Renal cancer in Adult Sudanese patients in Khartoum State:
Clinico pathological Study

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A thesis submitted in partial fulfillment for the requirements of the degree of Clinical MD in Pathology of the University of Khartoum
January 2011

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Dedication

To my beloved father and mother

To my lovely family

My husband Mohammed Abbas and my children Asma, Banan & Ahmed

For their patients
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Acknowledgement

I would like to thank my supervisor Dr. Mohammad Mohammad Othman, who devoted a great deal of his time to review this study, and gave me instructions and guidance which all led to the final production of this work.
Special thanks to my family members, for their infonaut support and tolerance.
I wish to thank the head of department of histopathology at Soba teaching hospital, IbinSina hospital, National Health laboratory and Khartoum teaching hospital for making the records available for this study.
I am sincerely thankful to the technicians and staff of National Health laboratory, IbinSina hospital, Soba teaching hospital & Khartoum teaching hospital for their invaluable help to get the patients records and histopathological slides, and their willingness to work long hours.
I’m also grateful to Mr. Hassan Ali who performed the statistical analysis. Finally I wish to express my deep gratitude to every person who helped turning this work into a reality.
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<td>CD</td>
<td>Cluster of Differentiation</td>
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<td>CDC</td>
<td>Collecting Duct Carcinoma</td>
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<td>CK</td>
<td>Cytokeratin</td>
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<td>Cm</td>
<td>Centimeter</td>
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<td>CT</td>
<td>Computed Tomography</td>
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<td>EBRT</td>
<td>External Beam Radiation Therapy</td>
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<td>DNA</td>
<td>Deoxyribonucleic Acid</td>
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<td>e.g</td>
<td>For Example</td>
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<td>FU</td>
<td>Fluorouracil</td>
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<td>HIV</td>
<td>Human Immune Deficiency Syndrome</td>
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<td>MCRCC</td>
<td>Multi Locula Cystic Renal Cell Carcinoma</td>
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<td>IVC</td>
<td>Inferior Vena Cava</td>
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<td>MRI</td>
<td>Magnetic Resonant Imaging</td>
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<td>PET</td>
<td>Positron Emission Tomography</td>
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<td>PRCC</td>
<td>Papillary Renal Cell Carcinoma</td>
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<td>RCC</td>
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<td>TNM</td>
<td>Tumor Node Metastasis</td>
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<td>TS</td>
<td>Tuberous Sclerosis</td>
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<td>US</td>
<td>Ultra Sound</td>
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<td>VHL</td>
<td>Von Hippel-Lindau</td>
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<td>WHO</td>
<td>World Health Organization</td>
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Abstract

Objectives: Renal cancer became a noticeable tumor recently with high mortality rates in the developed countries.

The objective of this study to review the histopathological pattern of renal cancer and show the relationships between the histological type, the clinical presentation, the mode of surgical procedure, grading the tumors by using Fuhrman grading and staging the tumors by using TNM staging system.

Methods: This is a descriptive retrospective case series study of 108 adult renal cancer patients during the period from Jan 2007 to Aug 2010 from different histopathology departments in Khartoum state including Soba Teaching Hospital, IbnSina Hospital, Khartoum Teaching Hospital & National Health Laboratory.

Data was collected from the patients request forms and patients files including detailed personal, clinical and pathological data. Formalin fixed paraffin embedded blocks of processed histopathology specimens were recut, stained and examined by the candidate and reviewed by the supervisor to determine the histopathological type, tumor grade and clinical stage of the patients.

Results: The study included 108 patients, 59 were males and 49 females, with a M: F ratio of 1.13:1.0.

The youngest patient was 19 years and the eldest was 86 years.

Thirty three patients (31.4%) were below 46 years with a mean age of 53 years. The majority of patients were from central regions.

The clinical presentation included loin pain in 35.2% (n=37), abdominal mass in 31.4% (n=34), hematuria in 22.9% (n=24) and 4.8% (n=5) were incidental finding during ultra sound examination.

Two types of surgical procedures were performed: nephrectomy and partial nephrectomy in 92 and 11 patients respectively. Eleven patients had needle biopsy only.
Microscopic examination of the slides identified 7 histological types of renal cancer. These were clear cell RCC in 71.2%, papillary in 18%, sarcomatoid RCC in 3.8%, Chromophobe in 0.9%, collecting duct RCC in 0.9%, transitional cell carcinoma in 4.5% and squamous cell carcinoma in 0.9%

Using Fuhrman grading system showed grade II, III, I and IV in 48, 29, 16 and 12 patients respectively

TNM staging system showed stage III, II, I and IV in 41, 30, 13 and 8 patients respectively.

**Conclusions:** Sudanese patients share many pathological and some of unique epidemiological features for renal cancer.
الآهدف: يعتبر سرطان الكلى من السرطانات التي يتميز بمعدلات وفيات عالية وقد أصبحت في السنوات الأخيرة من السرطانات الشائعة نسبياً في الدول المتقدمة. هدفت الدراسة إلى مراجعة التغييرات المرتبطة في الأنسجة في سرطان الكلى ويبحث علاقة الأنماط النسيجية للورم مع كل من الأعراض السريرية، نمط العلاج الجراحى، درجة التسرب والمرحلة السريرية.

منهجية البحث: هذه دراسة إستقصائية وصفية عن سرطانات الكلى عند السودانيين أجريت وسط 108 من المرضى في الفترة من يناير 2007 حتى أغسطس 2010 بمعالج مختلفة في ولاية الخرطوم والتي شملت م. سويا الجامعى، م. ابن سينا، العمل الصحي القومي، م. الخرطوم.

تم جمع معلومات سريرية من سجلات المرضى وتقاريرهم في المستشفيات المذكورة أعلاه. تم إعداد نسج وصروف ورواية عيانى للمرضى المثبتة في الفئات المختلفة، ومن ثم تم تشخيص الأنواع النسيجية المختلفة. تحدد درجة التسرب وتحديد المرحلة السريرية بواسطة الدارس ومن ثم مراجعتها مع احتسابات الأنسجة المشرف على البحث.

نتائج: تضمنت الدراسة 108 مريض كان منهم 59 من الذكور و 49 من الإناث بنسبة 1:1 لكل نوع، وتراوحت أعمار المرضى من 19 سنة إلى 86 سنة.

وقد أبرزت النسبة العالية لمرضى سرطان الكلى في الفئات العمرية الصغرى حيث كان هناك 33.14% من المرضى تحت عمر 46 سنة وكان متوسط العمر لكل الفئة هو 52.72 سنة.

أشارت الدراسة إلى النسبة العالية للمرضى الذين يسكنون المناطق الوسطى من السودان.

وجدت الدراسة أن نسبة 32.8% (37) من المرضى يشكلون من ألم في الحاضرة، 31.4% من ورم البطين، 22.9% من البول الدموي 4.8% (5) تم اكتشافهم بالصدفة عند اجراء موجات فوق الصوتية.

أظهرت الدراسة ثلاثة أنواع من العينات هي: استئصال الكلي البشري، عينه صغيرة عن طريق الجلد، وكانت النسبة على التوالي 87.6%، 9.91% و 1.9%.

الفحص المجهرى للشرائح وصل إلى شك أنواع نسيجية من سرطان الكلى هي سرطان الخلية الكلوية ومنها 71.2% من النوع الاعتراضي، 18% من النوع الوركي و 3.8% من النوع الاصطيعي. 0.9% سرطان الفنون الحلبية 0.9% سرطان الخلايا المتحولة 5.4%، السرطانات المصلية.

أظهرت الدراسة أن المرحلة السريرية، اشتركت 41 من المرضى 30 من المرضى، 13 مريض وانها المرحلة الرابعة 8 مرضى.

الخلاصة: المرضى السودانيون يتعرضون مع المرضى في العالم في العديد من الخصائص السريرية والأمانية وسرطان الكلى.

أشارت الدراسة إلى أهمية التنوع القصوى للاختصاص، المرضى عن سرطان الكلى وذلك للاكتشاف المبكر والوصول إلى معدلات امرائية ووفاة أقل.
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Chapter One
INTRODUCTION AND LITERATURE REVIEW

Malignant tumors of the kidney constitutes a group of tumors that are highly heterogeneous with respect to morphology and clinical behavior.

Renal cell carcinoma accounts for 85% of renal cancer in adults and represent about 3% of adult malignancies.\(^{(1)}\)

Renal cell carcinoma is found among all ethnic groups and geographic areas. With the highest incidence reported in north America and northern Europe and the lowest incidence in Asian countries and areas of central and south America. There is a higher incidence among blacks than whites in the United States. Men are more affected than women in a ratio of about 2:1 in the sixth and seventh decades of life.\(^{(5)}\)

The most important etiologic factor for RCC is cigarette smoking.\(^{(11)}\) Other environmental factors, nutritional and cytogenetic abnormalities are also established etiological factors. There is also increased incidence in patients with chronic renal failure and acquired cystic diseases. Autosomal dominant familial renal cancers account for only 4%, and they are common in younger individuals.

