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Histopathological Spectrum of Renal Tumors in Adults in Nephrectomy Specimens in a Tertiary Care Center

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ABSTRACT

Introduction

Renal neoplasms are heterogeneous tumors with clinical picture, prognosis and therapeutic implications differing with the various histological subtypes. There are limited studies on adult renal tumors conducted in Nepal so far. This study aims to provide a better assessment on the histopathological spectrum of renal neoplasms in adult population.

Methods

This is a descriptive study of all the nephrectomy specimens of adults received at Department of Pathology, Tribhuvan University Teaching Hospital from January 2013 to January 2020.

Results

There were 75 males and 35 females with mean age being 51.8 years. Malignant tumors (99 cases, 90%) were more common than benign tumors (11 cases, 10%). Renal cell carcinoma (RCC) was the most common malignant tumor consisting of 91 cases (82.72%) followed by 6 cases of urothelial carcinoma (5.45%) and 2 cases of primitive neuroectodermal tumor. (PNET) (1.8%). Clear cell RCC (78 cases, 70.90%) was the commonest histological subtype of RCC followed by papillary RCC (8 cases, 7.2%) and chromophobe RCC (2 cases, 1.8%). 42.65% of the cases of clear cell RCC were of WHO/ISUP grade 2, whereas, most of the cases of papillary RCC were of low grade (Grade 1, 37.5%). Majority of Renal cell carcinomas were in stage pT1a (28 cases, 34.56%).

Conclusion

Clear cell RCC was the most common renal tumor in adults comprising the majority of cases. These tumors mostly demonstrated WHO/ISUP Nuclear grade 2 and early stage of presentation (pT1). Papillary RCC was the second commonest RCC and mostly presented at lower nuclear grade (WHO/ISUP Nuclear grade 1). Urothelial carcinomas demonstrated higher nuclear grade and stage compared with RCC.

Keywords
Grade, histologic subtypes, renal neoplasms, staging

INTRODUCTION

Renal neoplasm are heterogenous group of tumors arising from different components of renal parenchyma such as tubular epithelium, urothelium, interstitial tissue and primitive elements.[1] These neoplasms have distinct distribution pattern among the pediatric and adult population.[2] Wilms tumor is the commonest neoplasm in pediatric population while renal cell carcinoma (RCC) is the commonest one in the adults.[3] RCC constitutes more than 90% of renal malignancies in adults.[4] It is the thirteenth most common malignancy worldwide.[5] Following renal cell carcinoma, urothelial carcinoma and oncocytoma are the common neoplasms in adults. Other uncommon adult renal neoplasms include multilocular cystic renal tumor, renal medullary carcinoma, collecting duct carcinoma, metanephric adenoma, angiomyolipoma, leiomyoma, hemangioma, sarcoma, neuroendocrine tumor, and juxtaglomerular apparatus tumor.[6]

Renal tumors classically present with abdominal pain, hematuria, and palpable abdominal mass. Radical nephrectomy and partial nephrectomy are the common surgical treatment. We frequently receive nephrectomy specimens at our pathology department for histopathological examination and confirmatory diagnosis of renal neoplasms with histological subtyping. Tumor stage and nuclear grade are the most important prognostic factors along with histological subtypes and presence of necrosis.[2,7] Histological diagnosis is straightforward in many cases but in some cases immunohistochemistry (IHC) may be required to subtype the tumor and to differentiate renal cell carcinoma from benign mimickers.[8]

There are limited studies on renal neoplasms conducted in Nepal so far. This study aimed to study the histopathological spectrum of renal neoplasms in adult population at tertiary center and their distribution as per age and sex along with further emphasis on factors such as tumor size, tumor site, histologic types, histologic grade (WHO/ISUP system) and pTNM staging.

METHODS

A descriptive study was conducted to characterize adult renal neoplasms diagnosed from January 2013 to January 2020 at the Department of Pathology, Tribhuvan university teaching Hospital (TUTH). Ethical approval was obtained from Institutional Review Committee of the Institute of Medicine. Medical records of all confirmed adult renal neoplasms during the study period were retrieved. The data collected included age, sex, tumor size, tumor site, histologic types, histologic grade (WHO/ISUP system) and pTNM staging. Tumor staging was performed according to the American Joint Committee on Cancer (AJCC) 8th edition cancer staging system. Data entry and analysis were made using IBM SPSS software program and was depicted in tables as means and percentages. Pediatric renal tumors, cases of nephrectomy diagnosed as metastatic tumors, cases with inconclusive diagnosis and core biopsy samples were excluded from the study.

