



School of Medicine

Department of Anatomic Pathology

A histopathological spectrum of lesions in nephrectomy specimens in Department of pathology in SPHMMC of four years experience

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List of abbreviations

CRCC	Clear Renal Cell Carcinoma
CPN	Chronic Pyelonephritis
IT	Information Technology
NFK	Non Functioning Kidney
RCC	Renal Cell Carcinoma
SPHMMC	St. Paul Hospital Millennium Medical College
WHO	World Health Organization

Summary

Background: Nephrectomy is a common surgical procedure done for various indications. Histopathological spectrum of diseases in nephrectomy specimens may show geographic variations with different urologic causes in different countries worldwide.

Objective: To study the spectrum of histopathological lesions in nephrectomy specimens received by pathology department in SPHMMC since 2014.

Methodology: Facility based descriptive cross sectional was carried out from January 2014 to March 2019. Descriptive analysis was used to describe socio-demographic and clinical profile of the study subjects.

Result: Non neoplastic lesions accounted for 121 (55.8%) cases out of 217 total cases and neoplastic accounted for 96 (44.2%) cases. Chronic pyelonephritis was the leading histopathologic diagnosis accounting for 93.4% (113 cases) among the non neoplastic lesions and Renal cell carcinoma was the leading diagnosis among the neoplastic lesions accounting for 86.6% (83 cases). Clear cell renal cell carcinoma constituted for 50.6% of renal cell carcinoma.

Conclusion: This facility based descriptive cross sectional study have found non neoplastic lesions to be the major cause leading to nephrectomy and the commonest of non neoplastic lesions to be chronic pyelonephritis. It has also found that the major malignant tumor to be Clear cell renal cell carcinoma, occurring in the sixth decade with male preponderance.

Keywords: Nephrectomy, Histopathologic morphology, SPHMMC

1. Introduction

1.1. Background

Kidneys are vital organs of the body with multiple functions. They are essential for not only excretory function but also to maintain water and salt metabolism along with acid base balance. In addition they maintain the blood pressure through renin-angiotensin mechanism and produce erythropoietin required for hematopoiesis (1).

The kidneys are by and large a very resilient organ. The renal parenchyma though subjected to repeated trauma/insults of the noxious environment, they are the last to respond. The kidney can be involved in a number of pathological conditions (2).

Kidneys could be affected both by neoplastic and non neoplastic disease entities. Conditions like acute and chronic infections, obstructive diseases, calculus diseases, renovascular diseases, benign tumors and malignant lesions are to mention a few. Some require nephrectomy for treatment (3).

Nephrectomy is the surgical procedure of removing kidneys. It has been a standard surgical procedure in practice performed for neoplastic and non neoplastic conditions of kidney with end stage disease. It can be simple, partial and radical types (4).

Nephrectomy is a common surgical procedure. Indications for nephrectomy are varied including irreversible damage by chronic infections, obstructive causes including strictures & calculus disease, vesicouretric reflex, congenital dysplasia, nephrosclerosis, cystic diseases, traumatic injury and various renal tumors; malignant or benign (3).

Nephrectomy procedure may show geographic variations with variable urological causes. Indications for nephrectomy may show geographic variations with different urologic causes in different countries worldwide (5).

1.2. Statement of the problem

The department of Anatomic pathology in SPHMMC has been receiving an increasing amount of nephrectomy specimens since its establishment. Despite the abundance of cases there is no well studied literature done by the department to help identify objectively the commonest disease.

Currently, we have a large enough data to conduct this study thoroughly and compare it with existing literatures in order to have a clear picture of the histopathologic pattern of diseases leading to nephrectomy.

1.3. Significance of the study

This study will be give us a clear picture on what the histopathologic spectrum of the diseases leading to nephrectomy.

The result from this study will help in developing strategies for intervention targeting the most common disease affecting kidneys.

2. Literature review

Renal diseases are important causes of morbidity worldwide. The indications of nephrectomy range from inflammatory lesions causing extensive parenchymal damage to benign and malignant tumors (6)

Nephrectomy is a standard surgical procedure in urological practice performed in end stage/nonfunctioning kidney or in suspected malignant neoplasm (5). Indications for nephrectomy are varied including irreversible damage by chronic infections, obstructive causes including strictures & calculus disease, vesicouretric reflex, congenital dysplasia, nephrosclerosis, cystic disease, dysplasia and also severe traumatic injury, non-corrective renal artery disease leading to renovascular hypertension (3).

According to SPHMMC's surgical protocol for nephrectomy, elective nephrectomy is done in malignant diseases of the kidney, nonfunctioning kidney diagnosed on intravenous urogram (IVU), uncontrolled hematuria after operation for kidney stone, pyonephrosis, tumours and undiagnosed large renal mass.

Most common age groups subjected to nephrectomy is variable in different studies. Maximum number of patients are in the forth decade in studies done in India (23,24). However, in another study done common age group affected is 2nd to 3rd decade (25)

Male preponderance is seen among patients subjected to nephrectomies in various studies done in different parts of India (23,25,26,27). In a study done in other parts of India showed an equal male and female preponderance (24).

The most common clinical presentation among patients with nephrectomy is flank pain in studies done in India (23).

The most common indication for nephrectomy was non neoplastic conditions like obstructive nephropathy, hydronephrosis and chronic pyelonephritis according to studies done in Iran, Jordan and India (7,8,9). In a report of 423 consecutive nephrectomies performed in a general hospital of Sudan 70% cases were performed for benign conditions (10).