In Sudan, there are no published data on renal cancers. So, this study is designed to analyze the clinico-pathological patterns of renal cancer among adult Sudanese patients from different departments of pathology at Khartoum state during the period between 2007 to August 2010.

1-1 Normal anatomy and histology of the kidney

1-1-1 Anatomy

The kidneys are two somewhat bean-shaped, reddish-brown organs located in the retroperitoneal space on either side of the vertebral column. Each kidney weighs about 150 gms, measures 11 cm long and 6 cm wide and lies between T11-12 and L3. Each kidney has a convex lateral border and a concave medial border with the two borders merging at the poles.
superior and inferior portions). Surrounding each organ is the fibrous renal capsule, which is loosely adherent to it. Adipose tissue surrounds the capsule and is in turn surrounded by the renal fascia (Gerota's fascia), which secures the kidney to the posterior abdominal wall. Much of the medial border is occupied by an indentation, the hilum, through which the renal vessels, nerves, lymphatics and the renal pelvis enter or leave the renal sinus, the space enclosed by the renal parenchyma.

The bisected kidney through the hilum shows the parenchyma to consist of an outer cortex, which forms a continuous subcapsular band of tissue, and an inner medulla, which is discontinuous being interrupted by projections of the cortex towards the renal sinus, the renal columns (columns of Bertin). The medulla consists of several triangular structures, the pyramids, with their bases towards the cortex and their tips, called papillae, projecting into minor calyces. (2)

1-1-2 Blood Supply

The kidney is richly supplied by blood vessels as they receive about 25% of cardiac output. The cortex is receiving 90% of the total renal blood supply. The main renal artery divides into anterior and posterior sections at the hilum. From these, inter-lober arteries emerge, course between the lobes, and give rise to the arcuate arteries, which arch between cortex and medulla, in turn giving rise to the interlobular arteries. From the interlobular arteries, afferent arterioles enter the glomerular tuft, where they progressively subdivide into 20 to 40 capillary loops arranged in several units or lobules architecturally centered by supporting mesangial stalk. Capillary loops merge to exit from the glomerulus as efferent arterioles. In general, efferent arterioles from superficial nephrons form a rich vascular network that encircles cortical tubules (peritubular vascular network), and deeper juxtamedullary glomeruli give rise to the vasa recta, which descend as straight vessels to supply the outer and inner medulla. These descending arterial vasa recta then make several loops in the inner medulla and ascend as the venous vasa recta. (6)

1-1-3 Histology

The renal parenchyma is composed of functional units called the nephron, and connective tissue, the interstitium. Each nephron consists of a tuft of anastomosing capillaries called the glomerulus, formed from the afferent arteriole and draining into the efferent arteriole, and a tubular system called
the renal tubule. Epithelial cells called podocytes (or visceral epithelium of Bowman's capsule) invest the glomerulus, and are reflected to become continuous with the parietal epithelium of the Bowman's capsule. The Bowman's capsule is the bulbous, distended, closed proximal end of the tubular system and is invaginated by the glomerulus. The space between the glomerulus and capsule is the urinary space. Extending from the capsule is the proximal tubule, which is lined by tall cuboidal-to-columnar epithelial cells containing many mitochondria and a prominent brush border. The proximal tubule is the longest portion of the tubular system and is made up of convoluted proximal and distal straight (pars recta) segments. The pars recta descend into the medulla, where it forms the U-shaped loop of Henle. The latter reenters the cortex within which it forms the straight and convoluted segments of the distal tubule. The distal tubule, at about the junction between its two segments, runs close to the glomerular hilum and forms a specialized segment called the macula densa (see below). The distal tubule is lined by cuboidal epithelium that lacks a brush border. The distal tubule empties into collecting tubules, which in turn drain into collecting ducts. The latter converge, as they approach the medulla, to form the collecting ducts of Bellini, which run vertically through the medulla to the papillae. The collecting tubules and ducts are lined by pale-staining, cuboidal epithelial cells called clear cells scattered amongst which are darker-staining intercalated cells. The straight portions of the proximal and distal tubules and the collecting ducts run in parallel arrays in a portion of the cortex devoid of glomeruli and inaccurately called the medullary rays (because they appear to emanate from the medulla). The medullary ray and the glomeruli and convoluted tubules on either side of it form the cortical subunit, the lobule. The interstitium is made up of the interstitial cells, which are fibroblast-like, and matrix. In the cortex the interstitium is small and mainly occupied by small blood vessels and lymphatics and, at the hilum of glomeruli, lacis cells. However, in the medulla it increases considerably in amount. The lacis cells, together with the macula densa and specialized myoepithelial cells in the walls of afferent and efferent arterioles containing neurosecretory granules filled with renin form the juxtaglomerular apparatus.\(^2\)

1-2 Renal Pathology

1-2-1 Congenital Anomalies

About 10% of all people are born with malformations of the urinary system.\(^3\) Structural anomalies of the kidney include:
a) Agenesis of the kidney.
b) Renal hypoplasia.
c) Ectopic kidney.
d) Horseshoe kidney.

1-2-2 Cystic diseases of the kidney

Cystic diseases of the kidney are a heterogeneous group comprising hereditary, developmental and acquired disorders.

Classification of renal cysts is as follows:

1) Cystic renal dysplasia.
2) Polycystic kidney disease
   a) Autosomal dominant (adult)
   b) Autosomal recessive (child hood)
3) Medullary cystic disease
   a) Medullary sponge kidney
   b) Nephronphthisis
4) Acquired (dialysis associated) cystic disease
5) Localized (simple) renal cysts
6) Renal cysts in hereditary malformation syndromes (e.g, tuberous sclerosis)
7) Glomerulocystic disease
8) Extraparenchymal renal cysts (pyelocalyceal cysts, hilar lymphangiatic cysts)

1-2-3 Non Neoplastic Renal Diseases

Glomerular diseases

Glomerular diseases constitute some of the major problem in nephrology; chronic glomerulo nephritis is one of the most causes of chronic renal failure in humans.
The glomerular diseases are classified as:

1) Primary glomerulopathies, in which the kidney is the only or predominant organ involved. It constitute various types including: acute diffuse proliferative glomerulonephritis, rapidly progressive (crescentic) glomerulonephritis, membranous glomerulopathy, minimal change disease, focal segmental glomerulosclerosis, membranoproliferative glomerulonephritis, IgA nephropathy and chronic glomerulo nephritis.

2) Secondary glomerular diseases, in which the kidney is injured by a variety of factors and in the course of a number of systemic diseases eg, systemic lupus erythermatosis, vascular disorders such as hypertension and polyarteritis nodosa, metabolic diseases such as diabetes mellitus, and some hereditary conditions such as Fabry disease.\(^{(5)}\)

**Diseases affecting tubules and interstitium**

This includes:

1) Ischemic or toxic tubular injury that leading to acute tubular necrosis and acute renal failure.

2) Inflammatory reactions of the tubules and interstitium (tubulointerstitial nephritis).

3) Other tubulointersitial diseases, eg, urate nephropathy, hypercalcemia, nephrocalcinosis & multiple myeloma.

**Diseases of blood vessels**

Nearly all diseases of the kidney involve the renal blood vessels secondarily. Systemic vascular diseases, also affect the renal vessels, this includes:

- Benign nephrosclerosis.
- Malignant hypertension and accelerated nephrosclerosis.
- Thrombotic Microangiopathies.
- Renal artery stenosis.
Obstrucive diseases

- Obstructive uropathy.
- Urolithiasis (renal stones). \(^{(5)(6)}\)

1-3 WHO classification of kidney tumors

Renal cell tumours
Clear cell renal cell carcinoma 8310/31
Multilocular clear cell renal cell carcinoma 8310/3
Papillary renal cell carcinoma 8260/3
Chromophobe renal cell carcinoma 8317/3
Carcinoma of the collecting ducts of Bellini 8319/3
Renal medullary carcinoma 8319/3
Xp11 translocation carcinomas
Carcinoma associated with neuroblastoma
Mucinous tubular and spindle cell carcinoma
Renal cell carcinoma, unclassified 8312/3
Papillary adenoma 8260/0
Oncocytoma 8290/0

Metanephric tumours
Metanephric adenoma 8325/0
Metanephric adenofibroma 9013/0
Metanephric stromal tumour 8935/1

Nephroblastic tumours
Nephrogenic rests
Nephroblastoma 8960/3
Cystic partially differentiated nephroblastoma 8959/1

