www.jmscr.igmpublication.org
Impact Factor 5.84
Index Copernicus Value: 71.58
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v5i9.55

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Histopathological Analysis of Nephrectomy Specimens: Experience from A Tertiary Care Hospital

Authors
Dr Suma M T[1], Dr Usha Poothiode[2]
[1]Associate Professor, Department of Pathology, Government Medical College, Thrissur Kerala, India
Mobile no: 9847678928, Email: *suma1879@gmail.com*
[2]Professor of Pathology, MOSC Medical College, Kolenchery

Abstract
Introduction: *Renal Cell carcinoma is a malignancy of renal tubular epithelium and constitute 3% of all adult malignancies and constitute 80-90% of renal tumors. The morphological features including the histopathologic type, nuclear grade and extent of tumor involvement determine the aggressiveness and prognosis of Renal Cell Carcinoma.*
Methods: *83 cases who underwent radicalor simple nephrectomy in a tertiary health care centerover a span of 4 years were included in the study. Their gross and microscopic features were studied.*
Results: *Renal cell carcinoma shows varying morphologic features in gross and histologic appearance. The predominant histologic variant is Clear cell variant and predominant nuclear grade of tumors is grade II.*
Conclusion: *Thorough evaluation of morphological parameters in Renal Cell Carcinoma is very essential for planning therapy and predicting the disease outcome.*
Keywords: *Kidney, Renal cell carcinoma, Clear cell carcinoma.*

INTRODUCTION

Nephrectomy is a common surgical procedure done for neoplastic and non-neoplastic lesions of kidney. First successful nephrectomy was performed by German surgeon Gustav Simon in 1869. There are various neoplastic and non-neoplastic indications for this procedure such as renal cell carcinoma, non functioning kidneys and congenital cystic lesions. Renal cell carcinoma in adults and wilms tumor in children predominates among malignancies which needs radical nephrectomy[1]. Nephrectomy for renal cell carcinoma is rapidly being modified to allow partial nephrectomy. Hydronephrosis, pyelonephritis, cystic lesions and non functioning kidneys are the common indications for simple nephrectomy. About 2,10,000 new cases of renal cell carcinomas are detected every year and more than 10,000 deaths are due to renal cell carcinoma annually. Globally there is 25% increase in incidence of renal cell carcinoma including almost all regions and ethnic groups.[2] Cigarette smoking, hypertension and obesity are the most important risk factors of renal cell carcinoma. Other risk factors are Tuberousscl-erosis, epithelioid angiomyolipoma, von Hippel-Lindau disease and other familial syndromes, renal transplantation, dialysis and acquired renal cystic disease.

Renal cell carcinoma is a disease of adults with average age of 55–60 years at diagnosis. About two third cases of renal cell carcinoma are localised at

presentation. 40% of patients develops metastases and die from the disease even with complete excision. Numerous prognostic factors have identified including tumor stage, grade, histological type, renal sinus involvement and extra-renal spread. Histopathological parameters have gained acceptance for assessing prognosis in routine clinical practice, especially the Fuhrman nuclear grading. Most urothelial (transitional cell) carcinomas of the renal pelvis occur in adults (in whom they constitute about 7% of all primary renal carcinomas), but pediatric cases also have been documented[3]

In this study analysis of various neoplastic and non neoplastic diseases of kidney was done. Histopathological sub typing of renal cell carcinoma is very important in prognosis because each subtype is associated with distinct genetic abnormalities and clinical behavior. Morphological subtyping of RCC was done and prognostic factors like stage, grade, extra capsular extension, involvement of perinephric fat and invasion of renal vein was studied.

OBJECTIVES

1. To study the spectrum of diseases in nephrectomy specimens
2. Morphological subtyping of renal malignancies and to analyze different tumor related prognostic factors in Renal cell carcinom

MATERIALS AND METHODS

The present study was conducted in a tertiary care center in South India for a period of 4 years. Study group included both adults and children who underwent radical nephrectomies for a clinical diagnosis of renal malignancies or for non neoplastic lesions of kidneys. Clinical data were collected by proforma given to the patient, chart review and from surgical records. Pathology reports and materials were reviewed and data including histopathological diagnosis, size, pathological stage and grade of tumor were recorded.