RESULTS

Total 110 cases of adult renal neoplasms were included in the study. It included 16 radical nephrectomy specimens, 11 partial nephrectomy and remaining 83 simple nephrectomy specimens. The mean age was 51.8 years with standard deviation of 13.78. There were 75 males (68.1%) and 35 (31.8%) females with male to female ratio being 2:1(Table 1). Maximum cases (35 cases, 31.8%) were seen in the sixth decade (Figure 1).

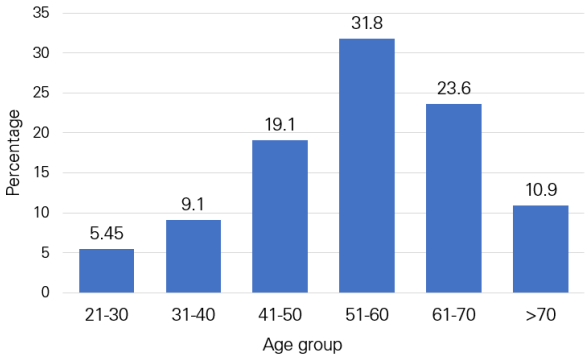

Figure 1. Bar diagram showing percentage of distribution of different age groups

Renal cell carcinoma was the commonest adult renal neoplasm (91 cases, 82.7%). Clear cell RCC was the most common histological subtype (78 cases) comprising 84.78% of total RCC. Papillary RCC was the second commonest histological subtype (8 cases) comprising of 8.7 % of total cases followed by Chromophobe RCC (2.19%).

On histopathological examination, Clear cell RCC showed tumor cells arranged in nests separated by fibrous septa (Figure 2a). Chromophobe RCC showed tumor cells arranged in nests and trabeculae surrounded by fibrovascular septa with raisinoid nuclei and perinuclear halo (Figure 2b). Likewise, tumor cells with bland nuclei and abundant eosinophilic cytoplasm were seen in Oncocytoma (Figure 2c). Sometimes, the distinction between Chromobhobe RCC and Oncocytomas becomes difficult. Few such cases were sorted with Cytokeratin 7 (CK7) immunohistochemistry (IHC) staining where diffuse CK7 positivity was noted in chromophobe RCC differentiating from oncocytoma. Out of 8 cases of papillary RCC, seven

