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Original Article

Pathology Section

Study of Histopathological Spectrum of Renal Neoplasms in Nephrectomy Specimens from a Tertiary Hospital in North Karnataka, India

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ABSTRACT

Introduction: Renal Cell Carcinoma (RCC) ranks 13th most common malignancy worldwide. Majority of the renal tumours are RCCs with very few cases presenting with the classical triad of flank pain, haematuria and mass per abdomen. Partial or total nephrectomy remains the treatment of choice in these patients. A systematic gross and microscopic examination of nephrectomy specimens is pivotal in determining the tumour type and its prognostic indicators namely tumour grade and stage for arriving at a complete treatment protocol.

Aim: This study from a tertiary care hospital was undertaken to determine the most common clinical presentation, with age and sex distribution of renal tumours and to analyse the histomorphological spectrum of renal tumours from resected nephrectomy specimens.

Materials and Methods: A total of 32 nephrectomy cases were studied during this period. Histopathological parameters were assessed as per CAP guidelines 2017. Tumours were sub typed according to WHO classification 2016 and Fuhrman's nuclear grade and TNM tumour stage were assessed. The statistical analysis was done using the Statistical Package for the Social Sciences version 20.0 (SPSS Inc. Chicago, IL, USA).

Results: The present study included 32 cases. The mean age of presentation was 43.43 years with flank pain being the most common clinical presentation in 17 (53.1%) cases. Histopathological evaluation revealed malignant neoplasm in 28 (87.5%) cases and benign neoplasm in 4 (12.5%) cases. Among malignant tumours, clear cell RCC was the most frequent tumour in our study observed in 15 (46.9%) cases, followed by papillary RCC in 5 (15.6%) cases, 3 (9.4%) cases of Wilms tumour, 2 (6.3%) cases of squamous cell carcinoma, and 1 (3.1%)case each of synovial sarcoma, chromophobe rcc and rhabdoid tumour.

Conclusion: Malignant renal tumours far out numbered the benign tumours in our study with RCC being the most common malignant tumour in adults. Wilms tumour was the most common malignancy in paediatric age group. Majority of the tumours showed Fuhrman's nuclear Grade 2 seen in 50% of the cases.

Keywords: Chromophobe, Oncocytoma, Renal cell carcinoma, Synovial sarcoma, Wilms tumour

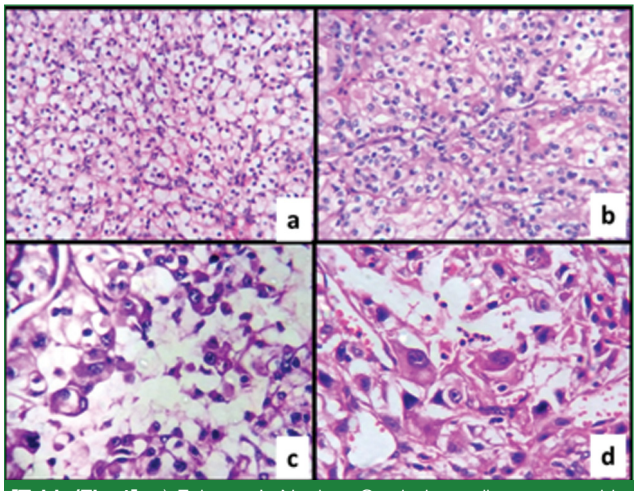
INTRODUCTION

RCC is the 13th most common malignancy worldwide [1]. In the Asian population, the incidence ranges between 1.1 and 6.0/100,000 population [1]. Renal neoplasms include wide spectrum of entities both in adults and in children, with few rare tumours. Renal neoplasms can arise from the different components of the renal parenchyma,which includes the tubular epithelium, interstitial tissue and from primitive elements [2]. Due to the widespread use of imaging modalities, 70% of the renal neoplasms are diagnosed incidentally in developed countries and in early stages as compared to the scenario in developing countries where malignancies are detected at advanced stages [3]. Nephrectomy is the standard curative as well as palliative procedure for renal neoplasms. The most significant prognostic indicators include tumour stage and nuclear grade followed by histological subtype, and tumour size which can only be established by systematic gross and histopathological examination of nephrectomy specimens. This study from a tertiary care hospital was undertaken to determine the most common clinical presentation, with age and sex distribution of renal tumours and to analyse the histomorphological spectrum of renal tumours from resected nephrectomy specimens.