Specimens were fixed in 10% formal in for about 18-24 hours and examined grossly for abnormalities including hydronephrotic changes, inflamatory changes, stones and PUJ obstructions. In case of malignancies size of tumor, invasion of perirenal fat, capsule, ureter, renal vessels, adrenal were noted. Sampling was done from tumor, capsules, renal pelvis, adjacent parenchyma, ureter, renal vessels and lymph nodes. Tissue was processed and H &E staining was done.

A specific diagnosis was given to non neoplastic-specimens like pyelonephritis, hydronephrosis, nephrolithiasis, congenital malformations including cystic diseases of kidney. Renal malignancies were sub classified morphologically according to WHO classification. The grading done by Fuhrman system and staging according to TNM system. Extracapsular extension, involvement of perinephric fat, renal vein and adrenal were noted. In case of Wilms tumour it was reported as tumors with favorable histology or tumors with unfavorable histology. Study was done after getting ethical approval from institutional ethical committee. No statistical analysis was required.

OBSERVATIONS

A total of 83 nephrectomies received, 51 nephrectomies done for malignancies including pediatric neoplasms and 32 nephrectomies done for non-neoplastic lesions of kidney.

Table 1. Type of nephrectomy specimens

Type of lesion	Number	Percentage
Neoplastic	51	61
Non neoplastic	32	39
Total	83	100

57% of renal malignancies were Renal cell carcinoma and 21% Transitional cell carcinoma. Pediatric neoplasms constitute 16%. There was two cases of Angiomyolipoma and one case of multilocular cyst.

Table 2 Types ofRenal tumors.

Type of lesion	No	percentage%
Rcc	29	57
Tcc	11	21
Wilms	6	12
Css	2	4
Aml	2	4

Multilocular cyst	1	2
Total	51	100

Of the 51 cases of malignancies 71% of patients were male and 29% were female with male: female ratio of 2.4:1. Renal cell carcinoma is generally a disease of adult and 31% cases was seen in between 61-70 years. Four cases were in the younger age group (20-40). 69% cases of renal cell carcinoma were on the right side and 31% were on the left side and all the cases of RCC were unilateral.

Presentation of renal tumors

Patients presented with costovertebral pain (45%) hematuria (27%) and mass (15%). 13% of patients showed other mode of presentations. The classic triad of mass, hematuria and flank pain were seen only in 6% of patients. Most of the TCC patients presented with flank pain. One of the patients came with bone pain due to bone metastasis from TCC of renal pelvis. Two cases of angiomyolipoma were included in this study. One of the patient came with complaints of infertility. Renal mass was an incidental finding in this patient. This patient had tuberous sclerosis with adenoma sebaceum, subungualfibromas and bilateral angiomyolipomas.

Table 3: Presentation of renal tumours

Presentation	Number	Percentage %
Flank pain	24	48
Hematuria	14	27
Mass	8	15
Fever	2	4
Bone pain	1	2
Infertility	1	2
UTI	1	2

Morphological profile of Renal cell carcinoma

31% of RCC observed in 61-70 years (male 66%, female 34%). Four cases were in the younger age group (20-40years). Renal cell carcinoma has got predilection to develop on the right side of the kidney. In the present study 20 cases of RCC were on the right side (69%) and 9 were on the left side (31%). The commonest location of tumor was in the upper pole of kidney (78%) Grossly more than 80% of RCC showed the classical variegated appearance composed of yellowish tumor with hemorrhage and necrosis. Rest of them presented as large tumors with extensive necrotic areas. Sarcomatoid RCC showed grey white solid areas.

The most common variant of Renal cell carcinoma was the conventional clear cell type constituting about 69 percent. Clear cell RCC were of high nuclear grade and high stage compared to other morphological variants of Renal cell carcinoma.

