

**CLINICOPATHOLOGICAL PROFILE OF
GLOMERULAR DISEASES AT THE KENYATTA
NATIONAL HOSPITAL.**

A DISSERTATION SUBMITTED IN PART FULFILLMENT OF THE
REQUIREMENT FOR THE DEGREE OF MASTER OF MEDICINE IN
INTERNAL MEDICINE, UNIVERSITY OF NAIROBI.

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DECLARATION

I hereby declare that this is my original work and has not been presented for a degree in any other university.

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DEDICATION

I dedicate this dissertation to my loving parents Mr. and Mrs. John Muthui who have given me only the best, and to my husband Gideon Mutua for his endless love and support.

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ABBREVIATIONS

AGN	-Acute glomerulonephritis
ANA	-Antinuclear antibodies
ASOT	-Antistreptolysin O titers
AUA	-Asymptomatic urinary abnormality
BP	-Blood pressure
CGN	-Chronic glomerulonephritis
CKD	-Chronic kidney disease
ESRD	- End stage renal disease
FGS	-Focal segmental glomerulosclerosis
GN	-Glomerulonephropathy
HBV	-Hepatitis B Virus
HCV	-Hepatitis C Virus
HepBs Ag	-Hepatitis B surface antigen
HIV	-Human Immunodeficiency Virus
IQR	-Interquartile range
KNH	-Kenyatta National Hospital
LN	-Lupus nephritis
MCD	-Minimal change disease
MN	-Membranous nephropathy
MPGN	-Membranoproliferative glomerulonephritis
MSPGN	- Mesangioproliferative glomerulonephritis
NaOH	- Sodium hydroxide
NHANES	- National Health and Nutrition Examination Survey
NSAIDS	-Non steroidal anti-inflammatory drugs
PAS	-Periodic Acid Schiff
RPGN	-Rapidly proliferative glomerulonephritis
SBE	-Sub acute bacterial endocarditis
SD	-Standard deviation
UACR	-Urine Albumin Creatinine Ratio
UON	-University of Nairobi
VDRL	-Venereal Disease Research Laboratory

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ABSTRACT

Background

Kidney disease is a worldwide public health problem. Glomerular diseases are the most common cause of end stage renal disease worldwide accounting for 51% of end-stage renal disease. Glomerular diseases in the tropics differ from those in temperate countries in their epidemiology, aetiology and natural history.

Objective of the study

The purpose of this study was to describe the clinical and pathological profile of patients presenting with glomerular diseases at The Kenyatta National Hospital.

Methods

A cross-sectional descriptive survey with both retrospective and prospective arms was carried out at The Kenyatta National Hospital. For the retrospective arm, records of patients who had renal biopsies between January 2007 and September 2009 were reviewed. For the prospective arm, new patients aged 14 years and above presenting to the renal clinic between November 2009 and March 2010 with proteinuria of 1g/dl and above were studied. A targeted history, physical examination, relevant laboratory investigations and a renal biopsy were done.

Results

In total 193 patients were reviewed (149 in the retrospective arm and 44 in the prospective arm). The mean age was 27.3 ± 12.3 while the male to female ratio was 1.14:1. Nephrotic syndrome was the most common clinical presentation (76.2%). The most common histological lesion was FSGS (30.1%) followed by MN (18.1%), MPGN (15.4%), MCD (14.5%) respectively. Idiopathic GN accounted for most of the glomerular diseases. The secondary causes of glomerular diseases identified included lupus nephritis, human immunodeficiency virus, hepatitis B virus and post-streptococcal infection.

Conclusion

Consistent with other studies, nephrotic syndrome was the most common clinical presentation. FSGS was the most common histological lesion showing a significant increase in frequency when compared with previous local studies.

1. LITERATURE REVIEW

1.1 INTRODUCTION

Kidney disease is a worldwide public health problem. There is an increasing incidence and prevalence of end stage renal failure requiring replacement therapy. Glomerular diseases are the most common cause of end stage renal disease worldwide. They account for 51 percent of end-stage renal disease [1].

Glomerular diseases in the tropics differ from those in temperate countries in their epidemiology, aetiology and natural history [2-3].

Data from surveys of the nephrotic syndrome have also shown that it is 60-100 times more common in some tropical countries compared to the United States of America and the United Kingdom [4-7].

The first report of glomerular diseases in Kenya was published by Carothers in 1934 [8].

1.2 PATHOGENESIS OF GLOMERULAR DISEASES

Various factors involved in the pathogenesis of glomerular diseases include hereditary, immunological and non immunological factors [9-12]. Glomerular injury of immune origin occurs via the actions of multiple elements of the immune system, thereby resulting in diverse clinical and pathologic manifestations [9-12].

The extent and severity of glomerular injury, and accordingly of the clinical presentation are determined by the nature of the primary insult and the secondary mediator systems that it invokes; the site of injury within the glomerulus; and the speed of onset, the extent, and intensity of disease.

1.3 CLASSIFICATION OF GLOMERULAR DISEASES

Glomerular diseases are classified as either primary or secondary [13].

Primary glomerular diseases are disorders in which the glomeruli are the sole or predominant tissue involved. These diseases are idiopathic.

Secondary glomerular diseases are disorders in which glomerular injury is a feature of a systemic disease involving multiple organs or systems. Table 1 shows the classification of glomerular diseases and the various causes of glomerular diseases.

TABLE 1. CLASSIFICATION OF GLOMERULAR DISEASES ACCORDING TO THE PRESENCE OR ABSENCE OF PROLIFERATIVE CHANGES.

TYPE OF DISORDER	PROLIFERATIVE CHANGES	NO PROLIFERATIVE CHANGES
Primary renal disorder	IgA nephropathy IgM nephropathy Other mesangioproliferative glomerulonephritides Crescentic glomerulonephritis With immune deposits Pauci-immune Membranoproliferative glomerulonephritis	Focal segmental glomerulosclerosis Membranous glomerulopathy Minimal-change disease Thin basement membrane disease
Secondary disorder	Lupus nephritis Postinfectious glomerulonephritis Glomerulonephritis related to hepatitis B or C Systemic vasculitides Wegener's granulomatosis Polyarteritis nodosa Henoch-Schönlein purpura Idiopathic	Diabetic nephropathy Amyloidosis Light-chain nephropathy Human immunodeficiency virus nephropathy Alport's syndrome Drug-induced glomerulopathies

Different infective agents and diseases have been implicated in the causation of glomerular disease in the tropics. These include schistosomiasis [14, 15], quartan malaria [7, 8, 16], filariasis, streptococcal infection, hepatitis B and C, and HIV [6, 17, 18]. Others include syphilis, mumps, measles, varicella, toxoplasmosis and infective endocarditis

Use of skin lightening cosmetics has also been implied in the causation of glomerular diseases in some studies [21, 22].

1.4 CLINICAL PATTERNS OF GLOMERULAR DISEASES

Glomerular diseases generally present with one of five clinical syndromes: asymptomatic urinary abnormality, acute glomerulonephritis, rapidly progressive glomerulonephritis, nephrotic syndrome, or chronic glomerulonephritis [13].

Nephrotic syndrome is characterized by massive proteinuria (> 3.5 g/day), hypoalbuminaemia, oedema, lipiduria and hyperlipidaemia.

Acute glomerulonephritis (acute nephritic syndrome) is characterized by abrupt onset of glomerular haematuria (RBC casts or dysmorphic RBC), non-nephrotic range proteinuria, oedema, hypertension and transient renal impairment.

Rapidly progressive glomerulonephritis is characterized by features of acute nephritis, focal necrosis with or without crescents and rapidly progressive renal failure over weeks.

Asymptomatic urinary abnormality is characterized by proteinuria and/or haematuria found on routine check-up, without oedema, hypertension and abnormal renal function.

Chronic glomerulonephritis is characterized by proteinuria lasting greater than three months.

NEPHROTIC SYNDROME

In adults, primary glomerular diseases causing nephrotic syndrome are membranous glomerulopathy, focal segmental glomerulosclerosis, minimal-change disease, and membranoproliferative glomerulonephritis [19, 20].

A study by Mcligeyo in patients older than 15years [3] found the most common histological types in Kenya to be mesangioproliferative glomerulonephritis, minimal change nephropathy, and focal segmental glomerulonephritis each accounting for about 20% of the cases.