MATERIALS AND METHODS

This six-year retrospective study was performed in the Department of Pathology, Sri Dharmasthala Manjunatheshwara College of Medical Sciences and Hospital, Dharwad, Karnataka, India. from 2011 to 2016. A total of 32 nephrectomy cases were studied during this period. Clinical details and patient particulars were retrieved from Medical Records Department. Histopathology slides and paraffin blocks of all patients who underwent nephrectomy for renal neoplasms were retrieved from the archives and reviewed. The specimens were fixed in 10% formalin and photographed. Specimen was oriented and sections were given to look for the tumour and tumour

particulars were noted with respect to size, surface, margins and extension. Stripping of the capsule was done to look for invasion. Sections were given according to CAP protocol. Histomorphology was studied on H&E slides, and special stains and IHC were performed wherever required. Patient particulars were recorded in detail in the proforma, which included age, sex, clinical findings, gross and microscopic findings. Histopathological parameters were assessed as per CAP guidelines 2017. Tumours were subtyped according to WHO classification 2016 and Fuhrman nuclear grade [Table/Fig-1a-d] and TNM tumour stage were assessed. Ethical clearance was obtained from the institutional ethical committee. All the nephrectomy specimens harbouring renal neoplasm were included in the study and the cases which were received for second opinion and review of slides only were excluded.



[Table/Fig-1]: a) Fuhrman's Nuclear Grade I, small monomorphic nuclei with inconspicuous nucleoli (H&E, 10x); b) Nuclear Grade II, slightly irregular nuclei with conspicuous nucleoli (H&E, 10x); c) Nuclear Grade III, moderately irregular nuclei with prominent nucleoli (H&E, 40x); d) Nuclear Grade IV, bizzare nuclei with prominent nucleoli (H&E, 40x).

STATISTICAL ANALYSIS

The statistical analysis was done using the Statistical Package for the Social Sciences version 20 (SPSS Inc. Chicago, IL, USA).

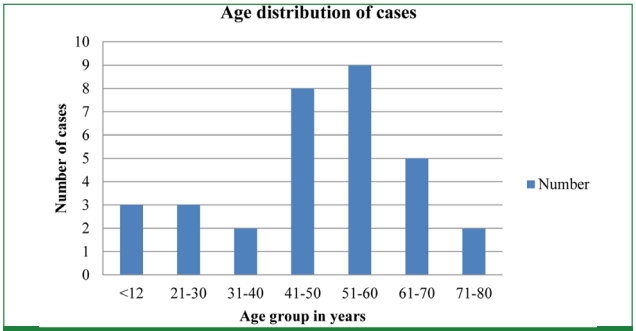
RESULTS

The present study included 32 cases. Of these, 22 (68.8%) cases were males and 10 (31.3%) were females with male to female ratio of 2.19:1. The mean age of presentation was 43.43 years (range 1 to77). Peak incidence in this study was between 51 to 60 years seen in 9 (28.1%) cases, followed by 41 to 50 years with 8 (25%) cases. Among these, 3 cases were paediatric (age < 12 years) with mean age 3.33 years (range1 to 6 years). The laterality of tumour was equal on both sides with ratio of 1:1[Table/Fig-2].

The most common clinical presentation was flank pain in 17 (53.1%) cases, followed by pain with haematuria in 4 cases (12.5%), mass per abdomen in 4 (12.5%) cases, pain with mass and isolated haematuria in 3 (9.3%) cases each. One (3.1%) case was incidentally detected. None of the cases showed triad of pain, mass and haematuria [Table/Fig-3].

Total 31 (96.8%) cases were managed by total nephrectomy, and 1 (3.1%) case which had tumour size of 2 cm size was managed by partial nephrectomy.