Table 4: Histologic variants of rcc

VARIANT	N0	%
Clearcell	20	70
Papillary	3	10
Rcc–Sarcomatoid	2	7
Unclassified	2	7
Chromophobe	1	3
Multicystic RCC	1	3
Total	29	100

RCC at younger age group

3 of our patients were young adults between 24 -37 years they presented with large tumors with average size 19 cms. Histologically two were of clear cell Type and one was papillary RCC, all of them showed higher nuclear grades 3or 4. Two cases showed extensive sarcomatoid areas along with clear cell areas. Predominant age group affected was 61-70 years and stage2 disease was common.

Table 5: Distribution of patients by Tumor stage

Age	Stage 1	Stage 2	Stage 3	Total	%
21-30		1		1	3
31-40	1	2		3	10
41-50	3	4	1	8	28
51-60	1	3	2	6	21
61-70	3	4	3	10	35
71-80			1	1	3
Total	8	14	7	29	100

40 % of RCC was stage T1 (40%) among this 63% belonged to T1 a stage and 37% to T1 b stage.

Table 6: T1 tumors

AGE	NUCLEAR GRADE	SIZE in cm	HISTOLOGY
50	1	6X4	RCC
67	2	5x4	RCC
50	3	5X3.5	RCC
61	2	4 X 4	RCC
53	2	3.5X3.5	RCC
35	3	3.5X2.5	RCC
50	2	2.5X2.5	RCC
65	3	1X1	RCC

T2 Tumors

Most of the tumors were T2 stage and nuclear grade2. Irrespective of the stage of RCC, majority of tumors were of nuclear grade 2 constituting about 55%.

Table 7: T2 Tumors

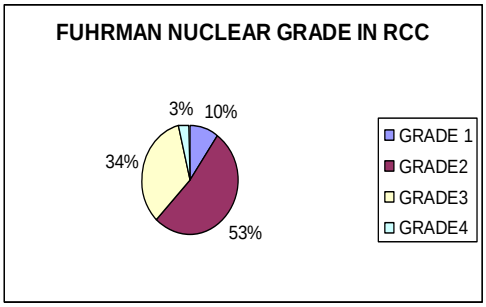
AGE	NUCLEAR GRADE	SIZE in cm	HISTOLOGY
68	1	8X5.5	RCC
37	1	17X12	RCC
46	2	10.5X7.5	RCC
42	2	8X7	RCC
52	2	12X5	RCC
48	2	10X6	RCC
70	2	8X5	RCC
59	2	7X5	RCC
62	2	7X6x5	RCC
40	2	8 X4	RCC
65	3	9.5X6.5	RCC
60	3	8X5	RCC
41	3	9.5 X 7.5	RCC
24	4	20X17	RCC

Out of 29 cases of RCC 7were stage 3 tumors including four cases ofT3a ,one case ofT3b, T3a N1 and T 3b N2 one case each.

Table 8: T3 Tumours

AGE	NUCLEAR GRADE	SIZE in cm	HISTOLOGY
6	2	8.5X4	RCC
60	2	8X6	RCC
61	2	7.5X6.5	RCC
72	2	4X4	RCC
65	2	10X5	RCC
66	3	5.5	RCC
49	3	9X7	RCC

53% of Rcc were of grade 2.



Pediatric neoplasm

We received 8 pediatric neoplasms, 6 cases of wilms tumor and two cases of clear cell sarcoma. All these cases were treated by radical nephrectomy. Morphologically wilms tumor showed triphasic pattern and favorable histology.

Table 9 : Paediatric renal tumours

Histology	Age	Sex	Presentation	size
Wilms	1	M	Haematuria	8x6x4
Wilms	1.5	M	Mass	12x7
Wilms	1.5	F	Mass	9x8.5x3
Css	2	M	Mass	8x6
Wilms	2.5	M	Mass	12x9
Wilms	3	M	Mass	10x7x4
Wilms	4.5	M	abd pain	11x8
Css	2.5	F	mass	7x6

Transitional cell carcinoma

Transitional cell carcinoma constitute about 21 percent of all renal malignancies. All the cases were of higher grade at presentation and most of the patients presented with flank pain. One of the patient came with bone pain. Histopathological examination showed TCC of renal pelvis with bone metastasis. Two of the patients were having duplex kidney with double ureters, of which one patient had synchronous malignancy of urinary bladder. Urine sediments were examined for all patients with clinically suspected or CT diagnosed malignancy of kidney and renal pelvis. Out of eleven patients with a histological diagnose of TCC of renal pelvis six patients (55%) showed positive urine cytology before surgery. One case of TCC showed unusual morphology with sarcomatoid areas, mucinous areas and extensive necrosis in a 71 year old male patient.

