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# RENAL CELL CARCINOMA IN A SEMI-URBAN POPULATION OF SOUTH-WESTERN NIGERIA

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## ABSTRACT

***Objective:*** **To describe the demographic features, treatment challenges and prognosis of renal cell carcinoma (RCC) in a semi-urban population of south-western Nigeria**
***Design:*** **A retrospective review of RCC managed between January 2007 and December 2014**
***Setting:*** **Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, south-western Nigeria**
***Subjects:*** **Fifty-one patients with histologically confirmed RCC**
***Interventions:*** **Radical nephrectomy, Immunotherapy**
***Main outcome measures:*** **Surgical outcomes**
***Results:*** **A total of 51 cases were reviewed, representing 46.8/100,000 of all new patients. Age range was 21 to 83 years, with peak in third decade and male to female ratio of 1:1.5. Identified risk factors were systemic hypertension (15.7%), smoking (11.8%) and obesity (3.9%). Triad of haematuria, loin pain and loin mass was found in 13.7% while 5.9% were discovered incidentally. The right and left kidneys were involved in 41.2% and 58.8% respectively. Radical nephrectomy was the most common procedure done (78.4%). Surgical complications included excessive primary haemorrhage (8.5%), surgical site infection (6.4%) and duodenal injury (2.1%) while mortality was (2.1%). Adjuvant immunotherapy with sunitinib/sorafenib was given in 7.8% of patients. The histologic types were clear cell (60.8%), chromophobe (17.6%), papillary (13.7%), sarcomatoid (3.9%), mixed (1.9%) and multilocular cystic RCC (1.9%). Clear cell variant were low grade with good prognosis. Poor prognostic factors were sarcomatoid histology and late presentation**
***Conclusion:*** **RCC is more common in females mainly of the younger age group in our environment. Radical nephrectomy remains the mainstay of management, including in advanced cases.**

## INTRODUCTION

Renal cell carcinoma (RCC) is the most common malignant renal tumour in adults, accounting for 2-3% of all adult cancers and 2% of all cancer deaths (1). According to cancer statistics, it is projected to account for 62,700 of new cancer cases and 14,240 cancer deaths for 2016 in the United States alone (2). Its incidence has actually been on the rise since the 1970s by an average of 3% per year for whites and 4% per year for African-Americans, largely related to the more prevalent use of ultrasonography and computed tomography (CT) for the evaluation of a variety of abdominal complaints (3). However, not much has been documented epidemiologically about this tumour on the African continent, as literature on RCC in sub-saharan Africa is relatively sparse (4).
Though RCC can be asymptomatic, occurrence of symptoms may be due to local tumour growth, haemorrhage, paraneoplastic syndromes or metastatic disease. Constitutional symptoms such as weight loss, fever or night sweats may also be present, while minority of patients have features of venous obstruction such as varicocoele or pedal oedema (5). Due to the retroperitoneal location of the kidney, majority of RCC cases do not become symptomatic

until advanced disease develops and the tumour has achieved adequate size to displace or invade contiguous organs (6).

This article describes the incidence, risk factors, pattern of presentation, management challenges, histologic sub-types and prognosis of RCC in a cohort of patients attending a tertiary care centre in a semi-urban location of south-western Nigeria.

## MATERIALS AND METHODS

A retrospective review of all patients with histologically confirmed RCC in our university teaching hospital between January 2007 and December 2014 was done. Information was extracted from hospital records and analyzed using statistical package for social sciences

(SPSS) version 21 software for biodata, pattern of clinical presentation, identifiable risk factors, investigation results, intra-operative details, histologic subtypes, treatment outcome and follow up duration. Staging and grading were done using the Robson and Fuhrman systems respectively.

## RESULTS

A total of 51 cases of histologically confirmed RCC representing 0.59% of all cancer cases and 46.8 / 100,000 of all new patients seen in our hospital over the eight year period were reviewed. Their age range was 21 to 83 years (median 41.7 years) with peak incidence in the 3rd decade (Table 1). The male to female ratio was 1:1.5. Systemic hypertension was found in seven patients (15.7%), smoking in six patients (11.8%) and obesity in two patients (3.9%). In the remaining 36 patients (70.6%), no risk factor could be identified. Genetic screening for Von Hippel Lindau syndrome was not done in any of the patients.