Kinuthia *et al* [21], also looking at nephrotic syndrome in adults older than 15 years at KNH between 1973 -1977 found diffuse proliferative glomerulonephritis as the most common histological type.

Kungu *et al* [22] found minimal change disease as the most common histological type in nephrotic syndrome in both children and adults. Published data from Kenya and Nigeria indicate minimal change disease is more common in females [3, 21-23].

1.5 HISTOLOGICAL PATTERN OF GLOMERULAR DISEASE

There are various histological patterns of glomerular diseases.

Membranous Nephropathy

Membranous nephropathy (MN) is among the most common causes of the nephrotic syndrome in nondiabetic adults, accounting for up to one-third of biopsy diagnoses in USA and Spain [20, 24-26].

MN is most often idiopathic, although it has been associated with hepatitis B antigenemia, autoimmune diseases, malignancies, and the use of certain drugs such as gold, penicillamine, and nonsteroidal anti-inflammatory drugs (NSAIDs).

MN is seen in all ethnic and racial groups and in both sexes, but idiopathic MN is more common in white males over the age of 40 years. MN in young women should raise the suspicion of lupus. MN is less commonly seen in children, in whom it is often associated with hepatitis B [26, 27].

MN is common in children in Zimbabwe and also in adults in Sudan and Nigeria [6, 23]. In both Africa and Asia it is frequently a complication of Hepatitis B infection [24,26].

Minimal Change Nephropathy

Minimal change disease (MCD; also called nil disease) is the most common cause of the nephrotic syndrome in children, accounting for 90 percent of cases under the age of 10 and more than 50 percent in older children [28-30]. It accounts for 10 to 15 percent of cases in adults of all ages [20, 31, 33].

MCD is also common in Tropical Africa where it is found in between 4 and 30% of cases [3, 4, 5, 17, 21, 22].

In 2 studies in Kenya done in adults older than 15 years by Barr *et al* [17] and Mcligeyo[3] MCD was the commonest and the second most common histological variety respectively. It was highest in females where it was associated with the use of mercury skin lightening creams.

Focal Segmental Glomerulosclerosis

Focal segmental glomerulosclerosis, FSGS (also called focal glomerulosclerosis) has become an important cause of the nephrotic syndrome in adults and remains a frequent cause in children and adolescents, particularly in the United States, Brazil, and many other countries [20, 24, 34-36].

In the United States, for example, a survey of renal biopsies performed from 1995 to 1997 for idiopathic nephrotic syndrome in adults found that FSGS was the most common cause, accounting for 35 percent of all cases and over 50 percent of cases among blacks [20].

Based upon data from the United States Renal Data Systems (USRDS), FSGS is currently the most common primary glomerular disease underlying end-stage renal disease (ESRD) in the United States [34].

In 1980, FSGS was the cause of ESRD in only 0.2 percent of patients; by 2000, it was responsible for 2.3 percent of cases (excluding patients with HIV), an eleven fold increase. As observed in other series, an increased incidence was reported in blacks and males.

By comparison, other countries have found that FSGS is a relatively less common cause of the nephrotic syndrome. Among 2000 patients between 15 and 65 years of age with nephrotic syndrome noted in the glomerulonephritis registry of Spain, the most common histologic causes were membranous nephropathy (24 percent), minimal change disease (16 percent), lupus (14 percent), and focal segmental glomerulosclerosis (12 percent) [25].

FSGS is particularly common in Ghana and in Senegal. Renal biopsies from the patients described in Senegal had an unusual fibrillary splitting of glomerular capillary walls with interposition of basement membrane like material [37].

In a study by Mcligeyo in Kenya in 1994[3], FSGS accounted for 10% of patients with nephrotic syndrome older than 15 years.

Membranoproliferative Glomerulonephritis

Membranoproliferative glomerulonephritis (MPGN; also called mesangiocapillary or lobular glomerulonephritis) is an uncommon cause of glomerular disease that, in its idiopathic form, primarily occurs between the ages of 8 and 30 [38-40].

MPGN has been associated with a number of chronic immune complex disorders and certain other systemic diseases [40].

Multiple chronic infections including hepatitis B and C virus infection, SBE, and ventriculoatrial shunt infection can cause the MPGN pattern of injury. Others include chronic visceral abscess [41], schistosomiasis which can cause glomerular disease in 10 to 15 percent of patients with chronic hepatosplenic infection [42], malaria, and leprosy.

MPGN has also been associated with HCV infection [43-46]. In the tropics it is commonly seen in post-infectious glomerulonephritis and in association with Hepatitis C infection [2-6].

Previous studies from Kenya reported that MPGN accounts for about 5-10% of patients with nephrotic syndrome [3, 21, 22].

Other histological types of glomerulonephritis include diffuse proliferative glomerulonephritis and crescentic glomerulonephritis.

1.6 CHANGING PATTERN OF GLOMERULAR DISEASES

Recent studies have shown that the pattern of glomerular diseases has been changing over the last two decades.

Haas M. et al [20] studying the etiologies of adult nephrotic syndrome from 1976-1979 and 1995-1997 found an increase in FSGS with a decrease in MCD.

Simon P. et al [47] while studying primary glomerular diseases in western France over a 27 year period (1972-2002) found that the incidence of membranoproliferative glomerulonephritis and membranous nephropathy were declining while the incidence of crescentic proliferative GN was increasing.

A very recent study by Fu-de Zhou et al [48] found that the relative frequency of non-IgA mesangioproliferative glomerulonephritis, endocapillary proliferative glomerulonephritis and membranoproliferative glomerulonephritis decreased significantly, while that of minimal change disease and IgA nephropathy increased significantly. There was also a six fold increase frequency of FSGS in the last 15 years. The proportion of elderly patients also increased significantly from 0% in 1993 to 9.1% in 2007.

2. STUDY JUSTIFICATION

Kidney disease is a worldwide health problem and glomerular diseases account for 51% of ESRD [1].

Glomerular diseases are probably the most popular aspect of tropical nephrology due to their more common occurrence than the western world and their varying aetiology and histopathology [3].

The last published local study was done 17 years ago and included only patients with nephrotic syndrome. There is no study from Kenya looking at all the presentations of glomerular diseases. According to some recent studies, there has been change in the pattern and aetiology of glomerular diseases [20, 47, 48].

This study was aimed at revisiting glomerular diseases in Kenya with a view to characterizing them clinically and pathologically and attempting to establish if there is a shift in pattern over the last two decades.

3. STUDY OBJECTIVES

3.1 BROAD OBJECTIVE

To describe the clinicopathological profile of glomerular diseases at The Kenyatta National Hospital, Nairobi.

3.2 SPECIFIC OBJECTIVES

1. To describe the demographic characteristics of patients presenting with glomerular disease at KNH.
2. To describe the clinical pattern of glomerular diseases at KNH
3. To describe the pathological pattern of glomerular diseases at KNH
4. To document the aetiological factors associated with glomerular diseases at KNH

4. METHODOLOGY

4.1 Study design

The study was a cross sectional descriptive survey with retrospective and prospective arms.

4.2 Study area

The study was conducted at The Kenyatta National Hospital renal clinic.

4.3 Study population

For the retrospective arm: Patients who had biopsies between January 2007 and September 2009 were included. For the prospective arm, new patients presenting to The Kenyatta National Hospital with glomerular disease aged 14yrs and above.

4.4 Sampling

Consecutive sampling was used to recruit patients in the prospective arm while for the retrospective arm all patients who fit the inclusion criteria were included.

4.4 Sample size

Retrospective arm: All patients aged 14 years and above with renal biopsies from January 2007 to September 2009 were recruited.

Prospective arm: The study was time bound and patients were recruited at the renal clinic for a period of 5 months.

4.5 Patient selection

Inclusion criteria

- New patients presenting with proteinuria of +1 and/or haematuria of +1 to the renal clinic
- Patients aged 14 years and above.
- Signing of an informed consent by the patient or guardian for minors.
- For renal biopsy: patients with proteinuria of 1g/dl and above.
- *For the retrospective arm:* Patients aged 14 years and above who had renal biopsies done between January 2007 and September 2009.

Exclusion criteria

- Patients who declined to participate in the study.
- Diabetics
- *Exclusion criteria for renal biopsy:* Failure to give consent, uncontrolled blood pressure, hemoglobin <10g/dl, platelets <100* 10⁹/l, solitary kidney, small kidneys on renal ultra sound (less than 9cm), hemorrhagic diathesis, skin sepsis over biopsy site, diabetic nephropathy.
- *For retrospective arm:* Patients' records with no biopsy results.