Table 10 : Transitional cell carcinoma

SL NO	AGE SEX	PRESENTATION	SIZE	GRADE

1	78M	Flankpain	12x9x7	High
2	71M	Flankpain	22x18x10	High
3	46M	Bonepain	3x2x1	High
4	64M	Flankpain	16x10x8	High
5	56F	Haematuria	9x6x6	High
6	57M	Flankpain	10x5x2	High
7	58M	Haematuria	12z10x6	High
8	65M	Mass	8x4x3	High
9	57M	Flankpain	13x10x3	High
10	65F	Flankpain	4x5x4	High
11	59M	Flankpain	8x7x5	High

Non neoplastic lesions of kidney

We received 32 nephrectomy specimen which were removed for loss of function constituting about 39% of all total nephrectomies. All were simple nephrectomy specimens. Mainly they were removed for pyelonephritis, hydronephrosis, nephrolithiasis, congenital anomalies like Renal dysplasia and pelviureteric junction obstruction

Table 11: Non neoplastic lesions of kidney

Lesion	No of cases	Percentage
Hydronephrosis	10	31`
Pyelonephritis	11	31
Dysplastic kidney	5	16
Duplex kidney	3	7
Lithiasis	2	3
Stricture	1	3

Figure 1: Macroscopy of renaltumors

Figure 1 A renal cell carcinoma

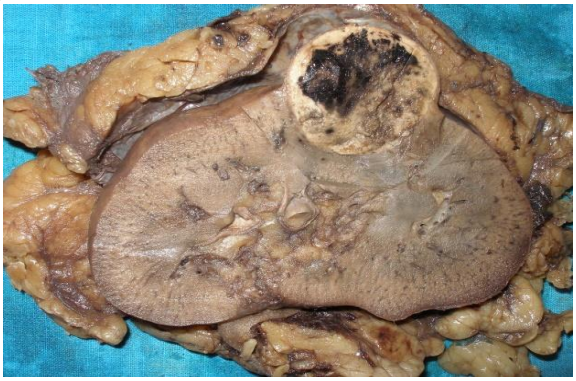


Figure 1 B Multi cystic nephroma

Figure 1C Xanthogranulomatous pyelonephritis

Figure 1 D Angiomyolipoma

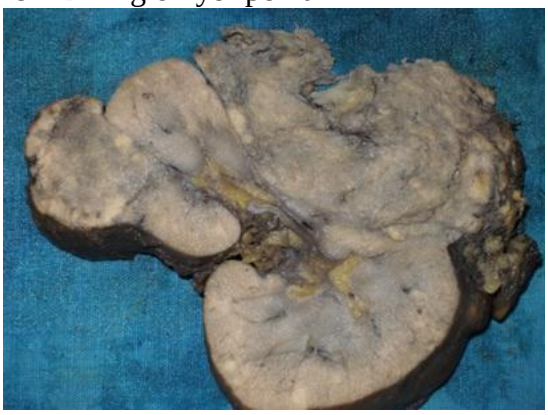


Figure 1 E Nephroblastoma

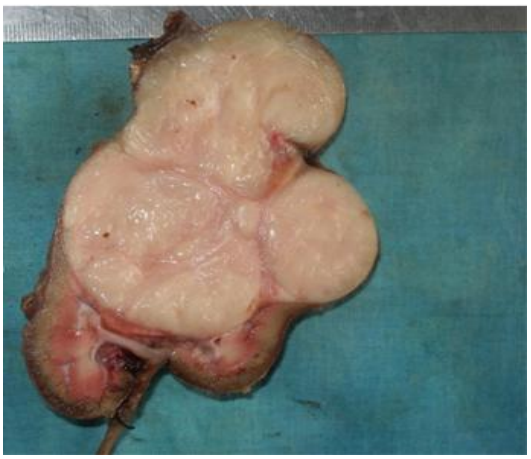


Figure 2 : Microscopic appearance of renal tumors

Figure 2A Clear cell carcinoma

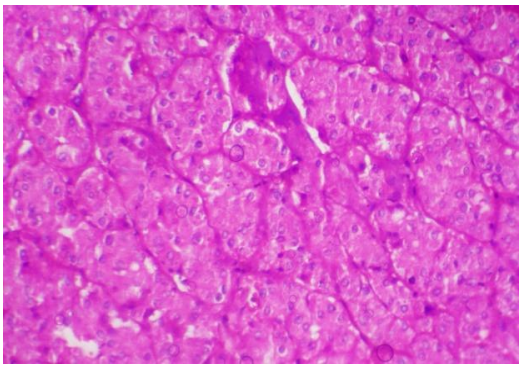


Figure 2 B Papillary renal cell carcinoma

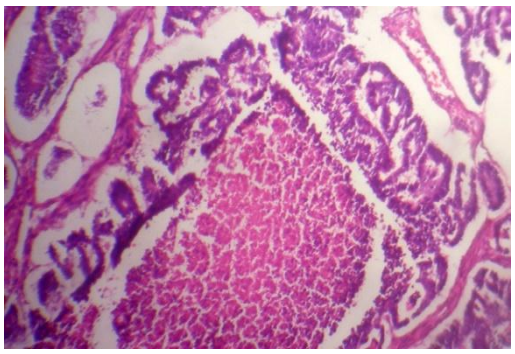


Figure 2 C Xanthogranulomatous pyelonephritis

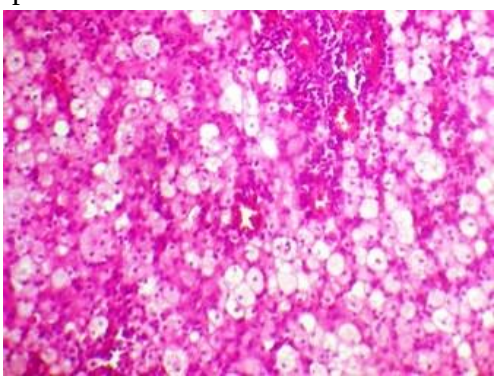
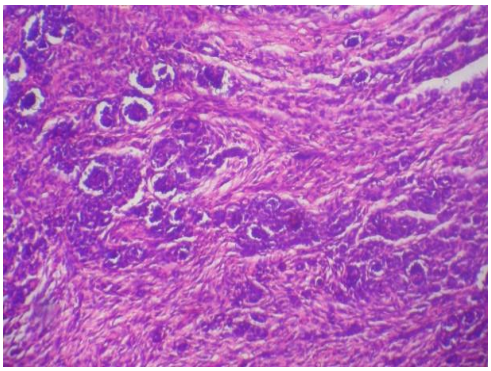


Figure 2 E Nephroblastoma



DISCUSSION

