

## **EDITORIAL**

### **Clinical Presentation and Histopathological Patterns of Renal Cell Carcinoma in Gezira Hospital for Renal Diseases and Surgery**

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#### **Abstract:**

**Background:** Renal cell carcinoma (RCC) is the most common primary tumour of the kidney in adults, responsible for (80-85%) of renal tumours<sup>(1)</sup>. Due to the absence of studies in Sudan in assessing the pattern and presentation of RCC, we conducted this retrospective study in Gezira Hospital for Renal Diseases and Surgery, in the period from January 2006 to January 2012.

**Objective:** To determine the clinical presentation, pathological pattern and stages of RCC in patients who were treated in (GHR) in the period of this study.

**Results:** A total of 60 patients were diagnosed as RCC in the period of six years. The disease was more common in males, with a peak incidence in the fifth and sixth decades. The classical triad were observed in 19 patients. Mean duration of symptoms was 4 months. Some patients had metastasis in the lung, bones or liver at diagnosis. Most of the patients presented with haematuria (66.6%), a small number with cervical lymphadenopathy (6.7%), lower limb edema (3.3%) and non reducible varicocele (5%).

**conclusion:** A large number of patients presented with a palpable loin mass, in contrast incidentally diagnosed cases were few. The age of presentation is one decade earlier than that in the western world.:

#### **Introduction:**

Renal cell carcinomas (RCCs) are the commonest primary renal tumours in adults responsible for 80 - 85 % of tumours, followed by transitional cell carcinoma (TCC). This tumour is relatively rare in paediatric practice where it is replaced by Wilms tumour.<sup>(1)</sup>

Globally, the incidence of RCC varies widely from region to region with the highest rates observed in the Czech Republic and North America<sup>(1)</sup>

The incidence of RCC has been increasing over last decades, but the size of tumour mass has been decreased at diagnosis and so is the stage, with proportional increases in 5years survival rate. This may be attributed to the wide use of new imaging techniques, and incidental diagnosis which approached more than (50%) in some settings along with early surgical intervention.

A number of environmental and clinical factors have been implicated in the aetiology of RCC<sup>(2, 3)</sup>. These include hypertension, acquired cystic disease of the kidney (typically associated with dialysis), obesity, hepatitis C, smoking, occupational exposure to toxic compounds such as cadmium and asbestos, analgesics. Genetic abnormalities as Von Hippel- Lindau gene, deletion of chromosome 3p and mutations in the p53 gene had been implicated.<sup>(2, 4, 5, 6, 7)</sup>

Previously, RCCs were classified by cell type and growth pattern<sup>(8)</sup>. This classification has recently changed so as to more accurately reflect the morphology, growth pattern, cell of origin, histochemical, and molecular basis of the different types of adenocarcinomas<sup>(9, 10)</sup>. Several distinct subtypes of RCC have been

## ***EDITORIAL***

identified, including: clear cell (75 to 85 %), which typically has a deletion of chromosome 3p, arises from the proximal tubule<sup>(11)</sup>. In addition to occurring as sporadic disease, clear cell carcinomas are specifically associated with von Hippel-Lindau disease. Papillary (chromophilic) carcinoma (10 to 15%) are frequently multifocal and bilateral, and commonly present as small, early stage tumours, Chromophobe (5 to 10%), Oncocytic (uncommon), collecting duct (Bellini's duct) carcinomas are very rare, and less than 5 % of RCCs are considered unclassified, these tumours have a worse prognosis compared with clear cell carcinomas.<sup>(12, 13)</sup>