Case definition

- Glomerular disease: New patients who presented to the renal clinic with glomerular proteinuria of 1g/d with or without haematuria.

Definition of clinical syndromes

Nephrotic syndrome: proteinuria (> 3g/d), serum albumin<30g/l, oedema, with or without hyperlipidaemia.

Acute glomerulonephritis (acute nephritic syndrome): haematuria, red blood cell casts and proteinuria (<3 g/d), with or without oedema/hypertension which persist less than 3 months

- Hypertension: blood pressure > 140/90 or patients on treatment for hypertension.

Rapidly progressive glomerulonephritis: features of acute nephritis with rapidly progressive renal failure over weeks but less than 3 months.

Chronic glomerulonephritis: proteinuria lasting more than three months

Asymptomatic urinary abnormality was defined as proteinuria and haematuria found by routine check-up, without oedema, hypertension and abnormal renal function.

Renal dysfunction: serum creatinine >150mmols/l.

4.6 Clinical and laboratory methods

a) The retrospective arm

The renal biopsy register in the renal unit was used to get a list of all patients who had renal biopsies from January 2007 to September 2009. The records of all these patients were then obtained from The Kenyatta National Hospital records department.

The files were retrospectively examined and records of patients aged 14 years and above were included in the study. Records with no renal biopsy results or inadequate biopsies were excluded.

Data with respect to the demographic characteristics, clinical presentation, laboratory investigations and histological pattern of their renal lesion were extracted from the files and entered into a data sheet. Corroborative biopsy results were obtained from Aga Khan Hospital pathology laboratory where the biopsies were analyzed. (Appendix I)

b) The prospective arm

All new patients aged 14 years and above attending the renal clinic between November 2009 and March 2010 were screened for eligibility after they were introduced to the study.

A urine dipstick was performed on all new patients. In patients with proteinuria of +1 and above and/or haematuria of +1 and above, UACR was carried and patients with proteinuria of 1g/dl and above were invited for recruitment into the study. Recruitment into the study began after informed consent was obtained from the eligible patients. Patients aged less than 18years gave assent and their guardians gave informed consent.

A targeted history and physical examination was performed on all recruited patients as per the study profoma (Appendix I). Relevant laboratory investigations which are done routinely on patients with glomerular diseases were then done. These included: HIV, HCV, HepBs Ag, VDRL, ANA, ASOT, RBS, urea, creatinine, electrolytes, total cholesterol, and blood slide for malaria parasites, haemoglobin, and urine microscopy. Other tests were guided by the clinical presentation. (Appendix II)

Renal biopsy: The patients were then prepared for a renal biopsy. A coagulation profile was done and a written consent was obtained from these patients or their guardians (for patients under 18 years) before the renal biopsy.

A percutaneous renal biopsy under ultrasound guidance was carried out on all patients with no contraindication to renal biopsy by one of the nephrologists.

Exclusion criteria for renal biopsy: Failure to give consent, uncontrolled blood pressure, hemoglobin <10g/dl, platelets <100* 10⁹/l, solitary kidney, small kidneys on renal ultra sound (less than 9cm), hemorrhagic diathesis, skin sepsis over biopsy site and diabetic nephropathy.

The biopsies were performed using a trucut needle producing a core tissue of approximately 1-2mm diameter and of varying length. They were transported in bottles containing 10% formalin. The standard procedure of processing renal tissue was performed using an automatic Shandon Citadel 1000 processor. (Appendix III)

The biopsies were then embedded in paraffin wax and histological sections cut using a microtome to 2-3microns for silver stains and 5 microns for the other stains (H&E stain, Periodic Acid Schiff, Masson's Trichrome, Jone's silver methalamine, and Congo red stain). The biopsies were then examined by one of the supervisors (Dr. S. Sayed). 10% of the biopsies were be examined by a second pathologist who was blinded to the first pathologist's diagnosis. This was done for quality assurance purposes.

The specific procedures for the various stains are described in appendix IV.

Quality Assurance

Internal quality control was performed to ensure precision of results and hence their reliability. Standard operating procedures were followed in carrying out the laboratory investigations.

5. DATA ANALYSIS

All data was collected on the study proforma and entered into MS access computer data base. Data entry and statistical analysis was done using the Statistical Package for Social science (SPSS) version 17.0. Data validation was carried out before analysis. Descriptive statistics were used in result presentation. Continuous data such as age, serum creatinine, serum urea, haemoglobin and serum albumin were described using means, standard deviations, medians, proportions and frequency distribution. Categorical data was be analyzed using percentages and their corresponding confidence interval. P value of less than 0.05 was considered significant.

The renal biopsy findings were used to describe the pathological pattern of glomerular diseases.

6. ETHICAL CONSIDERATIONS

The study was carried out after appropriate approval from the Department of Medicine (UoN) and KNH Scientific and Ethical Review Committee.

Patients were enrolled to the study only after giving informed written consent.

All information obtained from the study has been handled in confidence and used only for the intended purpose. The results were communicated to the primary care providers for the institution of proper management.

7. RESULTS

In the retrospective arm records of 162 patients who had renal biopsies between January 2007 and September 2009 were reviewed. 13 were excluded (8 had no biopsy results while 5 had inadequate biopsies).149 qualified and were enrolled into the study.

In prospective arm we screened 153 patients between November 2009 and March 2010. 48 who had diabetic nephropathy and 61 who had proteinuria of less than 1g/dl on UACR were excluded. A total of 44 patients were recruited into the study.

Preliminary analysis showed results from both retrospective and prospective arms were similar and the total 193 patients were therefore analyzed together as shown in table 2. For ease of describing the results of the study, the patients were grouped in 10-year age groups.

Table 2: Comparison between the results of the retrospective and prospective arms.

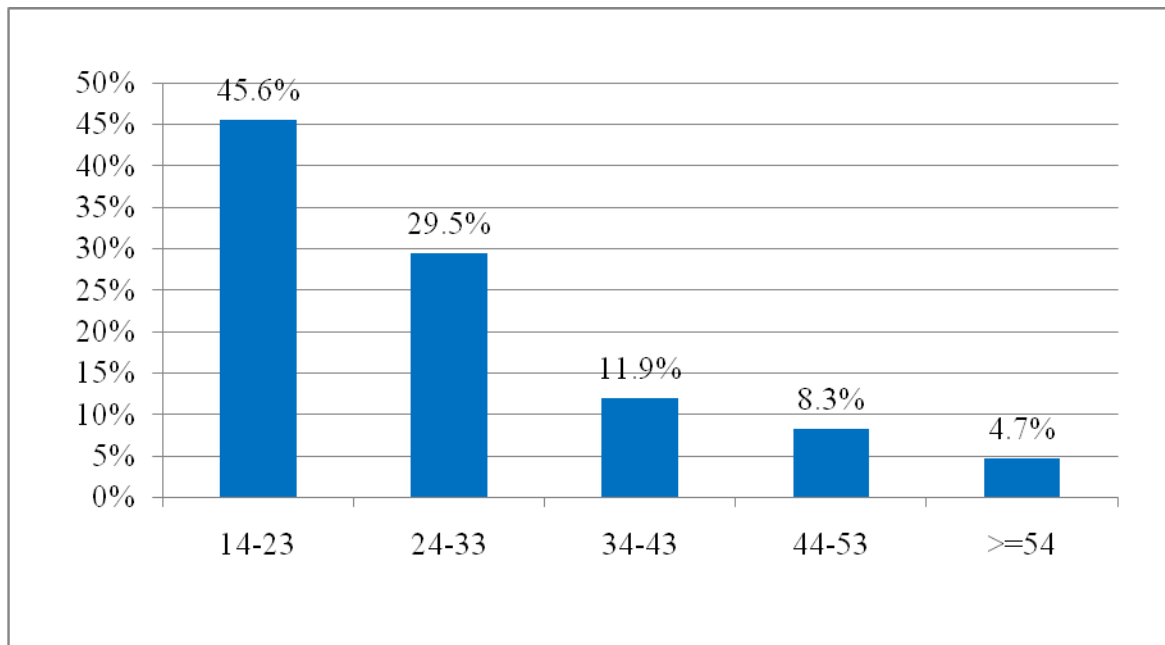
Variable	Retrospective (n=149)	Prospective (n=44)	P value
Mean age (yrs)	26.8 (12.3)	28.7 (12.3)	0.368
Sex			
Male	83 (55.7%)	20 (45.5%)	0.041
Female	66 (44.3%)	24 (54.5%)	
Clinical syndromes			
AGN	12 (8.1%)	1 (2.3%)	0.549
Nephrotic syndrome	113 (75.8%)	34 (77.3%)	
RPGN	15 (10.1%)	7 (15.9%)	
CGN	8 (5.4%)	2 (4.5%)	
Proteinuria	1 (0.7%)	0 (0.0%)	
Histological lesions			
MPGN	22 (15.1%)	7 (15.9%)	0.408
MSPGN	16 (11.0%)	6 (13.6%)	
MGN	28 (19.2%)	5 (11.4%)	
MCD	19 (13.0%)	9 (20.5%)	
FSGS	47 (32.2%)	11 (25.0%)	
DPGN	0 (0.0%)	1 (2.3%)	
LN	9 (6.2%)	5 (11.4%)	
Amyloidosis	2 (1.4%)	0 (0.0%)	
Normal	3 (2.1%)	0 (0.0%)	