83 nephrectomies were included in this study out of this 51 cases were renal malignancies and 32 were non neoplastic lesions. Renal cell carcinoma was the commenest malignancy, constituting about 57% similar to the observation made by Storkel et al[4]. Males were affected more than females [males : females – 2.3:1] This pattern is similar to observations made by [Chang TS, Chang SK etal 1980][5]. The increased RCC incidence may be linked to certain risk factors like smoking, hypertension, obesity, occupational factors and genetic factors. Age of patients ranged from 20 to70 years with peak incidence in fifth to seventh decade. The commonest presentation of renal cell carcinoma were flank pain (46%) haematuria (28%) abdominal mass (16%) repeated urinary tract infection (2%) and non specific symptoms like fever and body ache in (4%). The classical triad of symptom was seen only in 6% of the patients similar to observations by Hiroaki Masuda et al,[6] and they also found out that if a patient presents with above mentioned classical triad of symptoms the overall prognosis was poor. All the cases of TCC were of higher grade malignancies and 55% showed positive urine cytology for malignant cells. Study results of Raica M, Mederle O et al[7] suggested the urine cytology as a simple screening test for the early detection of urinary tract malignancy. Out of 11 patients with transitional cell carcinoma 9 patients underwent radical nephrectomy and 2 patients nephroureterectomy with bladder cuff resection. Two patients with TCC showed duplex kidney in the same side of malignancy. One case of Transitional cell carcinoma presented with bone pain due to metastasis and bone marrow biopsy showed osteoblastic metastasis from transitional cell carcinoma which is a rare occurrence. In our study 2 cases of Angiomyolipoma were included of which one case was that of a young lady who presented with infertility and features of Tuberous sclerosis. A total of 8 cases of pediatric neoplasms were received, 6 cases of Wilms tumor and 2cases of clear cell sarcoma. In patients with Wilms tumor, radical nephrectomies were performed and