Tumour was located in the upper pole in 9 (28.1%) cases, mid pole in 4 (12.5%) cases, lower pole in 8 (25%) cases and involving all the poles in 7 (21.9%) cases.



[Table/Fig-2]: Depicting the distribution of renal tumours among different age groups with majority of the tumours falling in the range of 51-60 years.

Clinical presentation		
Symptoms	**Number**	**Percentage**
Flank Pain	17	53.1
Flank Pain with hematuria	4	12.5
Mass	4	12.5
Hematuria	3	9.3
Flank Pain with Mass	3	9.3
Incidental finding	1	3.1
Triad	0	0

[Table/Fig-3]: Clinical presentation of cases with renal tumours.

Histopathological evaluation revealed malignant neoplasm in 28 (87.5%) cases and benign neoplasm in 4 (12.5%) cases. Among malignant tumours, Clear cell RCC was the most frequent tumour in our study observed in 15 (46.9%) cases, followed by papillary RCC in 5 (15.6%) cases, 3 (9.4%) cases of Wilms tumour, 2 (6.3%) cases of squamous cell carcinoma, and 1 (3.1%)case each of synovial sarcoma, chromophobe RCC and rhabdoid tumour [Table/Fig-4].

Among the benign neoplasms, commonest was oncocytoma in 3 (9.4%) cases followed by 1 (3.1%) case of papillary adenoma.

Nuclear grade was assessed in clear cell and papillary variants of RCC (20 cases). Most frequent nuclear Grade was II in 10 (50%) cases followed by Grade III in 5 (25%) cases, Grade I in 4 (20%) cases and Grade IV in 1 (5%) case [Table/Fig-5].

Subtype of tumour		
Subtype	**Number**	**Percentage**
Benign		
Oncocytoma	3	9.4
Papillary adenoma	1	3.1
Malignant		
RCC		
Clear cell RCC	15	46.9
Papillary RCC	5	15.6
Chromophobe RCC	1	3.1
Non RCC		
Wilms tumour	3	9.4
SCC	2	6.3
Rhabdoid tumour	1	3.1
Synovial sarcoma	1	3.1
Total	32	100.0

[Table/Fig-4]: Depicting the distribution of benign and malignant tumours along with different subtypes of renal cell carcinoma.

Among 28 malignant neoplasms, radial margin was involved in 8 (32.1%) cases, of which 4 were clear cell RCC, 2 were papillary RCC, one case each of chromophobe RCC and rhabdoid tumour. Renal vein was involved in one case of clear cell RCC, which also showed radial margin involvement.

Nuclear grade				
Nuclear grade	**Clear cell RCC**	**Papillary RCC**	**Total**	**Percentage**
I	3	1	4	20%
II	7	3	10	50%
III	4	1	5	25%
IV	1	0	1	5%
	15	5		

[Table/Fig-5]: Depicting Fuhrman's nuclear grading in RCC, with Grade II being the commonest nuclear grade displayed by majority of the tumours.

Tumour necrosis was present in 16 (57.14%) malignant cases. 11 out of these 16 (68.75%) were clear cell RCC, 3 (18.75%) were papillary RCC, 1 (6.25%) case of synovial sarcoma and 1 (6.25%) case of Wilms tumour.

Staging of RCC				
Stage	**Clear cell RCC**	**Papillary RCC**	**Chromophobe RCC**	**n (%)**
T1	6	1	0	7 (33.3%)
T2	5	2	0	7 (33.3%)
T3	4	2	1	7 (33.3%)

[Table/Fig-6]: Showing distribution of RCC along with the stage depicting equal distribution in T1, T2 and T3.

Tumour staging was done for 21 cases of RCC. There were 7 cases (33.3%) in stage T1, T2 and T3 each [Table/Fig-6].

DISCUSSION

Unfortunately, majority of the renal neoplasms do not present with the classic triad of haematuria, pain and mass. Incidental detection is on the rise now due to advancements in radiological diagnostic modalities. Early detection of renal neoplasms aids in effective treatment which includes partial or total nephrectomy. Since, systematic gross and histopathological evaluation is very essential to grade and stage the tumour and guide in further management, we have attempted to evaluate the histomorphological spectrum of renal neoplasms and adopt the CAP guidelines reporting format for nephrectomy cases in a tertiary care hospital catering to significant population of North Karnataka, India.

