Magna Scientia Advanced Research and Reviews

eISSN: 2582-9394

Cross Ref DOI: 10.30574/msarr

Journal homepage: https://magnascientiapub.com/journals/msarr/

(RESEARCH ARTICLE)

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Histological pattern of nephrectomy specimens: A fifteen-year review

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Magna Scientia Advanced Research and Reviews, 2023, 08(01), 019–029

Publication history: Received on 16 March 2023; revised on 28 April 2023; accepted on 01 May 2023

Article DOI: https://doi.org/10.30574/msarr.2023.8.1.0056

Abstract

Background: Nephrectomy is the surgical removal of all or part of a diseased kidney in a living person. Pathological assessment of the tissue specimen is required in most cases for eventual diagnosis and disease prognostication.

Objective: To demonstrate the pathological patterns of nephrectomy specimens in Nnewi, South East Nigeria.

Methods: The data of all the nephrectomy specimens submitted to the Department of Histopathology of the Nnamdi Azikiwe University Teaching Hospital, Nnewi, as well as Triple Green Diagnostic Clinics Ltd, Nnewi, from 2007 to 2021 were retrospectively reviewed. Their pathological features were analyzed.

Results: Of the 153 nephrectomy specimens, 141 that had complete data were used for the study. Those that had neoplastic lesions were 84(59.6%), while 57(40.4%) were non-neoplastic. Of the neoplastic lesions, 79 (94%) were malignant and renal cell carcinoma (RCC) accounted for 60%, with a mean age of 48.8±18.1 years and median age 52.5 years. RCC occurred commonly in the sixth decade of life (26%) with male preponderance (56%) and predominantly involving the left kidney (64%). Clear cell variant of renal cell carcinoma was the most common (52%), followed by papillary variant (34%). Nephroblastoma was the most common malignancy in the first decade with a modal age of 2years. Chronic pyelonephritis was the most common non-neoplastic lesions.

Conclusion: Nephrectomy is done for a wide range of renal pathology, with more done for neoplastic conditions than non-neoplastic ones.

Keywords: Nephrectomy; Specimen; Renal Cell Carcinoma; Chronic Pyelonephritis

1. Introduction

The kidneys are paired retroperitoneal organs that play key roles in fluid and electrolyte balance, acid-base balance as well as excretion of waste from the body. Its major functions are carried out through the physiological processes of glomerular filtration, selective reabsorption and secretion.[1] Like any other organ, it can be afflicted by a wide range

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of pathological processes, which can be congenital, traumatic, inflammatory or neoplastic, necessitating the removal of the kidney.[2] The removal of part or all of a kidney is compatible with life because the contralateral kidney, if healthy, can satisfactorily compensate for the function of the diseased kidney.

Nephrectomy refers to the surgical removal of the kidney and this can be done by open, laparoscopic or robotic-assisted approaches.[3] It is indicated in irreversible kidney damage or in renal cancers. Nephrectomy can be simple, partial or radical. Simple nephrectomy involves the removal of the poorly functioning kidney without the Gerota's fascia and is indicated in the settings of renal trauma; infections like chronic pyelonephritis; in cases of obstructive nephropathy like pelvi-ureteric junction obstruction or renal damage from a pelvic stone as well as in other benign conditions.[4] Partial nephrectomy is the removal of a diseased part of a kidney, often with a rim of normal tissue. It is indicated in tumour in a solitary kidney, poor contralateral renal function, bilateral renal tumours, poor overall renal function, tumours involving horse-shoe kidney or where contralateral kidney is at great risk of damage by comorbidities like diabetes mellitus or hypertension.[5,6] In recent times, there is growing interest in partial nephrectomy and other nephron-sparing modalities to treat localized malignant lesion.[7] Radical nephrectomy is indicated in localized renal tumour, where the contralateral kidney is normal and involves removal of the kidney with the covering Gerota's fascia, as well as the adrenal gland and regional lymph nodes enblock.[8,9] In our environment, where patients often present late and where access to modern imaging modalities that allow early detection of renal tumours is limited and may not be easily affordable, radical nephrectomy is almost always the modality for the management of malignant renal conditions, rather than any form of renal conserving surgery.