Three patients (5.9%) were asymptomatic and were detected incidentally during abdominal ultrasonography for pregnancy (two patients) and pre-employment evaluation (one patient). The symptomatic patients had symptom duration ranging from 6 to 32 weeks. A combination of loin pain and loin mass was the commonest feature at presentation (19, 37.2%). The triad of haematuria, loin pain and loin mass were found only in seven (13.7%) of the patients (Table 1).

Abdominal ultrasound was done in all the patients. CT scan (Figure 1) and other investigations are as highlighted in Table 1. History and investigation results confirmed that eight patients (15.7%) had features of metastasis at presentation.

The RCC involved the right kidney in twenty one patients (41.2%) Two of the patients with right RCC had solitary right kidney while a third patient had RCC in an ectopic (pelvic) right kidney. There were no bilateral RCC cases seen in our study.

Forty-seven patients (92.2%) had surgical intervention while the remaining four patients (7.8%) were inoperable and managed symptomatically. Radical nephrectomy was the commonest surgical procedure done (40, 78.4%). Tumour debulking was done in five patients (9.8%) while incisional biopsy of intra-abdominal metastatic deposit was done at laparotomy for the remaining two patients (3.9%).

Weight of the nephrectomy specimen ranged between 420-8400g. Surgical complications included excessive primary haemorrhage (8.5%) necessitating blood transfusions, surgical site infection (6.4%) managed with local wound care, duodenal injury (2.1%) managed conservatively in conjunction with the gastrointestinal surgeons and operative mortality (2.1%).

Immunotherapy with sunitinib or sorafenib was given as adjuvant treatment in four patients (7.8%), while two patients (3.9%) had radiotherapy to palliate bone pains from metastatic deposits. One patient was given medroxyprogesterone acetate as adjuvant hormonal therapy. No patient was given chemotherapy.

Follow up was for 15-48 months, with a mean duration of 17 months. This was by regular clinical evaluation, abdominopelvic ultrasound scan and electrolytes, urea and creatinine assay. The patients that were inoperable and those that had laparotomy and biopsy died within 6 months of presentation. The patients in whom tumour debulking was done died within 6-12 months while 95% of those that had radical nephrectomy survived for more than 12 months. Four (7.8%) of those that had radical nephrectomy developed recurrence within 18 months of follow-up. One was managed with sunitinib immunotherapy, two were referred for radiotherapy and the last one died from complications of cerebral and lung metastasis. Up to 55% of them have been followed up for at least 24 months and are alive and well.

Pathologic specimen was obtained either from surgery or autopsy for those without surgical intervention. Gross examination of the specimen showed the tumour was commoner in the upper pole (23, 45.1%), with lower pole tumour, centrally located tumour and tumour already taking up the whole of the kidney in twelve (23.5%), six (11.8%) and ten (19.6%) patients respectively. Histology revealed clear cell variant as the most common histologic sub-type, occurring in 31 (60.8%) cases (Figure 3); followed by chromophobe (9, 17.6%), papillary (7, 13.7%), sarcomatoid (2, 3.9%), mixed (1, 1.9%) and multilocular cystic RCC (1, 1.9%). Robson staging showed that 10 (19.6%) were stage 1, 14 (27.5%) were stage 2, 18 (35.3%) were stage 3 while nine (17.6%) were in stage 4. The nuclear grading of the tumour revealed that ten patients (19.6%) had grade I, 21 patients (41.2%) had grade II, eleven patients (21.6%) had grade III and nine patients (17.6%) had grade IV disease. Clear cell variant were essentially low grade and had the best prognosis while the sarcomatoid variant were all high grade and had the worst prognosis.

