

Renal Cancers in Ibadan, Nigeria (2013-2022): An update

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ABSTRACT

Background: Renal cancer (RC) is projected to be stable in the developed countries and increase in the developing countries. In the last review in our environment over 5 years; 69 patients had RC, a rise in clear cell carcinoma, tumours in young adults and less use of abdominal CT scan. We present an update of RC in Ibadan. **Methods:** This was a retrospective study of patients who presented with clinical, imaging studies and histological diagnosis of RC between 2013 to 2022. We analysed these data as well as histology types, treatment offered and outcome of management using Kaplan-Meier survival curve. **Results:** There were 68 patients with RC, mean age was 49.7 ± 14.8 years. Males were 52.9% and 47.1% were females. They presented with pain and total haematuria (20.6%), pain and swelling (19.1%), pain alone (17.6%) and 7.4% had incidental RCs. Abdominal CT scan performed in all that confirmed 98.5% and 1.5% were unilateral and bilateral respectively. Localized and locally advanced renal cancers accounted for 79.4% while 20.6% were metastatic disease. Paraneoplastic manifestations of RC were seen in 57.4%. RC rose gradually and peaked in 2019 and thereafter stabilized. The commonest histological types were clear cell RC (36.9%) and papillary RC (27.9%). Rare RCs were neuroendocrine RC (3.9%) and collecting duct RC (2.0%). The treatments offered were radical nephrectomy (RN), unresectable tumours, and targeted therapy in 72.1%, 13.2%, and 7.4% respectively. The median overall survival (OS) was 37 months ($p=0.000$, Chi-square 63.413, $df=3$). **Conclusion:** There was a gradual increase number of RC that later stabilized in the last 2 years of the study. There was increased utilization of CT scan. The majority of the patients presented with locally advanced disease. RN remained the main stay of treatment with best survival rate. Neuroendocrine and collecting duct carcinoma are rare.

Keywords: update, renal cancer, overall survival, histology, imaging study.

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INTRODUCTION

Kidney cancer is the 16 most common cancer with an estimate of 431,288 (2.2%) new cases and mortality of 179,368 new deaths worldwide [1]. The highest burden of RC is North America and Europe with gradual increase in the incidence over time. Most cases are discovered incidentally from imaging studies. In the United States about two-thirds of the tumours are found in men at a mean age of 64 years. Patients with Von Hippel-Lindau disease tends to present 20 years earlier than the general population. The reported modifiable risk factors are hypertension, smoking, obesity, diet and alcohol [2].

In Africa and middle East, the incidence of kidney cancer for male and female is 1.8-4.8/100,000 populations and 1.2-2.2/100,000 populations respectively. While in Nigeria it is 0.3%-2.3% for both sexes. The mean ages are 47 and 45 years for Africa/middle East and Nigeria [3,4].

At the time of presentation in Africa most patients are symptomatic. This includes combination of symptoms pain, swelling, haematuria. The classical triad continues to be significant 16.4% and 26.7% in southwestern part of Nigeria. The incidence of incidental tumours was as low as 6.3% [3,5,6].

In Africa the identifiable risk factors for kidney cancers includes hypertension 15.7% in Nigeria; 19% in Somalia [5,7], cigarette smoking (11.8%) and obesity (3.9%) [5].

The overall survival in Africa is poor and is comparable to that of metastatic renal cell carcinoma in the United States [2,3]. Despite the late presentation of patients in Africa, the main stay of treatment is open radical nephrectomy. In the industrialized nations, a reasonable number of patients with metastatic disease are offered combination of targeted therapy (vascular endothelial growth factor inhibitor & mammalian target of rapamycin) and immune check point inhibitors. This combination increased the patient free survival and overall survival. In Africa only a very small number of patients can afford the monotherapy targeted therapy

how much more the addition of immune check point inhibitors [3,5-7]. The aim of this study is to give an update on the management of renal cell carcinoma in our environment.