7.1 DEMOGRAPHIC CHARACTERISTICS

Age

Figure 1 shows the age distribution of all the patients. The mean age was 27.3 ± 12.3 years, with the youngest being 14 and the oldest 67 years. The majority were aged between 14-23 years.

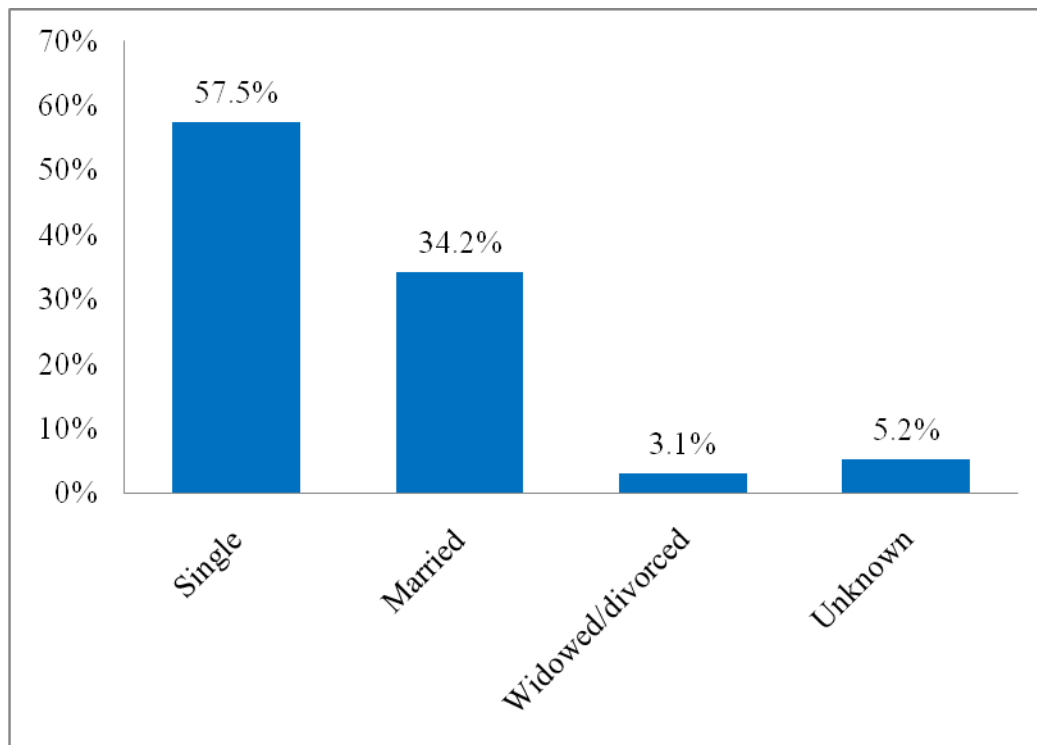
Figure 1: Age distribution of the study population



Sex distribution: 53.4% of the patients were males with an overall male to female ratio of 1.14: 1.

Marital status: Most of the patients were single as indicated in Figure 2.

Figure 2: Marital status of the study population



Occupation

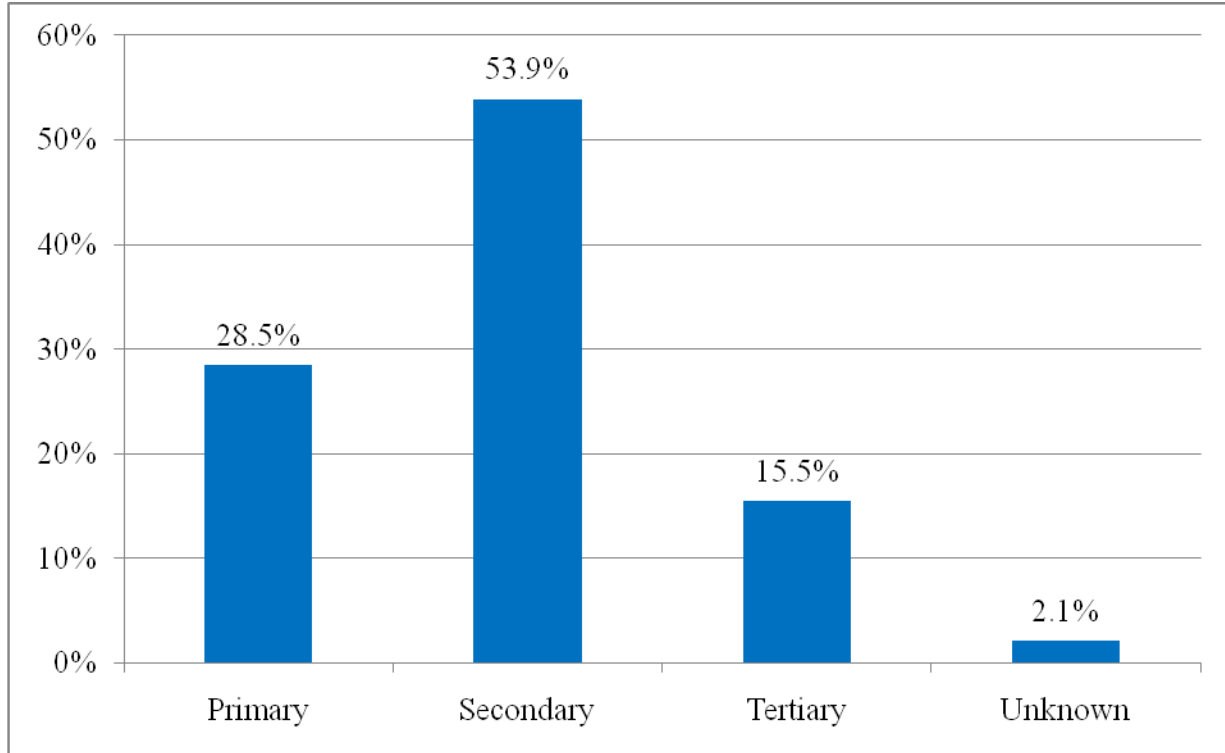
36.7% of the patients were employed, 38.9% were students while 18.7% were unemployed.

56.5% of the study population resided in urban centers.

10.9% took alcohol while 5.2% were smokers.

Majority of the patients had attained secondary education as shown in Figure 3.

Figure 3: Level of education of all patients



7.2 CLINICAL PATTERN OF GLOMERULAR DISEASES

Oedema was the most common presenting symptom as shown in Figure 4. The median duration of illness before presentation was 8.0 weeks (IQR 4.0-16.0 weeks) with the shortest being one week and the longest duration being 156 weeks (3years) Majority of patients were normotensive with a mean blood pressure of $126.2/77.4 \pm 21.6/15.1$ mmHg. The mean haemoglobin was 12.0 ± 2.2 g/dl. Most patients were in stage 2 CKD with a mean glomerular filtration rate of 70.4 ± 25.2 ml/min with a range of 13-122 ml/min as shown in Figure 5.