**Table 1**
**Clinical presentation and investigations**

| | | Frequency | Percentage |
|---|---|---|---|
| **A** | **AGE-RANGE** | | |
| | 21 to 30 | 17 | 33.3 |
| | 31 to 40 | 15 | 29.5 |
| | 41 to 50 | 7 | 13.7 |
| | 51 to 60 | 7 | 13.7 |
| | 61 to 70 | 4 | 7.8 |
| | 81 to 90 | 1 | 2.0 |
| | Total | 51 | 100.0 |
| **B** | **CLINICAL FEATURES** | | |
| | Loin Pain, Loin Mass | 19 | 37.2 |
| | Haematuria, Loin Pain, Loin Mass | 7 | 13.7 |
| | Haematuria | 6 | 11.8 |
| | Loin Mass, Constitutional features | 5 | 9.8 |
| | Loin Pain | 4 | 7.9 |
| | Haematuria, Loin Pain | 3 | 5.9 |
| | Incidental finding | 3 | 5.9 |
| | Haematuria, Loin Mass | 2 | 3.9 |
| | Hematuria, Paraneoplastic features | 2 | 3.9 |
| | Total | 51 | 100.0 |
| C | **INVESTIGATIONS** | | |
| | Ultrasound only | 3 | 5.9 |
| | Ultrasound and IVU | 17 | 33.3 |
| | Ultrasound and CT-urography | 28 | 54.8 |
| | Ultrasound/IVU/CT-urography | 1 | 2.0 |
| | Ultrasound and MRI | 1 | 2.0 |
| | Ultrasound/CT Urograpgy/Angiography | 1 | 2.0 |
| | Total | 51 | 100.0 |

*IVU: Intravenous urography*
*CT: Computerised tomography*
*MRI: Magnetic resonance imaging*