MATERIALS AND METHODS

This was a retrospective study in a tertiary hospital in the Western part of Nigeria spanning a period of ten years (January 2013 to December 2022). The data of patients with clinical and radiological features of renal cell carcinoma were retrieved from the patient's surgical outpatient records, theatre operation books and subsequently entered on Microsoft Excel spread sheet during the study period. The data studied include demography, clinical presentations, stage of disease, presence of paraneoplastic syndromes obtained from the biochemical and haematological results. In addition, imaging studies used were documented. The histological types, treatments offered, and outcome of treatment offered.

Patients with clinical presentations (total haematuria, flank pain or swelling), paraneoplastic syndromes such as unexplained anaemia, Stauffer's syndrome, weight loss, and thrombocytosis). Radiological features (often well-defined, heterogeneous, contrast enhancing and sometimes containing calcifications or cystic areas, with specific patterns helping to differentiate subtypes such as clear cell (intense enhancement) from papillary (hypovascular) or chromophobe (less dense) and histological diagnosis of renal cell carcinoma. Patient with diagnosis of benign renal tumours or xanthogranulomatous pyelonephritis were excluded. The primary outcome measure was overall survival (OS) (alive or dead), the median overall survival time in months.

The data was analysed using statistical software for social sciences version 20 (SPSS IBM). The categorical variable was expressed in mean while non categorical variables were expressed in percentages, and graphs. The overall survival for the treatment options was determine using the Kaplan-

Meier survival curve and a p-value < 0.01 was deemed significant.

RESULTS

A total of 68 patients with renal cancers (RC) were managed during the study period. There was an initial reduction in number of cases from 2013 to 2014 then followed by a slow increase in number of renal carcinomas till 2017. Thereafter, was a reduction in 2018 that rose to a maximum number of cases in 2019. By the year 2020 during the covid 19 pandemic there was a another drop that rose again and remained stable in the last two years of the study. In Figure 1.

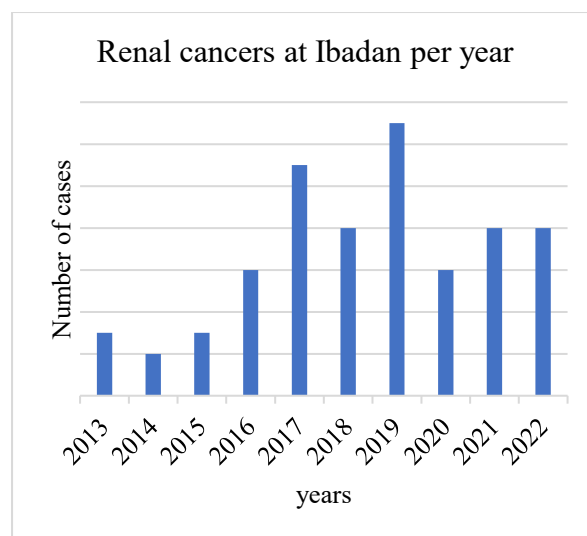


Fig. 1: Yearly distribution of number of renal cancers at Ibadan (2013-2022)

The mean age was 49.7±14.8years with age ranged of 16-76 years. There was a preponderance of male (52.9%) compared to 47.1% females. Tumours were found on the right side in 38 patients (55.9%), left side 29 (44.1%) and both sides in one case (1.5%). The commonest clinical presentations were pain and haematuria in 20.6% patients, pain and swelling in 19.1% patients, pain alone in 17.6% patients and incidental tumour was seen in 7.4% as shown in Table 1.

Table 1: The Clinical Presentations of renal carcinoma at Ibadan (2013-2022)

Clinical Presentation	N (%)	r	p-value
Pain and haematuria	14 (20.6)		
Pain and swelling	13 (19.1)		
Pain	12 (17.6)		
Incidental	8 (11.8)		
Classical Triad	6 (8.8)		
Swelling	6 (8.8)		
Haematuria	6 (8.8)		
Swelling & haematuria	3 (4.4)		
Paraneoplastic syndrome	39(57.4%)	-0.123	0.317
Abnormal LFT (Stauffer's syndrome)	19 (27.9)		
Weight loss	9 (13.2)		
Thrombocytosis	6 (8.4)		
Unexplained anaemia	4 (5.9)		
Fever	1 (1.5)		

All the patients had abdominal CT scan done that confirmed 98.5% being unilateral and 1.5% was bilateral. The smallest tumour volume 2.10 cm³ and biggest was 13,572 cm³ with a mean of 945.9 cm³ and these corresponded to a minimum tumour length of 2.00 cm and maximum tumour length of 30.00cm with a mean of 13.10cm.