The mean age of patients at clinical presentation was 43.4 years. Similar studies by Datta B et al., reported mean age of 47.3 years [2], Duchene DA et al., reported mean age of 57.4 years [4] and Bashir N et al., reported 54 years [5]. Majority of the cases in our study were males with male to female ratio of 2.19:1. Similar results were reported by Datta B et al., [2], Stinga AC et al., [6] and Bashir N et al., [5].

Majority of the cases presented with flank pain in 17 (53.1%) cases, followed by pain associated with haematuria in 4 (12.5%) cases and mass per abdomen in 4 (12.5%) cases. Ray R et al., reported haematuria as the most common presentation in 53.33% cases followed by pain abdomen in 50.67% of the cases [1]. Bashir N et al., reported pain in 35.86% cases followed by mass and haematuria [5]. Datta B et al., reported pain in 73% cases, haematuria in 61% cases and mass in 20% cases [2]. One case (3.1%) was incidentally detected in our study. Duchene DA et al., reported 48% [4] and Ray R et al., reported 9.33% of incidental tumour detection [1].

In our study, renal tumours were found to be equally distributed on either sides. Amin AN et al., reported right sided tumours in 53.1% and left sided in 46.9% cases [7]. Bashir N et al., observed in his study that 53.8% tumours were left sided and 46.1% of the tumours were right sided [5].

The most common location of the tumour in our study was upper pole in 9 (28.1%) cases, followed by lower pole in 8 (25%) cases. Amin AN et al., reported upper pole in 18.7% of cases [7]. Lower pole was the most common tumour location in the study reported by Bashir N et al., [5].

In our study, majority of the tumours were malignant amounting to 87.5% and 12.5% cases were benign. Similar findings have been reported by Aiman A et al., [8] and Duchene DA et al., [4] who have reported malignancies in 87.5% cases and 86% cases respectively.

The most common malignancy encountered in our study was RCC in 65.6% cases. Of these, clear cell variant was the most common histological subtype observed in 46.9% cases followed by papillary RCC in 15.6% cases and chromophobe

RCC in 3.1% cases. Stinga AC et al., [6] reported RCC in 95% of the malignant lesions with clear cell variant in 73.6% cases, papillary RCC in 16.6% cases and chromophobe RCC in 16% cases. Bashir N et al., reported RCC in 79.8% cases with clear cell variant in 60.8% cases, papillary RCC in 14.7% cases and 1.1% case of chromophobe RCC [5]. Duchene DA et al., [4] reported 100% RCC among malignant lesions with Clear cell variant in 93% cases and chromophobe RCC in 7% cases.

Nuclear grade was assessed in clear cell RCC and papillary RCC using Fuhrman's nuclear grade (20 cases). Most frequent nuclear Grade was II observed in 50% of cases followed by Grade III in 25% cases. Amin AN et al., reported Grade I as the most frequent in 44.4% cases followed by Grade III in 33.3% [7]. Stinga AC et al., reported nuclear Grade II in 59.72% cases followed by Grade III in 31.95% cases [6]. Aiman A et al., reported nuclear Grade II in 52% cases followed by Grade III in 24% cases [8],which is comparable to the present study [Table/Fig-7].

Tumour staging was done for 21 cases of RCC. There were 7 cases (33.3%) in Stage T1, T2 and T3 each. Ray R et al., reported 42.67% of Stage III, followed by 28% of Stage II RCC [1]. Agnihotri S et al., has reported 34.1% of Stage I followed by 24.9% of Stage II RCC [9].

Studies	Grade I	Grade II	Grade III	Grade IV
Stinga AC et al., [6]	5.55%	59.72%	31.95%	2.77%
Amin AN et al., [7]	44.4%	33.3%	22.2%	0%
Aiman A et al., [8]	16%	52%	24%	8%
Present study	20%	50%	25%	5%

[Table/Fig-7]: Comparison of nuclear grade in RCC with other studies.

