

## PATHOLOGICAL SPECTRUM OF NON- NEOPLASTIC DISEASES IN THE NEPHRECTOMY SPECIMENS

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**ABSTRACT: INTRODUCTION:** There is an increase in the number of nephrectomies with the extensive use of imaging techniques in the recent years. In India management of chronic kidney diseases is posing a great challenge as dialysis and kidney transplantations are expensive for the patients. **OBJECTIVES:** 1. To analyze all the nephrectomy specimens received over a period of ten years, from 2004 to 2014 at K.I.M.S. Hospital and Research center, Bengaluru. 2. To determine the age and sex distribution in various non-neoplastic diseases. 3. To categorize the various types of non-neoplastic conditions of the kidney. **MATERIALS AND METHODS:** The study included retrospective and prospective cases over a period of ten years between 2004 to 2014. For the retrospective cases, blocks, slides and records were retrieved and studied. For the prospective cases, nephrectomy specimens sent for histopathological evaluation were studied. Along with routine hematoxylin - eosin stain, special stains were done when required. **RESULTS:** Our study included a total of 116 nephrectomy specimens of which 84(72.41%) were non-neoplastic and 32(27.59%) were neoplastic lesions. Of the 84 non-neoplastic lesions age distribution varied from 1 month to 70 years. Gender distribution included 54.76% males and 45.23 % females. The male to female ratio being 1.2:1. The commonest non-neoplastic lesion was chronic pyelonephritis (54.31%) and cystic lesions were the least. **CONCLUSION:** We observed that the number of nephrectomies has increased gradually over the years. Amongst non-neoplastic diseases of kidney chronic pyelonephritis is the commonest cause leading to nephrectomy.

**KEYWORDS:** Nephrectomy, non- neoplastic lesions, chronic pyelonephritis.

**INTRODUCTION:** Nature has provided two kidneys in the human body which are essential organs and each one weighs around 150gms. Our entire blood volume gets filtered 20 to 25 times per day by kidneys, working constantly every minute, every day on all 365 days. Kidney is a complex organ with 30 different cell types comprising about one million nephrons as functional units.

Kidneys are vital organs essential for the excretory function and they also maintain water and salt metabolism along with acid base balance. Kidneys also have endocrine functions as they produce renin-angiotensin to control blood pressure and erythropoietin required for haemopoiesis.

Renal diseases are responsible for a great deal of morbidity. Millions of people are affected annually by non- fatal kidney diseases mainly infections and calculi. The functional reserve of the kidney is large, and much damage would occur before there is evident functional

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impairment.<sup>1</sup> Kidneys are affected by conditions like pyelonephritis, nephrosclerosis, vesico-ureteric reflux, pyonephrosis, tuberculosis and so on.<sup>2</sup>

Nephrectomy is a common procedure in surgical practice, performed in the context of end stage renal disease (ESRD) where kidney is damaged severely, non-functional and in cases of malignant renal neoplasms.

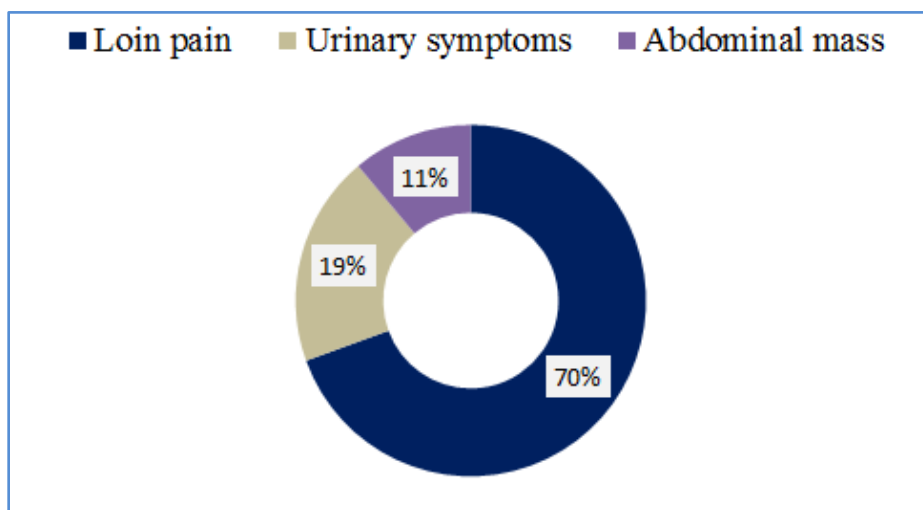
The objectives of this study were 1) to analyze all the nephrectomy specimens received over a period of ten years, from 2004 to 2014 at K.I.M.S. hospital and research center, Bengaluru, 2) to determine the age and sex distribution in various non- neoplastic diseases and 3) to categorize the various types of non- neoplastic diseases and neoplasms of kidney. In this article we are presenting only the non-neoplastic lesions.