In addition nephrectomies performed at al Bashir Hospital, Saudi, 77.6% cases of nephrectomy were done for benign conditions (11). Similarly, in a series of 135 nephrectomies reported from Pakistan, 76.6% cases were due to benign causes (12).

However neoplastic diseases were found to be commonest according to another study done in India (13) where similar findings were also seen in other studies done.

Non neoplastic renal diseases like obstructive nephropathy, hydronephrosis and chronic pyelonephritis leading to end stage renal disease are the most common indications for nephrectomy in both adults and children (5).

Chronic pyelonephritis and its variants still continue to be the leading cause of nephrectomies despite the advent of newer and more effective antibiotics. In studies done in different facilities, chronic pyelonephritis followed by hydronephrosis and tuberculosis were the commonest non neoplastic indications for nephrectomies (6, 10, 16).

Other non neoplastic kidney diseases leading to nephrectomy are hydronephrosis, tuberculous pyelonephritis, xanthogranulomatous pyelonephritis, interstitial nephritis and pyelolithiasis (14). In one study hydronephrosis followed by xanthogranulomatous pyelonephritis and tuberculosis were the prevalent findings among the non neoplastic conditions (17).

In other study done, nephrolithiasis followed by trauma, non functioning kidney due to medical causes and congenital developmental anomalies was identified (2).

Renal tumors both benign and malignant are among the most common indications for nephrectomy. Nephrectomy is recommended for a tumor measuring more than 3 cm or for those of smaller sizes that are associated with persistent hematuria or rapid growth, because on nephrectomy many of the latter tumors turn out to be unequivocal RCCs (20,22).

In many cases, in spite of sophisticated imaging techniques, preoperative differentiation between cysts with infection or bleeding and tumors is not possible. The complex and variegated renal changes may preclude assessment of tumor size, a main determinant of benign versus malignant. Empirical nephrectomy is usually performed for these cases (20,22).

According to WHO 2017, tumors of the renal were classified into nine each having their own subtyping (14).

Renal cell tumors, being one of the WHO classes of tumors of renal, represents over 90% of all malignancies of the kidneys that occur in adults in both sexes. It is almost exclusively a cancer of adults, comprising only 2% of all pediatric renal tumors, with male predominance (14).

In a study done in India renal cell tumor was the most common tumor identified among the malignant tumors in nephrectomy specimens. Similar findings were also found in studies done in Jordan and Iran (7,8).

Among the malignant renal cell tumors, clear cell renal cell carcinoma followed by papillary renal cell carcinoma and chromophobe renal cell carcinoma are the most common tumors encountered (15) Studies done in India have identified for clear renal cell carcinoma to be the most common malignant tumor in nephrectomy specimens (8)

The most common benign renal cell tumor is the papillary adenoma of the kidney. Since majority are asymptomatic and incidental findings in autopsy studies, the true prevalence and incidence is not known (14,15)

In pediatrics age group primary renal tumors are uncommon. However, they constitute the fifth most common group of pediatric cancers (15). Wilms tumor is the most common renal tumor encountered in this group. Similar findings were reported among nephrectomy specimens in studies done in India and Jordan (7,8).

In most of the reported series from developing countries, benign diseases of the kidney were the leading causes of nephrectomy (18). The incidence of nephrectomies for benign conditions such as chronic pyelonephritis is decreasing and nephrectomies for malignant lesions are increasing in the developed countries (19).

3. Objectives

3.1. General objectives

- ✓ To observe the spectrum of histopathological lesions in nephrectomy specimens received by pathology department in SPHMMC since 2014.

3.2 Specific objectives

- ✓ To study the age and gender distribution among patients subjected to nephrectomy.
- ✓ To study the histopathological features of lesions in the nephrectomy specimen.
- ✓ To analyze the histopathology of non neoplastic lesions of kidney according to age and gender.
- ✓ To analyze the histopathology of neoplastic lesions of kidney according to age, gender and site.
- ✓ To analyze the trend of diseases in nephrectomy specimens over the 5 year period.

4. Methodology

4.1. Study area

The study was conducted in SPHMMC Addis Ababa Ethiopia. SPHMMC is a specialized teaching university hospital that provides medical specialty services to patients who are referred from all over the country. The inpatient capacity is 700 beds and sees an average of 1200 emergency and outpatient clients daily. It is a fast growing hospital having more than 20 departments.

The pathology department is one of the many practicing departments in SPHMMC, having a total of 10 staffs.

4.2. Study design and period

Facility based descriptive cross sectional was carried out from January 2014 to March 2019.

4.3. Population

4.3.1. Source population

All surgical samples received in the pathology department during the study period.

4.3.2. Study population

All nephrectomy specimens received in the pathology department during the study period.

4.4. Inclusion and exclusion criteria

4.4.1. Inclusion criteria

All nephrectomy specimens received in the pathology department were included.

4.4.2. Exclusion criteria

All cases that are not nephrectomy were excluded.

All cases that have incomplete data were excluded.

4.5. Sample size determination

All nephrectomy specimens received in the pathology department during the study period were included.

4.6. Data collection

4.6.1. Data collection instruments

Demographic and clinical information of each case along with the final pathology report was collected from the archives of the department of pathology in SPHMMC during the study period.