Figure 4: Presenting symptoms of the patients

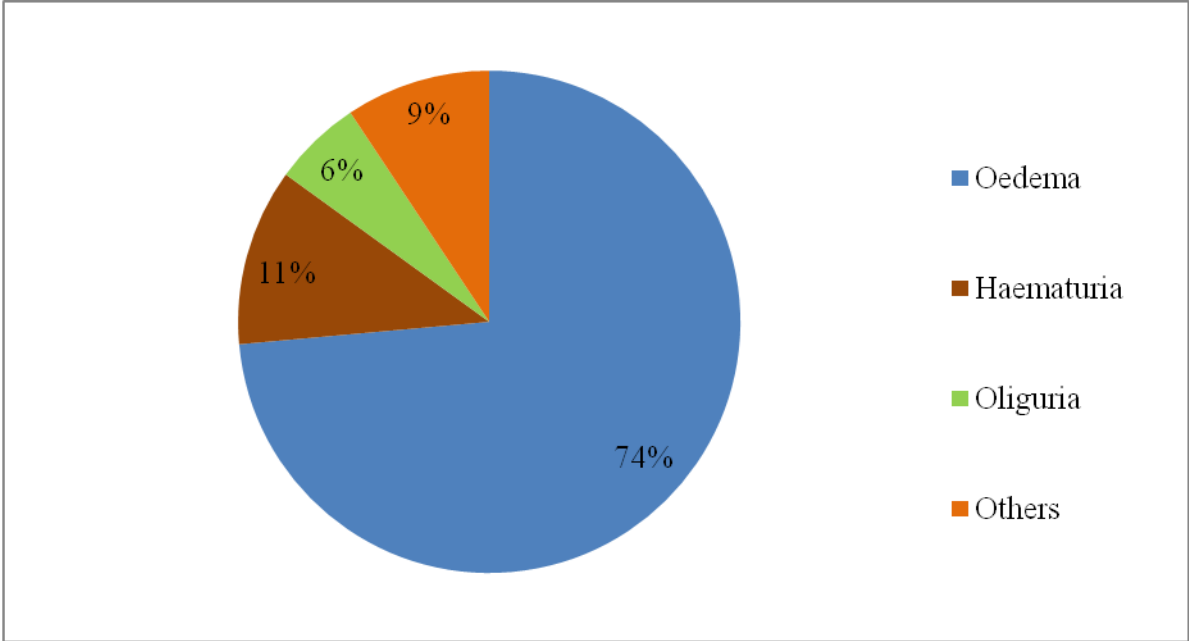
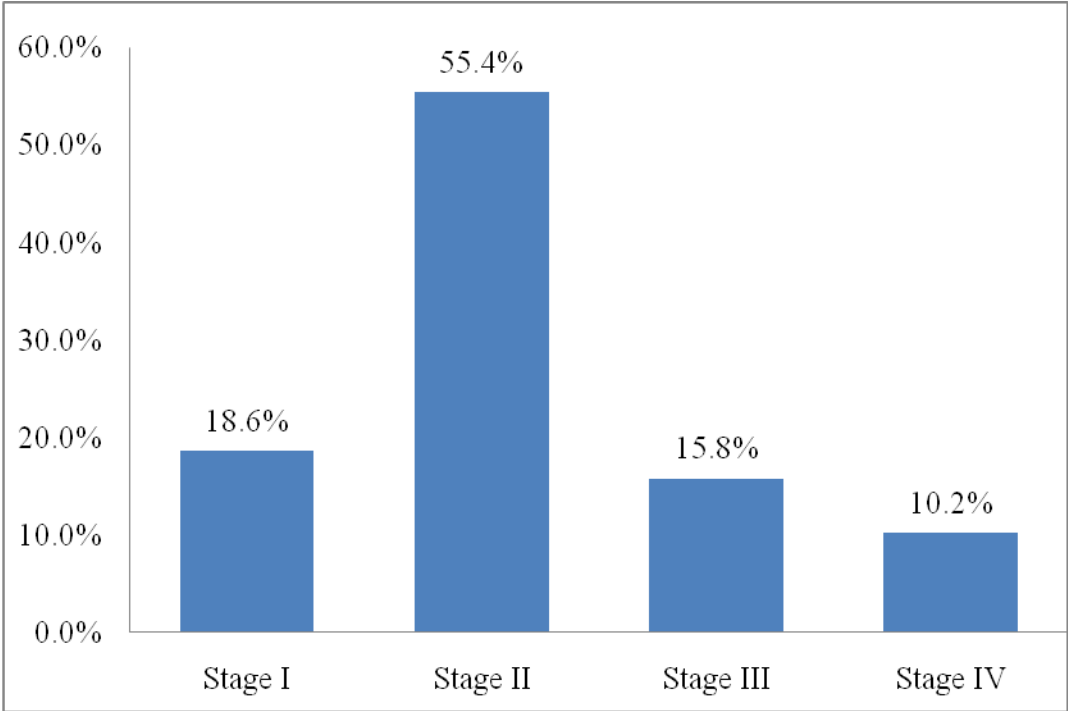


Figure 5: CKD stages of all the patients



The clinical syndromes Nephrotic syndrome was the most common clinical syndrome as shown in Figure 6. The age and gender distribution of various clinical syndromes is shown in Table 3.

Figure 6: Frequency of various clinical syndromes in the study population

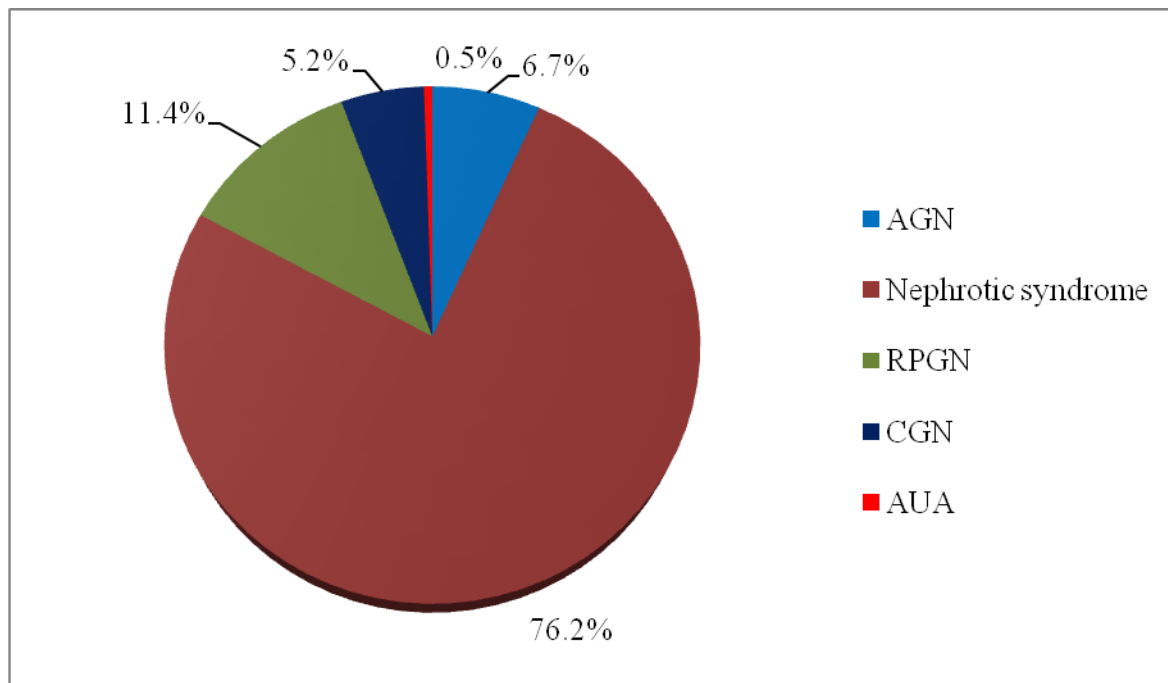


Table 3: Age and gender distribution of various clinical syndromes in the study population

<i>Clinical pattern</i>	<i>n (%)</i>	<i>Mean age(SD)</i>	<i>Sex</i>	
			Male (%)	Female (%)
AUA	1 (0.5)	22.0	1 (1.0)	0 (0.0)
AGN	13 (6.7)	21.2 (6.3)	9 (8.7)	4 (4.4)
Nephrotic syndrome	147 (76.2)	28.4 (13.1)	74 (71.8)	73 (81.1)
RPGN	22 (11.4)	24.7 (9.1)	13 (12.6)	9 (10.0)
CGN	10 (5.2)	24.2 (9.8)	6 (5.8)	4 (4.4)
Total	193 (100.0)	27.3 (12.3)	103 (100.0)	90 (100.0)

Laboratory parameters

Serum albumin was markedly depressed with elevated serum cholesterol in nephrotic syndrome as shown in Table 4.