**MATERIALS AND METHODS:** This study was carried out in the Department of Pathology, Kempegowda Institute of Medical Sciences, Bengaluru, which included one and a half years of prospective (JAN 2013 to JUNE 2014) and eight and a half years of retrospective study (JUNE 2004 to DEC 2012). All nephrectomy specimens received in ten years from 2004 to 2014 were studied with the clinical features, radiological findings, gross and microscopic features. For prospective cases, the specimens of surgically resected kidneys sent for routine histopathological evaluation were studied. For retrospective cases, paraffin blocks and slides along with the case records were retrieved and studied. All the nephrectomy specimens were fixed in 10% formalin, the weight, size of specimens were recorded. Position of the kidney in relation to the blood vessels and ureter at the hilum was noted. Kidney was cut sagittally and the capsule was examined. The morphology of cortex, medulla, renal pelvis, and ureter was noted. The required number of bits were processed from parts of the lesion and from adjacent normal kidney including bits from renal vessels and ureter. After routine processing of the tissue bits, serial sections of 4-5 microns thickness were taken and stained with Hematoxylin and Eosin. Special stains like Ziehl-Neelsen, Periodic Acid Schiff and others were done wherever necessary. A final diagnosis was made after correlating the clinical, radiological and histopathological findings.

**RESULTS:** The present study was conducted in the Department of Pathology, Kempegowda Institute of Medical Sciences and Research Center, Bengaluru. 116 cases of nephrectomy specimens received from June 2004 to June 2014 were studied. Of these 84(72.41%) cases were non-neoplastic lesions and 32(27.59%) were neoplasms.

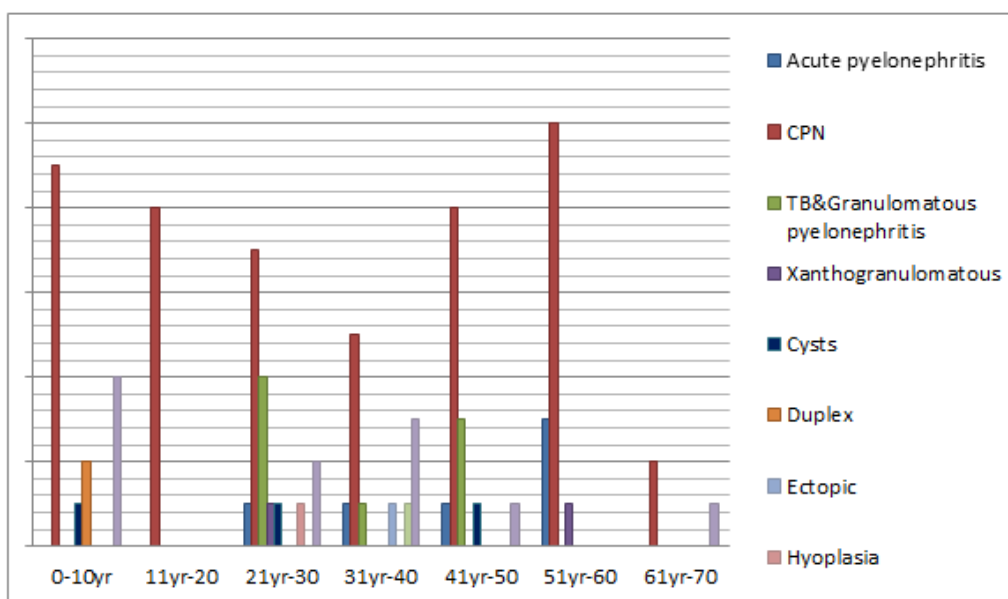
Loin pain was the main presenting complaint noted, followed by urinary symptoms like burning micturition and increased frequency of micturition. 4 cases presented with abdominal mass (Fig. 1).