Mesenchymal tumours
Occurring Mainly in Children
Clear cell sarcoma 9044/3
Rhabdoid tumour 8963/3
Congenital mesoblastic nephroma 8960/1
Ossifying renal tumour of infants 8967/0
Occurring Mainly in Adults
Leiomyosarcoma (including renal vein) 8890/3
Angiosarcoma 9120/3
Rhabdomyosarcoma 8900/3
Malignant fibrous histiocytoma 8830/3
Haemangiopericytoma 9150/1
Osteosarcoma 9180/3
Angiomyolipoma 8860/0
Epithelioid angiomyolipoma
Leiomyoma 8890/0
Haemangioma 9120/0
Lymphangioma 9170/0
Juxtaglomerular cell tumour 8361/0
Renomedullary interstitial cell tumour 8966/0
Schwannoma 9560/0
Solitary fibrous tumour 8815/0

**Mixed mesenchymal and epithelial tumours**
Cystic nephroma 8959/0
Mixed epithelial and stromal tumour
Synovial sarcoma 9040/3

**Neuroendocrine tumours**
Carcinoid 8240/3
Neuroendocrine carcinoma 8246/3
Primitive neuroectodermal tumour 9364/3
Neuroblastoma 9500/3
1-4 Epidemiology & risk factors of renal cancer

1-4-1 Epidemiology

Renal cancer accounts for about 2% of all cancers. And around 208,500 new cases are diagnosed each year. \(^{(8)}\)

The incidences varies widely, with the highest rates being in North America and Scandinavia. There is higher incidence among blacks than whites in the United States. Estimated new cases and deaths from kidney and renal pelvis cancer in the U.S in 2010 :\(^{(9)}\)

- New cases 58,240
- Deaths 13,040

Renal cell carcinoma represents 85% of renal parenchymal malignancies. Among urologic tumors it is the worst in cancer specific mortality, since more than 40% of the patients with RCC die of the disease.\(^{(10)}\) RCC may occur at any age, with peak incidences in the sixth and seventh decades of life .They occur twice as frequently in men as in women.

1-4-2 Risk Factors

Environmental factors play a significant role in the development of renal cancers.
1) Tobacco, whether smoked or chewed, heavy smoking double the risk of RCC, directly related with the number of cigarettes and inversely with age of beginning of the habit.\textsuperscript{(11)}

2) Obesity, particularly in women, increased the risk up to 5 fold higher risk in those with highest 5 percent body mass index compared with lowest quartile.\textsuperscript{(12)}

3) Hypertension has been identified as a significant risk factor. Despite the exact mechanism is not known\textsuperscript{(13)}, it seems that metabolic and/or functional changes in the renal tubular cells produce carcinogenesis.

4) Chemical

Cadmium was demonstrated to have influence on the development of RCC in cigarettes smokers\textsuperscript{(14)}. The well known chemicals associated with RCC are:

- Asbestos increases the risk of RCC especially in insulation workers and asbestos products workers, where it found to be deposited in kidney tissue.\textsuperscript{(15-16)}
- Organic solvents, pesticides, copper sulphate, benzene herbicides, and vinyl chloride increased risk of RCC in prolonged exposure.\textsuperscript{(17)}
- Polycyclic aromatic hydrocarbons e.g. Coal oven workers and firefighters.\textsuperscript{(18)}

5) Estrogen therapy in post menopausal women’s and as contraceptives.

6) Diuretics: there are high incidences of RCC in patients with chronic intake of diuretics.\textsuperscript{(19-20-22)}

7) Analgesics: although this is a controverted topic, several studies reported increase the risk of RCC with the use of analgesics like paracetamol, salicylates and phenacetin.\textsuperscript{(23-24)} Drugs that contain phenacetin, increase the risk for transitional cell carcinoma of the renal pelvis.

8) Radiations: Ionizing radiation appears to increase the RCC among patients treated for ankylosing spondylites and cervical cancer.\textsuperscript{(25-26)}

Other less recognized risk factors include:
- Viruses, especially immune suppressant state in HIV.\(^{(27)}\)
- Dietary studies have generally found reduced risk with increased consumption of fruits and vegetables.\(^{(28)}\)
- Alteration in development of the kidney eg, horse shoe kidney.\(^{(29-30)}\)

1-4-3 Hereditary causes

Most of the cases of RCC are sporadic; however there are some defined types of RCC with a hereditary pattern.

(1) Von Hippel-Lindau (VHL) disease

The VHL disease is inherited through an autosomal dominant trait. The syndrome is caused by germline mutations of the VHL tumor suppressor gene, located on chromosome 3p25-26; these mutations can virtually always be identified. The VHL protein takes part in cell cycle regulation and angiogenesis.\(^{(31)}\) Patients develop capillary haemangioblastomas of the central nervous system and retina, clear cell carcinoma, phaeochromocytoma, pancreatic, and inner ear tumors.

The clinical diagnostic criteria of VHL disease consist of:

i. Presence of capillary haemangioblastoma in the central nervous system or retina.

ii. Presence of one of the typical VHL associated extra neural tumors, within pertinent family history.

Fourty to sixty percent of the patients with VHL disease present with RCC. Although they are usually low-grade tumors, the progress rate to metastasis is around 30 %.\(^{(32)}\)

Renal lesions in carriers of VHL germline mutations are either cysts or clear cell RCC. They are typically multifocal and bilateral.

(2) Hereditary papillary renal carcinoma
This type of renal carcinoma is an inherited tumor syndrome with autosomal dominant trait and of late onset, with multiple and bilateral papillary renal cell carcinomas type 1. The disease is caused by activating mutations of the MET oncogene which maps the chromosome 7q31.

(3) Hereditary leiomyomatosis and renal cell carcinoma
This is an autosomal dominant tumor syndrome with germline mutations in the FH gene (chromosome 1q42.3–q43). These patients have the tendency to acquire benign leiomyomas of the skin and the uterus, and occasionally papillary renal cell carcinoma type 2 and uterine leiomyosarcomas. (34)

(4) Birt-Hogg-Dube syndrome
This syndrome is characterized by benign skin tumors, specifically fibrofolliculomas, trichodiscomas, and acrochordons. Multiple renal tumors and spontaneous pneumothoraces are also frequent. (35) We can find chromophobe RCC, typical RCC, hybrid oncocytoma, papillary RCC, or oncocytic tumors.

The Birt-Hogg-Dube gene maps the chromosome 17p11.2 and encodes the protein called folliculin. This gene is also involved in sporadic RCC.

(5) Familiar clear cell renal cell carcinoma
These families present a hereditary form of multiple, bilateral clear cell RCC but without any clinical evidence of suffering the von Hippel-Lindau disease. (36)

This hereditary cancer is characterized to present translocations affecting the chromosome 3. Translocations have been described among the chromosome 3 and the 8, 6, 2, 1& 4.
Acquired cystic disease/chronic dialysis
Approximately the 35 to 47% of the patients on dialysis and specially those with a very long history present acquired cystic disease\textsuperscript{(37)}. Some patients with this disease develop a papillary hyperplasia in the epithelium of the cysts that would be the origin of the RCC. Approximately the 5 to 9% of the patients with acquired cystic disease will develop an RCC, showing a higher incidence in population.\textsuperscript{(38)}

1-5 Localization of renal cancer
The RCC; putative cell of origin and genetics correlation \textsuperscript{(39)}

\begin{itemize}
  \item **Proximal Nephron**
    \begin{itemize}
      \item Cells of the proximal convoluted tubule
        \begin{itemize}
          \item Clear cell RCC
            genetic 3p-
        \end{itemize}
      \item Cells of the distal convoluted tubule
        \begin{itemize}
          \item Papillary RCC
            genetic +, 17+, 3+, Y- and t(x; 1), (x; 17)
        \end{itemize}
    \end{itemize}
  \item **Distal Nephron**
    \begin{itemize}
      \item Loop of Henle or collecting ducts
        \begin{itemize}
          \item Tubular & spindle cell
            1-,4q-,8-.11q-,13-,17+,20q+
        \end{itemize}
      \item Intercalated cells of the renal cortex
        \begin{itemize}
          \item Chromophobe RCC
            Y-,1-,2-,6-,10-,17-,21-
        \end{itemize}
      \item Collecting ducts of the renal medulla
        \begin{itemize}
          \item Medullary carcinoma
            (sickle) cell
          \item Collecting duct carcinoma
            1-,6-,14-,22-.13q-
        \end{itemize}
    \end{itemize}
\end{itemize}
1-6 Metastasis and spread of renal cancer

Renal cell carcinoma have higher propensity for extensive venous invasion, which is more common in clear cell type (18-29%). Extension of the tumor into the renal vein is one of the common features of the disease is it’s tendency to metastatize hematogenously before giving rise to local symptoms and signs.\(^{(2)}\)

The most common localizations of distant metastasis are the lungs (where cannon ball secondary tumors are produced), with regional lymph nodes, liver, and bone showing about equal frequencies, next followed by the adrenal, the other kidney and the brain. Unusual sites for metastasis include nasal cavity, parotid, heart, thyroid, pituitary, and genital organs.\(^{(40)}\)

1-7 Diagnoses

1-7-1 Clinical picture of renal cancer

The majority of patients with renal cell carcinoma are asymptomatic. 50% of cases are now detected incidentally (radiologist tumor)\(^{(41)}\)

The symptoms and signs include: triad of RCC haematuria 40%, pain 40% and flank mass 25%. A combination of all three components of the classical triad occurs in less than 10% of cases.\(^{(42)}\) Other non specific symptoms include weight loss, fever, fatigue, nausea, vomiting, and varicocele (left sided) secondary to obstruction of the spermatic vein is observed in a few patients.