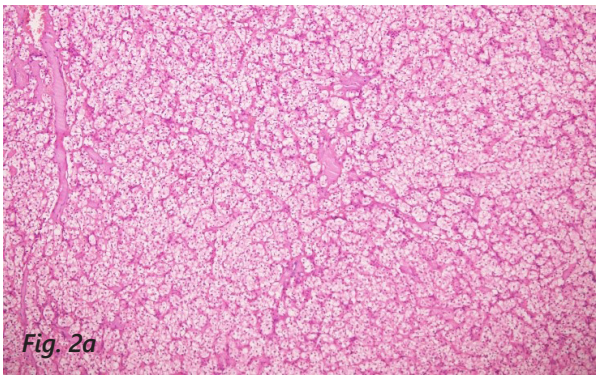
Fig. 2a

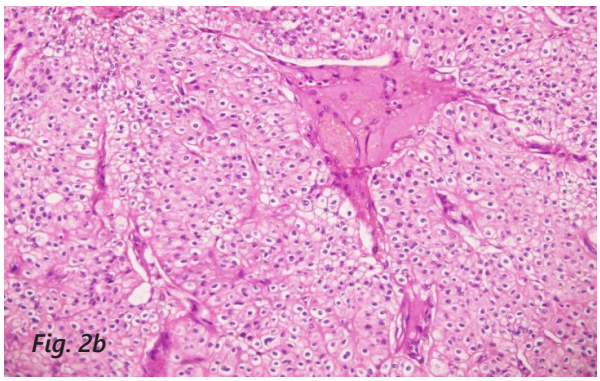
Fig. 2b

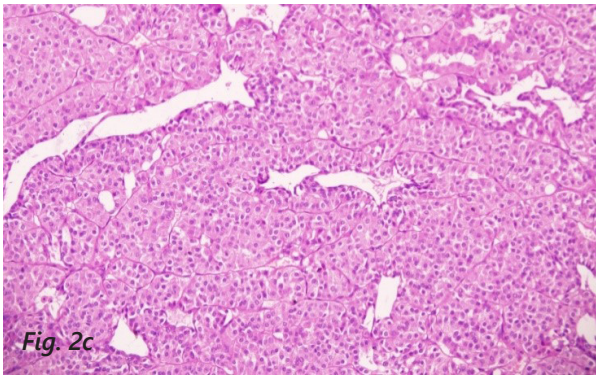
Fig. 2c

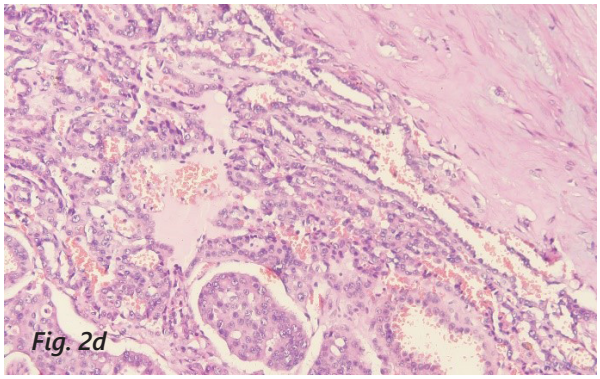
Fig. 2d

Figure 2a. Clear cell RCC showing tumor cells arranged in nests separated by fibrous septa (HE stain, X100). Figure 2b. Chromophobe RCC showing prominent perinuclear halos (HE stain, X200). Figure 2c. Renal oncocytoma showing cells with bland nuclei and abundant eosinophilic cytoplasm (HE stain, X100). Figure 2d. Type1 papillary RCC showing tumor cells arranged in papillae lined by small cuboidal cells (HE stain, X100).

Table 1. Frequency of different adult renal neoplasms and distribution by sex

Renal neoplasm type	Number		Total number (%)
	Males	Females	
Clear Cell RCC	55	23	78 (70.9)
Papillary RCC	8	-	8 (7.2)
Urothelial carcinoma	5	1	6 (5.4)
Primitive neuroectodermal tumor (PNET) PNET	-	2	2 (1.8)
Chromophobe RCC	1	1	2 (1.8)
Clear cell papillary RCC	1	-	1 (0.9)
Multilocular cystic neo-plasm of low malignant potential	1	-	1 (0.9)
Mucinous tubular spindle cell carcinoma	-	1	1 (0.9)
Oncocytoma	2	3	5 (4.5)
Angiomyolipoma	1	3	4 (3.6)
Papillary adenoma	1	-	1 (0.9)
Adult cystic nephroma	-	1	1 (0.9)
Total	75	35	110 (100)

were type 1 papillary RCC and showed tumor cells arranged in papillae lined by small cuboidal cells (Figure 2d).

Rest of the malignant renal tumors consisted of urothelial carcinoma and primitive neuroectodermal tumor (PNET) constituting 5.45% and 1.8% of total adult renal tumors. (Table 1)

Benign renal tumors consisted of 5 cases (4.5%) of oncocytoma, 4 cases (3.6%) of angiomyolipoma and 1 case (0.9%) each of papillary adenoma and

Table 2. Frequencies of distribution of Clear cell and Papillary RCC as per ISUP/WHO grade[9]

WHO/ISUP grade	Clear cell RCC n (%)	Papillary RCC n (%)
Grade 1	18 (23.07)	3 (37.5)
Grade 2	36 (46.15)	2 (25)
Grade 3	19 (24.35)	2 (25)
Grade 4	5 (6.41)	1 (12.5)
Total	78	8

Table 3. Distribution of Renal cell carcinoma as per pTNM staging, AJCC 8th edition[10]

pTNM Stage	Number (%)
pT1a	28 (34.56%)
pT1b	20 (24.69%)
pT2a	12 (14.81%)
pT2b	10 (12.34%)
pT3a	5 (6.27%)
Total	81

adult cystic nephroma. (Table 1).