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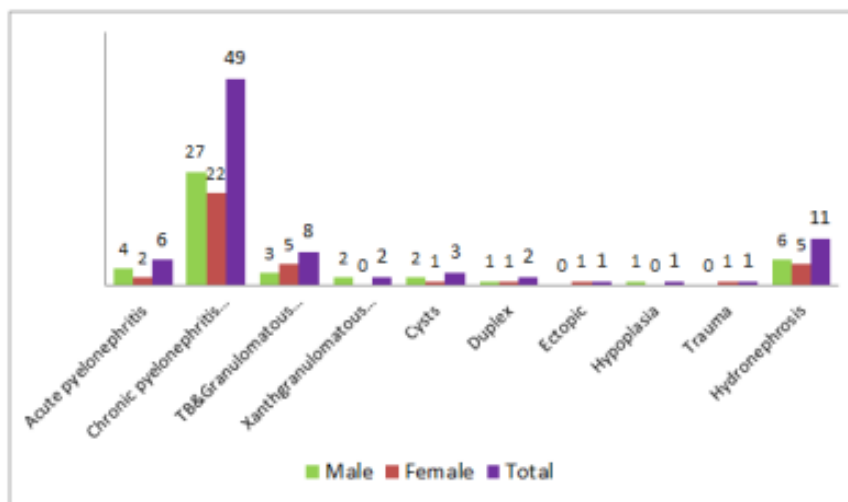


**Fig. 1: Presenting complaints in 84 cases of non-neoplastic kidney lesions**

Age of the patient ranged from 1 month to 70 years. The highest percentage of patients belonged to the age group of 21-30 years (20.2%), followed by 0-10 years (19%), 14 cases (16.6%) in the age group of 41-50 years and 51-60 years, 12 cases (14.2%) in the age group of 31-40 years, 8 cases (9.52%) in the age group of 11-20 years and 3 cases in the age group of 61-70 years (Fig. 2).



**Fig. 2: Age wise distribution of non-neoplastic diseases**



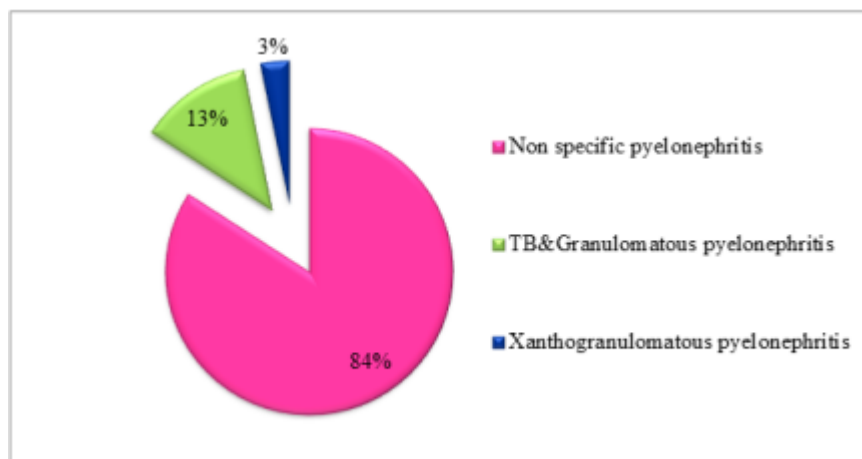
**Fig. 3: Gender wise distribution of non-neoplastic diseases**

Gender distribution included 54.76% (46 cases) males and 45.23% (48 cases) females. The male to female ratio being 1.2:1. Gender wise distribution of non-neoplastic diseases is explained in fig. 3.