4.6.2. Data collection procedures

Data was collected by the principal investigator who is a final year pathology resident with the aid of the IT expert in the department.

4.7. Study variables

4.7.1. Dependent variables

Histopathologic diagnosis

4.7.2. Independent variables

Age of the patient

Sex of the patient

Clinical presentation of the patient

Clinical diagnosis of the patient

4.8. Data processing and analysis

The collected data was entered into SPSS version 20 computer software for analysis. Data was checked for outliers and corrected accordingly. Descriptive analysis was used to describe socio-demographic and clinical profile of the study subjects.

4.9. Data quality management

The principal investigator was responsible for collecting data for which the quality was checked by using a checklist at the end of each data collection dates and assure its completeness.

4.10. Ethical considerations

Permission to conduct the study was obtained from the research ethical committee of SPHMMC.

4.11. Dissemination of results

Result will be submitted to SPHMMC pathology department and other concerned bodies and publication on peer reviewed journals.

5. Result

5.1. Distribution of nephrectomy specimens according to age, gender and disease

A total of 217 nephrectomy cases are studied and analyzed during a period of 5yrs (2007 to 2011EC). Among the 217 cases , 117 (53.1%) are males and 100 (46.1%) are females. The male to female ratio is 1.2:1. (Table 1)

The peak age of incidence is from 31-40 yrs. The youngest patient is 2yrs and the oldest is 83 yrs of age. (Table 1)

Majority of the nephrectomy specimens are due to non neoplastic conditions. Non neoplastic conditions accounting for 121 of cases (55.8%) and neoplastic ones for 96 cases (44.2%). (Table 1)

Table 1: Distribution of nephrectomy specimens according to age, sex and disease

Variables	Number	Percent(%)
Age (In completed years)		
0-20	13	5.9
21-30	37	18.3
31-40	50	24.8
41-50	27	13.4
51-60	48	23.8
61-70	19	9.4
71-80	6	3
81-90	3	1.5
Sex		
Male	117	53.1
Female	100	46.1
Disease		
Non neoplastic	121	55.8
Neoplastic	96	44.2

5.2. Histopathologic spectrum of non neoplastic lesions

Among the total 217 nephrectomy cases 121 (55.8%) are due to non neoplastic conditions. Higher incidence of non neoplastic conditions are observed in the third and forth decades of life with slight male preponderance (Male:female ratio 1.1:1). (Figure 1)

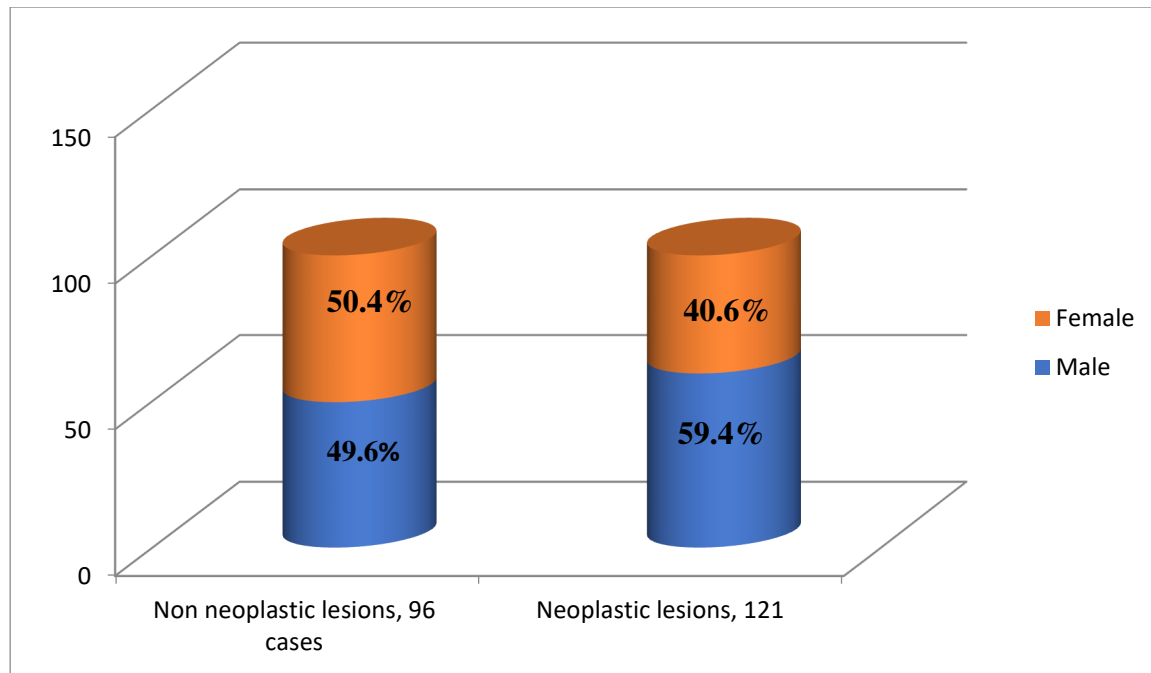


Figure 1: Cross relation between disease conditions and gender

The non neoplastic conditions identified in our current study include chronic pyelonephritis, obstructive uropathy and cystic lesions. (Table 2)

Table 2: Histopathologic spectrum of non neoplastic lesions in nephrectomy specimens