Table 4: Laboratory parameters of all patients

Clinical pattern	Biochemistry parameters, Mean (SD)					
	Serum Albumin (g/L)	Serum Creatinine (umols/L)	GFR (ml/min)	RBS (mmol/L)	Cholesterol (mmol/L)	Hb (g/dl)
AUA	33	82	95.4	4.8	5.1	15.6
AGN	36.2 (4.5)	214 (187)	36.8 (21.6)	5.2 (0.9)	4.8	12.2 (2.0)
Nephrotic	24.8 (8.3)	100 (67)	79.5 (17.3)	5.8 (7.9)	9.7 (8.3)	12.3 (2.2)
RPGN	32.8 (5.5)	514 (529)	37.2 (25.1)	5.3 (1.0)	4.1 (0.5)	10.4 (1.8)
CGN	30.1 (4.1)	286 (197)	50.8 (24.8)	5.3 (0.6)	4.8 (0.6)	10.6 (2.5)

7.3 PATHOLOGICAL PATTERN OF GLOMERULAR DISEASES

The most common histological lesion was FSGS (30.1%) followed by MN, MPGN, MCD respectively (Fig 7). 3 biopsies were reported as normal.

Renal amyloidosis occurred in 2 patients 1 male and 1 female, aged 32 and 51 respectively.

Among the subgroup of patients with nephrotic syndrome, the picture was the same with FSGS (32.2%), MN (21.9%) and MCD (19.2) being the most common. In patients with AGN, 6 patients (50%) had MSPGN, followed by MPGN 5 patients (41.7%). FSGS was the most common histological lesion among patients with CGN (Fig 8).

Figure 7: Frequency of various histological lesions of the study population

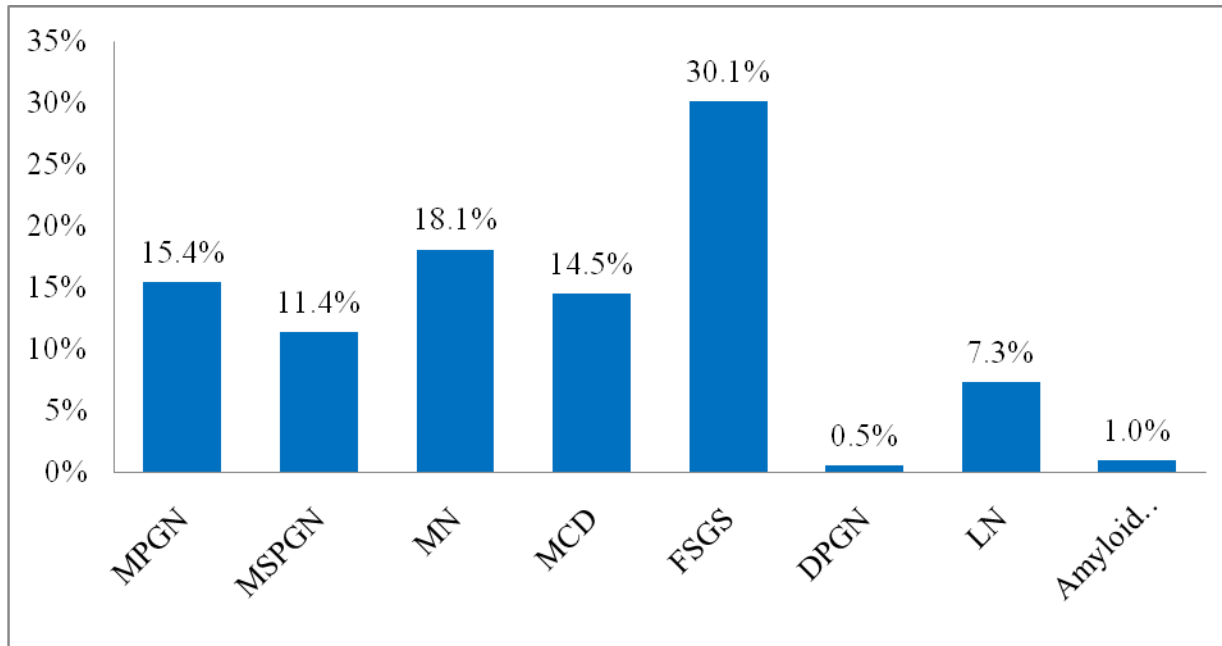
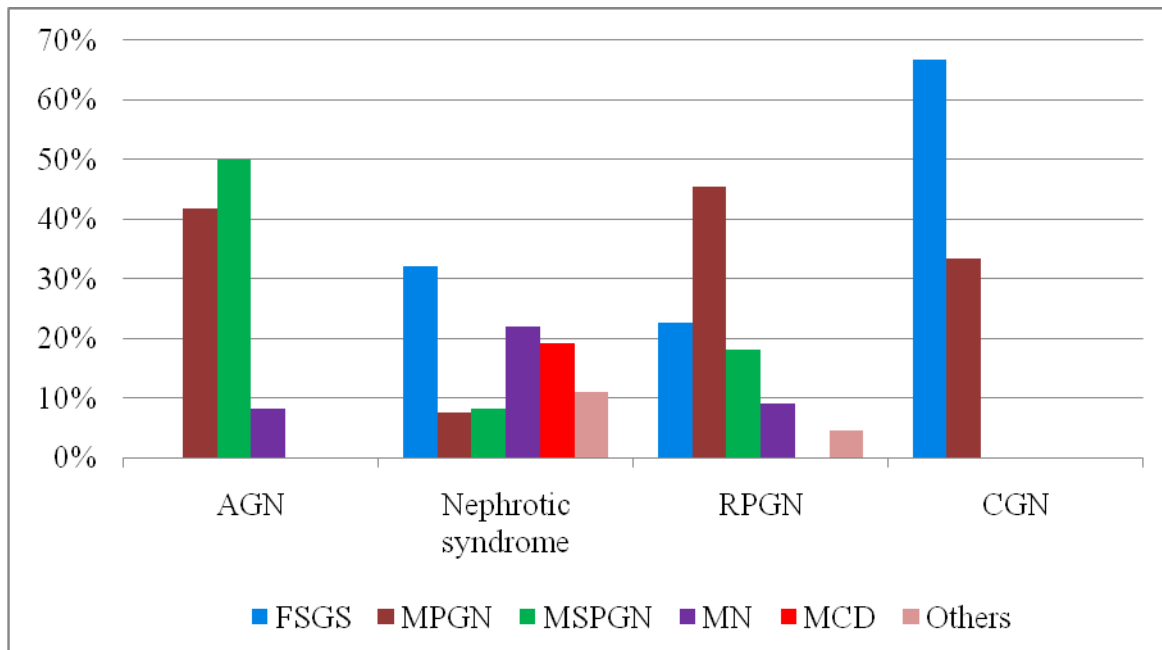


Figure 8: Distribution of histological lesions by the clinical pattern



Urinalysis findings and histological lesions

The presence of isolated proteinuria on urinalysis was found to be significantly higher among patients with MCD (71.4%) than those without MCD (36.6%) (P=0.001). In fact, detection of proteinuria together with haematuria and/or granular casts in urine was found to be more likely among the patients with other histological lesions (63.4%) as shown in Table 5.

Table 5: Correlation between urinalysis results and histological lesions

Urinalysis	MCD		P value
	Yes	No	
Proteinuria	20 (71.4%)	56 (36.6%)	0.001
Proteinuria with haematuria/casts	8 (28.6%)	97 (63.4%)	

The major histological patterns according to age and gender are shown in Table 6. There was a male predominance in most of the histological lesions.