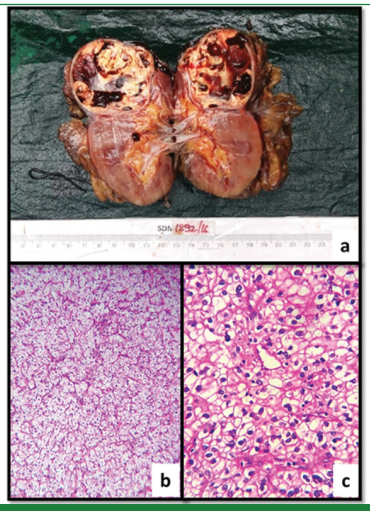
Clear Cell Carcinoma

This tumour is known to originate from the renal tubular epithelium and accounts for about 70% to 75% of all RCCs [10]. The 'clear' cytoplasm of the tumour cells is due to the presence of intracytoplasmic glycogen and lipids which gets dissolved during tissue processing [11]. Higher grade tumours have more granular-eosinophilic cytoplasm. Gross examination reveals golden yellow coloured tumour due to abundant intracytoplasmic lipid. The high grade tumours display variegated appearance because of less lipid and glycogen and with areas of haemorrhage and necrosis. Microscopically, the tumour displays cells arranged in acinar and solid nest patterns, along with arborizing intricate capillaries [12].

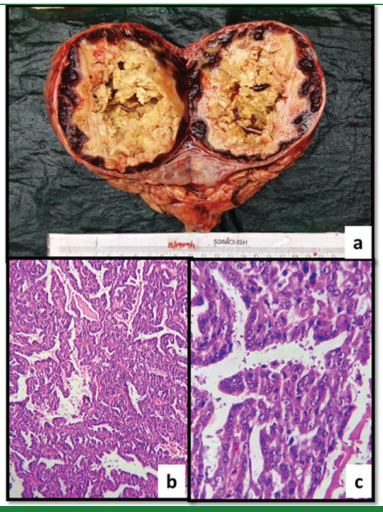
In our study, we observed 15 cases of clear cell RCC. The age ranged from 30 to 73 years with a mean age of 52.06 years. Majority of them involved the upper pole with a mean size of 8.04 cm [Table/Fig-8a-c].

Papillary (Chromophil) RCC

The second most common histological variant of RCC is papillary RCC, which accounts for about 10% of the cases [10]. It arises from the proximal convoluted tubules and grossly reveals a discrete mass in the renal cortex with areas of haemorrhage, necrosis and cystic degeneration [11]. Microscopically, it shows papillae, tubule-papillae and tubular structures. These papillae contain thin and delicate fibrovascular cores with foamy histiocytes [13]. Histologically, there are two variants. Type 1 displays short and delicate papillae with single layer of cells having scant cytoplasm and low grade nuclear features. Type 2 displays large papillae lined by cells with abundant eosinophilic cytoplasm and large nuclei showing pseudostratification and prominent nucleoli [13].



[Table/Fig-8]: a) Clear cell carcinoma: Nephrectomy specimen showing yellowish tumour in the upper pole of kidney with variegated appearance; b) Microphotograph displaying tumour cells in sheets and organoid pattern (H&E, 10x); c) Clear cell RCC showing tumour cells with clear cytoplasm and well defined cell borders (H&E, 40x).



[Table/Fig-9]: a) Papillary RCC : Cut surface showing tumour in the upper and mid pole with areas of haemorrhage and necrosis; b) Tumour arranged in papillae with fibrovascular core lined by tumour cells (H&E, 10x); c) Tumour displaying oval cuboidal to columnar tumour cells with eosinophilic cytoplasm (H&E, 40x).

In our study, we observed 5 (15.6%) cases of Papillary RCC. The age ranged from 45 to 61 years with a mean age of 51.4 years. Majority of them involved the lower pole with a mean size of 10.37 cm [Table/Fig-9a-c].