Recent advances in imaging technology have resulted in marked improvement in the characterization of renal masses. However, differentiating between benign and malignant renal masses and the precise diagnosis of renal tumour types on imaging remains a challenge.[10] For accurate diagnosis, histopathology evaluation of renal tumour is necessary. Percutaneous renal mass biopsy (PRMB) is a safe means of obtaining renal tissue for the histological diagnosis of renal masses, with a diagnostic accuracy in differentiating between benign and malignant specimens being in the range of 76% to 92%.[11,12] However, with respect to tumour grading, tissue obtained by PRMB is less accurate than nephrectomy specimens, as up to 20% of low-grade tumours on PRMB have been reported to be upgraded to high-grade tumours after nephrectomy.[12-14] Despite the benefits of PRMB in diagnosis of renal masses and in potentially reducing unnecessary nephrectomies, many urologists still underutilize or even fail to use it and this has been projected to contribute to about 6000 unnecessary nephrectomies annually worldwide.[15] As such, nephrectomy still serves as the ultimate therapeutic and diagnostic option for most renal masses.

Histopathological examination of nephrectomy specimens thus affords opportunity for comprehensive and definitive diagnosis of renal lesions.[16] Pattern of histological diagnosis obtained from nephrectomy specimens have been demonstrated to show geographic variations worldwide.[17] This study seeks to determine the histological patterns of nephrectomy specimens in our environment and to compare with what obtains in other geographical regions.

2. Material and methods

This is a retrospective study of nephrectomy specimens submitted to the Department of Histopathology of the Nnamdi Azikiwe University Teaching Hospital, Nnewi and Triple Green Diagnostic Clinics Ltd, Nnewi between January 2007 and December 2021. Currently, these are the two facilities in Nnewi that offer specialist anatomic pathology services.

Routinely, nephrectomy specimens are received in the pathology laboratory fixed in 10% buffered formalin. The formalin-fixed tissues are examined macroscopically by the pathologist and representative samples taken into tissue cassettes for tissue processing. The submitted samples are next dehydrated by passing them through increasing concentration (70% to 100%) of alcohol and the dehydrated samples cleared of remaining water molecules by passing them through xylene (a clearing agent). The tissues are thereafter infiltrated and embedded in paraffin wax to form formalin-fixed paraffin embedded (FFPE) tissue blocks. From these FFPE tissue blocks, thin sections are made using a microtome set at 4-5microns. The paraffin tissue ribbons are floated in a warm water bath and picked unto a plain glass slide. The glass slide with the tissue ribbon are placed in a warm oven for about 15minutes to allow the tissue section adhere to the slide (temperature set at 2^0C less than the melting point of the paraffin wax). The slides with the tissues are then subjected to routine Haematoxylin and Eosin (H&E) staining protocols.

The tissue sections on the slides were de-paraffinised by passing it through xylene and then rehydrated in decreasing alcohol concentrations (100% to 70%). The slides are then treated with the basic dye (Haematoxylin) that stains the acidic component (nuclei) of the cell, and then passed through the acidic dye (Eosin), which stains the basic component (cytoplasm) of the cell.

The stained tissue sections on the slides are dehydrated by passing through increasing concentrations (70% to 100%) of alcohol, and then cleared using xylene. A resinous substance (Epoch resin) is placed on the slide sections and a thin glass coverslip placed over the sections. This is allowed to dry before viewing under the microscope. The produced H&E stained slides were viewed using a diagnostic compound binocular microscope (Carl Zeiss Axioscope 40). The features observed were then reported by the pathologists.

The gross and microscopic features of all the nephrectomy specimens thus examined were obtained from the pathology reports.