<i>Histopathologic diagnosis</i>	<i>Number</i>	<i>Percent(%)</i>
Chronic pyelonephritis	113	93.4
Obstructive uropathy	5	4.1
Chronic glomerulonephritis	1	0.8
Cystic lesion	2	1.7

Chronic pyelonephritis accounts for the majority of the non neoplastic lesions, 113 (93.5%). (Table 2) It affects all age groups however the peak incidence of age is 31-40yrs (32, 28.1%) with equal male and female preponderance (Male to female ratio is 1:1). (Figure 2)

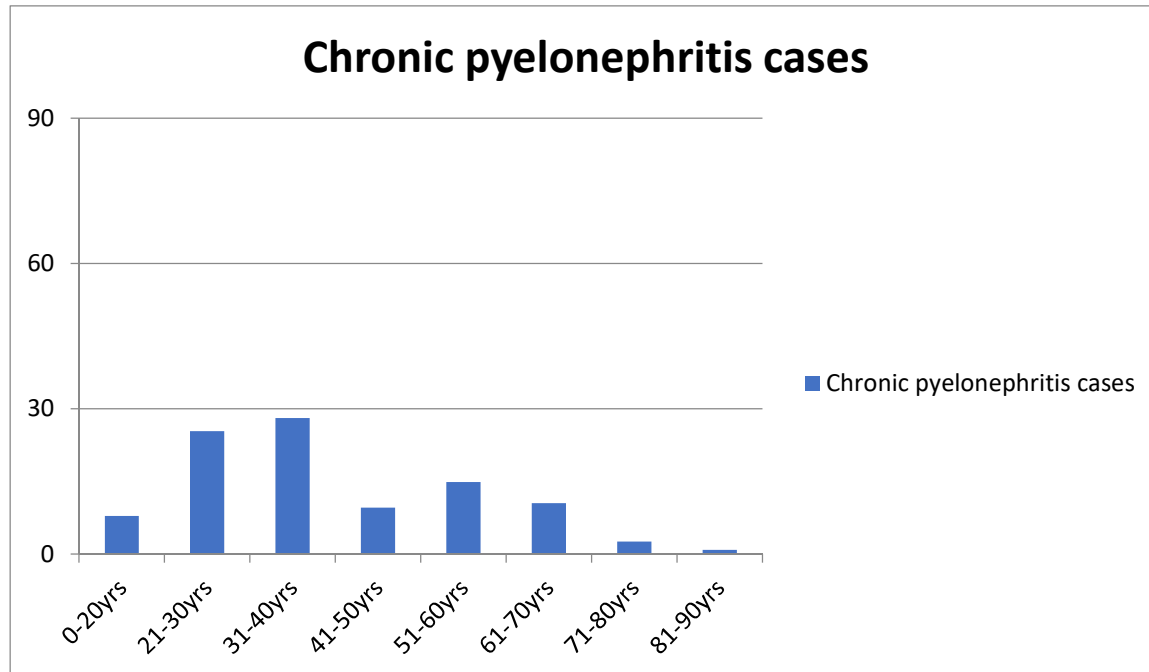


Figure 2: Distribution of chronic pyelonephritis cases according to age

Chronic pyelonephritis is found to be associated with other histologic factors like hydronephrosis, nephrolithiasis, pyonephrosis, granuloma and xanthogranulomatous lesions. The most common associated feature is hydronephrosis accounting for 64.6% (73) of the cases followed by nephrolithiasis (12, 10.6%). (Figure 3)

Out of the total cases of CPN identified, only 82.3% (93) of them are found with complete data to analyze the following variables.

In gross findings in pyelonephritis, most cases are found to have dilated pelvicalyceal system with 65.6%, and loss of cortico-medullary junction with 64.5%. 12.9% are found to have stones .(Table 3)

In microscopic findings, 93.5% of cases show tubular atrophy, tubular dilation and thyroidization with moderate to dense mononuclear inflammatory cell infiltrates. 78.4% show interstitial fibrosis and 20.4% show glomerular sclerosis. (Table 4)

Table 3: Gross findings of CPN in nephrectomy specimen

Gross findings	Number	Percent
Dilated pelvi-calyceal system	61	65.6
Loss of cortico-medullary junction	60	64.5
Renal stones	12	12.9
Enlarged kidney	52	55.9

Table 4: Microscopic findings of CPN in nephrectomy specimen

Microscopic findings	Number	Percent
Tubular changes	87	93.5
Glomerular changes	19	20.4
Vascular changes	23	24.7
Interstitial fibrosis	73	78.4
Mononuclear inflammatory cells	93	100