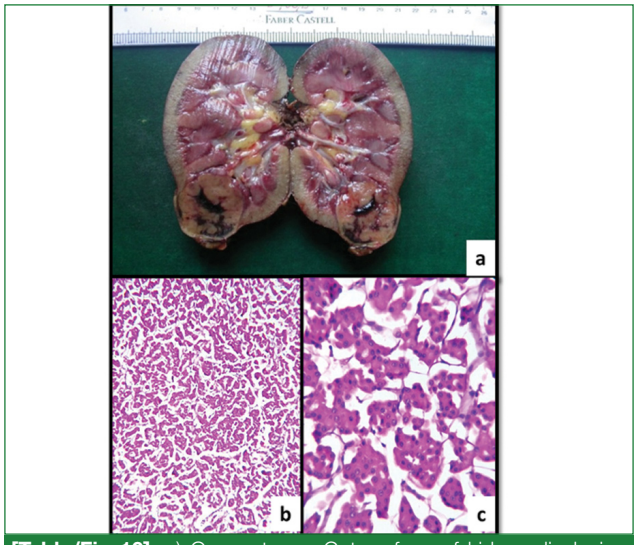
Renal Oncocytoma

Renal oncocytoma is a benign epithelial neoplasm accounting for about 3-7% of all primary renal neoplasms. Grossly, it reveals a well circumscribed mahogany brown solid lesion with central stellate scar. Histologically, it is composed of tumour cells arranged in nests, cords and tubules. The cells display adundant densely eosinophilic cytoplasm with monomorphic round vesicular nuclei and prominent central nucleoli.

In our study, we observed 3 (9.4%) cases of oncocytoma. The age ranged from 39 to 55 years with a mean age of 49.33 years. Majority of them involved the lower pole with a mean size of 5.66 cm. All the cases in our study presented with flank pain [Table/Fig-10a-c].

Papillary Adenoma

These are epithelial neoplasm with papillary or tubular architecture measuring less than 5 mm in size with low grade nuclei [13]. They are present in around 20% of the adult kidney [14]. Nearly 50% of the adenomas are identified in papillary RCC [15].



[Table/Fig-10]: a) Oncocytoma: Cut surface of kidney disclosing well defined mahogany brown tumour in the lower pole with central scar; b) Microphotograph displaying tumour cells arranged in cords, nests and sheets (H&E, 10x); c) Tumour cells with round to oval monomorphic nuclei with abundant granular eosinophilic cytoplasm (H&E, 40x).

In our study, we observed 1 (3.1%) case of papillary adenoma in 77 years male, who presented with flank pain and non functioning kidney. Grossly, it was contracted kidney with dilated pelvicalyceal system. Microscopy revealed features of pyelonephritis with focal areas showing cells arranged in papillae.

Renal Sarcomas

Sarcomas of various types can arise in the adult kidney including leiomyosarcoma, angiosarcoma, osteosarcoma, synovial sarcoma and others.

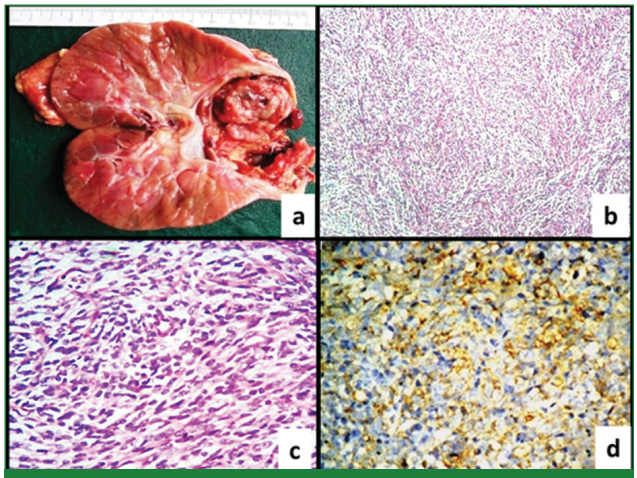
Synovial Sarcoma

Primary renal synovial sarcoma is very rare tumour accounting for about 1% of all primary renal neoplasms [16]. Grossly, tumour presents as an irregular large well defined mass ranging from 5-20 cms in size and may show cystic areas [17]. Microscopically, tumour displays either monophasic or biphasic pattern. Biphasic variant is composed of both epithelial and spindle cell component. The epithelial cells are arranged in the form of glands, and spindle cells with plump nuclei arrayed in short fascicular pattern. Monophasic variant contains only spindle cell component [18].