WHO/International Society of Urologic Pathology (ISUP) Grading was applied for grading of all the cases of Clear cell RCC and Papillary RCC. Majority of the cases of clear cell RCC were of WHO/ISUP grade 2 (36 cases, 46.25%) followed by grade 3 (19 cases, 24.35%) and grade 1 (18 cases, 23.07%). Whereas, most of the cases of papillary RCC were of low grade (Grade 1, 37.5%). Sarcomatoid features were noted in six cases (5 cases of clear cell RCC and one case of papillary RCC) resulting in WHO/ISUP nuclear grade 4. (Table 2) The size of RCC ranged from 1.9 cm to as large as 14 cm with mean size being 4.95 cm.

Pathological staging was done using TNM staging (AJCC eighth edition) in total 81 cases of RCC excluding 10 cases of partial nephrectomy. Majority of Renal cell carcinomas were in stage pT1a (28 cases, 34.56%). Tumors in advanced stage (pT3a) consisted of 5 cases, 6.27% (Table 3). Perinephric fat invasion was seen in one case, renal sinus fat along with renal vein invasion were seen in 3 cases and renal sinus fat invasion alone was seen in a single case. In case of urothelial carcinoma, three out of six cases were seen in stage pT3 with invasion of peri-pelvic fat. One case showed invasion of subepithelial tissue resulting in stage pT1. Amongst the remaining two cases, one was stage pTa (noninvasive papillary urothelial carcinoma) and the other was pT4 with invasion of perinephric fat. None of the malignant renal tumors showed lymph node metastasis.

DISCUSSION

There exists a limited body of literature on adult renal tumors carried out in Nepal. We describe here the compilation of the findings on adult renal tumors in TUTH, the largest tertiary care center in Nepal. Renal tumors are common in adult population with nephrectomy specimens comprising major share of the histopathological examination. In adult population, Renal cell carcinoma is the most common renal tumor and shows male preponderance. Our study also revealed male preponderance with male to female ratio of 2: 1. This is in concordance with the studies conducted by Datta et al, Bashir et al, and Yamakanamaradi et al with reported male to female ratio of 1.9:1, 1.7:1, and 2.19:1 respectively.[1,11,12]

Maximum number of cases were seen in the sixth decade with mean age being 51.8 years. However, in the study conducted by Sannaboraiah et al and Latif et al, renal tumor was common in the fifth decade with mean age being 48 years and 47.9 years respectively.[13,14]

In our study, malignant tumors were more common than benign tumors. Malignant tumors constituted 99 cases (90 %) of total cases. Renal cell carcinoma was the most common malignant tumor similar to the studies done by Sannaboraiah et al, Aiman et al and Ngairangbam et al.[13,15,16] In the current study, the most common location of RCC was upper pole followed by lower pole and mid region. Likewise, the size of RCC ranged from 1.9 cm to as large as 14 cm with mean size being 4.95 cm. The findings were similar to the study done by Turun et al which reported the mean size of RCC being 5.02 cm.[17]

Clear cell RCC was the most common histological subtype of RCC in our study followed by papillary RCC and chromophobe RCC similar to the studies conducted by Latif et al, Bashir et al and Yamakanamardi et al.[11,12,14] Clear cell RCC morphologically showed presence of polygonal tumor cells arranged in nests separated by fibrovascular septa. These cells had moderate to abundant clear cytoplasm with distinct cell membrane. (Figure 2a) Eight cases of papillary RCC were noted comprising seven cases of type 1 and one case of type 2. Type 1 papillary RCC on histopathology showed papillae lined by single layer of cells with scanty cytoplasm and low nuclear grade. Morphology of type 2 papillary RCC showed tumor cells arranged in papillae and tubules with predominance of papillae, some fused and arborising. The findings were similar to the study done by Muglia et al.[18]

Chromophobe carcinoma morphologically showed tumor cells arranged in nests and trabeculae surrounded by fibrovascular septa with raisinoid

nuclei and perinuclear halo. (Figure 2b) Study done by Manipadam et al also demonstrated similar findings.[19] Sometimes it is difficult to distinguish these tumors from oncocytoma. In such cases, we should pay attention to nuclear features such as raisinoid shape and perinuclear halo as well as immunohistochemistry can be of help.[20] In our study IHC marker CK7 was used to distinguish Chromophobe RCC from oncocytoma. The former showed diffuse staining and the latter showed negative staining. Study by urologic pathologist has also shown CK7 to be the most utilized marker with <5% of cells staining positively as supportive of oncocytoma and diffuse staining for chromophobe RCC.[21]