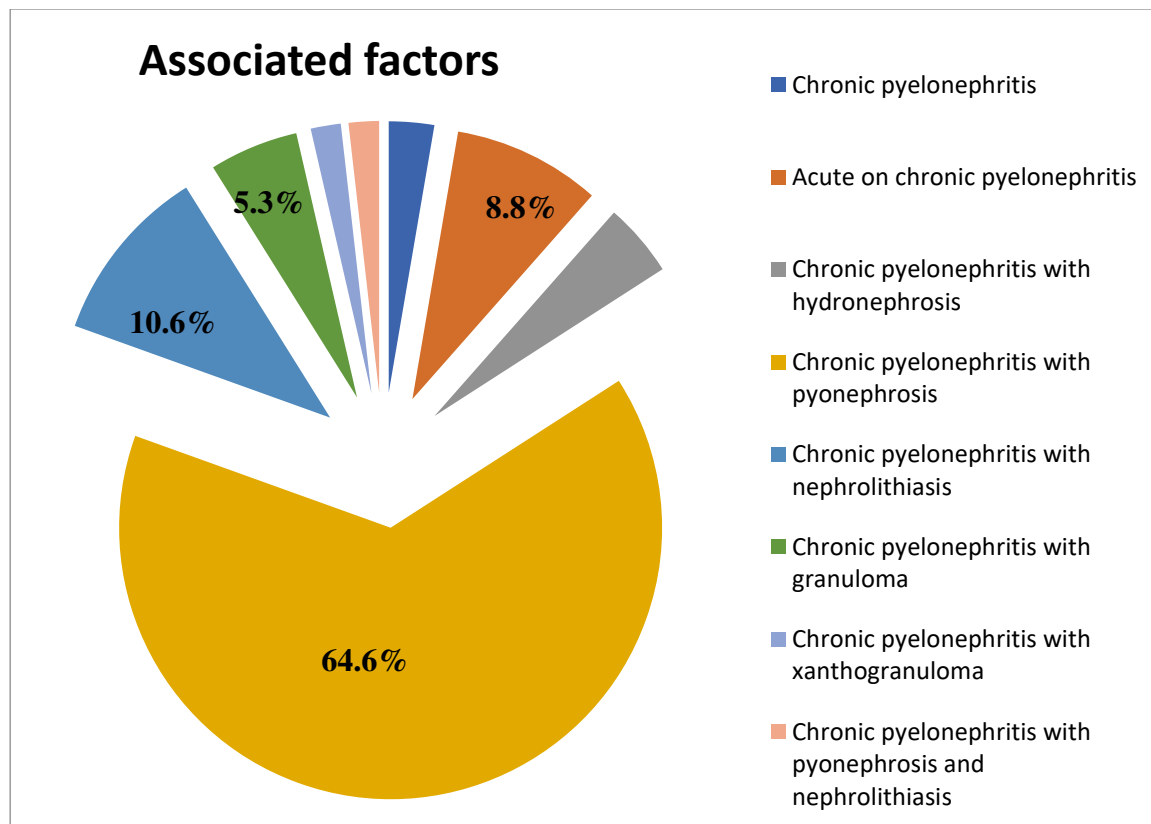


Figure 3: Frequency of associated features of Chronic pyelonephritis

5.3. Histopathologic spectrum of neoplastic lesions in nephrectomy specimens

Among the total 217 nephrectomy cases, 96(44.2%) are due to neoplastic conditions. Majority of cases are observed in the sixth decade of life with male preponderance (Male : Female is 1.46:1). (Figure 1)

According to WHO's classification of renal tumors, neoplastic lesions are classified into five classes, and renal cell tumors accounts for maximum number of cases 83 (86.6%), followed by mesenchymal tumors 4(4.1%) and nephroblastic tumors 3 (3.1%). (Table 5)

Table 5: Frequency of neoplastic lesions in nephrectomy specimens

	Number	Percent (%)
Renal cell tumors	83	86.6
Mesenchymal tumor	4	4.1
Mixed epithelial and stromal tumor	3	3.1
Nephroblastic tumor	3	3.1
Squamous cell carcinoma	1	1
Transitional cell carcinoma	2	2.1

Malignant tumors account for majority of 88.5% (85 cases) of neoplastic lesions and benign lesions account for 11.5% (11 cases). (Figure 4)