Hepatomegally that is associated with hepatic dysfunctions in patients with RCC is known as Stauffer syndrome, where the main morphological change in the liver is sinusoidal dilation.

RCC is associated with para neoplastic syndrome in form of polycythemia, hypercalcemia, Cushing’s syndrome, and neuropathy.\(^{(43)}\)
1-7-2 Diagnostic strategy

Detailed medical review of past health state

One of the first steps in establishing a renal cell carcinoma diagnosis is a detailed and complex medical review of a patient's past health problems and general health state, family medical history, kidney cancer risk factors, and symptoms.

Physical examination:
During a physical examination, look for noticeable signs of the kidney cancer such as the high body temperature, high blood pressure, the presence of any large tumor in the abdominal cavity.

Laboratory tests

Urine tests: These set of tests check for several indicators of the cancer such as blood, sugar, proteins, and bacteria.

Blood tests: These set of tests measure the amount of several kidney cancer indicators, (red blood cells and creatinine).

Imaging Techniques

Ultrasonography: the initial investigation as it safe, non invasive, and fastest procedure. \(^{(41)}\)

Computed tomography scan: Sensitivity of 78%.it is used for tumor detection and involvement of renal vein and inferior vena cava.

Magnetic resonant imaging (MRI): It reveal the complete image of the kidneys and are indicated in local advanced malignancy, venous involvement, renal insufficiency, and distinguish tumor thrombus from bland thrombus. \(^{(44)}\)

Positron emission tomography (PET scan): For detection of metastases.

Bone scan: Used for symptomatic patients or patients with abnormal alkaline phosphatase.

Others like intra venous pyelography, chest x-ray, and angiography.
1-7-3 Pathological diagnoses

Imaging studies usually provide enough information for a surgeon to decide if an operation is needed. However, fine needle aspiration (FNA) biopsy or needle core biopsy is sometimes used to get a small sample of cells from a suspicious area if imaging test results are not conclusive enough to warrant removing a kidney. Biopsy may also be done to confirm the diagnosis of cancer if a person's health is too poor for surgery and other local treatments (such as radiofrequency ablation, arterial embolization or cryotherapy) are being considered. (45)

Fine needle aspiration and needle core biopsy are 2 types of percutaneous kidney biopsy.

1-8 Renal tumors

1-8-1 Benign renal tumors

i. Papillary adenoma

Grossly, papillary adenomas are yellow to pale nodules within the renal cortex. Histologically, the tumours show varying proportions of papillary and tubular architecture. The cytoplasm is usually scant and mitotic figures are rare. Foamy macrophages and psammoma bodies are common. There may be a pseudocapsule. (46)

Papillary adenomas show lower proliferative activity than both papillary and clear cell renal cell carcinomas. Some studies have found that papillary adenomas frequently have trisomy of chromosomes 7 and 17 and loss of the Y chromosome in males. (15) Positive immune histochemical reactions for cytokeratins and vimentin in papillary adenoma.

ii. Metanephric adenoma and adenofibroma

Metanephric adenomas are rare epithelial tumours (< 1% of renal cell neoplasms) that occur at any age and are more common in females. These tumours are variable in size, ranging up to 15 cm in diameter. The cut surface is fleshy and is grey to yellow, often with areas of cystic change and haemorrhage.

Histologically, metanephric adenomas consist of small tubules with occasional blunt papillae reminiscent of glomeruli. Psammoma bodies are common. Unlike papillary renal carcinoma, metanephric adenomas are rarely multifocal, are not associated with renal scarring, and usually lack a
pseudo capsule. They are also of uniformly low grade with small nuclei, inconspicuous nucleoli, and rare or absent mitotic figures. Metanephric adenoma appears to be related to two other entities, metanephric adenofibroma and metanephric stromal tumor. Metanephric adenofibroma (originally called ‘nephrogenic adenofibroma’) is a rare tumour originally considered to be related to mesoblastic nephroma and nephroblastomatosis. The tumour consists of nests of epithelial elements identical to metanephric adenoma surrounded by bands and sheets of fibroblast-like spindle cells. Metanephric stromal tumour appears related to metanephric adenofibroma but is composed entirely of the stromal component. These recently described tumours are frequently CD34-positive and appear benign.

iii. Renal Oncocytoma

Oncocytomas are well-circumscribed and are frequently brown, both when fresh and when fixed in formalin. A central stellate zone of oedematous stroma is common but non-specific. Multifocality occurs in 13% and bilaterality in 4–5% of cases. Rarely, numerous oncocytic nodules are present within the same kidney, sometimes exhibiting a spectrum of histological features ranging from oncocytoma to chromophobe renal carcinoma. Histologically, oncocytomas most often show solid growth with delicate inconspicuous vasculature and microcystic growth pattern. As is characteristic of oncocytes in general, the cells have voluminous eosinophilic cytoplasm, although clusters of smaller cells and pyknotic cells are fairly common. Scattered cells with pronounced nuclear pleomorphism, including multinucleated giant cells, are also seen in oncocytoma. Mitotic activity is absent or rare. Microscopic infiltration into peri renal fat is occasionally present and intravascular extension has been reported. Oncocytomas appear to originate in the intercalated cells of collecting duct epithelium. Several genetic abnormalities are frequent in oncocytoma: loss of chromosomes 1 and Y, translocations involving breakpoint 11q13, and a variety of chromosomal abnormalities.
iv. Angiomyolipoma

Angiomyolipomas are benign lesions characterized by the presence of mature adipose tissue, smooth muscle and thick-walled blood vessels. The true nature of these lesions is uncertain, but they are usually regarded as hamartomas. About 33% of patients with angiomyolipoma have tuberous sclerosis and more than 80% of tuberous sclerosis patients have angiomyolipoma.

Typically, the lesions are asymptomatic but may present with flank pain, mass, hematuria or a combination of these especially in patients with tuberous sclerosis. Grossly, the tumors are typically multifocal, bilateral and small in patients with tuberous sclerosis, and single, unilateral and large in those without. They are well circumscribed but not encapsulated and have varied appearances depending on the proportions of the constituent elements. In 25% of cases the tumors may be confused with malignancy because of extension outside the renal capsule.

The tumors show a wide variation in microscopic appearances due to differences in the amount of each component present in a particular tumor. There is no definite organization and the three components are haphazardly arranged. The bizarre mixture of elements may lead to confusion with malignant tumors.

v. Juxtaglomerular Cell Tumor

This is a rare, usually benign neoplasm of the juxtaglomerular cells of the kidney. Clinically, they occur mainly in young people, all of whom present with hypertension. Grossly, the tumors are small, usually less than 3 cm in diameter, well circumscribed and located in the cortex. Histologic appearances are variable.

