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Original Article

A Histopathological Spectrum Of Nephrectomy Specimens In A Tertiary Hospital In Southern India.

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ABSTRACT

Like any other human organ kidney may be involved by neoplastic and non neoplastic diseases requiring the removal of the organ. This study has been taken up to analyse kidney diseases histopathologically, to record and report the various lesions of the kidney and their subtypes , to analyse the gender and the age incidence and record the various lesions which have lead to partial nephrectomy,total nephrectomy,unilateral and bilateral nephrectomies.This study was a retrospective and prospective study (May 2003 –June 2012). undertaken on 70 nephrectomy specimens during the time period of 2 years The final diagnosis was arrived at after correlating the clinical features, gross , microscopic findings ,histochemistry wherever required.A total of 70 nephrectomy specimens were studied of which Simple and radical nephrectomy accounted for 92.9% and 7.1% respectively. The spectrum of pathological lesions included inflammatory,benign and malignant lesions. Non-neoplastic lesions were the most common reasons for nephrectomy with chronic pyelonephritis being the most common lesion .Renal cell carcinoma (RCC) was the most common malignant tumour seen in this study. Benign tumour were rare in the study with a single case each of congenital mesoblastic nephroma and angiomyolipoma. Other rare tumours like collecting duct carcinoma ,sarcomatoid carcinoma and hemangiopericytoma were also encountered in this study.

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1. Introduction

Simple Nephrectomy is a standard therapeutic urological procedure for irreversibly damaged non functioning kidneys involved by different benign pathological conditions like extensive renal stone disease, obstruction due to impacted calculus in the kidney or ureter,trauma,nephrosclerosis,neglected pelviureteric junction obstruction(PUJO),congenital malformations, renovascular hypertension due to non correctable renal artery abnormalities 1. The causes of loss of renal function which leads to nephrectomy differ between the adult and pediatric patient population 2,3,4.,Nephrectomy brings in relief to patient from various chronic and life threatening diseases and in some cases makes way for renal transplant.

On the other hand radical nephrectomy is indicated to treat different malignant neoplastic conditions of the kidney.In the last few years,there has been a growing interest on nephron- sparing surgeries or partial nephrectomies to treat selected cases of localized renal cell carcinomas by open or laproscopic approach 5,6,7.In the developed countries, laproscopic procedures have already replaced the open nephrectomy procedures.But in a developing country like India, in many centres especially those in rural and semi-urban setup, most of the nephrectomies are still being performed by open surgical procedures.

This study aimed aimed at determining the indications for nephrectomy in the community, studying the wide spectrum of renal diseases, to study the frequency of neoplastic and non neoplastic conditions and correlation with respect to age and sex of the patients.

Materials and Method

The present study was a 2 year study done on the nephrectomy specimens sent for histopathology evaluation to the Department of Pathology,Yenepoya Medical college from Yenepoya Medical College Hospital, Yenepoya Speciality Hospital, , private nursing homes and other hospitals in Mangalore during a period of 9 years (May 2003 to June 2012) .This is 8 years retrospective and 1 year prospective study. Required relevant clinical and imaging details were obtained from case sheets.

Grossing of the formalin fixed nephrectomy specimens was done according to the standard procedure . After routine paraffin processing, sections of 3 μ m thickness were cut and routinely stained with haematoxylin and eosin stain. Detailed light microscopic features were studied and recorded.. The final diagnosis was arrived at after correlating the clinical features, gross and microscopic findings. Special stains and immunohistochemistry were used as and when required

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Results

Out of 70 cases, 38 (54.2 %) and 32 (45.7 %) were non neoplastic and neoplastic respectively. The spectrum of cases included inflammatory, benign and malignant. (Table 1) (Figures 1-5)