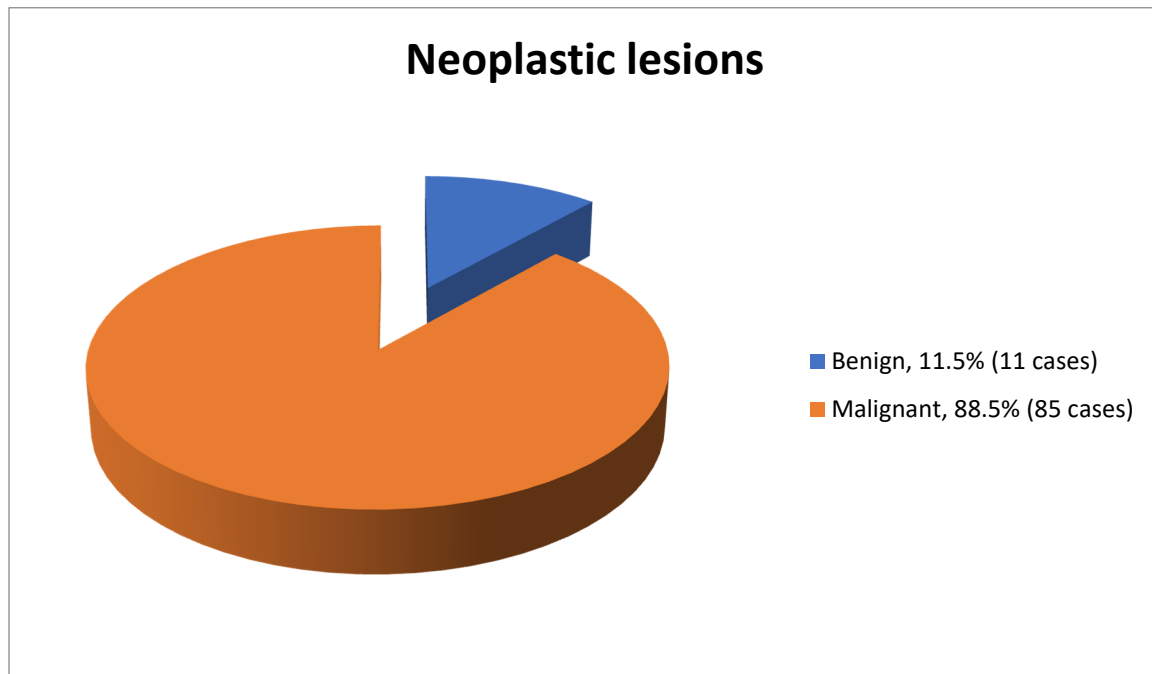


Figure 4: Frequency of benign versus malignant lesions

Clear cell renal cell carcinoma accounts for majority of 49.4% (42 cases) of the malignant neoplastic lesions identified. The second and third malignant cases are papillary renal cell carcinoma (23.5%, 20 cases) and chromophobe renal cell carcinoma (17.6%, 15 cases) respectively. (Figure 5)

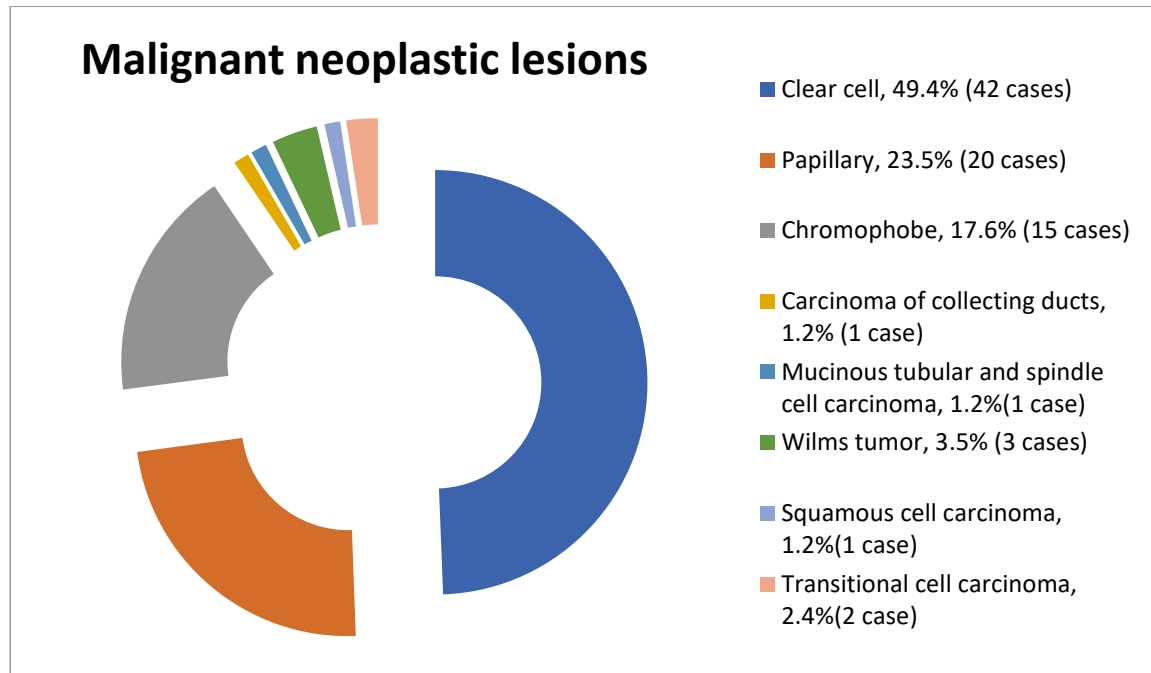


Figure 5: Histopathologic spectrum of malignant neoplastic lesions

Clear cell renal cell carcinoma's peak age of incidence is the sixth decade of life accounting for 17 cases (40.5%) with male preponderance (Male to female ratio is 2.2:1).

Out of 42 cases of clear cell renal cell carcinoma only 35 cases have been found with complete data to analyze the following variables.

Table 6: T stage of clear cell renal cell carcinoma

Pathologic stage (T)	Number	Percent
T1	11	31.4
T2	15	42.9
T3	8	22.8
T4	1	2.9

Most (15, 42.9%) of clear cell renal cell carcinoma has been stage as T2 followed by T1 and majority with Furhman grade 2. Two cases are identified to have sarcomatoid and rhabdoid changes.(Table 4)

Table 7: Furhman nuclear grade of clear cell carcinoma

Fuhrman nuclear grade	Number	Percent
Grade 1	13	37.1
Grade 2	14	40
Grade 3	8	22.9
Grade 4	-	-

Oncocytoma is the most common benign tumor identified accounting for 4 cases of neoplastic lesions followed by Angiolipoma (3 cases) and cystic nephroma (3 cases). (Figure 6)