**Figure 1**
**CT image in one of the patients**

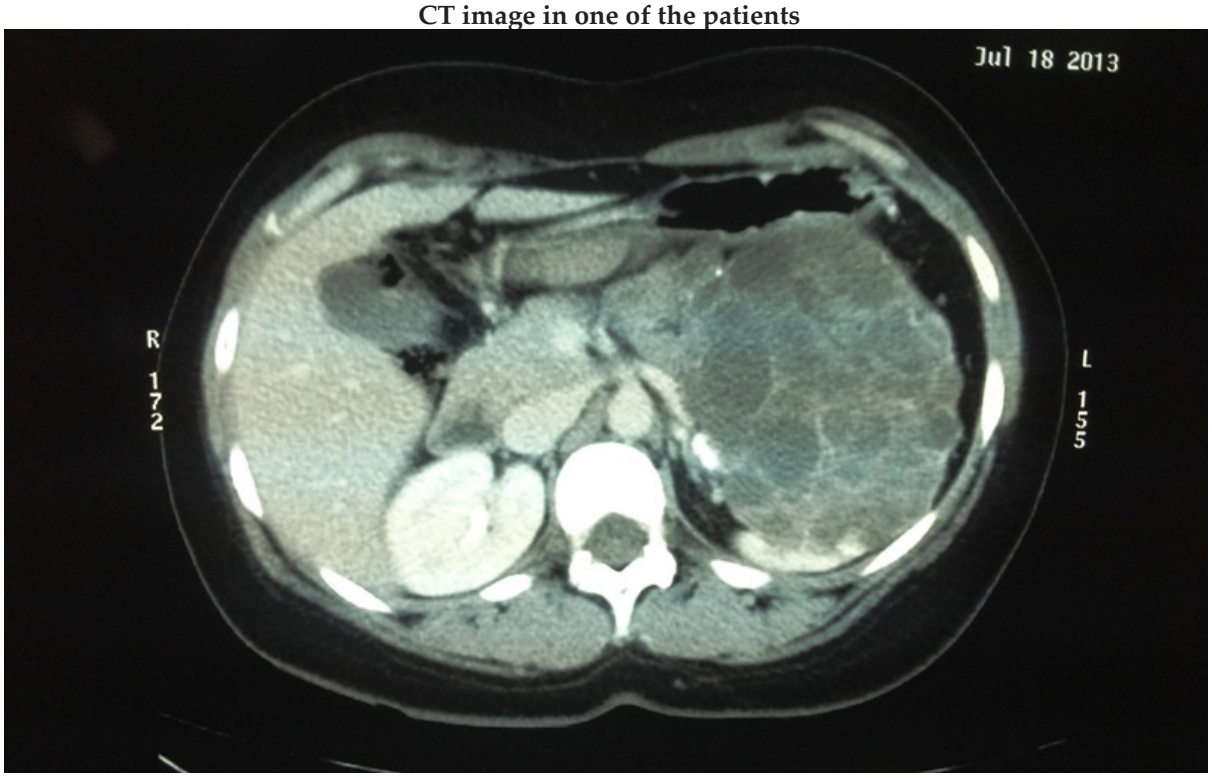



**Figure 2**
**Nephrectomy specimen (bisected) for one of the patients showing tumour in lower pole of the kidney**

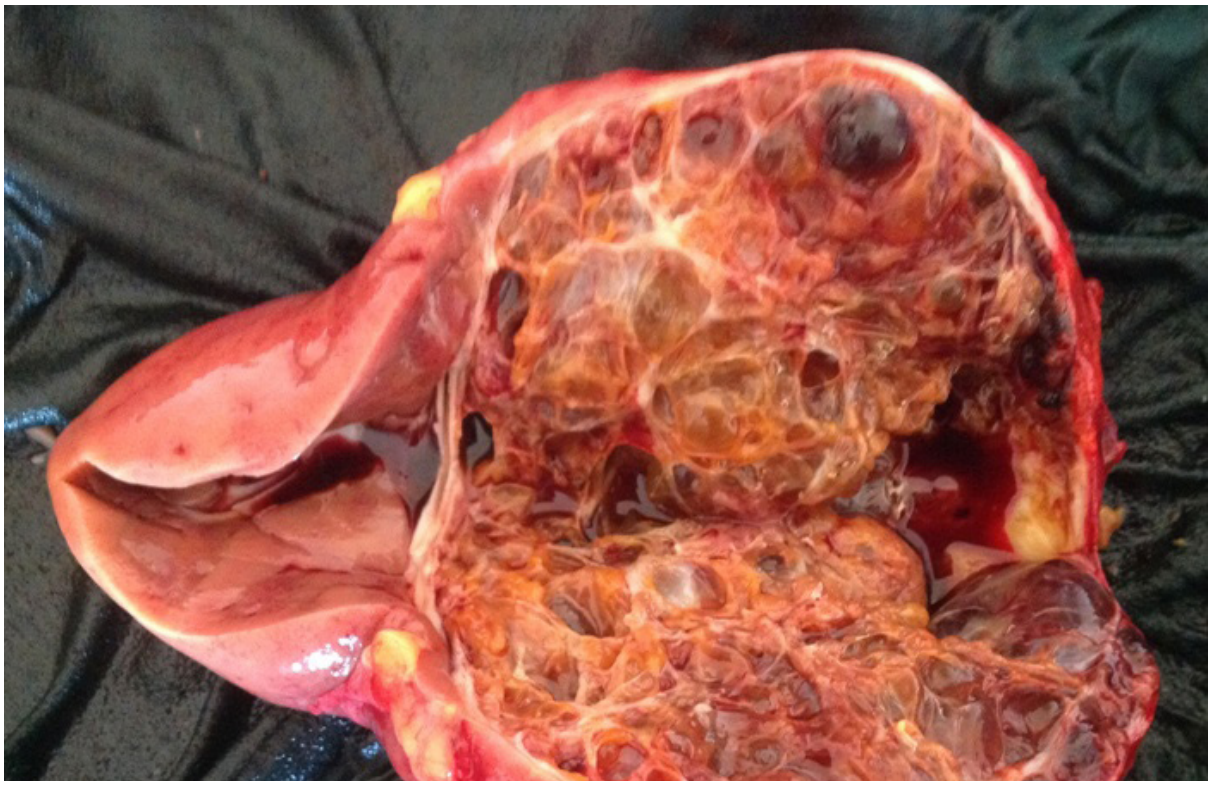
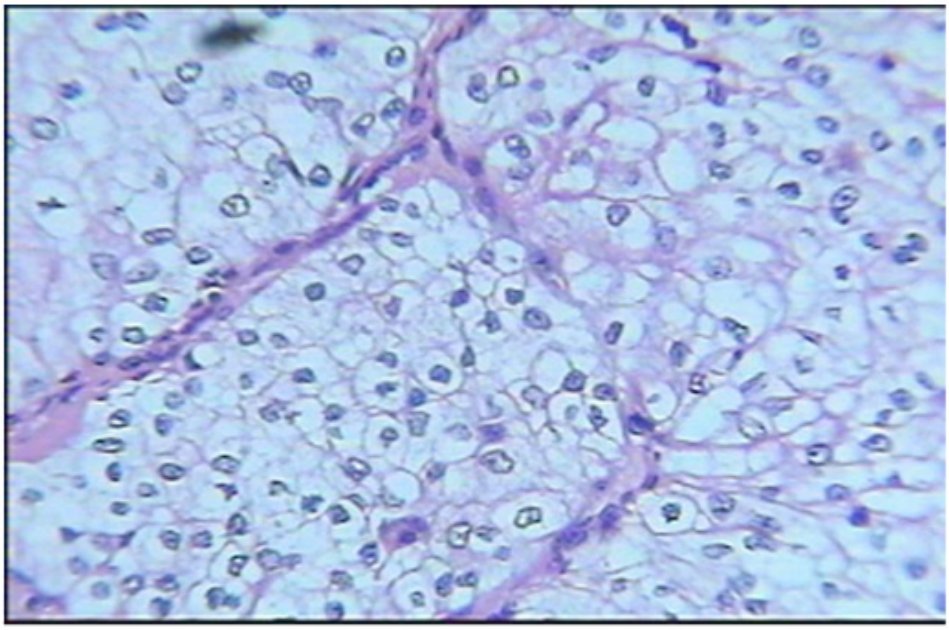