Following RCC, urothelial carcinoma was the second most malignant renal tumor in our study comprising of 6 cases (5.45%). These tumors arise from the urothelial lining of renal pelvis or ureter. Three cases showed origin from renal pelvis and remaining three cases presented as upper ureteric mass. On histopathological examination, 4 out of 6 cases presented as infiltrating urothelial carcinoma, one case presented as invasive high grade papillary urothelial carcinoma and remaining one case as noninvasive low grade papillary urothelial carcinoma. Squamous differentiation was seen in one case of infiltrating urothelial carcinoma.

In our study, we noted 11 cases of benign tumors. (Table 1) It included 5 cases of oncocytoma, 4 cases of angiomyolipoma and one case each of papillary adenoma and adult cystic nephroma. Oncocytoma and angiomyolipoma were also the common benign renal tumors in the studies conducted by Bashir et al, Latif et al and Shah et al.[11,14,22] However, in these studies angiomyolipoma was more common than oncocytoma.

In our study, we applied WHO/International Society of Urologic Pathology (ISUP) nuclear Grading system for grading of all cases of Clear cell RCC and Papillary RCC. Most of the clear cell RCC showed WHO/ISUP nuclear grade 2 (46.15%) followed by grade 3 (24.35%) and grade 1(23.07%) respectively. This finding is also in concordance with other studies done by Shah et al and Narang et al.[22,23] On the contrary, in a study done by Ashima et al, nuclear grade 1 was more commonly reported in about 44.4 % of cases followed by nuclear grade 2 in 33.3 %.[24] In cases of papillary RCC, lower nuclear grade (grade 1) was commonly noted, 37.5% of total cases. Whereas nuclear grades 2 and 3 were seen in 25% of cases each. This is similar to the studies by Latif et al and Gudbjartsson et al.[14,25]

In the present study, pathological tumor staging was done as per AJCC eighth edition and CAP protocol in total 81 cases of RCC (excluding 10 cases of partial nephrectomy). Most RCC presented in lower stage with pT1 constituting 28 cases (34.5% of total cases) followed by pT2 (20 cases, 24.69%) and pT3 (12 cases, 14.81%). This is similar to the other studies and showed that majority of RCC are being detected at early stage.[13,26,27] Tumor detected at earlier stage have better prognosis.[28] In the present study, only five cases presented in advanced stage (pT3a). Among them, perinephric fat invasion was seen in one case, renal sinus fat along with renal vein invasion were seen in three cases and renal sinus fat invasion alone was seen in a single case. However, in the study conducted by Latif et al, higher percentage of cases were seen in advanced stage compared to lower stage (36.5% vs 34.1%).[14] In the present study, majority of cases of urothelial carcinoma were seen in advanced stage. Three out of six cases were seen in stage pT3 with invasion of peri-pelvic fat and one case was in stage pT4 with invasion of perinephric fat. This was similar to the study by Korkes et al and Olgac et al.[29,30]

This study has a few limitations. Retrospective study design in itself is a limitation. Also, this being a single institutional study, the data may not reflect the burden in population of Nepal. Hence, further research in a larger sample size could be conducted. This study was also not able to look into the outcomes and survival of this malignancy which could be an area of future research.

CONCLUSION

Clear cell RCC was the most common renal tumor in adult comprising the majority of the cases. These tumors were mostly of WHO/ISUP nuclear grade 2 and presented at an early stage (pT1). Papillary RCC was the second most common RCC and demonstrated lower nuclear grade. Oncocytoma was the most common benign renal tumor in adult followed by angiomyolipoma. Given the limited research on the histomorphological spectrum of heterogenous adult renal tumors, more studies if conducted from different parts of the country would facilitate in diagnosis and prognostication.

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CONFLICT OF INTEREST

The author(s) declare that they do not have any conflicts of interest with respect to the research, authorship, and/or publication of this article.

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