We encountered 1 (3.1%) case of synovial sarcoma in our study in a 57 years old male who presented with mass per abdomen. Cut section of kidney showed tumour in lower lateral aspect which was fleshy with haemorrhage and necrosis. Microscopically, it showed both glandular and spindle cells. Immunohistochemically, tumour cells were positive for CD99 and vimentin [Table/Fig-11a-d].

Squamous Cell Carcinoma

It is a rare unusual tumour of the kidney arising from the collecting system. It accounts for 0.5% to 15% of all the urothelial malignancies [19]. The presence of renal calculi, infections, imbalance of hormone, radiotherapy and vitamin A deficiency are few of the risk factors [19,20].



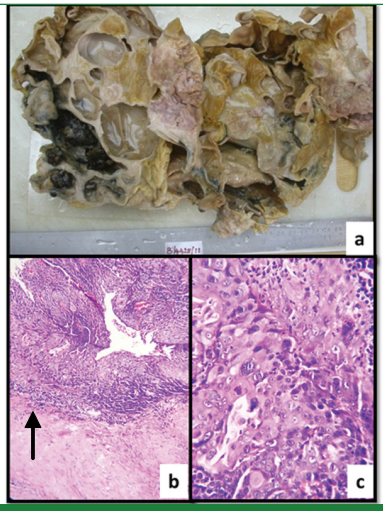
[Table/Fig-11]: a) Synovial sarcoma : Cut surface of kidney showing fleshy tumour in the lower pole with hemorrhagic and necrotic areas; b) Microphotograph displaying biphasic tumour cells arranged in interlacing bundles (H&E, 10x); c) High power view showing epithelial and spindle shaped tumour cells (H&E, 40x); d) Tumour cells showing IHC positivity for CD99 (40x).

In our study, we observed 2 (6.3%) cases of squamous cell carcinoma. One of the patient was aged 55 years male, who presented with hydronephrosis. Grossly, kidney was massively enlarged. Cut section revealed

thinned out cortex and dilated pelvicalyceal system. Microscopically, renal pelvis revealed features of well differentiated squamous cell carcinoma with focal areas of squamous metaplasia and carcinoma in situ. Other case was a 60 years old male patient who presented with non functioning kidney with renal calculi. Grossly, it showed dilated pelvicalyceal system with thinned out cortex and 3 calculi each measuring 1.5 cm. Microscopy revealed features of chronic pyelonephritis with foci of invasive squamous cell carcinoma [Table/Fig-12a-c].

Wilms Tumour

Wilms tumour also known as nephroblastoma, is one of the most common solid malignant neoplasm of children. It is an embryonal type of renal cancer accounting for 90% of all paediatric tumours of the kidney [21]. Grossly, they present as solitary, spherical well circumscribed mass with soft consistency. The size can vary from small to very large



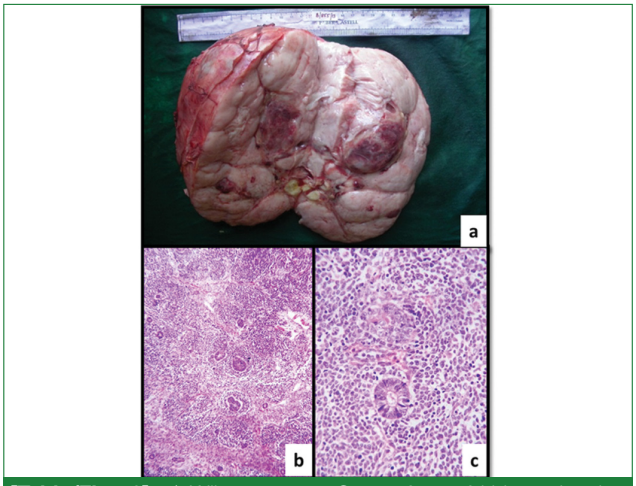
[Table/Fig-12]: a) Specimen of hydronephrotic kidney with dilated pelvicalyceal system; b&c) Dysplastic stratified squamous epithelium with tumour showing invasion (Squamous cell carcinoma) (H&E, 10x and 40x).

lesion. Cut surface reveals predominantly solid areas, pale grey or tan in colour with areas of haemorrhage, necrosis and cystic change [14]. Microscopically, tumour displays triphasic elements with features of attempt to form various stages of nephrogenesis [22].