Chronic pyelonephritis (CPN) was the commonest non- neoplastic disease encountered in all the age groups. Out of 84 lesions, 69(82.1%) cases were inflammatory conditions, 4(4.76%) cases were non-inflammatory conditions, 11 cases (13%) were hydronephrosis. 63(91.3%) of 69 cases were chronic pyelonephritis and 6 (8.69%) were acute pyelonephritis.

Chronic pyelonephritis (non-specific) was seen in 53(84%) cases, 8(13%) were cases of granulomatous pyelonephritis and 2(3%) cases were xanthogranulomatous pyelonephritis (Fig. 4).

Of the 8 cases of granulomatous lesions noted in the study, 5 showed positivity for acid fast bacilli with Ziehl-Neelsen stain and were diagnosed as tubercular pyelonephritis.



**Fig. 4: Distribution of 63 cases of chronic pyelonephritis**

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There were 4 cases of non-inflammatory conditions of which 3 were cysts and 1 was a lacerated kidney due to trauma. Among 3 cases of cysts, 2 were simple cysts and 1 was a case of Adult polycystic kidney disease.

There were 11 cases (13%) of hydronephrosis which were commonly seen in paediatric age (1month – 10yrs). Most of these cases were due to vesicoureteric reflux (7 cases), followed by pelvi-ureteric junction obstruction and ureteric stricture.

There were 2 cases of duplex kidney, a case of ectopic kidney and a case of hypoplastic kidney with persistent fetal lobulations. They had chronic pyelonephritis which necessitated nephrectomy. Supernumerary kidneys are rare and there are very few reports in literature. Some of them are reported as being contents of inguinal hernial sac. We encountered one such rare case of supernumerary kidney which presented as a content of sac excised from indirect inguinal hernia along with cryptorchid testis. This patient was an adult male who had two normal kidneys as per the scan report. Prior to surgery all these patients were diagnosed as having non – neoplastic lesions on imaging studies which correlated with the histopathological findings. All cases underwent simple nephrectomy and 1 case had laparoscopic nephrectomy done.

Anatomically 43(51.19%) cases were seen in the left kidney, 41(48.8%) cases were encountered in the right kidney. Congenital anomalies (duplex, hypoplasia, ectopia) of the kidneys were seen more commonly in the left kidney (Table 1). Hence there was not much difference in the total number of lesions in the right and left kidneys.

<b>Non-Neoplastic lesions</b>	<b>Right</b>	<b>Left</b>
Acute pyelonephritis	05	01
Chronic pyelonephritis(non-specific)	24	25
TB&Granulomatous pyelonephritis	04	04
Xanthogranulomatous pyelonephritis	01	01
Cysts	01	02
Duplex	00	02
Ectopic	01	00
Hypoplasia	00	01
Trauma	01	00
Hydronephrosis	04	07
<b>Total</b>	<b>41</b>	<b>43</b>

Table 1: Frequency of involvement of right and left kidney in non-neoplastic lesions

Of the 84 cases of non-neoplastic lesions, gross morphology included the following.10 cases showed necrosis, 81 cases showed hydronephrotic changes with loss of normal cortico medullary junction and dilatation of pelvi-calyceal system. Apart from hydronephrotic changes we noticed scarred, shrunken kidneys in 17 cases and calculi were noted in 17 cases (Table 2).

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Gross findings	Number of cases
1. Shrunken	17 (20.2%)
2. Enlarged	15 (17.8%)
3. Loss of cortico medullary junction	81 (96.4%)
4. Dilatation of pelvi-calyceal system	81 (96.4%)
5. Stone	17 (20.2%)
6. Pus and caseous necrosis	10 (11.9%)

**Table 2: Gross findings of the kidney in 84 cases**

Microscopically periglomerular fibrosis, glomerular sclerosis were seen in 52 cases, tubular changes like atrophy and thyroidisation were seen in 76 cases, 8 cases showed granulomas, 67 cases had chronic interstitial inflammation. 6 cases showed acute inflammatory cells, 2 cases had sheets of foamy macrophages and arterial changes such as sclerosis were seen in 43 cases (Table 3). Some of the rare cases like ectopic kidney, hypoplasia and duplex kidneys were seen in our study which also showed features of chronic pyelonephritis.

