublished personal data).

More than 80% of the patients in this study presented late with advanced disease, thus compounding the problems of management, and limiting the clinician to only palliative measures.[14] For renal tumours, nearly 97% presented at the late stages of the disease. The problems of late presentation with accompanying inoperability and poor survival are characteristic features common to malignant diseases and indeed most diseases encountered in Nigeria. These, along with scarcity of appropriate chemotherapeutic agents, are responsible for the dismal survival rates of cancer victims in Nigeria in general, and in our region in particular. This seems to be a direct consequence of poverty, superstitious and religious beliefs and practices which influence patients' attitudes to disease causation and management, and inevitably, of clinical outcomes.

Only two patients in our series presented with early-stage (Stage 1) Wilms tumours which also responded favourably to treatment. This tumour is a little more prevalent in people of African descent and constituted 55% of all renal tumours in the series. This is in line with observations elsewhere that after hydronephrosis and multicystic dysplastic kidney disease, Wilms tumour is the most common renal mass in childhood, accounting for 6% of malignancies in children.[15,16] It presents a peak incidence between 3-4 years, though this was in the age group of 0-3 years in our series.

Our success with the management of nephroblastoma can be described as poor to moderate on average. Apart from two children with Stage 1 disease, one of which was associated with hemihypertrophy, most patients never survived beyond two years, a far cry from the outcomes in western countries. This patient was our longest survivor; he was also unique in the sense that he kept his follow-up appointments for just over six years and remained healthy before he was lost to follow-up. The second patient was lost to follow-up early, following radical nephrectomy. Proper assessment of clinical outcomes in one patient with stage II disease was made impossible by an early death from unrelated causes. Bilateral disease is usually seen in 7-12% of cases, 6.25% in our series.

The management of adult renal cancer was even more problematic. The patients treated with additional medroxyprogesterone survived for longer periods than those without this additional therapy. The numbers responding to this innovation in treatment were however too few to draw conclusions about its efficacy or to establish it as routine treatment.

Furthermore, the use of medroxyprogesterone for the treatment of renal cancer has since become obsolete, in favour of targeted treatments such as Interleukins, Interferons and several other biological response modifiers.

Malignant tumours of the testis are relatively rare, accounting for only 1% of all male malignancies. It is even rarer among blacks, while the incidence in Nigeria is reportedly among the lowest in the world accounting for 0.1 per 100,000 per annum.[17,18] Its worldwide incidence has however increased three-fold in the last five decades.[19] It is the most common solid malignancy affecting young males between the ages of 15 to 35 years.[20] Onuora *et al,* (1989) from Benin, Nigeria, reported sixteen cases in ten years, while Magoha GA, (1995) in Lagos, Nigeria, saw only eight in five years with a mean age of 37.7 years.[17,21] In the latter study, the incidence was divided equally between germ cell tumours (GCT) and non-GCT Tumours. Unlike the Lagos experience, however, more than 70% of the non-germ cell testicular Tumours (non-GCT) in the Benin study were Hodgkin's lymphomas. This finding was corroborated by a more recent report from Yaoundé, Cameroon, where lymphomas constituted about 64% of the malignant testicular tumours, Burkitt's lymphoma (35.7%) being the commonest variety encountered.[22]

A report from Calabar, Nigeria, also indicated that all the testicular cancers as well as the sacrococcygeal tumours encountered

among children were of the same histological type, embryonal carcinomas (endodermal sinus tumours, EST).[9] It has been suggested that testicular cancers and sacrococcygeal tumours could have a common aetiological factor in the environment.[23, 24] In this study, testicular cancers among adults presented a mixed picture, with germ-cell tumours predominating (4 seminomas, including one spermocytic seminoma] (30.8%), but with two high-grade non-Hodgkin's lymphomas (15.4%), and one adenomatoid tumour (7.7%) which is thought to be a benign lesion. This contrasts with the findings in Benin City, Nigeria, where 70% of the paratesticular tumours were Hodgkin's lymphomas. [21] The histology reports of two of our patients were not found.

Chemotherapy for advanced GCT has achieved important breakthroughs during the past three decades. The discovery of cisplatin as a highly effective anti-neoplastic agent in 1965, and its later use in the treatment of germ cell tumours of the testis (GCT), was an important breakthrough.[25] It was initially discovered to be effective as a single agent in patients that were refractory to actinomycin D and/or vinblastine plus bleomycin, and later became the major component of a curative combination chemotherapy regimen.[26,27] By the 1970s, combination therapies such as cisplatin, vinblastine and bleomycin had been shown to produce objective responses; 57% complete response rates and 45% long-term disease-free survival rates were reported.[28] In 1974 and beyond, the combination of cisplatin, vinblastine and bleomycin was investigated by the Indiana group and 100% of the 47 patients in the initial phase II study achieved a response.[29] Thirty-five (74%) of these patients achieved complete remission; the remaining patients achieved partial remission, establishing this combination as the treatment of choice.