Most of the specimens were enlarged (57.1%), contracted (31.4%) and normal sized (11.5%). Majority were males (40 cases-57.1%) with the remaining (30 cases -42.9%) being females. Maximum number of cases were seen between the 4th and 5th decade (14 cases-20%) (Table 2). The non neoplastic category included both inflammatory as well as congenital disorders. Pyelonephritis as a pure lesion and associated with hydronephrosis formed the most common lesion (31 cases-44.3%). In the infection-inflammatory lesions, there was slight female predominance in the ratio of 0.8:1. Maximum number of cases were found in the age group of 41-50. On the whole, infection-inflammatory lesions were common above 40 years of age (61.3%). Tuberculous and xanthogranulomatous pyelonephritis were found to be common in the third decade. Right kidney (51.6%) was involved slightly more frequently than the left kidney (48.4%) in non neoplastic lesions. Majority showed dilatation and distortion of the pelvi-calyceal system followed by thinning of the cortex (Table 3). There were 2 cases of renal calculi measuring 6x4x3 cms and 2x2x2 cms. Both the calculi were observed in the wall of the renal pelvis. There were 3 cases of tuberculous pyelonephritis and in all the cases the cut section showed distortion of the pelvicalyceal system along with multiple cysts filled with caseous material.

The second most common lesion in the non neoplastic category was multicystic renal dysplasia (7 cases-10 %) with a slight female predominance (0.7:1). Most of the cases (57.12%) were seen in the age group below 5 years. All the cases were unilateral. Microscopically the lesions, were characterized by fibrofatty tissue with nerve bundles, mature kidney tissue and immature tubules surrounded by concentric layers of smooth muscle fibres, immature mesenchyme and occasionally by cartilage (Table 4).

There were 32 cases of neoplastic lesions of the kidney with majority- 93.8% being malignant tumors. Most of the neoplastic lesions were observed in males (23 cases-79.9%) and 9 cases (28/1%) were seen in females with a ratio of 2.6:1. Right sided neoplastic lesions were slightly more (53.1%) than the left side (46.9%).

The most common neoplastic lesion was Renal cell carcinoma (17 cases). Only 2 cases of benign tumors, one case each of congenital mesoblastic nephroma and angiomyolipoma were seen. Wilms tumor formed the most common malignant paediatric tumor with 8 cases. The other malignant tumors being Transitional cell carcinoma of the renal pelvis and clear cell sarcoma of the kidney (2 cases each) and Hemangiopericytoma (1 case each) were seen in this study.

In the present study majority of the renal cell carcinomas were seen in the 8th decade-5 cases (15.6%) with a predominance of left kidney involvement (10 out of 17 cases) whereas most of the Wilms tumors were observed in the 1st decade-11 cases (34.4%) with predominance of right kidney involvement (6 cases of 8 cases). Male preponderance was seen on both renal cell carcinoma (3.2:1) and Wilms tumor (1.6:1). The most common type of renal cell carcinoma was clear cell type, other types seen were that of papillary, sarcomatoid, chromophobe and collecting duct type of RCCs (Table 5). The predominant pattern observed in renal cell

carcinomas was alveolar pattern which was observed in 8 cases (47%). Solid pattern was next commonly pattern observed 5 cases (29.4%). The other patterns observed were papillary and tubulopapillary pattern. The predominant cell type observed were clear cells in 8 cases (47.1%). In 6 cases (35.3%) both clear cells as well as granular cells were observed. The nuclear grade I was the most common nuclear grade observed in the present study (Table 6). Evidence of capsular infiltration was seen in 9 cases. There was no evidence of lymph node metastasis or adrenal gland involvement in any of the cases of renal cell carcinomas.

FIGURES

Table 1: Frequency of various renal lesions encountered in the present study:

Histopathological diagnosis	No. of cases	Percentage
NON-NEOPLASTIC		
Inflammatory		
Chronic pyelonephritis (CPN)	11	15.7%
Hydronephrosis with CPN	11	15.7%
Tuberculous pyelonephritis	3	4.3%
CPN with calculi	2	2.9%
Pyonephrosis	2	2.9%
Xanthogranulomatous pyelonephritis	1	1.4%
Acute pyelonephritis	1	1.4%
Congenital		
Multicystic renal dysplasia	7	10%
NEOPLASTIC		
Benign		
Angiomyolipoma	1	1.4%
Congenital mesoblastic nephroma	1	1.4%
Malignant		
Renal cell carcinoma	17	24.3%
Wilm tumor	8	11.4%
TCC of renal pelvis	2	2.9%
Clear cell sarcoma	2	2.9%
Hemangiopericytoma	1	1.4%