Of the 32 cases of neoplasms, Renal cell carcinoma (RCC) was the commonest tumour with rare cases like RCC with osseous metaplasia, Chromophobe RCC, Liposarcoma arising from Angiomyolipoma and Mucinous adenocarcinoma of renal pelvis with renal calculus. There was a case of Leiomyosarcoma which was confirmed with immunohistochemistry for smooth muscle actin and a case of Adult Wilms' tumour was encountered.

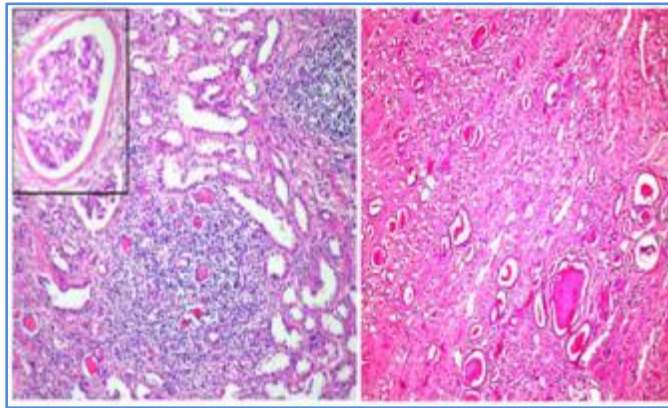
Microscopic findings	Number of cases
Periglomerular fibrosis	52 (61.9%)
Glomerular sclerosis	52 (61.9%)
Atrophy of tubules	76 (90.4%)
Thyroidisation of tubules	76 (90.4%)
Interstitial inflammation	
Acute	06 (7.1%)
Chronic	67 (79.7%)
Granulomas	08 (9.52%)
Foamy macrophages	02 (2.38%)
Interstitial fibrosis	77 (91.6%)
Hyaline Arteriosclerosis	43 (51.1%)

**Table 3: Microscopic findings in 84 cases of non-neoplastic kidney lesions**

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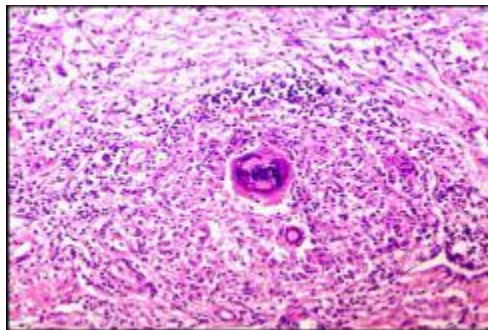
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**Fig. 5:** Microphotograph of Chronic pyelonephritis showing (a) periglomerular fibrosis (inset), interstitial inflammation (b) thyroidisation of tubules and interstitial fibrosis (H & E, 100x)



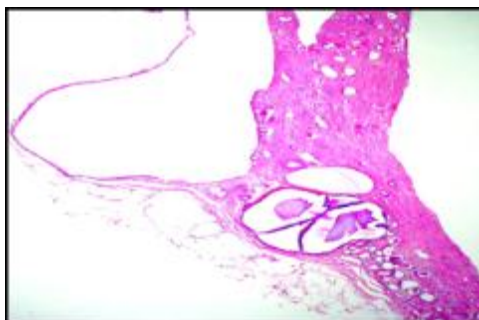
**Fig. 5**

**Fig. 6:** Microphotograph of a granulomatous pyelonephritis showing granuloma with multinucleate giant cells. (H & E, 100x)



**Fig. 6**

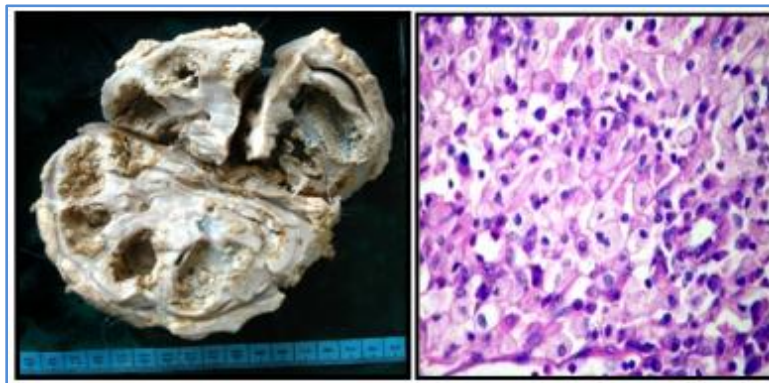
**Fig. 7:** Microphotograph of a simple cyst showing cyst lined by flattened epithelium with wall showing renal tubules. (H & E, 40x)