The data analysis was done using the IBM, Chicago Statistical Package for Social Sciences (SPSS) software version 20.0 and the result presented with tables and charts.

3. Results

A total of 40,387 specimens were received at the two facilities during the period under review. Of these, 153 were nephrectomy specimens. Following exclusions due to incomplete biodata, 141 were used for the study. Some of the pathologic (macroscopic and microscopic) images of the lesions observed were as shown in Figures 1a-e.

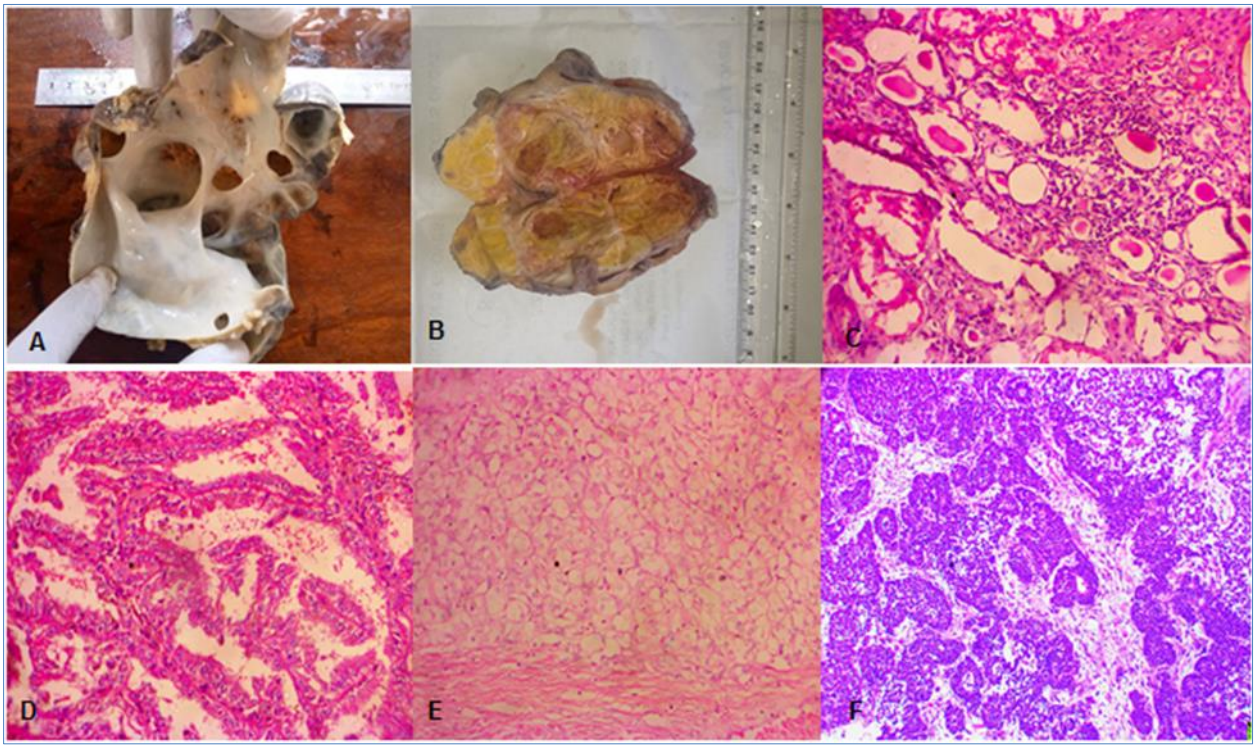

Figure 1 A is a gross picture of hydronephrosis, showing thinned parenchyma and dilated pelvicalyceal area. B is a cut section of nephrectomy specimen with a circumscribed nodular tumour. C is a photomicrograph of chronic pyelonephritis showing interstitial lymphocytic inflammation, fibrosis, dilated tubules with eosinophilic materials (H&E x100). D is a photomicrograph of papillary renal cell carcinoma (H&E x100). E is a photomicrograph of clear cell renal cell carcinoma (H&E x100). F is a photomicrograph of Nephroblastoma, showing predominantly blastema element and the stromal component (H&E x50)