Table II: Age and sex distribution of the cases studied:

Age group (years)	Males	Females	Total no. of cases	Percentage
0-10	9	9	18	25.72%
11-20	1	3	4	5.71%
21-30	0	5	5	7.14%
31-40	3	2	5	7.14%
41-50	8	6	14	20.0%
51-60	7	3	10	14.29%
61-70	6	2	8	11.43%
71-80	6	0	6	8.57%
Total	40	30	70	100%

Table III: Cut section of non neoplastic lesions:

Feature	No of cases	Percentage
Distortion/dilatation of pelvicalyceal system	21	67.74%
Thinning of cortex	15	48.39%
Cysts	5	16.13%
Renal stones	2	6.45%
Filled with pus/necrotic material	5	16.13%
Grey white homogenous areas	8	25.81%

Table IV : Microscopic features in renal dysplasia.

Microscopic findings	No. of cases (n=7)
Cysts lined by cuboidal epithelium	7
Primitive ducts	7
Blastemal tissue	4
Primitive mesenchyme	4
Cartilage	2
Calcification	3

Table V:Frequency of histological types of renal cell carcinoma

Histopathological types	No. of cases	Percentage
Clear cell	9	52.9%
Papillary	3	17.6%
Chromophobe	2	11.8%
Sarcomatoid	2	11.8%
Collecting duct	1	5.9%
Total	17	100%

Table V1:Frequency of nuclear grade in clear cell renal cell carcinoma

Nuclear grade	No. of cases	Percentage(%)
I	4	44.4%
II	3	33.3%
III	2	22.2%
IV	0	0%

Figure 1:Cut section showing yellowish areas in xanthogranulomatous pyelonephritis



Figure 2: Cut section of kidney with a large calculi in the pelvis



Figure 3:Gross photograph of congenital mesoblastic nephroma exhibiting firm whorled texture



Figure 4 :Gross photograph of angiomyolipoma with yellow and grayish areas with haemorrhage



Figure 5: Photomicrograph of angiomyolipoma of the kidney with mixture of fat, blood vessels and smooth muscles. (H & E,40 x).

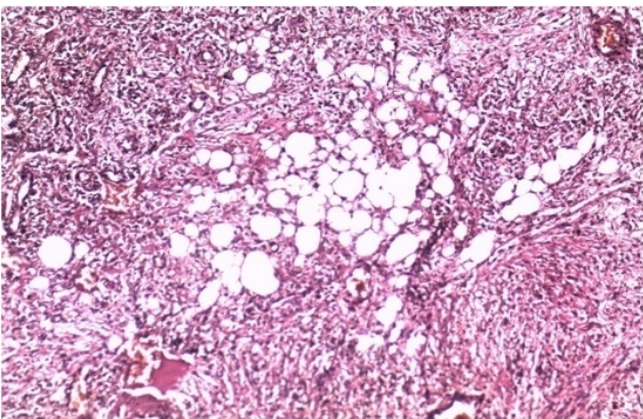


Figure 6: Photomicrograph of interlacing fascicles of fibroblastic cells with entrapped tubules.