**Fig. 7**

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**Fig. 8:** Xanthogranulomatous pyelonephritis (a) Gross - showing yellowish necrotic areas (b) Microscopy shows sheets of foamy macrophages (H & E, 400x).



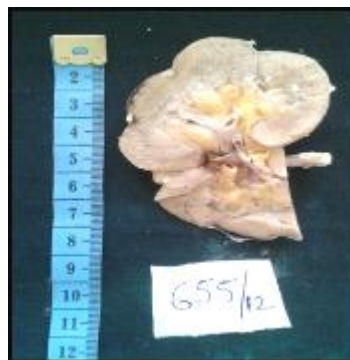
**Fig. 8**

**Fig. 9:** Cut surface of kidney with CPN & Hydronephrosis showing dilated pelvi-calyceal system.



**Fig. 9**

**Fig. 10:** Hypoplastic kidney with persistent fetal lobulations.



**Fig. 10**



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**DISCUSSION:** Gustav Simon performed the first planned nephrectomy for the treatment of urinary fistula in 1869 and one year later in 1870 Simon performed partial nephrectomy for hydronephrosis.<sup>3</sup>

Kidneys are involved in various pathological conditions, some of which require surgical removal. Diseases which commonly affect kidney are the chronic infections and obstructive conditions. Nephrectomy is also indicated in cases of renovascular hypertension, traumatic injury and congenital dysplasia. The kidneys are affected by different tumours and 99% of renal neoplasms are malignant.<sup>2</sup> Recent advances in early diagnosis and management of renal disease have reduced the number of nephrectomies performed for benign lesions.<sup>1</sup> There is a geographic variation regarding the indications for nephrectomy. In spite of availability of health care facilities, many advanced treatment, the number of nephrectomies has been increasing for benign conditions.

In our study, 116 nephrectomy cases were analyzed. There were 84 (72.41%) non-neoplastic diseases and 32 (27.59%) neoplastic diseases. It showed an increase in the number of nephrectomies over last 5 years compared to the first 5 yrs of study period (Table 4).

	<b>Non-neoplastic cases</b>	<b>Neoplastic cases</b>	<b>Total</b>
2004-2009	<b>35</b>	<b>07</b>	<b>42</b>
2010-2014	<b>49</b>	<b>25</b>	<b>74</b>
<b>Total</b>	<b>84</b>	<b>32</b>	<b>116</b>

Table 4 : Distribution of cases in the study period

In the present study there were 46 males and 38 females with a ratio of 1.2:1. Most of the cases were in 3<sup>rd</sup> decade (20.2%) followed by 1<sup>st</sup> decade (19%). A study of 192 cases by S. Sujatha.et.al, showed similar male preponderance, where 102 males and 90 females. In their study, highest incidence was in 3<sup>rd</sup> decade.<sup>4</sup> Aiffa Aiman.et.al, study of 104 cases showed female preponderance, 62 females and 44 males and they observed highest incidence in age group of 21-40yrs.<sup>2</sup> A study by Mohammad Rafique Zaki.et.al, showed male to female ratio was 2:1 & most cases were in the 3<sup>rd</sup> and 4<sup>th</sup> decade.<sup>1</sup>

In the present study, loin pain was the commonest symptom followed by urinary symptoms. This observation was similar to a study by Mohammad Rafique Zaki.et.al and Aiffa Aiman.et.al who reported loin pain as the most common clinical feature.<sup>1,2</sup>

Of 84 non-neoplastic lesions, 8 (9.52%) cases were granulomatous pyelonephritis. Of 8 cases, 5 cases were diagnosed as of tubercular etiology. Most of the cases occurred in 3<sup>rd</sup> decade with slight female preponderance. Biswajit Datta.et.al, reported 9 (17.3%) out of 52 non-neoplastic lesions<sup>5</sup> and 9 (5.35%) out of 168 cases were found in a study by Ibrahim Fathi Ghalayini.<sup>6</sup> In a developing country like India nephrectomies done for tubercular pyelonephritis are far higher than in the western countries.