The neoplastic lesions accounted for 84 (59.6%) of the nephrectomy specimens, while 57(40.4%) were non-neoplastic. Of the 57 non-neoplastic cases, chronic pyelonephritis occurring independently or with other pathologies, accounted for more than half of the diagnoses (58.7%). Six cases, accounting for 10.5% of the nephrectomy specimens had nephrolithiasis with non- functioning hydronephrotic kidney (Table 1).

Table 1 Distribution of non-neoplastic renal lesions

Diagnosis	Frequency	Percent
Chronic pyelonephritis	27	47.7
Simple renal cyst	7	12.3
Hydronephrosis	7	11.9
Nephrolithiasis with Hydronephrosis	6	10.5
Ureteric obstruction with Chronic pyelonephritis	4	7
Hydronephrosis with Chronic pyelonephritis	2	3.4
Polycystic kidney disease	1	1.8
Pyonephrosis	1	1.8
Reflux nephropathy with Chronic pyelonephritis	1	1.8
Chronic rejection	1	1.8
Total	57	100

Seventy-nine of the 84 specimens with neoplastic conditions were malignant while 5 were benign. Most of the neoplastic (53.6%) and malignant (54.4%) lesions occurred in the males as shown on Figure 1.

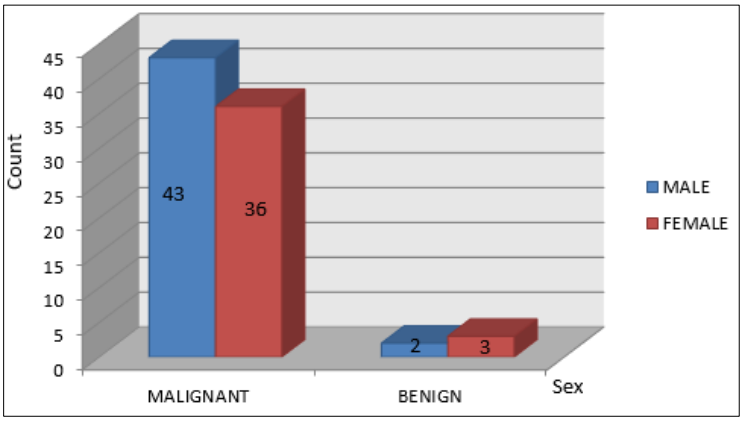

Figure 2 Distribution of the neoplastic lesions

Table 2 Pattern of distribution of neoplastic renal lesions

Diagnosis	Right	Left	Not Indicated	Frequency	Percent
Renal cell carcinoma	16	32	2	50	59.5
Nephroblastoma	10	8	3	21	25.0
Squamous Cell Carcinoma	2	1	1	4	4.8
Embryonal Rhabdomyosarcoma	1	1	0	2	2.4
Oncocytoma	1	0	1	2	2.4
Mesoblastic nephroma	0	1	0	1	1.2
Fibromatosis	0	1	0	1	1.2
Mucinous adenocarcinoma	1	0	0	1	1.2
Rhabdoid tumour	0	1	0	1	1.2
Transitional cell carcinoma	0	1	0	1	1.2
Total	31	46	7	84	100

From Table 2, renal cell carcinoma accounted for 59.5% and 63.3% of the neoplastic and malignant diagnoses respectively, with left-side preponderance (64%). Nephroblastoma accounted for 25% of the neoplastic renal specimens, occurred mostly in the 1st decade of life with a modal age of 2 years. Generally, the neoplastic lesions occurred more on the left side (54.8%) than the right (36.9%), while for 7 (8.3%), the side of the specimen was not specified in the histology request form.