In our study, we observed 3(9.4%) cases of Wilms tumour. Two cases in paediatric age group within the age ranging from 01 to 06 years, with mean age of 3.5 years and mean size of 13.25 cm. There was one case of adult Wilms tumour in 23 years female with size of 6.5 cm. All Wilms tumours were situated in upper pole [Table/Fig-13a-c].

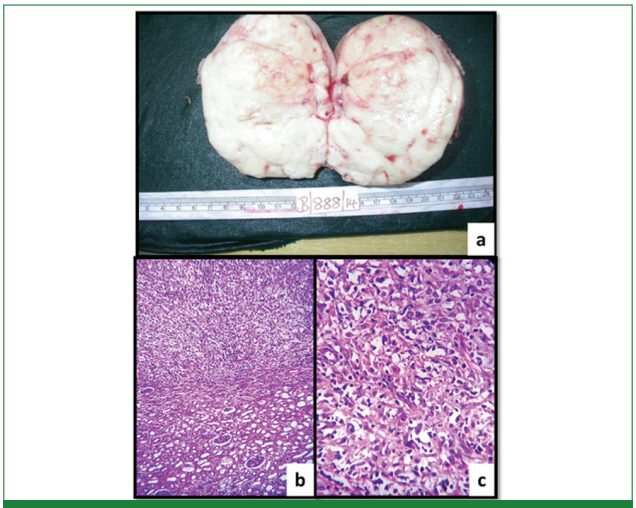
Rhabdoid Tumour

It is a highly malignant tumour, seen mainly in children younger than 2 years of age. It accounts for about 0.9% of all paediatric renal tumours [23]. In our study, we observed this tumour in one child aged 3 years, clinically presenting with mass per abdomen. Grossly tumour was grey white homogenous lesion with a rim of compressed renal tissue.



[Table/Fig-13]: a) Wilms tumour: Cut surface of kidney showing grey white homogenous tumour with fleshy appearance; b) Microphotograph showing tumour composed of blastemal cells, stromal cells and epithelial elements (H&E, 10x); c) High power view displaying blastemal cells with small monomorphic nuclei and scant cytoplasm with a central abortive tubule (H&E, 40x).

Histologically, the tumour was composed of sheets of large cells exhibiting vesicular nucleus, prominent nucleoli and eosinophilic cytoplasm with cytoplasmic inclusions. IHC was positive for vimentin and EMA [Table/Fig-14a-c].



[Table/Fig-14]: a) Rhabdoid tumour: Cut surface showing grey white homogenous tumour with narrow rim of normal kidney; b) Microphotograph depicting tumour cells in sheets with adjacent normal renal parenchyma (H&E, 10x); c) Tumour cells displaying pleomorphic eccentric nuclei with abundant eosinophilic cytoplasm (H&E, 40x).

LIMITATION

The limitation of the study includes the small sample size because of which the histologically vital prognostic factors such as tumour grade and stage were not statistically significant in our study. The strength of our study includes the significant variety of rare tumours with very few case reports published in the literature such as primary renal synovial sarcoma and squamous cell carcinoma.

CONCLUSION

Malignant renal tumours far outnumbered the benign tumours in our study with RCC being the most common malignant tumour in adults. Wilms tumour was the most common malignancy in paediatric age group. Majority of the tumours showed Fuhrman's nuclear Grade II observed in 50% of the cases. Nuclear grade and stage of tumour are essential for therapeutic decisions and help in prognostication, thus necessitating a systematic gross and histopathological examination of nephrectomy specimens.

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