1-8-2 Malignant renal cell tumors

Renal Cell Carcinoma

1- Clear cell RCC

Clear cell renal cell carcinoma comprises approximately 70% of malignant renal cell neoplasms.\(^{(48)}\). Most clear cell RCC are solitary cortical neoplasms that occur with equal frequency in either kidney. Multicentricity (4%) and bilateralism (0.5 to 3.0%) may be seen. The size is variable, but the frequency of small lesions increases due to imaging techniques. Clear cell RCC is typically golden.
yellow. Necrosis, cystic degeneration, hemorrhage calcification, ossification (49)

Histology
Clear cell RCC is architecturally diverse, with solid, alveolar and acinar patterns, the most common. The carcinomas typically contain a regular network of small thin-walled blood vessels, a diagnostically helpful characteristic of this tumour. No lumens are apparent in the alveolar pattern but a central, rounded luminal space filled with lightly acidophilic serous fluid or erythrocytes. The alveolar and acinar structures may dilate, producing microcystic and macrocystic patterns (50) Infrequently, clear cell renal cell carcinoma has a distinct tubular pattern and rarely a pseudopapillary architecture is focally present. The cytoplasm is commonly filled with lipids and glycogen, which are dissolved in routine histologic processing, creating a clear cytoplasm surrounded by a distinct cell membrane. Many tumours contain minority populations of cells with eosinophilic cytoplasm; this is particularly common in high grade tumours and adjacent to areas with necrosis or haemorrhage. In well preserved preparations, the nuclei tend to be round and uniform with finely granular, evenly distributed chromatin. Depending upon the grade, nucleoli may be inconspicuous, small, or large and prominent. Very large nuclei lacking nucleoli or bizarre nuclei may occasionally occur. (52-53)

Immunoprofile
Clear cell RCCs frequently react with antibodies to brush border antigens, low molecular weight cytokeratins, CK8, CK18, CK19, AE1, Cam 5.2 and vimentin.
The majority of clear cell RCCs react positively for renal cell marker, CD10 and epithelial membrane antigen. MUC1 and MUC3 are consistently expressed.
Extension into the renal vein and sarcomatoid change may occur. The term “granular cell” indicates RCC with acidophilic cytoplasm. Micro vascular invasion might be a relevant clinical prognostic parameter for low clinical stage RCC and could be the only independent predictor of disease-recurrence after radical surgery. Sarcomatoid change may be seen in all types of RCC with no evidences supporting that RCC develops “de novo” as sarcomatoid carcinoma. Clear cell RCC has a worse prognosis when compared with Chromophobe or papillary subtypes. However, the response rate to systemic therapy is higher than other histological types.
Fuhrman nuclear grade after stage is the most important prognostic predictor in RCC.
Sporadic clear cell RCC displays frequent chromosome 3p losses.
2- Multilocular cystic renal cell carcinoma (MCRCC)
This is a tumor with excellent outcome and entirely composed of cysts of variable size separated from the kidney by a fibrous capsule. The cysts are lined by a single layer of clear to pale cells but occasionally shows a few small papillae. The septa are composed of fibrous tissue that may have epithelial cells with clear cytoplasm that resemble those lining the cysts. VHL gene mutations in MCRCC support its classification as a type of clear cell RCC\(^{(54)}\). There is a male predominance of 3:1 with age ranging 20 to 76 years. No progression of MCRCC has been observed.

3- Papillary renal cell carcinoma (PRCC)
PRCC has a less aggressive clinical course than clear cell RCC. PRCC has variable proportions of papillae and may be bilateral or multifocal with frequent hemorrhage, necrosis and cystic degeneration. The papillae contain a fibro vascular core with aggregates of foamy macrophages, calcified concretions and frequent hemosiderin granules.\(^{(56)}\) Cellular type 1 and type 2 tumors have been recognised with papillae covered by small cells with scanty cytoplasm arranged in a single layer in type 1, and tumor cells of higher nuclear grade, eosinophilic cytoplasm and pseudostratified nuclei in type 2. Trisomy or tetrasomy 7, trisomy 17 and loss of chromosome Y are the earliest karyotypic change. Fuhrman’s tumor grade, stage, tumor proliferation and sarcomatoid change being correlated with outcome. Type 1 tumors have longer survival.

4- Chromophobe RCC
Characterized by huge pale cells with reticulated cytoplasm and prominent cell membrane. It accounts for 5% of renal epithelial tumors. Chromophobe RCC is solid and appears orange turning grey or sandy after fixation. When the cytoplasm is pale, the cytoplasmic borders are prominent and there is a high cytoplasmic/nuclear ratio, with perinuclear clearing producing a halo effect. Nucleoli are often visible and do not correlate well with nuclear size. These tumours are characterised by diffuse cytoplasmic staining with Hale’s colloidal iron stain.\(^{(57)}\) Eosinophilic variant needs to be differentiated from oncocytoma as both of them are considered to be derived from the intercalated cell of the collecting duct, both have alterations of mitochondria.\(^{(58)}\) In addition, there are reports of hybrid tumor composed of oncocytic and chromophobe elements. Cytogenetic and molecular studies show widespread loss of chromosomes and chromosomal regions with monosomy of chromosomes 1, 2, 6, 10, 13, 17 and 21 being most frequent. At the time of diagnosis
most patients are in the sixth decade, stage T1 or T2 (86%) and similar gender incidence.\(^{(69)}\)

5- Carcinoma of the collecting ducts of Bellini
Collecting duct carcinoma (CDC) is centrally located in the kidney, ranges 2.5 to 12 cm and typically shows a firm grey-white appearance. When small, origin within a medullary pyramid may be seen \(^{(60)}\). Histologically they are composed of a mixture of dilated tubules and papillae lined by a single layer of cuboidal to columnar cells that often have a hobnail pattern. The cytoplasm is amphophilic to acidophilic. There is marked nuclear pleomorphism with vesicular to coarse chromatin and single or multiple nucleoli. Mitosis is frequent with abnormal ones. Most tumors are in advanced stage with metastasis at diagnosis. The cells of CDC display Fuhrman iii and iv nuclear features. The main differential diagnoses of CDC include type 2 PRCC, renal pelvic adeno carcinoma or urothelial carcinoma with glandular differentiation. CDC accounts for <1% of renal malignancies and derives from the “principal cells” of the collecting duct. Mean patient age is 55 years with a slight male predominance. Upper tract imaging often suggests urothelial carcinoma and patients may have positive urine cytology.\(^{(61)}\)

6- Renal medullary carcinoma
It is a rapidly growing rare tumor of the renal medulla regarded as an aggressive variant of CDC. With few exceptions this tumor is seen in young male blacks with sickle cell trait (mean age 22 years), presenting with hematuria, flank pain, weight loss and palpable mass. Metastatic deposits may be the initial clinical evidence. Prognosis is poor.\(^{(62)}\) Histologically, the most characteristic feature is a reticular or yolk sac like appearance. Other patterns include solid nests or tubules. Infiltration by polymorphonuclear leukocytes is common. Tumor cells are pleomorphic, with large nuclei containing macronucleoli and with moderate to abundant acidophilic cytoplasm within desmoplastic stroma.

7- Renal carcinoma associated with Xp11.2 translocations/TFE3 gene fusions.
This type of RCC is defined by different translocations involving chromosome Xp11.2, all resulting in gene fusions involving the TFE3 gene. This carcinoma predominantly affects children and young adults. The ASPL-TFE3 translocation carcinomas characteristically present at an advanced stage associated with lymph node metastases.\(^{(63)}\) RCC associated with Xp11.2 translocations resemble clear cell RCC on gross examination and seems to have an indolent evolution, even with
metastasis. The histopathological appearance is that of a papillary carcinoma with clear cells and cells with granular eosinophilic cytoplasm. These cells display nuclear immunoreactivity for TFE3 protein.

8- Renal cell carcinoma associated with neuroblastoma
A few cases of RCC arise in long term survivors of childhood neuroblastoma. This group is heterogeneous, shows oncocytoid features. Allelic imbalances occur at the 20q1 locus. The prognosis is similar to other RCC. Males and females are equally affected with a mean age of 13.5 years, being uni- or bilateral.

9- Mucinous, tubular and spindle cell carcinoma
This is a low-grade carcinoma composed of tightly packed tubules separated by pale mucinous stroma and a spindle cell component. It seems to derive from the distal nephron. This tumor has a combination of losses involving chromosomes 1, 4, 6, 8, 13 and 14 and gains of chromosome 7, 11, 16 and 17. There is a female predominance and the mean age is 53 years. It presents as circumscribed asymptomatic mass on ultrasound examination.

10- Renal cell carcinoma, unclassified
In surgical series, it represents 4–6% of renal tumors and at presentation, most of them are of high grade and stage with poor survival. Features which might place a carcinoma in this category include: (i) composites of recognised types, (ii) pure sarco-matoid morphology without recognisable epithelial elements, (iii) mucin production, (iv) rare mixtures of epithelial and stromal elements, and (v) unrecognizable cell types.

Urothelial carcinomas of renal pelvis

They represent about 5% to10% of primary renal tumors.

Grossly tumors may be papillary, polypoid, nodular, ulcerative, or infiltrative. High grade tumors may appear as ill defined scirrhous mass that involve the renal parenchyma and may be multicentric.

Tumor grades either low grade or high grade depend on architectural and cytological features as their counterpart in the bladder.

Prognosis depends on grading and staging (depth of invasion).
**Squamous cell carcinoma**

They are more common in renal pelvis and ureter, next to urothelial carcinomas. These tumors are usually high grade and may invade the whole kidney. They grow in the back ground of nephrolithiasis with squamus metaplasia.\(^{64-65}\)

**Tumors Metastatic to the kidney**

The most common primary sites of renal secondaries are lung, breast, skin (malignant melanoma), contra lateral kidney, GIT, ovary and testes.