Fifty-four (79.4%) of the patients presented with localised and locally advanced diseases (stages 1, 2 and 3) while 14 (20.6%) presented with metastatic disease (stage 4). Thirty-nine (57.4%) of these patients had paraneoplastic manifestations of which the commonest was Stauffer's syndrome in 19 (27.9%). There were no correlations between the presence of paraneoplastic syndrome and the outcome of treatment (r = -0.123, p= 0.317). (Table 1). The commonest histological types were clear cell RC (36.9%) and papillary RC (27.9%) while the rare RCs were urothelial RC (2.9%), RC with neuroendocrine component (2.9%) and collecting duct RC (1.5%) as documented in Table 2. Seventeen (25%) that were not available because the

tumours were unresectable or inoperable (13.2%) and 7.4% each had targeted therapy or were lost to follow up.

Table 2 further showed the treatment offered were radical nephrectomy in 72.1%, 13.2% were inoperable while 7.4% each received sorafenib and were lost to follow up. The overall median survival

was 37 months which was statistically significant (Chi-square 63.413, $df = 3$, $p = 0.000$). However, radical nephrectomy had the highest median survival of 40 months and least survival of 2 months was documented in patients who were treated with targeted therapy as shown in Figure 2.

Table 2: Clinical stage and histology of patients with renal cancer at Ibadan (2013-2022)

Stage of disease	n (%)				
Stage I (T1, N0, M0)	4 (5.9)				
Stage II (T2, N0, M0)	40 (58.8)				
Stage III (T3, N0, M0) or T1, T2, T3, N1, M0	10 (14.7)				
Stage IV (T4, Any N, M0) or t, Any N, M1	14 (20.6)				
Histology	n (%)				
Clear cell RC	25 (36.9)				
Papillary RC	19 (27.9)				
Chromophobe RC	2 (2.9)				
Urothelial RC	2 (2.9)				
Renal cancer with neuroendocrine component	2 (2.9)				
Collecting duct carcinoma	1 (1.5)				
Not available (TG-5, LTFU-5, unresectable-7)	17 (25)				
Treatment/Intervention	n (%)	MS (months)	95%CI Lower	Upper	p-value
Radical nephrectomy	49 (72.1)	40	35.999	44.001	0.000
Unresectable (2 Lymph node biopsy)	9 (13.2)	3	2.076	3.924	
Target therapy	5 (7.4)	2	0.000	4.147	
Lost to follow up	5 (7.4)	NA	NA	NA	
Total	68	37	18.385	55.615	

TG – target therapy, LTFU – lost to follow up, RC – renal cancer, CI – confidence interval, NA -not available.

The comparison of the previous study and the current update is shown in Table 3.

Table 3: Comparison of previous study and updated study at Ibadan

Variable	Previous Study	Updated Study	Remark
Study period	2007 - 2012	2013 - 2022	5 years versus 10 years
Number of patients	69	68	Covid-19
Mean age (years)	48	49.1	Comparable
Sex (male/female)	1:1	1.1:1	Similar
Classical triad	7	6	Slight reduction
Side if tumours	100% unilateral	Unilateral (98.5%) Bilateral (1.5%)	Appearance of bilateral disease
CT scan	11.6%	98.5%	Improved
Metastatic disease	15 (21.7%)	14 (20.6)	Stable
Histology	CCRC (24), PRC (1), CRC (1)	CCRC (25), PRC (19), URC (2), NERC (2), CDC (1)	Increased PRC, URC, NERC and CDC
Median survival (months)	31	37	Improved
Lost to follow up	37 (53.6)	5 (7)	Improved

CCRC – clear cell renal cell carcinoma, PRC – papillary renal cell carcinoma, CRC -chromophobe renal cancer, CDC – collecting duct renal cancer, URC – urothelial renal cancer, NERC – renal cancer with neuroendocrine component.