combined radiation and/or chemotherapy after surgery were given for cure of tumor.

Grossly more than 80% of RCC showed the classical variegated appearance. Rest of which included very large tumours with extensive necrotic areas, sarcomatoid RCC with grey white solid areas and tumors with cystic change. Histological subtyping is important in prognosis of renal cell carcinoma. According to various studies there are significant differences in outcome for the different histologic subtypes of RCC, highlighting the need for accurate subtyping (Mahul B. Amin, M.D.; Mitual B.)[8] and among the morphological subtypes classical clear cell variant has got the worst prognosis. In our study also clear cell RCCs were of larger size and higher stage at presentation compared to other morphological variants of Renal cell carcinoma like papillary and chromophobe RCC. This observations are similar to studies conducted by (B. A. Birnbaumet al)[9]

Smoking habit was found in 70 percent of the male patients. A significant association was noted between smoking and renal cell carcinoma and Transitional cell carcinoma. 94 percent patients were normotensive and only 6 percent were hypertensive at the time of surgery. 3 of our patients were young adults between 24 -37 years, they presented with large tumors of average size 19cms. Histologically these tumors showed nuclear grade 3 and 4 and clear cell and papillary morphology. Studies conducted by Renshaw AA, Fletcher JA[10] that the clinicopathologic features of renal cell carcinomas in children and young adults differ from those arising in older adults and these tumors are characteristically high-grade, papillary tumors with numerous calcifications. Leuschner I, Harms D and Schmidt D[11]et al found that young patients presenting with large masses shows high grade RCCs with poor prognosis. RCC with sarcomatoid areas showed extensive spindle cell areas along with clear cell areas.Both cases were observed in female patients in the fourth decade contributing about 6% of total Renal cell carcinomas.

40% of RCC was stage T1 (40%) among this T1a tumors showed high nuclear grade and papillary architecture. T1b tumors was predominantly of nuclear grade2.Same observation was mace by Bretheu Lechivallier E et al.[12] Study conducted by Gauraguptha et al shows that symptomatic T1b RCC had higher nuclear grade and papillary architecture. Studies conducted by Raymond M. Hsuet al found out that there is no significant difference in stage and nuclear grade in tumors of 3 cm size and tumors between 3-7cm .Most of the tumors in our study was T2 stage and irrespective of the stage of RCC majority of tumors were of nuclear grade 2 constituting about 55%.Out of 29 cases of RCC 7were stage T3 tumors. The distribution of tumors were T3a 4 cases,T3b 1case,T3a N1and T 3b N2 one case each

Transitional cell carcinoma constitute about 21 percent of all renal malignancies. All the cases were of high grade tumors and common presentation wasflank pain similar to studies conducted by Nielsen k & Ostri P et al[13]. Two of the patients had duplex kidney with double ureters of which one patient had synchronous malignancy of urinary bladder. Urine sediments were examined for all patients with clinically suspected or CT diagnosed malignancy ofkidney and renal pelvis. Out of eleven patients with a histological diagnose of TCC of renal pelvis six patients (55%) showed positive urine cytology. One case of high grade TCC showed unusualmorphology with sarcomatoid areas mucinous areas and extensive necrosis in a 71 year old male patient. Perez Montiel D et al states that unusual morphology are usually of high grade.