The use of bleomycin, etoposide and cisplatin (BEP) and etoposide and cisplatin (EP) combination chemotherapies for the treatment of testicular cancers, has led to better treatment outcomes elsewhere. In our country, Nigeria, we are limited to whatever chemotherapeutic agent happens to be available, hence the poor to modest results often obtained. The high cost of chemotherapy is also a limiting factor in treatment outcomes since most of our patients could not afford them.

Among Caucasians the male to female ratio in bladder cancer is usually around 2:1; in our series, it was 14:1, though there appears to be a slightly different picture in the northern parts of Nigeria. This confirms that bladder cancer is uncommon in our environment and rare among women. The reason for this lopsided gender difference is difficult to adduce at this time. However, men are more likely to be exposed to the risk factors of bladder cancer than women through their occupation in the rubber industry, etc. With an incidence of only 0.3%, cancer of the penis is a rare disease in this environment (Fig.5). This very low incidence may be related to the cultural practice of childhood circumcision which is almost universal in our catchment area.

CONCLUSION

The need to update cancer statistics in the country and to establish a baseline for future reference in our region was the motivation to embark on this study among Nigerians in our geographical zone. Uro-genital cancers were found to be largely an adult disease in our environment, with cancers of the cervix, prostate and renal cancers at all ages predominating. Prostate cancer frequency was found to be on the increase, in comparison to earlier studies throughout the country. More than 80% of patients in our environment usually present with advanced disease because of reliance on alternative means of treatment which are often ineffective. This and the resulting high degree of inoperability and non-availability of the appropriate chemotherapeutic agents and/or radiotherapy, in our environment, were the major reasons for the poor results of treating cancers generally and urogenital cancers in particular. Only 15% of patients in advanced economies present with advanced cancers. This guarantees much better treatment outcomes. The low incidence of testicular cancer, penile cancer and bladder

cancer among Nigerians was confirmed in this study. Regional variations in incidence and geographical epidemiology of cancers were also established.

To reverse the trend of late presentations and inoperability, a new multi-pronged policy approach has become necessary, namely, to embark on massive public education for men and women, aimed at adjusting lifestyles and other attitudes toward personal health. Such education will also have the salutary effect of reducing the number of late presentations for better treatment outcomes. As a country, we must also develop strategies along the lines of targeted screening of patients to radically improve the numbers presenting with early disease. In the West and other advanced countries, this is a controversial subject. But it is pertinent to note that through mass screening, they have been able to reduce late presentations to only about 15%. To ignore screening in Nigeria at this time is inimical to our aspirations to reduce the astronomically high rates of late presentations and inoperability among our patients. For women, there is already an established screening modality for the commonest female cancer, cervical cancer, called PAP smear, for women in the childbearing age groups. If adopted massively, it has the potential for early detection of cervical cancers and improved outcomes of treatment. Moreover, it should be mandatory for all females to be screened for human papilloma virus which has been implicated as an aetiologic factor in cervical cancer.

Because patients were few and far between, it was difficult to evolve a standard policy of treatment, due to the difficulty of evaluating success through the use of technology. Since a single centre does not see enough of the common urological cancers such as Wilm's Tumour, and because of the high potential for treatment outcomes of 90% or more, it is advocated that government should establish a national Wilm's tumour centre where these children can be treated under a unified treatment policy. Furthermore, the professional bodies in collaboration with the government should enforce a policy of screening among men for early detection of prostate cancer and cervical cancer, as well as prevention of cervical cancer in women through vaccination against human papillomavirus as a public health strategy in Nigeria. This we must do regardless of present Western policies if we must reduce the level of late presentations and the resulting inoperability among our Nigerian patients.