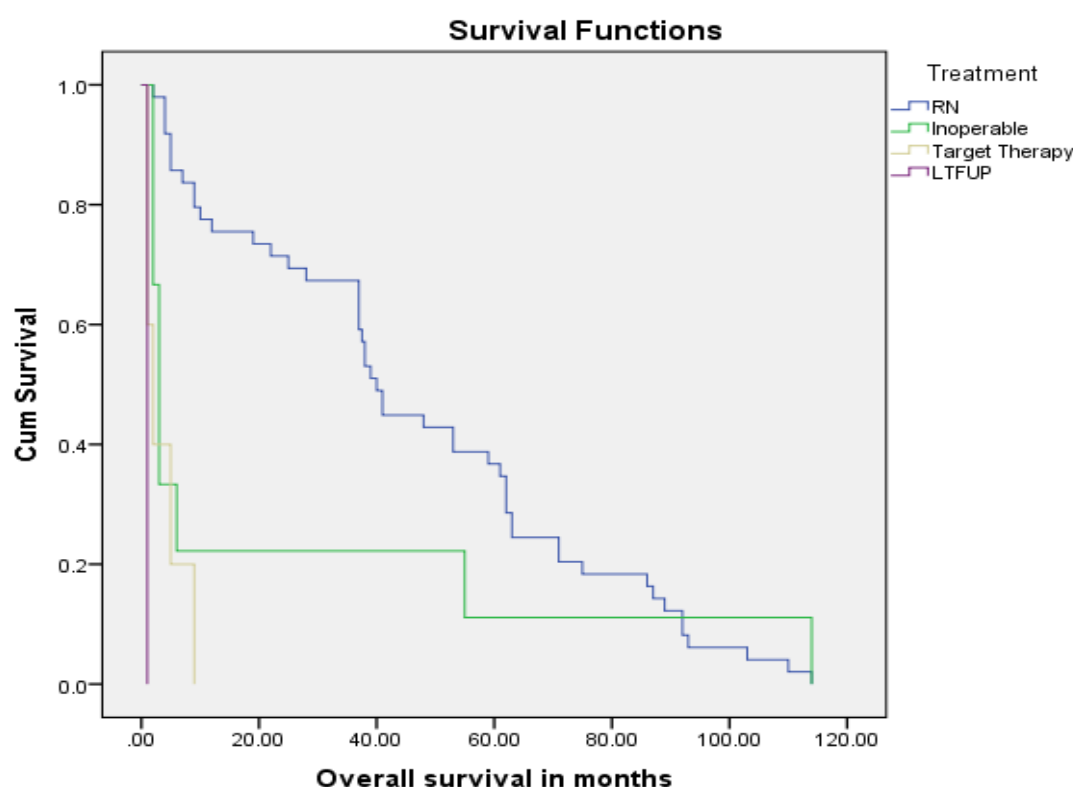


Fig. 2: Median survival in months of different treatment offered to patients with renal cancers at Ibadan.

DISCUSSION

There was a gradual increase in new cases of kidney cancers in this study inconsonant with the progressive increase reported worldwide. [2,8,9] Du et al. [14] predicted a significant increase in the incidence of renal cancer in the developing countries with a decrease in the developed countries from 2018 to 2030. The implication is that the developing countries should be more vigilant in the early detection of renal cancer to ensure better survival and decrease in the typical late presentation. Enlisting routine abdominal ultrasound as part of screening modality during pre-employment, obtaining driver's license, preadmission into tertiary institutions will assist in the early detection of renal masses that may require further CT scan. Of note was decline in cases reported during industrial

strike action by health workers in Nigeria and impact of the Covid-19 pandemic in 2018 and 2020 respectively in this present study. In the last two years of this study, the incidence of renal cancer remained stable, contrary to the prediction for the developing counties [2,8,9].