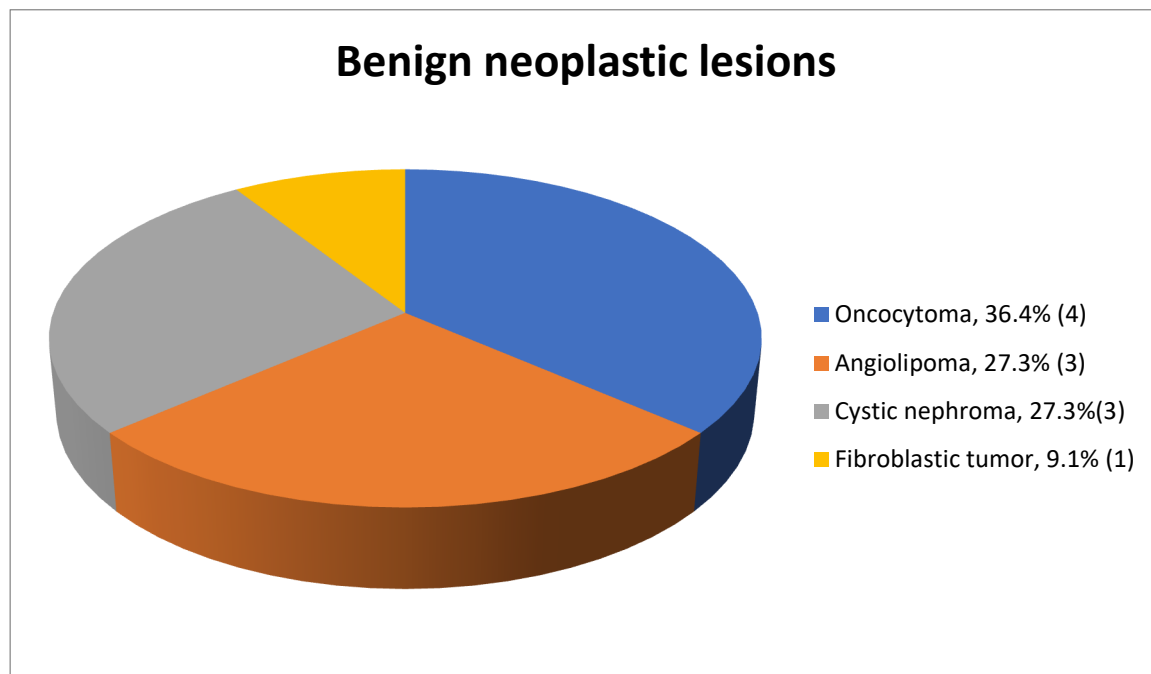


Figure 6: Histopathologic spectrum of benign neoplastic lesions

Grossly all of the cases of oncocytoma show a well delineated lobulated solid mass with a homogenous tan brown cut surface. Only half of the cases have a central stellate scar. Microscopically all cases have similar histology with diffuse sheets, cellular nests & dilated tubular structures of cells with uniform abundant granular eosinophilic cytoplasm, distinct cell borders, central located round nuclei, coarse clumped chromatin pattern, and conspicuous nucleoli.

5.4. Trend of renal lesions over the four years

Nephrectomy specimens is progressively increasing over the four years. Non neoplastic to neoplastic ratio is progressively reversing over the years. (Figure 5)

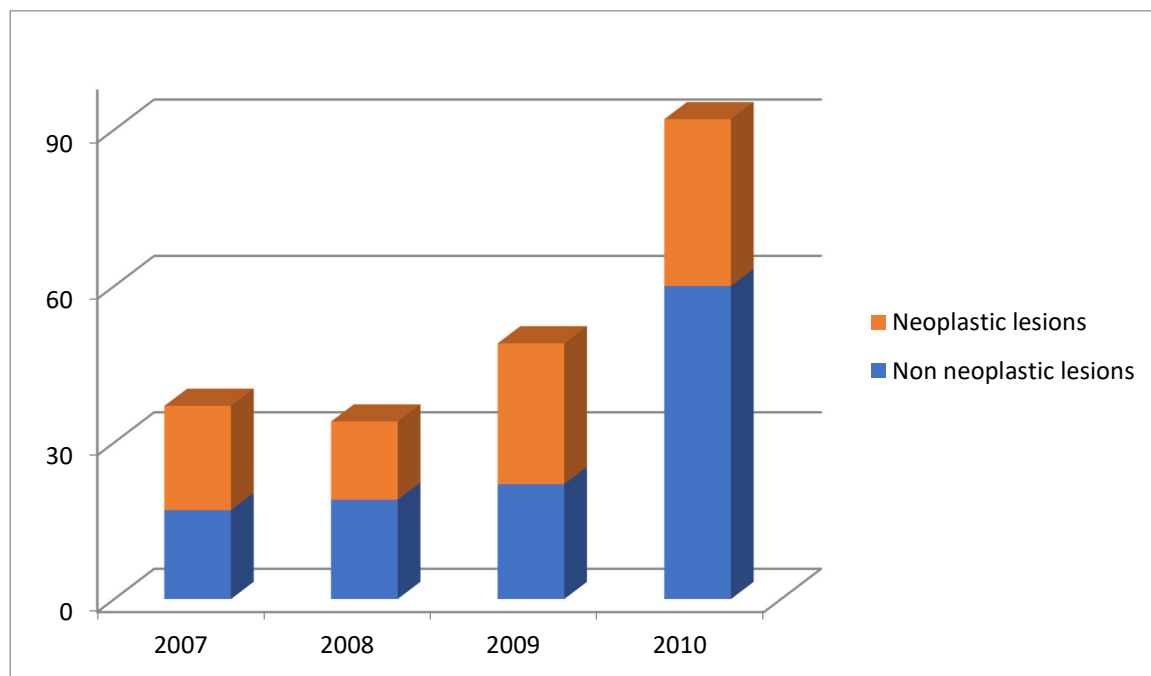


Figure 7: Trend of diseases in nephrectomy specimens over 4 years

Non neoplastic lesion proportion is progressively increasing over the 4 yrs period.