There were 11 cases (13%) of hydronephrosis which were more common in paediatric age (1 month -10 yrs) in this study. Most of the cases were due to vesicoureteric reflux (7 cases), followed by pelvi-ureteric junction obstruction and ureteric stricture. In a study by S.Sujatha.et.al,

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of the 192 nephrectomy cases, hydronephrosis was seen in 77 cases and the commonest cause was pelvi-ureteric junction obstruction.<sup>4</sup>Prasanna.L.C, studied 30 cases of hydronephrosis which showed peak incidence in 3<sup>rd</sup> decade and ureteric calculus was the commonest cause.<sup>7</sup>

Worldwide incidence of Xanthogranulomatous pyelonephritis is 0.6 to 1%, and literature shows a female preponderance.<sup>8</sup>In our study both the cases were in males which is very unusual. And these two cases were associated with calculi. A study by Ibrahim Fathi Ghalayini, showed 13 cases of xanthogranulomatous pyelonephritis and the association with calculi was seen in 11 cases.<sup>6</sup>

Ectopic kidneys are usually asymptomatic and detected incidentally. We have reported one such case as of ectopic supernumerary kidney presenting as the content of hernial sac of the inguinal hernia.<sup>9</sup> Samaila I Shuaibu, reported a case of ectopic kidney in the right iliac fossa. Pathologic conditions can affect these kidneys included hydronephrosis, pyonephrosis, pyelonephritis, cysts, papillary cystadenoma and Wilms'tumour. These cases require long term follow up because of occurrence of complications and malignancy.<sup>10</sup> Our study had 2 cases of duplex kidney. Duplex is the most common congenital abnormality of the urinary tract with an incidence of 2% with a male preponderance. Azzawi M. HadiAljumaily, reported a case of pelvi ureteric junction obstruction in a duplex kidney.<sup>11</sup> In our study both the cases of duplex kidney had features of chronic pyelonephritis and hydroureters.

Simple cysts are detected on imaging studies. In the present study we encountered 2 cases of simple cysts, one in 1 month old child and another in a 48 year old male. Simple cysts are rare in younger individuals and incidence is low in females. A study by Ken Marumo.et.al, showed higher incidence in females.<sup>12</sup>

Our study had 1 case of Adult polycystic kidney. Grossly kidney was enlarged showed multiple cysts of varying sizes. Histology showed cyst lined by cuboidal epithelium and hyperplasia of tubular epithelium with papillary formations. Various studies showed higher number of cases of Adult polycystic kidney disease. I. A Mungadi. et. al and Mohammad Rafique Zaki. et. al, showed 8 out of 33 and 24 out of 189 cases respectively.<sup>13,1</sup>

The present study included 1 case of lacerated kidney due to abdominal trauma. Nephrectomy remains the standard treatment for severely damaged kidney. Aiffa Aiman. et.al, showed 4 cases of traumatic kidney out of 106 non-neoplastic cases.<sup>2</sup>

In this study we encountered a rare case of Leiomyosarcoma<sup>14</sup> and one case of Wilms' tumour in an adult male.<sup>15</sup>

**CONCLUSION:** The present study provides a fair insight into the morphological pattern of lesions in the nephrectomy specimens at our institution. In the recent years kidney lesions are being detected at an early stage and relatively in younger patients with the emergence of sophisticated laboratory investigations and imaging techniques. Hence there was marked increase in the number of nephrectomies in the second part of the study period. Non- Neoplastic lesions were 72.41% and chronic pyelonephritis was the commonest lesion. The commonest cause for nephrectomy in children was vesico-ureteric reflux. A wide histopathological spectrum of lesions comprising both neoplastic and non-neoplastic diseases was encountered in the nephrectomy

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specimens. Hence it is mandatory to study each specimen in detail along with clinical and radiological findings.

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