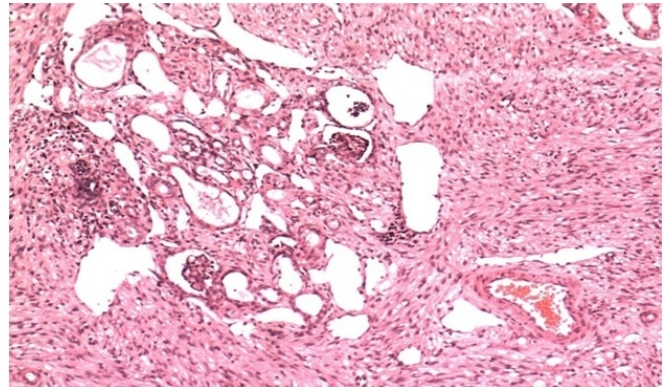
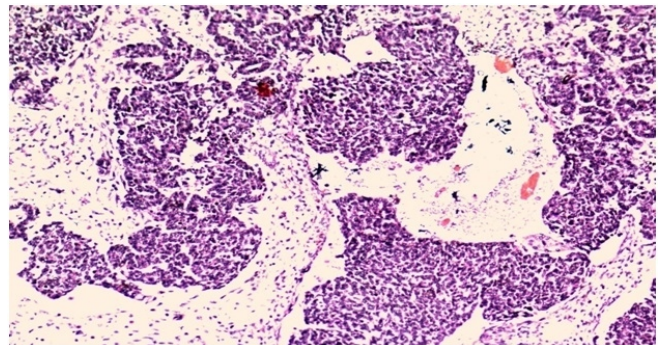


Figure 7: Photomicrograph of Blastemal, stromal and epithelial component in Wilms tumor (H& E, 40 x).



Discussion

Many non neoplastic and neoplastic lesions constitute an indication for nephrectomy in urology today .The present study was an analysis of 70 nephrectomy specimens . 92.9% (65 cases) of the 70 nephrectomy specimens were that of simple nephrectomy. No partial nephrectomy specimens were encountered .Radical nephrectomies which were done for malignant tumors accounted for 7.1% in the present study in comparison to 16.7% and 22% in the nephrectomy studies done by Badmus et al and Fadil et al respectively^{8,2}.

The highest number of cases included in this study were below the age of 10 years (25.7%) followed by the age group of 41 to 50 years (20%). The least number of cases were seen between 11-20 years(5.7%). The youngest patient in this study was a 10 day old infant and the oldest patient was an 80 year old male patient .The male to female ratio of all the nephrectomy specimens was 1.3:1. El Fadil et al (1997) and Lathif et al (2011) concluded that the male to female ratio in their respective studies was 1.9:12.9. Male : Female ratio of 2:1 was also seen in the nephrectomy study done by Badmus T et al (2008)⁸. There was a slight female predominance in the nephrectomy study done by Rafiq et al with a M:F ratio of 2.3:110. In the present study right and left sided lesions were affected equally, in contrast to the nephrectomy studies done by Dutta et al and Fadil et al where there was preponderance of left sided lesions and Diniz et al where there was predominance of right sided lesions^{11,2,1}.

From the review of literature it appears that there is a geographical variation in indications for nephrectomy. Beisland et al and Kubba et al from Norway and UK respectively have

reported that there has been a change in the indications for nephrectomy in their countries during the last few decades with more nephrectomies now being performed for malignant conditions^{12,13}. Kim et al divided his study into 3 groups, period 1 from January 1980 to December 1987, Period 2 from January 1990 to December 1997 and period 3 from January 2000 to December 2005 and concluded that the incidence of nephrectomies for benign renal diseases has markedly decreased over time. In comparison to the nephrectomy study done by Kim K et al, the frequency of infection - inflammatory diseases was much higher in the present study (54.2%)¹⁴. This could be attributed to the fact that India being a developing country, inflammation-infection forms a majority of our case load.

Pyelonephritis is seen in all age group with peak incidence in infancy and childhood, women of child bearing age and both men and women older than 60 years. In the present study majority of pyelonephritis were seen between 4th to 7 th decade. Non obstructive pyelonephritis is said to be less common than obstructive pyelonephritis. In a necropsy study by Farmer et al (1971) the incidence of non obstructive chronic pyelonephritis was found to be only 0.23%¹⁴. In the present study, non obstructive pyelonephritis was found to be more common as compared to obstructive chronic pyelonephritis, with only 2 cases showing renal calculi. The reason for this could be that most cases of renal calculi are being treated conservatively and hence nephrectomy is not required in most cases. The most important cause of non obstructive chronic pyelonephritis is vesicourethral reflux. Kim et al in his analysis of causes of nephrectomy from 1980 to 2005 showed a steady decrease in the incidence of infection-inflammatory diseases from 28.75% to 8.57%¹⁴. In our study there was an equal sex distribution and predilection for left kidney in case of chronic pyelonephritis.