Symptoms associated with RCC can be due to local tumour growth, haemorrhage, paraneoplastic syndromes, or metastatic disease<sup>(14)</sup>. With the more pervasive use of non-invasive imaging for the evaluation of nonspecific symptoms, more than 50% of RCCs are now detected incidentally<sup>(15-16)</sup>. The classic trait of flank pain, haematuria and abdominal mass are present in about 10 – 15 % of patients and indicate an advanced disease (too late to treat). Before the advent of ultrasonography and CT, most patients with RCC presented with one or more of these signs or symptoms, and many were incurable. Other indicators of advanced disease include constitutional symptoms, such as weight loss, fever, night sweats. Physical examination findings are such as palpable cervical lymphadenopathy, non reducing varicocele, or bilateral lower extremity oedema due to venous involvement. A minority of patients present with symptoms directly related to metastatic disease. Paraneoplastic syndromes are found in 20% of patients, like hypertension, nonmetastatic hepatic dysfunction, hypercalcaemia, Cushing syndrome, polycythaemia, hypoglycaemia and other hormone related disorders.

### **Patients and Methods:**

This is a retrospective and prospective, descriptive, cross sectional and hospital based study conducted in Gezira Hospital for Renal Diseases and Surgery in Wad Madani, which is a governmental class (A) hospital. It is a tertiary care hospital which provides service to the population of Gezira and neighbouring states. The hospital offers 24 hours emergency, laboratory, blood bank and pharmacy services. The patients with renal cell carcinoma were diagnosed and managed in the hospital during the period from January 2006 to January 2012, they agreed to participate and were enrolled in the study.

The sample size was 60 patients. Data were collected by detailed and structured questionnaire to be filled directly by the patients. Data were analyzed by computer using statistical package for social science (SPSS) software (v:17).

### **Results:**

The males were 36(60%) and the females were 24 (40%), with a male to female ratio of 3:2. The majority of the patients were above 50 years (81%), and 61% of them reside in the central Sudan (Gezira and Khartoum states).

About 75 % of patients had duration of symptoms more than one month when presented first time. Asymptomatic patients were few, 6 patients ( 10% ), but more than half of them had loin mass when presented first time 34 ( 57 %), the classical triad of ( Hematuria, loin pain and loin mass ) occurred in about 31.6%. (Table 1). In more than half of the patients (57%) physical examination revealed a palpable loin mass. Few patients had palpable cervical lymph nodes (6.7%), non reducible varicocele (5%) or lower limb oedema (3.3%).

**EDITORIAL**

All patients had abdominal ultrasound as initial imaging of the mass followed by enhanced CT scan; only four patients underwent MRI to assess the vascular system and bones. Chest X ray as a tool for assessing lung and chest wall metastases was done in all patients.

Two thirds of the patients 40(66.7%) had clear cell carcinoma representing the most common type. About 15 % were papillary type, (10%) were chromophobe and (5%) were collecting duct carcinoma .Two cases were unclassified.

Early disease stages constituted 40 %( stage I ten and II fourteen). The rest (60%) were advanced stages (III twenty and IV sixteen).

**Discussion:**

This study is a retrospective prospective, descriptive, cross sectional and hospital based study. Due to lack of local studies in pattern and presentation of RCC in Sudan we had been obligated to compare the results with available regional and international studies. The analysis of patients’ demographic data showed that the distribution between sexes is in keeping with international standards, 2:3 for female: male respectively. A regional study in Nigeria showed female predominance with male to female ratio of 1:1.7.<sup>(17)</sup> Most of the cases in this study were above 50 years, and the peak incidence was between the fifth and sixth decades of life (46.7%), which is one decade earlier than in the western world population where RCC is primarily a disease of the elderly with typical presentation in sixth and seventh decades.<sup>(15, 16)</sup> Similar to our findings were reported in Nepal.<sup>(18)</sup> The mean age at time of diagnosis was (58.3 years) which was near to what was found in Nepal, which was (55year). In contrast the mean age at Lagos and Obafemi hospitals was 41.8 years and 47.5 years respectively<sup>(20)</sup>.The majority of RCC are a symptomatic until advanced disease develops.This is due to the retroperitoneal location of the kidney. Local symptoms arise only after tumor achieves a size large enough to displace or invade other organs.<sup>(19)</sup>

In this study the common presenting symptoms were haematuria (66.7%), loin pain (48.3%) and loin mass (57.3%). Occurrence of the first two was more common in females and quite similar to the international one<sup>(19)</sup>, but presence of loin mass was more in males and it was higher than that in the international figures. This indicates that male patients do not seek medical advice until the mass drew their attention.