**Figure 3**
**Photomicrogragh showing Clear cell variant of renal cell carcinoma**



## DISCUSSION

Though findings from a previous study in our hospital showed that RCC was more common in males (7), our result in this study suggests a changing gender profile, as we had more women than men with RCC. Similar female preponderance was noted by Tijani *et al* (4) also in south-western Nigeria. Some authors have suggested that estrogens play a role in aetiology of RCC (8), and this may be partly responsible for the increase in RCC occurrence in females compared to males. Another possible explanation is that since women routinely have abdominal ultrasound scans for pregnancy, they stand a higher chance of having any solid renal mass picked up during such ultrasound evaluation, as was the case in a few of our patients. As adduced by Mohammed *et al* (6), another contributory factor may be that females are generally very sensitive and are more likely to seek medical attention earlier than males.

There is a reduction in the age of RCC occurrence in our practice as its peak incidence was in the third decade of life from this study, as against fifth decade reported ten years ago from our hospital (7). Our second peak was in the fourth decade and more than 50% of all our patients were less than 40 years of age. Though definitive reason for this is unknown at present but is an area for future research, a study in Lagos, also in south-western Nigeria, equally found that a significant proportion of their patients with RCC had similar younger age at presentation (4). This is however a clear departure from peak incidence in fifth decade from other parts of Africa (9) and sixth decade reported for Caucasians (10).

The risk factors identified in our patients were cigarette smoking, obesity and hypertension, consistent with reports from literature (11). It is known that RCC in younger age groups is more likely to have a familial tendency (12). None of our patients however had a positive family history of the disease. Genetic screening for conditions such as Von Hippel Lindau syndrome would have been desirable for further screening, but was not available in our environment.