In our study, congenital malformations accounted for 10% of all renal lesions. All the cases were that of Multicystic renal dysplasia. The mean age was 4.3 years. Adamson et al reported a M:F ratio of 7:1 with 11 out of 16 cases seen in the left kidney and the mean age being 1.816. In the present study 85.7% cases were seen in the 1st decade and 14.3% were seen in the 2nd decade. Risdon¹⁷ (1971) reported 34% cases of multicystic renal dysplasia in a necropsy study of 121 children. He describes an equal incidence in either sex. In our study left kidney was affected in 71.4% of cases of multicystic renal dysplasia. This is in concordance to the study done by Risdon and Adamson et al. Renal dysplasia may be complete, segmental or focal. Bilateral total renal dysplasia results in death in the first few years of birth. In the present study all the cases of renal dysplasia were unilateral and complete.

Neoplastic lesions constituted 45.7% of all renal lesions with a M:F ratio of 2.2:1. Among the neoplastic lesions, 93.8% were malignant and 6.2% were benign which is concordance with the study done by Latif et al⁹. The mean age was 39.5 years which is lower than the previously published studies. The prevalence of neoplastic lesions in the right kidney and left kidney was 53.1% and 46.9% respectively. Latif et al in their study reported 54% of the tumors in left kidney and 46% occupied the right kidney⁹.

There was no significant difference between the involvement of the upper pole and lower pole in case of RCC with upper pole and mid portion being involved in 18.7%, lower pole in 16.6%, entire cut surface in 43.8% and pelvis in 6.3%.

The incidence of renal cell carcinomas increases with advancing age¹⁷ and thus majority of the patients in the present study were between 61 to 80 years of age (28.1%). The male : female ratio is 3:1 for renal cell carcinoma. In the present study, it was 3.2:1. Renshaw (2002) states that clear cell or conventional renal cell carcinoma comprise 75% of all renal cell carcinoma¹⁸. In the present study, 52.9% of all renal cell carcinomas were of the clear cell type. Collecting duct carcinoma was found in 5.9% of renal cell carcinomas.

Nuclear grade of the tumor as determined in microscopic sections is an important predictor of survival. The nuclear grade I was the most common nuclear grade observed in the present study (44.4%). Grade II and III were seen in 33.3% and 22.2% cases respectively. Most common secondary changes noticed in the surrounding kidney were necrosis and haemorrhage (8 cases); chronic pyelonephritis (7 cases) and tumor infiltration (7 cases). In the study done by Usha et al (1987) who studied 26 cases of RCC and observed chronic interstitial nephritis in 18 cases, out of which 4 also showed hydronephrotic changes and 3 showed features of renal adenoma apart from RCC¹⁹. In the present study the most common microscopic pattern observed was alveolar (47.0%) followed by solid pattern (29.4%), papillary pattern (11.8%) and tubulopapillary pattern (11.8%). Syrjamen and Hjelt (1978) in a study of 138 cases of RCC found papillary pattern as the commonest architectural pattern (48.7%) followed by tubular (25.6%), undifferentiated (22.4%) and glandular (3.3%)²⁰.

In the present study, Wilm's tumor was seen in 28.2% of all primary renal tumors. Lemerle et al (1976) reported a mean age of 3 years and a left sided predominance 21. In this study, the youngest patient was 10 months old and the oldest patient was 8 years of age with a mean age of 3.5 years and right sided predominance. Most Wilm's tumors have been found to be triphasic, with a representation of blastemal, mesenchymal and epithelial components. In our study, 7 cases (87.5%) showed triphasic pattern. Only 1 case (12.5%) showed biphasic pattern with mesenchymal and blastemal element.

CONCLUSION

Open nephrectomy still remains the local surgical technique. Nephrectomies done for non neoplastic lesions were more common than neoplastic lesions of the kidney in our setup. Malignant tumors of the kidney forms the majority of the kidney tumors with clear cell renal cell carcinoma predominating. Benign tumors of the kidney are very rare.

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