Clear cell variant was the most frequent of the renal cell carcinoma variants, accounting for 52% of the cases, followed by the papillary cell variant, 34%. The medullary and the sarcomatoid variants were the least in occurrence, each accounting for 2% of the renal cell carcinoma variants (Table 3).

Table 3 Pattern of distribution of renal cell carcinoma variants

RCC variants	Frequency	Percent
Clear cell	26	52
Papillary	17	34
Oncocytic	3	6
Chromophobe	2	4
Medullary	1	2
Sarcomatoid	1	2
Total	50	100

RCC= Renal cell carcinoma

Table 4 shows that RCC occurred commonly in the sixth decade of life (26%) with male preponderance (56%). The mean and median ages of RCC occurrence were 48.8±18.1 years and 52.5 years respectively. Nephroblastoma was the most common paediatric renal malignancy, occurring largely in the first decade, with a modal age of 2 years. Of the fifty cases of RCC, four (8.0%) occurred in the first 2 decades of life; one of which (papillary variant) was observed in the first decade of life in a 5-year old male and another in a 13year old female with ipsilateral duplex ureter.

Table 4 Distribution of neoplastic renal lesions with their sex and age groups

Pathologic diagnosis			Patient's Sex		Total
			Male	Female	
Embryonal Rhabdomyosarcoma	Age group of patient	0-10	1	1	2
	Total		1	1	2
Mesoblastic nephroma	Age group of patient	0-10	0	1	1
	Total		0	1	1
Fibromatosis	Age group of patient 31-40		0	1	1
	Total		0	1	1
Mucinous adenocarcinoma	Age group of patient	41-50	1	0	1
	Total		1	0	1
Nephroblastoma	Age group of patient	0-10	9	10	19
		11-20	0	2	2
	Total		9	12	21
Oncocytoma	Age group of patient	31-40	0	1	1
		61-70	1	0	1

	Total		1	1	2
Renal cell carcinoma	Age group of patient	0-10	1	0	1
		11-20	0	3	3
		21-30	4	2	6
		31-40	3	4	7
		41-50	6	1	7
		51-60	5	8	13
		61-70	7	3	10
		71-80	1	1	2
		81-90	1	0	1
	Total		28	22	50
Rhabdoid tumour	Age group of patient	0-10	0	1	1
	Total		0	1	1
SCC	Age group of patient	41-50	1	0	1
		51-60	0	1	1
		61-70	1	0	1
		71-80	1	0	1
	Total		3	1	4
Transitional cell carcinoma	Age group of patient	41-50	1	0	1
	Total		1	0	1
Total	Age group of patient	0-10	11	12	23
		11-20	1	5	6
		21-30	4	2	6
		31-40	3	6	9
		41-50	9	1	10
		51-60	5	9	14
		61-70	9	3	12
		71-80	2	1	3
		81-90	0	1	1
	Total		44	40	84

SCC=Squamous cell carcinoma

Table 5 shows that for most (56.95%) of the nephrectomy specimens with neoplastic lesions, definitive diagnoses were made post-surgery following pathologic evaluation. Only 44.04% of the cases had pathologic diagnosis in agreement with the clinical diagnosis (see bold and underlined figures in table 5).

Table 5 Correlation between pre-surgery and pathologic diagnoses for neoplastic lesions

Clinical Diagnosis	**Pathologic diagnosis**										**Total**
	Embryonal Rhabdomyosarcoma	**Mesoblastic nephroma**	**Fibromatosis**	**Mucinous adenocarcinoma**	**Nephroblastoma**	**Oncocytoma**	**Renal cell carcinoma**	**Rhabdoid tumour**	**SCC**	**Transitional cell carcinoma**	
Adrenal Tumour	0	0	0	0	0	0	1	0	0	0	1
Rhabdomyosarcoma	1	0	0	0	0	0	0	0	0	0	1
Not Indicated	0	0	0	1	2	0	18	0	1	1	23
Recurrent Retroperitoneal Tumour	0	0	0	0	0	0	1	0	0	0	1
Intraabdominal tumour	0	0	0	0	0	0	3	0	0	0	3
Renal Tumour	1	0	1	0	0	1	7	0	1	0	11
Cystolithiasis	0	0	0	0	0	0	0	0	1	0	1
Renal Cell Carcinoma	0	0	0	0	0	1	13	0	1	0	15
Nephroblastoma (Wilm's Tumour)	0	1	0	0	19	0	1	1	0	0	22
Hypernephroma	0	0	0	0	0	0	4	0	0	0	4
Polycystic Kidney	0	0	0	0	0	0	1	0	0	0	1
Total	2	1	1	1	21	2	50	1	4	1	84