REFERENCES

1. Williams AO. Tumours of childhood in Ibadan, Nigeria. Cancer 1975;36:370-8.
2. Baquet CR, Horn JW, Gibbs T, Greenwald P: Socio-economic factors and cancer incidence among blacks and whites. Journal of National Cancer Institute 1991;83: 551-7.
3. Bankole MA, Familusi JB, Ngu VA. Nephroblastoma in Ibadan. Afr J Med med Sci. 1971;2:65-75.
4. Nkposong EO, Lawani, J. Primary Carcinoma of the Prostate in Ibadan. West African Medical Journal 1973;108-111.
5. Lawani J, Nkposong EO, Aghadiuno PU *et al*. A twenty-year review of urologic tumours of the genito-urinary tract. In: Solanke, TF, Osunkoya BO, Williams CKO *et al,* eds, Cancer in Nigeria, Ibadan; Ibadan University Press 1982;67-71.
6. Solanke TF. Cancer in Nigeria. Oyo State NMA Annual Lecture, Ibadan April 16, 1996.
7. Osegbe DN. Prostate Cancer in Nigerians: facts and non-facts. Journal of Urology. 1997;157:1340-43.
8. Udeh FN. Prostatic Carcinoma in Nigeria: a ten-year retrospective study. International Urology and Nephrology 1981;13:159-166.
9. Ekanem IA, Asindi AA, Ekwere PD, Ikpatt NW, Khalil MI. Malignant childhood tumours in Calabar, Nigeria. African Journal of Medicine and Medical Science 1992;21:63-69.
10. Antia-Obong OE, Ekwere PD, Ekpo MD, Archibong, EI. Congenital Hemihyperttrophy and Wilms

Tumour: a case report. Nigerian Journal of Paediatrics 1988,15:47.
11. Akang EEU, Aligbe JU, Olisa EG. Prostatic Tumours in Benin City, Nigeria. West African Journal of Medicine 1996;15:56-60.
12. Ogunbiyi JO, Shittu OB. Increased incidence of prostate cancer in Nigerians. Journal of the National Medical Association 1999;91:159-164.
13. Dawan D, Rafindadi AH, Kalayi GD. Benign Prostatic Hyperplasia and Prostate carcinoma in native Africans. BJU International 2000;85:1074-77.
14. Ekwere PD, Egbe SN. The changing pattern of prostate cancer in Nigerians: current status in the south-eastern states. Journal of the National Medical Association 2002;94:619-627.
15. Pastore G, Znaor A, Spreafico F, Graf N, Pritchard-Jones K, Stellarover-Foucher E. Malignant Renal tumours incidence and survival in European children (1978-1997): report from the Automated Childhood Cancer Information System project. Eur. J. Cancer 2006;42:2103-14. http://www.ejcancer.com/article/S0959-8049(06)00448-5/abstract).
16. Dahnert W. Uro-genital Tract. In: Radiology Review Manual 7th edition, Lippincott Williams & Wilkins 2011, p895-1012.
17. Magoha GA. Testicular cancer in Nigerians. East African Medical Journal 1995;72:554-6.
18. Rao AB, Sparke B. Tumours of the testis in Jamaica. Br Journal of Urology 1979;51:151-3.
19. Giwercman A, Carlsen E, Keiding N, Skakkeback NE. Evidence for an increasing incidence of abnormalities of human testis: a review. Environmental Health Perspectives 1993, 101 (suppl 2): 65-75.
20. Steele GS & Richie JP. The management of Non-seminomatous Testicular Cancer. Digital Urology Journal 2002:1-22.
21. Onuora V. Non-germ cell testicular tumours in Nigerians. Tropical Geographic Medicine 1989;41:458-60.
22. AngwafoFru F 3rd, Takongmo S, Mbakop A, Ngu VA. Testes tumours in a Sub-Saharan African city (Yaoundé). Incident cases and histopathology. European Urology 1996;30:345-8.
23. Ekwere PD. Penile agenesis and sacrococcygeal tumour: a possible link to environmental pollutants. Nigerian Journal of Surgery Dec. 1999;6:55-57.
24. Kennedy WA & Snyder III, HM. Paediatric andrology: the impact of environmental pollutants. BJU International 1999;83:195-200.
25. Rosenberg B, Vancamp L, Krigas T (1965): Inhibition of cell division in Escherichia coli by electrolysis products from a platinum electrode. Nature 205 (4972):698-9.
26. Higby DJ, Wallace HJ, Holland JF. Diamminedichloroplatinum II. A phase I study showing response in testicular and other tumours. Cancer 33;1219:1974-1225
27. Einhorn LH, Donohue JP. Combination chemotherapy with - diamminedichloroplatinum, vinblastine, and bleomycin disseminated testicular cancer. Annals of Internal Medicine 87;293:1977-298
28. Einhorn LH. Treatment of testicular cancer: a new and improved model. Journal of Clinical Oncology 8, No. 11 (Nov. 1990):1777-81.
29. Wiltshaw E. (1979). "Cisplatin in the treatment of cancer". Platinum Metals Review 23:90-8.