In most cases metastases are multiple and bilateral with well circumscribed nodules, but they can also be single with infiltrative borders.

Metastases may be limited to intra glomerular location, rarely resulting in renal failure.
1-9 Staging of renal cancer

Tumor staging is a numerical description of the degree of invasion and metastatic spread of the tumor. Staging of renal cancer is valuable both in treatment choice and as a prognostic factor.\textsuperscript{(66)}

Staging is based on the result of physical examinations, biopsies, imaging tests (CT scan, MRI, PET, and chest x-ray).

TNM classification

TNM Definitions

Primary tumor \((T)\)

- TX: Primary tumor cannot be assessed
- T0: No evidence of primary tumor
- T1: Tumor 7 cm or less in greatest dimension and limited to the kidney
  - T1a: Tumor 4 cm or less in greatest dimension and limited to the kidney
  - T1b: Tumor larger than 4 cm but 7 cm or less in greatest dimension and limited to the kidney
- T2: Tumor larger than 7 cm in greatest dimension and limited to the kidney
- T3: Tumor extends into major veins or invades adrenal gland or perinephric tissues but not beyond Gerota fascia
  - T3a: Tumor directly invades adrenal gland or perirenal and/or renal sinus fat but not beyond Gerota fascia
  - T3b: Tumor grossly extends into the renal vein or its segmental (i.e., muscle-containing) branches, or it extends into the vena cava below the diaphragm
  - T3c: Tumor grossly extends into the vena cava above the diaphragm or invades the wall of the vena cava
- T4: Tumor invades beyond Gerota fascia

Regional lymph nodes \((N)\)*

- NX: Regional lymph nodes cannot be assessed
• N0: No regional lymph node metastasis
• N1: Metastasis in a single regional lymph node

• N2: Metastasis in more than one regional lymph node

*Laterality does not affect the N classification.

If a lymph node dissection is performed, then pathologic evaluation would ordinarily include at least eight nodes.\(^{(67)}\)

Distant metastasis (M)

• MX: Distant metastasis cannot be assessed
• M0: No distant metastasis
• M1: Distant metastasis

AJCC Stage Groupings

Stage I

• T1, N0, M0

Stage II

• T2, N0, M0

Stage III

• T1, N1, M0
• T2, N1, M0
• T3, N0, M0
• T3, N1, M0
• T3a, N0, M0
• T3a, N1, M0
• T3b, N0, M0
• T3b, N1, M0
• T3c, N0, M0
• T3c, N1, M0

Stage IV

• T4, N0, M0
• T4, N1, M0
• Any T, N2, M0
• Any T, any N, M1

1-10 Grading

Tumor grading is numerical expression of the degree of its cellular differentiation. It is based on careful assessment of histological section under the microscope. Grading of renal cell carcinoma is based on nuclear grade which is one of the most important prognostic feature of RCC\(^6\). The preferred formulation is that of Fuhrman nuclear grading system and is currently used for grading clear cell renal cell carcinoma (CCRCC), as follows:

- Grade I: Nuclei are small (<10µm) and round, with dense chromatin and inconspicuous nucleoli.
- Grade 2: Nuclei are slightly larger (15 µm) with finely granular chromatin and small nucleoli.
- Grade 3: The nuclei are 20 µm in size and may be oval in shape, with coarsely granular chromatin and prominent nucleoli.
- Grade 4: The nuclei are pleomorphic with open chromatin and single or multiple macro nucleoli.

1-11 SCREENING FOR RCC: TARGET POPULATION

1. Patients with end stage renal failure – Screen patients with long life expectancy by periodic ultrasound or CT, starting from 3rd year of dialysis.
2. Patients with known VHL Syndrome: Biannual CT or Ultrasound beginning at 15-20 yrs, periodic radiographic screening for non renal manifestations.
3. Relatives of patients with VHL: Obtain genetic analysis, if positive; follow screening for patients with VHL syndrome.
4. Relatives of patients with other form of familial RCC periodic ultrasound and genetic analysis.
5. Patient with Tuberous sclerosis: Periodic screening with ultrasound or CT - increased incidence of RCC in TS is debatable.\(^6\)
6. Patients with autosomal polycystic kidney disease: Screening not justified.
1-12 Treatment of renal cancer
Renal cell carcinoma treatment varies from patient to patient. The treatment approach is adjusted to the patient’s needs and takes in consideration these following factors: (1) the renal cell carcinoma type, (2) the tumor size and location, (3) the cancer stage, (4) the general health state of the patient, and (5) the patient’s age.

The treatment options for renal cell carcinoma patients include surgery, arterial embolization, chemotherapy, radiotherapy, hormone therapy, targeted therapy, and biological therapy.

1-12-1 Surgical treatment
1-radical nephrectomy:
Considered as the gold standard treatment. It is include removal of the kidney, adrenal gland, peri renal fat, and Gerota fascia with or without regional lymph nodes resection. It is suitable for stage i, ii, iii, and some of iv.\(^{(70)}\)

2-Simple nephrectomy:
Removal of the kidney only.

3-Partial nephrectomy:
usually use for stage I A tumors or patients with bilateral tumors, patients with only one kidney, patients who already had reduced kidney functions or patients with Hipple Lindau disease.

1-12-2 Radiotherapy
External-beam radiation therapy (EBRT): is used before, after nephrectomy or as palliative therapy for selective patients.

1-12-3 Arterial embolization
May be employed preoperatively to reduce blood loss during nephrectomy or as palliative treatment in patients with inoperable disease.

1-12-4 Biological therapy
This cytokine therapy has been shown to induce objective response and have a modest impact on survival in selected patients.
Interferon, interleukine-2 or combination, cause the cancer cells to shrink and lose more than half of their original size in about 10%-20% of the patients.

1-12-5 Targeted therapy
Anti angiogenic drugs, which block tyrosine kinase enzyme. Sunitinib or Sorafenib (Nexavar). This is a drug which blocks the new blood vessel from growing and the growth-stimulating molecules within the cancerous cell. It has proven to be effective in advanced stages renal cell carcinoma patients by slowing down the cancer progression.\(^{(71)}\)

1-12-6 Chemo therapy
Unfortunately, kidney cancer cells are usually resistant to chemotherapy, and there is no standard way to treat it with these drugs. Some drugs, such as vinblastine, floxuridine, 5-fluorouracil (5-FU), capecitabine, and gemcitabine have been shown to help a small number of patients. Still, chemotherapy is often reserved for cancers in which targeted drugs and/or immunotherapy are not effective.\(^{(72)}\)
1-13 Prognosis

Depends on

1. Pathological stage
2. Tumor size
3. Nuclear grade

Histological subtype prove to be important prognostic factors.\textsuperscript{(73-74)}

Prognosis – RCC / Radical Nephrectomy

A tumor confined to the kidney is associated with a better prognosis.

Stage I - 5-year survival rate is approximately 94%,
Stage II - Survival rate of 79%.
Stage III - IIIB renal cell carcinoma is 18%.
Stage IV 0 - 20%

Surgical removal of renal vein or IVC thrombus – 5-yr survival 25 -50%,
15-20% reduction in survival over 5 year with invasion of perinephric fat.
Systemic metastasis 1 year survival rate less than 50%.

Patients with clear cell renal cell carcinoma (CCRCC) tend to have a worse prognosis than patients with other histological subtypes of renal cell carcinoma (RCC), with 5-year disease-specific survival rates of 50-69%, compared with 67-87% for papillary renal cell carcinoma (RCC) and 78-87% for chromophobe RCC (chRCC). However, analysis of 1000 patients showed very similar 5-year disease-specific survival rates for clear cell renal cell carcinoma (10.5%) and papillary renal cell carcinoma (10.3%) once metastatic disease was present.\textsuperscript{(75)}
Objectives

General Objectives:

To study the cases with renal cancer in the study area from January 2007 to August 2010, with the objective to determine the different epidemiological & clinicopathological features of this disease.

Specific Objectives:

1. To review the histological patterns of renal cancer among the study population.
2. To determine the frequencies of nuclear grades of renal cancer according to Fuhrman grading system among the study population.
3. To determine the different stages of renal cancer according to TMN classification system.
4. To review the clinical presenting features of renal cancer in the study population.
5. To determine the relation between histological patterns and age, sex and site of tumor.
Chapter Two
Methodology

2.1 Study design:

The study is a descriptive retrospective recorded data-based study.

2.2 Study area:

The study was conducted at different departments of histopathology including Ibn Sina hospital, Soba teaching hospital, Khartoum teaching hospital & National health laboratory (NHL).