4. Discussion

Nephrectomy is done for a wide range of kidney pathologies; and the indications and pattern of the lesions seem to vary with age and geographical location. In this study, of the 141 nephrectomy specimens analyzed over a fifteen-year period, 59.6% were neoplastic lesions while 40.4% were non-neoplastic. This pattern is similar to a local study in South-west Nigeria by Omisanjo *et al*., who reported 75% neoplastic lesions, all of which were malignant.[18] However, this is at variance with studies done in the Oriental world. Studies in India and Pakistan reported that 75% and 76% respectively, of nephrectomy lesions were non-neoplastic.[19,20] This lower frequency of neoplastic lesions in the oriental studies may be related to dietary and lifestyle factors, as the Orientals are noted to consume more of sea-foods reported to be inversely proportional to RCC.[21-22] As such, there is a geographical variation in the pattern of distribution of neoplastic and non-neoplastic renal lesions in nephrectomy specimens.[23]

Chronic pyelonephritis (CPN) and hydronephrosis were the most common and second most common histologically diagnosed non-neoplastic lesions in the nephrectomy specimens, occurring either singly or in combination, and accounting for 59.6% and 22.8% of cases respectively. This pattern has also been reported by other researchers.[24-26] CPN is characterized by chronic tubulo-interstitial inflammation and interstitial fibrosis. Usually it results as a complication of obstructive nephropathy with reflux of urine into the pelvi-calyceal system. On rare occasions, it results from contiguous or haematogenous spread and this occurs more in debilitated or immunosuppressed patients.[27] Both CPN and hydronephrosis occur in the most part as complications of obstructive nephropathy, later stage/severe cases of which are associated with non-functional kidney due to fibrosis and tubular atrophy.[28-29] Their high frequency in this study suggests late presentation for the management of the primary pathology.

Nephrectomy is the standard of care for most neoplastic lesions of the kidney, particularly the malignant ones which respond poorly to radiotherapy, chemotherapy or hormonal treatment.[30] Neoplastic lesions accounted for 59.6% of all the nephrectomy specimens, 94% of which were malignant and 6% were benign. The most common malignant lesion observed in this study is renal cell carcinoma in adults and nephroblastoma in children. This agrees with the reports of

other studies.[9,20,31-32] Other rarer malignant lesions observed included squamous cell carcinoma, transitional cell carcinoma, mucinous adenocarcinoma and embryonal rhabdomyosarcoma.

RCC refers to a group of malignancies arising from the epithelium of renal tubules, comprising of about 90% of all renal malignancies in adults and occurring mostly in the fifth decade of life.[33] However, in our study, RCC occurred commonly in the sixth decade of life with mean and median ages of 48.8±18.1 years and 52.5 years respectively. Although Thompson *et al.,* reported similar modal age group of sixth decade, the median age in our study contrasts with theirs with a median age of 64 years.[34] This contrast may be largely due to a large number of subjects used in their study. We observed a male preponderance (male: female ratio of 1.3:1) and more involvement of the left kidney with a left: right ratio of 2:1. These patterns are similar to what was observed by other authors.[24,35-36] In agreement with the works of Shaila *et al*.,[31] Chitra *et al.*,[37] and Bashir *et al*.,[38] we observed that the clear cell variant of RCC was the most frequent variant at 52%, followed by papillary variant at 34%. Other variants found included medullary, oncocytic, chromophobe and sarcomatoid variants occurring at 25%, 6%, 4% and 2% respectively. No collecting duct variant was observed in the index study.