The availability, improvement of CT scan and better understanding of the features has enabled categorisation and correlations of radiological features with histological types of renal cell carcinoma. The imaging equipment have led to early identification of small size cancers worldwide [10,11,12]. This is not the case in our study where increase utilization of CT scan established the length and volume of kidney cancers. However, the smallest size of RC in our series was neuroendocrine renal

cancers while the largest were in those with clear cells renal carcinoma.

Worldwide, the peak age incidence and mean age of KC is in the 6th to 7th decades. Unlike in Africa and Nigeria where the mean age is around the 4th and 5th decade of life. This appeared consistent with the younger age group of patients with Von Hippel Lindau's (VHL) disease. It is possible that we have a reasonable number of patients with VHL disease. Therefore, a close collaboration with countries where facilities for screening for VHL gene are available may help confirm the suspicion of and incidence of VHL disease among patients with kidney cancers in our community [2,3,4,5,6].

There seems to be persistence of slight male preponderance in this update as in the previous study. This is consistent with findings worldwide except for a report from Ile Ife where there were more females [1,4,5,6,7,13].

The clinical presentation of RC is maintained in this update except for a rise in incidental RC, paraneoplastic syndrome and a case of bilateral RC. The incidental tumour is similar to report by Salako et al [5] though over 50% of renal malignancies are discovered incidentally in the developed countries [11]. In Lagos there was a correlation between the paraneoplastic especially Stauffer's and outcome of treatment, there was none in this study [6]. The incidence of metastatic disease has remained stable around 21%. This is comparable to what obtained in Zaria. [8,13].

Sixty-four percent of patients presented at stages 2 and 3, this is evidence of locally advanced disease apart from the metastatic

disease. This is in consonance with typical presentation in Africa [3,4,5,6,7,13,14,15].

Compared to our previous study, this update showed an increase in papillary and chromophobe RC while maintaining clear cell as the commonest histological type. This is a consistent finding in Nigeria, Africa and worldwide [4,5,7, 10,12,13]. A patient had collecting duct carcinoma. This is very rare and is associated with poor prognosis [12,16]. World Health Organisation (WHO) recognised the non-classified RC. Although, it is debatable, but we may consider classifying the RC with neuroendocrine components and urothelial RC reported in this update as part of this non-classified RC. Both tend to have the worst prognosis that is also the case with collecting duct renal cancers [12].

Despite this late presentation, majority of the RC are treated by radical nephrectomy with varying degree of survival as low as 13.6% at 5 years. This update showed an increase median survival from 31 months to 37 months of patient who underwent radical nephrectomy which is the main stay of treatment in Africa [3,4,5,6,7,13,15]. The introduction of the use of vascular endothelial growth factor inhibitor (VEGFI) and mammalian target of rapamycin (mTOR) in the of advanced RC almost tripled their survival. This was not the case in this update, where the median survival was 2 months [16,17,18].

Akpayak et al [15], reported a high lost to follow up of patients with RC that is similar to our previous study. However, this update revealed a significant reduction to as low as 7.4% lost to follow-up [13]

CONCLUSION

This update showed a trend toward stable RC though yearly increase was observed. It also confirmed increased utilization of diagnostic CT scan. It is not surprising since majority of the patients presented with localised and locally advanced disease, RN still remained the main stay of treatment with an interesting best survival rate compared to other studies in the sub-region. With the increasing pathologist's expertise, rare renal cancers such urothelial, collecting duct RC with neuroendocrine components are being identified.

Declarations

We declare that the patients were managed at the University College hospital at no extra cost to their treatment. Information was obtained from the theatre and urology record books without revealing the identity of patients.

Study Limitations

Acknowledgement: We appreciate the surgical trainee for data entry per case. We are grateful to the theatre nurses for the supports during the surgery. We thank the staff in pathology department who assisted in retrieving the histology reports.

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Conflict of Interest: We declare no conflict of interest.

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