The increasing use of imaging procedures such as ultrasonography, CT-scan and magnetic resonance imaging (MRI) in the evaluation of gastrointestinal complaints in developed countries has led to increased incidental discovery of RCC (11). This was found to be true in our practice as a few of our patients (5.9%) were discovered incidentally during routine ultrasonography for other reasons. This is an improvement over previous report published 10 years ago in our hospital (7) during which none of the patients was discovered incidentally. With improved awareness, more affordable health care from advent of health insurance and increased screening, the number of incidentally discovered cases is further expected to increase in our environment in the immediate future.

For symptomatic patients, the classic triad of haematuria, loin mass and loin pain were not common in this study and was observed in only 13.7% of patients, comparable to other reports from similar settings as ours (13,14). This classic triad almost always denote advanced disease and was more common before the advent of routine ultrasonography and CT

scanning (15). The reduction in the number of patients with this triad may therefore signify improving diagnostic facilities, unlike what was obtainable in the past.

The tumour was more common on the left compared to the right with no case of bilateral disease in this series; similar to finding from previous study in our centre (7). It is interesting to note that we had cases of RCC in adult patients with previously undiagnosed background congenital renal anomaly. RCC was found in solitary right kidneys and also in patient with pelvic kidney. Because of the diagnostic dilemma that can result from clinical examination of such patients, a high index of suspicion should be entertained and RCC considered as a possible differential diagnosis for all abdominal masses, regardless of location on abdominal examination.

Surgical excision remains the mainstay of treatment, since RCC is relatively resistant to chemoradiation therapy (4), (7) and immunotherapy with sunitinib, sorafenib or bevacizumab is expensive and not readily available. We therefore offered surgery to almost all of our patients (92.2%). Radical nephrectomy was the primary treatment modality in majority of them (78.4%), despite the advanced nature of their disease. It offers good reduction of local tumour burden and there is also the possibility of spontaneous regression of some metastatic deposits following excision of the primary tumour in metastatic RCC (16). We routinely used an anterior, transperitoneal approach for the surgery due to large tumour size and need to explore the abdomen for local spread and metastasis. In addition, this approach allows early access to the renal vessels with minimal manipulation and attendant risk of tumour dissemination. We recorded huge sizes of nephrectomy specimen (Figure 2), ranging from 420 – 8400g, in similar manner to 480 – 3820g reported earlier from our hospital (7). This is however in contrast to the developed countries where the size of kidney tumours at presentation has steadily and consistently decreased over the years (5), hence increasing popularity of nephron sparing surgeries in those parts of the world.

The tumour was found to be more common in the upper pole than in any other part of the kidney from our study. In those with whole organ involvement, the tumour could have started from either of the poles and secondarily involved the whole organ since RCC has not been shown to have predilection for any poles of the kidney. Peculiar management challenge with upper pole tumours in our practice was associated difficulty in sparing the ipsilateral adrenal gland during radical nephrectomy. We thus routinely included the adrenal gland during radical nephrectomy for upper pole tumours.

It was not surprising that clear cell was the most common histologic sub-type from our review, since it is also the most common sub-type worldwide. The 60.8% recorded for the clear cell variant is however higher than the 46.2% reported from our centre in previous studies (7). Though the reason for this is unclear, our finding in this study is similar to the 60.0% reported for clear cell RCC in Lagos, southwestern Nigeria (4). The cytological grade of the tumour is known to have important predictive value in RCC (17). Though our follow-up was not without its shortcomings, contact tracing of our patients revealed that the low grade tumours (mainly clear cell RCC) had the best prognosis while the high grade tumour (mainly sarcomatoid RCC) had the worst prognosis. Up to a quarter of our patients died within 12 months of presentation, mainly among the inoperable patients and those that had either tumour debulking or biopsy. This high mortality compared to better survival in advanced countries (5) is a likely fall-out of late presentation generally prevalent among our patients.

In conclusion, this study showed reduced age of occurrence, female preponderance and increased number of incidentally discovered RCC in our practice in south-western Nigeria. Radical nephrectomy is safe and beneficial, even in advanced cases. Clear cell histologic type has the best prognosis while sarcomatoid tumours have the worst prognosis.

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