There were four cases of paediatric RCC (8.0% of all RCCs) observed in this study with an age range of 5-18 years, one of which was a Papillary RCC in a 5 year old male. The other three cases occurred in females in the second decade of life aged 13 years (in association with duplex ureter), 15 years and 18 years. Although rare, paediatric RCC has been reported in literatures, being commoner among adolescents above the age of ten years and found to be associated with some heritable syndromes such as Von Hippel-Lindau and Tuberous sclerosis complex.[39] The incidence of RCC in children is estimated to be between 1.8% and 6.3% of all malignant renal tumours,[40] with some noted to occur in association with anomalies of the urinary system.[41-43] Although the causal relationship between these anomalies and RCC in childhood remains to be established, Calderon-Margalit *et al.*, in a population based cohort study done between 1967 and 1997 and comprising of 1,510,042 adult subjects, reported that congenital anomalies of the kidney and urinary tract is associated with increased risk of urinary tract cancers.[44]

There were twenty-one cases of nephroblastoma in this study, accounting for 25.0% of the neoplastic lesions, with about 90.5% occurring in the first decade of life and involving the right (55.6%) more than the left (right: left=1.25:1). Similarly, Thakur *et al*. in central India[24] and Amin *et al*. in Southern India[25] reported occurrence of nephroblastoma largely in the first decade of life with slight preference for the right kidney. Nephroblastoma in this study, has a modal age of 2 years with a female preponderance (female: male=1.3:1). The study on paediatric nephrectomies in a tertiary healthcare facility in Southeastern Nigeria by Ezomike *et al*., showed that nephroblastoma accounted for 97.1% of the specimens affecting largely children in the first decade of life with slight left predominance.[45] A sided predominance of nephroblastoma therefore, may be a chance finding.

Only 44.04% of the nephrectomy specimens with neoplastic lesions had pathologic diagnosis in agreement with the clinical diagnosis. For majority (56.95%) of the cases, definitive diagnoses were made post-surgery following pathologic evaluation. It is usually difficult to make a definitive diagnosis of renal tumours without histopathologic evaluation.[42] Whereas majority (54.8%) of the neoplastic lesions involved the left kidney, the affected side was not specified in 7 cases (8.3%). Incomplete filling of requisition forms is one of the major challenges in clinico-pathologic consults; an inadequacy with potential negative impact on the interpretation of results, timely communication of critical values, turnaround times and ultimately the quality of patient care.[46-48] There is therefore, need to increase awareness among clinicians, by way of continuous medical education, on the importance of adequate and complete filling of laboratory request forms in patient care.

5. Conclusion

Nephrectomy is indicated in both neoplastic and non-neoplastic renal pathologies, essentially as a therapeutic option; though in many instances, histological assessment of the specimen can aid definitive diagnosis and better characterization of the disease entity. The most common non-neoplastic lesion in nephrectomy specimens in our environment is chronic pyelonephritis while the most common neoplastic lesion is renal cell carcinoma in adults, predominantly the clear cell variant, and nephroblastoma in children. The major limitation of the work is improperly filled pathology request forms that failed to supply all the requisite clinical information needed. We therefore recommend increased awareness creation among clinicians as a way to mitigating this malady. However, in general, the outcome of the study correlates with the pattern reported by other studies in Nigeria.

Compliance with ethical standards

Acknowledgments

We acknowledge the management and staff of Triple Green Diagnostic Clinics Ltd, Nnewi for granting us access to their records and helping to retrieve the slides.

Disclosure of conflict of interest

All the authors declare that there are no conflicts of interests.

Disclosure of conflict of interest

Ethical approval gotten from the Ethical committee of the Nnamdi Azikiwe University Teaching Hospital, Nnewi.

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