2.3 Study population:

Cases diagnosed as renal cancer in the study area from Jan 2007 up to Aug 2010.

2.4 Inclusion criteria:

Cases of renal cancer with full records and histopathological slides.

2.5 Exclusion criteria:

Cases with deficient records (missed request forms) or missed histopathological slides and blocks..

2.6 Data collection:

Data were collected from the patients request forms and patients files including detailed personal, clinical and pathological data. The slides were collected and reviewed by expert histopathologist to confirm the diagnosis of renal cancer, to determine the histological type using the WHO classification of renal cancer and to grade the tumor using Fuhrman grading system (nuclear grading depends on nuclear size, shape of the chromatin & presence of nucleoli so it was graded into four grades which have prognostic effects) was applied in this study. And lastly tumor staging using the TNM system (depend on the tumor size, lymph node involvement and the degree of invasion and metastases) was applied for this study.
2.7 Data analysis & statistics:

The data were analyzed by SPSS software.
Chapter Three
Results

The total number of patients with renal cancer during the study period was 117 patients; 6 of them had missed slides and consequently excluded from the study. The remainders (111) patients were selected and studied.

3.1 Characteristics of the studied patients:

3.1.1 Age distribution:

The age of the studied patients ranged from 19 to 86 years, with a mean of 52.72 years +-. The age group with highest frequency was (46 – 60) years \(\text{(Figure 1)}\).

3.1.2 Sex distribution of the patients:

Fifty nine patients (53.2%) of the patients were males, compared to fifty two (48.8%) females \(\text{(Figure 2)}\). Thus, the male to female ratio was 1.31:1

3.1.3 Residence distribution of patients with renal cancer:

Concerning the residence of patients, sixty eight (64% ) of them came from central regions including Khartoum and the four central states. Five (4.8%) patients were from the northern region. The west, east & south were represented with five (4.8%), five (4.8%) and one (1%) respectively. In twenty one patients (20% of the cases) the residency was not stated in the request form \(\text{(Figure 3)}\).

3.2 Distribution of the clinical symptoms among studied patients:

The various clinical presentations of the renal cancer in the studied group were shown in table (1). Thirty seven patients had loin pain (35.2%), abdominal mass in thirty three patients (31.4%). Haematuria in twenty four patients (22.9%) and five patients were diagnosed by incidental ultra sound. Other complaints: loss of weight, fever, bilateral hydro nepherosis and pleural effusion were observed in four patients (3.8%). \(\text{(table1)}\)
3.3 Site distribution of the renal cancer

Figure (4) demonstrates the site distribution of the renal cancer in the studied patients. Right sided & left sided cancer was found (45%) & (54.1%) respectively, no information concerning the site was given in (0.9%) of the set-up.

3.4 Mode of operation among Population Study

Three modes of operation were used to obtain the specimen from the studied patients. The most frequently used procedure was nephrectomy in 92 patients (87.61%), partial nephrectomy in 2 patients (1.8%) and core needle biopsy in 11 patients (9.9%) of the cases. (figure 5)

3.5 Histopathological characteristics of RCC among the studied patients

3.5.1 Histological types:
The diagnosis of renal cancer in this study is based solely on the histopathological examination of the surgical specimens.

The vast majority (94.6%) was RCC, while transitional cell carcinoma (4.5%) & squamous cell carcinoma in (0.9%) of the cases (table 3). Clear cell RCC was the predominant histological subtype seen in (71.2%) of cases, secondly comes papillary carcinoma (18%), sarcomatoid carcinoma (3.8%), chromphobe (0.9%) and collecting duct carcinoma (0.9%)

3.5.2 Grading:
Fuhrman grading system (nuclear grading) was applied in this study. The majority of cases (44.1%) 48 patients were considered as grade II, followed by grade III (26%) 29 patients, grade I (15.3%) 16 patients and lastly grade IV (14.4%) in 12 of patients (Table2)

3.5.3 Staging:
TNM staging system was applied in this study (depends on the tumor size, lymph node involvement and degree of invasion and metastases). The majorities of cases (39%) 41 patients were considered stage III, followed by stage II (28.6%) 30, stage I (12.4%) and lastly stage IV (8%). (table 3)
FIG (2) THE GENDER OF THE STUDY POPULATION

MALE, 53.33%

FEMALE, 46.67%
Fig (3) Residence for the Study Population

- Central: 86.95%
- North: 5.95%
- East: 5.95%
- West: 5.95%
- South: 1.19%
FIG (4) THE SITE FOR THE STUDY POULATION

LEFT, 56.73%

RIGHT, 43.27%
FIG (5) THE TYPE OF OPERATION FOR THE STUDY POPULATION
Clinical Presentation of Renal Cancer Among the Study Population

<table>
<thead>
<tr>
<th>Clinical Presentation</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loin pain</td>
<td>37</td>
<td>35.2%</td>
</tr>
<tr>
<td>Abdominal mass</td>
<td>33</td>
<td>31.4%</td>
</tr>
<tr>
<td>Haematuria</td>
<td>24</td>
<td>22.9%</td>
</tr>
<tr>
<td>Incidental U\S</td>
<td>5</td>
<td>4.8%</td>
</tr>
<tr>
<td>Other complains</td>
<td>4</td>
<td>3.8%</td>
</tr>
<tr>
<td>Not mentioned</td>
<td>2</td>
<td>2.9%</td>
</tr>
<tr>
<td>Total</td>
<td>105</td>
<td>100%</td>
</tr>
</tbody>
</table>
Grading Scores for Renal Cell Carcinoma Among the Study Population

<table>
<thead>
<tr>
<th>Grade</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>16</td>
<td>15.02%</td>
</tr>
<tr>
<td>II</td>
<td>48</td>
<td>45.7%</td>
</tr>
<tr>
<td>III</td>
<td>29</td>
<td>27.6%</td>
</tr>
<tr>
<td>IV</td>
<td>12</td>
<td>11.4%</td>
</tr>
<tr>
<td>Total</td>
<td>105</td>
<td>100%</td>
</tr>
</tbody>
</table>
Staging Scores for Renal Cell Carcinoma Among the Study Population

<table>
<thead>
<tr>
<th>Stage</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>13</td>
<td>12-4%</td>
</tr>
<tr>
<td>II</td>
<td>30</td>
<td>28-6%</td>
</tr>
<tr>
<td>III</td>
<td>41</td>
<td>39%</td>
</tr>
<tr>
<td>IV</td>
<td>8</td>
<td>7-6%</td>
</tr>
<tr>
<td>Not applicable</td>
<td>13</td>
<td>12-4%</td>
</tr>
<tr>
<td>Total</td>
<td>105</td>
<td>100%</td>
</tr>
</tbody>
</table>
## Histological Types Among the Study Population

<table>
<thead>
<tr>
<th>Histological Type</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCC clear cell</td>
<td>79</td>
<td>71.2</td>
</tr>
<tr>
<td>RCC papillary</td>
<td>20</td>
<td>18.0</td>
</tr>
<tr>
<td>RCC sarcomatoid</td>
<td>4</td>
<td>3.6</td>
</tr>
<tr>
<td>RCC chromphobe</td>
<td>1</td>
<td>0.9</td>
</tr>
<tr>
<td>Collecting duct</td>
<td>1</td>
<td>0.9</td>
</tr>
<tr>
<td>Transitional cell carcinoma</td>
<td>5</td>
<td>4.5</td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>1</td>
<td>0.9</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>111</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>
### Relationship Between Histological Types & Gender of the Patients

<table>
<thead>
<tr>
<th>Histological Type</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>RCC clear cell</td>
<td>41</td>
<td>38</td>
<td>79</td>
</tr>
<tr>
<td></td>
<td>(51.9%)</td>
<td>(48.1%)</td>
<td>(100%)</td>
</tr>
<tr>
<td>RCC papillary</td>
<td>11</td>
<td>9</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>(55%)</td>
<td>(45%)</td>
<td>(100%)</td>
</tr>
<tr>
<td>RCC sarcomatoid</td>
<td>3</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>(75%)</td>
<td>(25%)</td>
<td>(100%)</td>
</tr>
<tr>
<td>RCC chromophobe</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>(0%)</td>
<td>(100%)</td>
<td>(100%)</td>
</tr>
<tr>
<td>Collecting duct</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>(100%)</td>
<td>(0%)</td>
<td>(100%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>56</td>
<td>49</td>
<td>105</td>
</tr>
<tr>
<td></td>
<td>(53.3%)</td>
<td>(46.7%)</td>
<td>(100%)</td>
</tr>
</tbody>
</table>
## Relationship Between Histological Types & the Site of the Tumor