6. Discussion

In this facility based descriptive cross sectional study 217 nephrectomy specimens were analyzed. In this study highest number of cases included was in the age group of fourth decade followed by sixth decade, which was similar to findings in studies done in India (22), where the peak age of incidence was fourth decade. Male to female ratio of all the nephrectomies was 1.2:1, which was comparable with studies done in different facilities in India (22,26) but male predominance was observed in other studies with male to female ratio of 3:1 and in some with equal predominance (11, 23).

Non neoplastic lesions accounted for 55.8% of cases in nephrectomy specimens which is in slight concordance with some studies done in which non neoplastic lesions accounted for 70.5% and 62.8% (24, 25).

Chronic pyelonephritis with hydronephrosis followed with nephrolithiasis accounted for the majority of non neoplastic lesions in this study, which was in concordance with few studies (26,27,28). However in contrast with one study done in India (11) where the most common of non neoplastic lesions identified was due to renal stones.

Majority of chronic pyelonephritis case showed tubular atrophy, thyroidization and interstitial fibrosis which is in agreement done in some studies. (24)

In the present study, a total of 96 (44.8%) neoplastic lesions were observed; of these, a vast majority comprised renal cell carcinomas. This was similar to the findings found in studies done in 12 who observed that the majority of malignant neoplasms (97%) of the kidney were renal cell carcinomas. In our study, microscopically, the clear cell type of renal cell carcinomas was the predominant type of tumor observed. This was followed by papillary type and chromophobe which is in discordance with the findings in few studies. (24,25)

Clear cell renal cell carcinoma occurred in the sixth decade of life with male preponderance in our study which is in agreement with the various studies done by WHO.

Fuhrman nuclear grading revealed 14 (40%) cases showing Grade 2 nuclear features and 13 (37.1%) cases depicting Grade 1 nuclear features. Thus, majority of cases (76%) showed Grades 1 and 2 nuclear features. This is in disagreement when compared with studies done in India (25).

The most common benign tumor identified in our study is oncocytoma unlikely the studies done in different parts of India, where papillary adenoma is the commonest benign tumor identified (23, 25, 26).

Over the four years period, the incidence of non neoplastic lesions in nephrectomy specimens has exponentially increased which is in concordance with other studies.(17,18) Like many other developing countries the majority of cases of nephrectomy are due to preventable and early treatable non neoplastic conditions.

7. Conclusion and recommendation

7.1. Conclusion

This facility based descriptive cross sectional study have found non neoplastic lesions to be the major cause leading to nephrectomy and the commonest of non neoplastic lesions to be chronic pyelonephritis.

It has also found that the major malignant tumor to be Clear cell renal cell carcinoma, occurring in the sixth decade with male preponderance.

7.2. Recommendation

With regards to the findings found in this study the recommendations are:

To Ministry of Health

- To make policy and ensure its enforcement in preventing rather than treating renal diseases
- To participate and help associations in creating awareness of morbidity of renal diseases in our society
- To fund researches focusing on renal diseases

To kidney associations

- To engage more with the patients and give different education for health professional in relation to renal diseases.
- To work on awareness creation for the society using different media.
- To work in coordination with Ministry of health in making policies and enforcing them.

To public media

- To engage themselves with more health education programs.
- To create awareness and inform the society about the burden of renal diseases.
- To encourage the society in seeking medical help in cases of signs and symptoms of renal diseases.
- To teach and inform the society about the preventive and treatable nature of renal diseases.

To health care facilities

- To make the clinic setting in terms of infrastructure accessible and flexible in screening and treating patients with renal diseases.
- To have a separate trained staff and working spaces for the follow up clinics.
- To work together with kidney associations and government offices to have regular sessions of education for patients with renal diseases.

To general health professionals

- To update and train themselves continuously about renal diseases, risk factors, screening protocols, preventive techniques and treatment protocols.
- To identify risk factors of renal diseases during a visit of a patient.
- To integrate screening for renal diseases in each visits.

To General surgeons

- To record all necessary clinical information about a patient subjected to nephrectomy.
- To communicate and involve other health professionals in decision making.
- To participate in different meetings and forums regarding renal diseases
- To participate and engage in training other health professionals
- To participate in giving health education regarding renal diseases

To surgical pathologists

- To use standard format during grossing a nephrectomy specimen, and reporting cases.
- To use updated grading and staging protocols regarding neoplastic diseases
- To engage and participate in patients management and treatment

To researchers

- To do regular researches regarding the magnitude of renal diseases and associated risk factors, to update and influence the policy regarding renal disease patient management.

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Annexes

Questionnaire

S.no	Questions	Answers	Code
101	Biopsy no.		
102	Medical record no.		
103	Age		
104	Sex		
105	Clinical presentation		
106	Clinical diagnosis/radiologic findings		
107	Site of lesion		
108	Type of nephrectomy procedure		
109	Gross appearance		
110	Histopathologic diagnosis		