**Table 1: Clinical presentation**

Clinical presentation		NO	%
<b>Duration</b>	weeks	6	10
	months	45	75
	Years	9	15
<b>Presentation</b>	asymptomatic	6	10
	Haematuria	40	66.6
	Loin pain	39	65
	Loin mass	34	57
	Classical triad	9	15
<b>Conistitutional</b>	pyrexia	18	30
	Weight loss	27	45
	Anaemia	16	26.7

**EDITORIAL**

<b>Paraneoplastic</b>	AbnormalLFT	17	28.3
Hyper calcaemia		1	1.6
<b>Metastatic symptoms</b>	Lungs	3	5
	Bones	2	3.3
	Liver	4	6.7

**Table 2: Physical examination**

Examination	Number	Percentage
Palpable loin mass	34	57%
Palpable cervical lymph node	4	6.7%
Bilateral Lower limb edema	2	3.3%
Non reducible varicocele	3	5%
NAD	17	28. %3

The rate of symptoms in our cases was reversed when compared with the Lagos study; haematuria (40.6%), loin pain (86%) and palpable loin mass (90.6%).<sup>(17)</sup> The classical triad appeared in about one third of the patients, it's higher than in the international reports (7-10%), but similar to what reported in Nigeria (29-36%). In this study some patients presented with constitutional symptoms such as pyrexia, weight loss and anaemia<sup>(15, 17, 20)</sup>. Constitutional symptoms have a great correlation with disease duration and stage. The paraeneoplastic syndrome was observed in (33.3%) and this result is comparable with international studies (20-40%). Distant metastatic symptoms were found at time of diagnosis, surprisingly two thirds of them were males.

Concerning physical examination of the patients studied in this review more than half of them (57%) presented with palpable loin mass, this occurred in one third of patients in the western world<sup>(20)</sup>. This may be due to late presentation in our community. Other signs appeared with low frequency such as palpable cervical lymphadenopathy (6.7%), limb oedema (3.3%) and varicocele (5%) all are in keeping with international and regional reports.<sup>(15, 17)</sup>

All patients in this study had abdominal ultrasound as initial imaging, which was found to be very useful in diagnosing a renal mass. CT scan was also done for all cases; it is the method of choice for staging of tumour and more sensitive than sonography. It looks clear that when patients were directed into the right referral tract the diagnosis will be obvious. MRI as an additional imaging to CT has been done for only few cases, it is more sensitive in assessing the vessels and bone lesions but has no other advantages over CT scan. Regarding the histopathological patterns all these percentages are similar to the international ones<sup>(10, 18, 19)</sup>, but in Nigeria incidence of clear cell type was low (33.3%)<sup>(20)</sup>. The stage of disease in this study is in keeping with regional series where African people presented and diagnosed late (60%); had locally

**EDITORIAL**

advanced or metastatic disease <sup>(17, 18)</sup>. In contrast to the results of international studies where the rule is presentation in early stages and increased incidental diagnosis of cases. <sup>(15, 16, 19)</sup>

**Table 3: Histopathological types**

Type	Number	Percentage
Clear cell	40	66.7%
Papillary ( chromophilic )	9	15%
Chromophope	6	10%
Collecting duct	3	5%
Unclassified	2	3.3%

**Table 4: Staging**

Stage	Number	Percentage
Stage i	10	16.67%
Stage ii	14	23.33%
Stage iii	20	33.33%
Stage iv	16	26.67%

**Conclusion:**

RCC occurred one decade earlier in our cases than western population. The highest incidence was in the fifth and sixth decades. A large number of patients presented with the classical triad, most of them were males. Incidentally diagnosed were few and two third of them were females. The commonest histological type was clear cell

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***EDITORIAL***

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