<table>
<thead>
<tr>
<th>Histological Type</th>
<th>Site</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Right</td>
<td>Left</td>
</tr>
<tr>
<td>RCC clear cell</td>
<td>32</td>
<td>46</td>
</tr>
<tr>
<td></td>
<td>(41%)</td>
<td>(59%)</td>
</tr>
<tr>
<td>RCC papillary</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>(50%)</td>
<td>(50%)</td>
</tr>
<tr>
<td>RCC sarcomatoid</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>(25%)</td>
<td>(75%)</td>
</tr>
<tr>
<td>RCC chromophobe</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>(100%)</td>
<td>(0%)</td>
</tr>
<tr>
<td>Collecting duct</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>(100%)</td>
<td>(0%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>45</strong></td>
<td><strong>59</strong></td>
</tr>
<tr>
<td></td>
<td><em>(43.3%)</em></td>
<td><em>(56.7%)</em></td>
</tr>
</tbody>
</table>
## Relationship Between Histological Types & the Age of Patients

<table>
<thead>
<tr>
<th>Histological Type</th>
<th>Age Groups</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>16-30</td>
<td>31-45</td>
</tr>
<tr>
<td>RCC clear cell</td>
<td>8 (10.4%)</td>
<td>18 (23.4%)</td>
</tr>
<tr>
<td>RCC papillary</td>
<td>1 (5.6%)</td>
<td>4 (22.2%)</td>
</tr>
<tr>
<td>RCC sarcomatoid</td>
<td>1 (25%)</td>
<td>1 (25%)</td>
</tr>
<tr>
<td>RCC chromophobe</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Collecting duct</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>10 (9.9%)</strong></td>
<td><strong>23 (22.8%)</strong></td>
</tr>
</tbody>
</table>
### Relationship Between Histological Types & clinical Stages Among the Study Population

<table>
<thead>
<tr>
<th>Histological Type</th>
<th>Stage I</th>
<th>Stage II</th>
<th>Stage III</th>
<th>Stage IV</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCC clear cell</td>
<td>10 (14.1%)</td>
<td>21 (29.6%)</td>
<td>32 (45.1%)</td>
<td>8 (11.3%)</td>
<td>71 (100%)</td>
</tr>
<tr>
<td>RCC papillary</td>
<td>2 (12.5%)</td>
<td>7 (43.8%)</td>
<td>7 (43.8%)</td>
<td>0 (0%)</td>
<td>16 (100%)</td>
</tr>
<tr>
<td>RCC sarcomatoid</td>
<td>0 (0%)</td>
<td>2 (50%)</td>
<td>2 (50%)</td>
<td>0 (0%)</td>
<td>4 (100%)</td>
</tr>
<tr>
<td>RCC Chromophobe</td>
<td>1 (100%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>1 (100%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>13 (14.1%)</strong></td>
<td><strong>30 (32.6%)</strong></td>
<td><strong>41 (44.6%)</strong></td>
<td><strong>8 (8.7%)</strong></td>
<td><strong>92 (100%)</strong></td>
</tr>
</tbody>
</table>
### Relationship Between Histological Types & Fühman Grade Among the Study Population

<table>
<thead>
<tr>
<th>Histological Type</th>
<th>Fühman Grade</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Grade I</td>
<td>Grade II</td>
</tr>
<tr>
<td>RCC clear cell</td>
<td>15 (19%)</td>
<td>34 (43%)</td>
</tr>
<tr>
<td>RCC papillary</td>
<td>1 (5%)</td>
<td>14 (70%)</td>
</tr>
<tr>
<td>RCC sarcomatoid</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>RCC Chromophobe</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Collecting duct</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>16 (15.2%)</td>
<td>48 (45.7%)</td>
</tr>
</tbody>
</table>
Clear cell renal cell carcinoma
Papillary type of renal cell carcinoma
Sarcomatoid renal cell carcinoma
Squamous cell carcinoma of the kidney
Transitional cell carcinoma of the kidney
Chromophobe type renal cell carcinoma
Chapter Four
**Discussion**

This is a retrospective descriptive study on renal cancer in Sudanese patients; it was carried out in the period from January 2007 to August 2010.

This study has been faced by many difficulties and limitations due to deficient registration data, in particular the poor information regarding history and clinical information and in some labs the filing of records and slides was poor, so it is very difficult to compare this result with the international data especially in defining the risk factors.

There has been a significant increase in all cancers incidence all over the world and in Sudan as one of the African and developing countries a sharp increase in all types of cancer including renal cancer.\(^{(9,10)}\)

Regarding the age in this study, the mean age of the patients was 52.72 years it is about three years younger than the age of fifty five years in the USA and other European countries, RCC was found more frequently in the age group (46 – 60) years and 31.4% of the patients was under 46 years old.

This observation should alert the clinicians in Sudan to be more cautious in managing patients with urinary symptoms or patients with renal mass as malignant neoplasm’s are more common than benign ones.

In this study the sex distribution of RCC shows high female to male ratio as it is 1.13:1 while in most western countries and USA the ratio is 2:1 to 1.5:1.\(^{(1,6)}\)

The study shows no relation between the gender of the patient and the histological types.
Regarding the residency the majority (64%) of patients came from central regions – including the capital Khartoum and the four centre states -. The least frequent place of origin has been the most remote states. This can readily be explained on the bases of the demographic and economic characteristics of the Sudanese population, in that most Sudanese are clustered in the big towns and also the unjustified focusing of the medical services in the capital.

Regarding the occurrence of RCC was almost in equal rates between right and left kidney as observations shows left kidney 46.73% and right 43.27%, and this shows a clear similarity with the literature.

The present study found that about 92% of cases had symptoms at the time of diagnoses while in the literature is less than 20%(1); this is very alarming because most symptomatic patients of RCC have advanced disease.

In USA and western countries RCC is known as a radiologist tumor and as more than 60% of them are diagnosed indecently so they named it incident loma, so this must give another alert for the clinicians and radiologists.

The study showed three modes of diagnostic procedures were used, the most frequently used procedure was total nephrectomy in 92 patients (87.61%) followed by needle biopsy in 11 patients (9.9%) and lastly partial nephrectomy in 2 patients (1.9%), this is due to the advanced stage of the diagnosed patients.

The low percentage of needle biopsy as a diagnostic procedure may be due to the low awareness of renal cell carcinoma.

On the view of the limitations of this study the histological types showed the highest frequency of RCC (94.6%) and this has some agreement with the international data.

When we take a look at the sub-types of RCC the commonest is the conventional clear cell type (71.2%) followed by papillary type (18%), sarcomatoid (3.8%) and equal percentage of Chromophobe & collecting duct carcinoma (0.9%) each .these are similar to literature except for the lower percentage of chromophobe as it is about 5% in most studies. (1,57)
Five patients (4.5%) were diagnosed as transitional cell carcinoma three of them are males and two are females, their age range between 55 to 70 years, three of them present with hematuria. By using the WHO grading system for urothelial tumors, three were graded as high grade while the other two were low grade.

One patient (0.9%) as squamous cell carcinoma which is a rare type but there is some reported cases.

Most of the cases in this study were considered as grade II followed by grade III in Fuhrman grading system, this also highlights the aggressiveness of the types of RCC.

By using the TNM staging system the study showed that the majority of the cases are stage III followed by stage II, this is another clue for the advance stage of RCC at the time of diagnoses.

Unfortunately this study could not assess the importance of the different risk factors of RCC due to the deficiency of recorded data, although some patients have some risk factors such as hypertension, one patient with chronic renal failure on chronic dialysis and another patient with family history of renal cancer in her mother. So further heavy work is needed to identify the natural history of renal cancer in Sudan and this means team work including clinicians, radiologists, histopathologist and oncologists.
Conclusion

This is study on Renal cell cancer, with all the difficulties and limitations, it indicated that this type of cancer is common and have some similar pathological and clinical features with other countries.

These features include younger age group, high female: male ratio late presentation with advanced disease.

The study identified five sub types of RCC, transtional cell carcinoma and squamous cell carcinoma.
Renal cancer needs more studies and hard works, especial concentration on the risk factors (environmental, community related and familial ones.)

Cooperation and coordination between clinicians and pathologists for early detection and management.

Improvements of blocks and slide storage.

Use of very strict rejection criteria regarding the request forms.

Improvement of cancer registry all over the country.
References


53. Gobbo S, Eble JN, MacLennan GT, et al. Renal cell carcinomas with papillary architecture and clear cell components: the utility of
54. Involvement of multiple loci on chromosome 3 in RCC development. Vandenberge E, Bunys CH. Genes, chromosomes and cancer 1997 59-76
64. Li MK, Cheung WL. Squamous cell carcinoma of the kidneys. J Urol 1987; 138:269-71. (s)


Appendix I

Appendix II