Table 6: Gender and age characteristics of various glomerular diseases

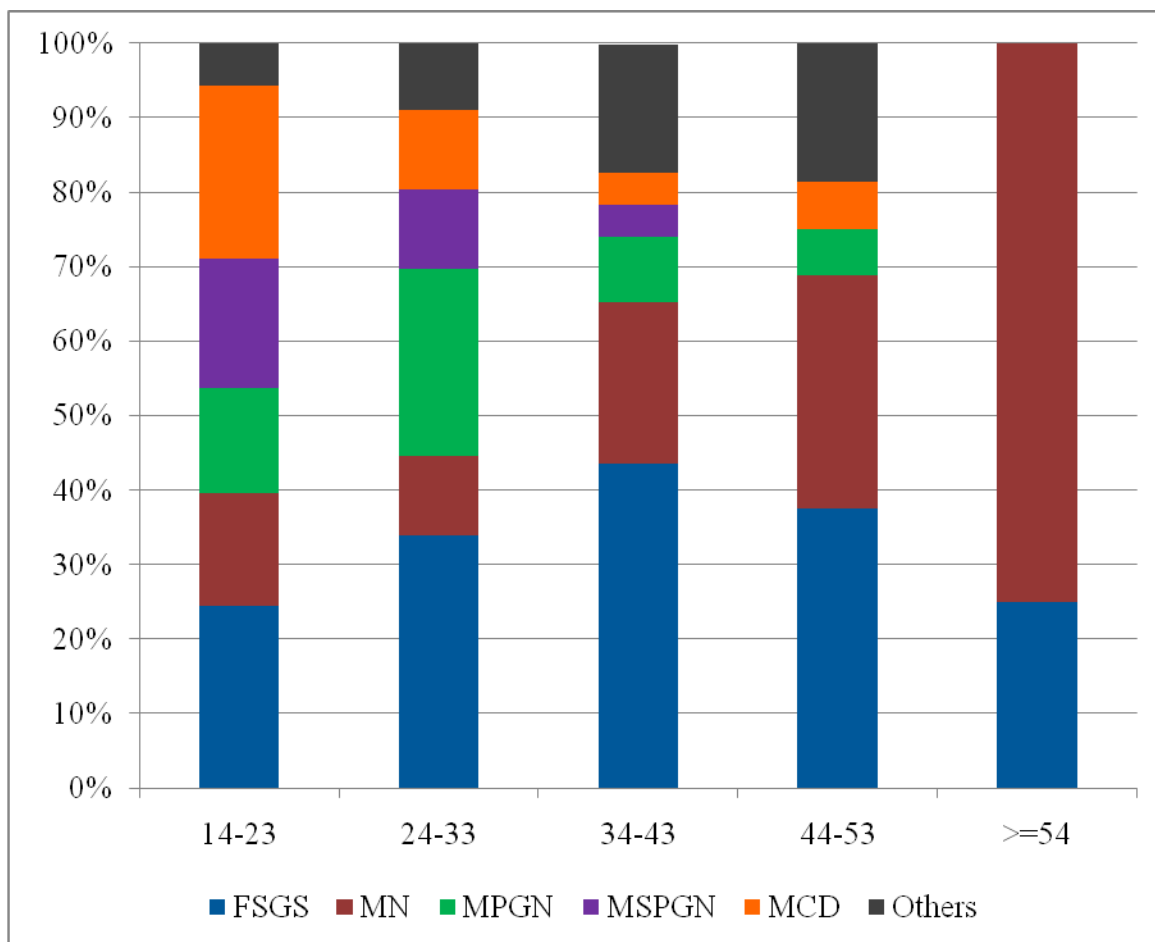
Histology	n(%)	M:F	Mean age (SD)	Age group (%)				
				14-23	24-33	34-43	44-53	>=54
FSGS	58 (30.1)	1.4:1	28.7 (11.4)	21 (24.4)	19 (33.9)	10 (43.5)	6 (37.5)	2 (25.0)
MPGN	29 (15.4)	1.2:1	24.7 (8.1)	12 (14.0)	14 (25.0)	2 (8.7)	1 (6.3)	0 (0.0)
MSPGN	22 (11.4)	1.2:1	20.2 (6.4)	15 (17.4)	6 (10.7)	1 (4.3)	0 (0.0)	0 (0.0)
MN	35 (18.1)	1.9:1	34.7 (15.4)	13 (15.2)	6 (10.7)	5 (21.7)	5 (31.3)	6 (75.0)
MCD	28 (14.5)	1:1	20.5 (9.2)	20 (23.3)	6 (10.7)	1 (4.3)	1 (6.3)	0 (0.0)
DPGN	1 (0.5)	0:1	43.0	0 (0.0)	0 (0.0)	1 (4.3)	0 (0.0)	0 (0.0)
LN	14 (7.3)	1:13	29.4 (10.6)	5 (5.8)	4 (7.1)	3 (13.0)	2 (12.5)	0 (0.0)
Amyloidosis	2 (1.0)	1:1	38.5 (9.2)	0 (0.0)	1 (1.8)	0 (0.0)	1 (6.3)	0 (0.0)

(%) percentage of age group

Trends with age

Age had a considerable influence on various categories of glomerulonephropathies. MCD and MSPGN had a peak incidence in the 14-23 year group with a mean age of 20.5 and 20.2 years respectively; subsequently, there was a steady decline in incidence with none diagnosed in those >54 years. FSGS increased with age with peak age of 34-43. MN also occurred among the older age groups (mean age 37.4) and accounted for 75% (6/8) among the patients aged 54 years and above. (Fig 9)

Figure 9: Distribution of the histological lesions by age among the study population



7.4 ASSOCIATED AETIOLOGICAL FACTORS

The majority of the patients had no associated aetiological factors identified as indicated in Table 7.

Table 7: Frequency of various aetiological factors looked for in the history

Aetiological factor	n (%)
Sore throat	11 (5.7)
Kidney disease	0
Family history of kidney disease	0
Diabetes	0
Hypertension	12 (6.2)
HIV	5 (2.6)
SLE	8 (4.1)
Lymphoma	1 (0.5)
Carcinoma	0
IV drugs	0
Blood transfusion	2 (1.0)
Antihypertensive drugs	8 (4.1)
Alcohol use	21 (10.9)
Smoking	10 (5.2)
Exposure to skin creams	1 (0.5)
Exposure to steroids	17 (8.8)
RA	2 (1.0)
Immunosuppressants	7 (3.6)
Gold	0

The various histologic lesions and the identified aetiological factors are shown in Table 8.

Table 8: Histologic lesions and associated aetiological factors

Histology	Aetiologic factor						
	ASOT	HIV	HBV	HCV	VDRL	LUPUS	RA
MSPGN	9	0	0	0	0	0	0
MN	2	1	3	1	1	6	2
MPGN	2	0	0	1	0	0	0
FSGS	1	7	1	1	0	0	0
MCD	0	0	0	0	0	0	0
OTHERS	0	0	0	0	0	8	0
TOTAL (%)	14 (7.3)	8(4.1)	4(2.1)	3(1.6)	1(0.5)	14(7.3)	2(1.0)

8. DISCUSSION

Glomerular diseases in the tropics differ from those in temperate countries in their epidemiology, aetiology and natural history [2-3]. In this cross sectional descriptive survey, we analyzed the clinical and pathological data of 193 patients.

The patient population in this study was young with a mean age of 27.3 ± 12.3 years with a majority aged between 14 and 23 years. This compares to other studies done locally. A study by Mcligeyo [3] found a peak age of 21-40 years while Kungu *et al* found a peak age of 21-30 [22]. The Kenya Demographic and Health Survey of 2007 reports that most the Kenyan population is young with 45% of the population aged less than 15 years and only 3% of the population aged above 65years[63].

However, glomerular diseases in the USA and European countries occur at later ages. Jennifer B. Hanko *et al* [49] in the changing pattern of adult primary glomerular disease in N Ireland found a mean age of 52 ± 17 years while Jae Hyun Chang *et al* [50] in a Korean study found an average age of 36 years.

Most patients in this study were male (53.4%) and this was similar in all the clinical and histological subtypes. This was also found by Kinuthia *et al* [21] who found a M: F ratio of 1.3:1 however Mcligeyo [3] found more females than males but his study included both children and adults. This is similar to other several published renal biopsy registers where males were predominant [25, 48, 50]. Fu-de Zhou *et al* [48] looking at the changing spectrum of glomerular diseases found a M: F ratio of 1.20:1 and there was a male predominance in all histological types. Nothing so far has been found to explain the male predominance in primary glomerular diseases.

In this study, nephrotic syndrome was the most frequent clinical presentation accounting for 76.4%. Data from surveys of the nephrotic syndrome have shown that it is 60-100 times more common in some tropical countries compared to the United States of America and the United Kingdom. The incidence of nephrotic syndrome as a percentage of medical admissions is 4% in

New Guinea, 2.4% in Nigeria, 2% in Uganda and 1.8% in Kenya as compared to 0.02, 0.03 and 0.04% for China, USA and UK respectively [4-7].