Most common pediatric neoplasm was nephroblastoma and Clear cell sarcoma. Most of the neoplasms were observed below three years. Main pathological changes observed in non neoplasticle-sions include pyelonephritis, hydron-ephrosis followed by congenital anomalies like dysplastic kidneys and duplex kidneys.Among the cystic lesions cystic dysplastic kidney predominated with abortive glomeruli,primitive ducts surrounded by condensed mesenchyme and immature cartilage.[14]

Two cases of angiomyolipoma were included in this study. One of the patient came with complaints of infertility. Renal mass was an incidental finding in

this patient. This patient had tuberous sclerosis with adenoma sebaceum, subungualfibromas and bilateral angiomyolipomas. EI Malik EM et al also described one case of angiomyolipoma with tuberous sclerosis.[15]

CONCLUSION

Renal cell carcinoma constituted 57percent of total renal malignancies. The age group of Renal cell carcinoma was 61-70 years with a male to female ratio of 2.3:1. Clear cell RCC was the predominant histological subtype of RCC. Majority of Renal cell carcinoma were stage II and Grade II.

REFERENCES

1. Ozen H, Colowick A, Freiha FS, Incidently discovered solid renal masses:What are they ? Br J Urol.1993;72:274-6.
2. Cohen HT, Mc Govern FJ: Renal-cell carcinoma. N Engl J Med2005;353:2477-2490
3. Guinan P, Vogelzang NJ, Randazzo R, Sene r S, Chmiel J, Fremgen A, Sylvester J: Renal pelvic cancer. A review of 611 patients treated in Illinois 1975–1985. Cancer Incidence and End Results Committee. Urology 1992; 40:393-399
4. Störkel S Rumpelt HJ Histopathology and classification of renal cell tumors (adenomas, oncocytomas and carcinomas). The basic cytological and histopathological elements and their use for diagnostics.Pathol Res Pract.1986 May;181(2):125-43.
5. Chang TS, Chang SK. 1980.PatientPlus articles, renal tumours, Egton Medical Information Systems DocID: 2722 Document Version: 22 DocRef: p 686.
6. Hiroaki Masuda et al, Can symptoms predict the prognosis of RCC a multivariate analysis of 320 patients.
7. Raica M Mederle O et al Urinary cytology in diagnosis of epithelial tumours of urotheliumDiagnCytopathol 1993,9;197-201
8. Mahul B. Amin, M.D.; Mitual B.) Prognostic impact of adult renal epithelial neoplasms an experience of 405 cases. Am J SurgPathol 2002,26;281-291.
9. B. A. Birnbaum et al:Renal cell carcinoma acorrelation of 100 tumours with ct findings – journal abdominal imaging volume 19-may 1999 pages 262-266.
10. Renshaw AA, Granter SR, Fletcher JA: Renal cell carcinoma in hildren and young adults increased incidence of papillary architecture and unique subtypes Am J surg path 1999; 23;795-802.
11. Leuschner I, Harms D and Schmidt D1991 Renal Cell Carcinoma in children: Histology, immunohistochemistry , and follow up 10 cases. Med PediatrOncol19 : 33-41.
12. Bretheu Lechivallier E et al.Prognostic value of nuclear grade of renal cell carcinoma. Bretheau D, Lechevallier E, de Fromont M, Sault MC, Rampal M, Coulange C. Department of Urology, Salvator Hospital, Marseille, France.
13. Nielsen k Ostri P 1988 Primary tumours of the renal pelvis : evaluation of clinical and pathological features in consecutive series of 10 years. J Urol 140: 19-21
14. Maizals M, Simpson SB. Primitive ducts of renal dysplasia induced by culturing ureteric buds denuded of condensed renal blastema. Science.1983;219: 509 – 510
15. EI Malik EM, Mmon SR,Ibrahim AL, AI Gizawi. Nephrectomy in adults:Asir Hospital Experience. Saudi J Kidney Dis Transpl 1997;8:423-7.