Fu-de Zhou *et al* [48] also found that the most common clinical presentation was NS, followed by chronic nephritic syndrome, asymptomatic urinary abnormality, acute nephritic syndrome and RPGN.

Asymptomatic urinary abnormality was the least frequent clinical presentation (only 1 patient). This may be due to the fact that most of these patients will not come to seek medical care since they are asymptomatic and routine screening of urine for haematuria or proteinuria is not usually carried out in our local setup. Some studies in countries with an active urine-testing programme noted AUA as the most frequent indication for renal biopsy [56].

FSGS was the most common (30.1%) histological lesion overall followed by MN, MPGN and MCD accounting for 18.1%, 15.4% and 14.5% respectively. The picture was the same among the patients with nephrotic syndrome. This is a shift in pattern from local studies done previously showing a significant increase of FSGS with a decrease in MSPGN. Mcligeyo in 1994 [3] and Kungu *et al* in 1978 [22] looking at nephrotic syndrome in adults found the frequency of FSGS to be 9.9 % and 9.3% respectively compared to 30.1% found in this study. In this study MSPGN accounted for 11.4% compared to 27.8% in the study by Mcligeyo [3]. MPGN also increased from about 10% in the studies by Mcligeyo [3] and Kungu [22] compared to 15.4% of all patients with nephrotic syndrome in this study.

Among the patients with elevated ASOT, 64% had MSPGN. With improvement in standards of living, better public health and the early effective antibiotic treatment of pharyngeal infections, it has been reported that the proportion of post-streptococcal acute glomerulonephritis declined in many countries. This has been reported in Spain [51], Tunis [52], the USA [20], India [53] and Brazil [35] as well. This may explain the decline in the proliferative GN.

This study showed that there has been a significant increase in FSGS. Similar results have been demonstrated elsewhere in the USA, Brazil and India [20, 24, 53-55] making this the most common identified primary glomerulopathy in some centers.

In the United States, for example, a survey of renal biopsies performed from 1995 to 1997 for idiopathic nephrotic syndrome in adults found that FSGS was the most common cause, accounting for 35 percent of all cases and over 50 percent of cases among blacks [20].

Of note a higher incidence of FSGS in African Americans has been reported [54, 55]. In a rural area in Massachusetts, Braden *et al.* reviewed the relative frequency of FSGS among adult patients which increased from 13.7% during 1975–1979 to 25% during 1990 to 1994 [24]. Stratified analysis showed a significant increase in the frequency of FSGS in both blacks and Hispanics, and the relative frequency of FSGS increased slightly in whites but did not reach statistical significance.

FSGS is also common in Ghana and in Senegal. Renal biopsies from the patients described in Senegal had an unusual fibrillary splitting of glomerular capillary walls with interposition of basement membrane like material [37]

By comparison, other countries have found that FSGS is a relatively less common cause of the nephrotic syndrome. A Chinese study found no increase in FSGS while in most European studies, IgA nephropathy is the most common histologically diagnosed primary renal disease with no significant increase in FSGS over time [25, 47, 57-58].

This increase trend found in different regions and different races indicated that some genetic and environmental factors might play a role in the pathogenesis of FSGS.

The increase in FSGS in our study population cannot be explained by the use of steroids since among the 18 patients on steroids only 2 were diagnosed with FSGS while the rest had other histological lesions.

There are also a number of well-documented causes of secondary FSGS including infections such as human immunodeficiency virus (HIV) and obesity. The high rates of HIV in our local set up may also partly explain the rising incidence of FSGS this study. Among the patients with HIV in our study, 87.5% (7/8) had FSGS on biopsy. There may also be other unidentified aetiological factors in our local set up that may explain the increase. In this study we did not find an aetiological role for heroin abuse which has also been associated with FSGS.

Data from this population is consistent with the reported differences in frequency of renal disease with patient age. MCD and MSPGN occurred in the younger age groups. Studies have shown MCD is the most common cause of nephrotic syndrome in children [28-31] and in the adults it occurs in the younger age groups as shown by Mcligeyo [3], Kungu *et al* [22] and Barr *et al* [17]. MsPGN is thought to be a variant of MCD or resolving post infectious glomerulonephritis hence its occurrence at an earlier age group.

In this study, MN was found in the older age groups with a mean age of 34.7 years and it occurred in 75% of the patients older than 54 years. This is similar to other studies where it is common in patients older than 40 years [20, 24-26]. MN is also frequently associated with secondary causes like chronic infections, malignancies and use of certain drugs hence its occurrence in the older population.

In most tropical countries, primary glomerular diseases (PGD) are more common than secondary glomerular diseases. In this study, majority of the patients had no associated aetiological factors identified. Local studies by Mcligeyo [3], Kungu *et al* [22] and Kinuthia *et al* [21] also found very few associated etiological factors. This is similar to studies elsewhere. Fu-de Zhou *et al* [48] found that PGD remained the most common renal disease, accounting for 61.7%.

Different infective agents have been implicated in the causation of glomerular disease in the tropics. These include schistosomiasis [14, 15], quartan malaria [7, 8, and 16], filariasis, streptococcal infection, HIV and use of skin lightening cosmetics. [6, 17, 18]

In this study malaria was not implicated in any of the patients while poststreptococcal infection was implicated in the aetiology of proliferative glomerulonephritis.

Skin lightening creams were not found to be of aetiological significance as reported in previous studies. A study by Mcligeyo [3] found that 75% of females with MCD had used a skin lightening cream while in this study only 1 patient reported the use of skin lightening creams.

This study showed that lupus nephritis is an emerging cause of secondary glomerular disease in adults accounting for 7.3%. Most of the previous local studies had not reported lupus as a major secondary cause. Studies by Kungu *et al* [22] and Kinuthia *et al* [21] in the 1970s reported no case of lupus nephritis while a study by Mcligeyo [3] found lupus nephritis in 2.3% of the

patients. This increase may be due to the fact that ANA is currently done routinely on all patients before renal biopsy at KNH and this may not have been the case previously.

HIV was also found to be an emerging aetiological factor (4.1%). The role of HIV in glomerular diseases had not been reported in previous local studies which were done 17 years ago [3, 21, 22]. This can be attributed to the rise of the HIV pandemic in our set up. The majority of patients with HIV (87.5%) had FSGS on biopsy. Emily Koech [64] in 2004 (unpublished data) looking at the clinicopathological manifestations of kidney disease HIV also found FSGS to be the most common histological lesion (83%).

This study shows that post infectious glomerulonephritis still remains an important secondary cause of glomerular disease in our setup especially the younger age groups. 7.3% of the patients had raised antistreptolysin titer with 62.3% having MSPGN on biopsy indicating that MSPGN in our set up is associated with resolving post infectious glomerulonephritis.

9. CONCLUSION

Glomerular diseases still remain an important aspect of tropical nephropathy and are mainly seen in the young age groups with nephrotic syndrome being the most common clinical presentation of glomerular diseases.

Patients with nephrotic syndrome and isolated proteinuria with no microscopic haematuria or casts on urinalysis are likely to have MCD.

FSGS is the most common histological lesion and there has been a significant increase in FSGS over the last few years.

9.1 RECOMMENDATIONS

- Routine screening of urine for proteinuria should be carried out so as to identify patients with asymptomatic urinary abnormality.
- A larger prospective study with all the investigational modalities is indicated to identify secondary causes of glomerular diseases in our local set up.

9.2 STUDY LIMITATIONS

A shortcoming of this study is that we were unable to carry out immunopathological and electron microscopical studies, missing out on secondary causes and making comparisons with studies carried out in industrialized countries less valid.

Another limitation is that the study was carried out in a referral center and thus missed out on patients with asymptomatic urinary abnormality and less severe disease. In this study only one patient was seen with asymptomatic urinary abnormality.

A limitation of the retrospective arm was the incompleteness of some patients' records.

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APPENDIX I: STUDY PROFOMA

BASIC INFORMATION

1. Study No
2. Hospital No
3. Telephone contact
4. Address
5. Age
6. Sex Male¹, Female 2
7. Marital status single, married, separated divorced, widowed
8. Residence Rural periurban urban
9. Educational level none primary, secondary, tertiary
10. Occupation

HISTORY

YES is indicated by 1, NO is indicated by 2

11. Presenting symptoms
dysuria oliguria hematuria flank pain
Other specify.....
12. Duration of current illness in weeks
13. History of oedema- facial , pedal generalized
14. History of previous sore throat
15. Previous kidney disease
16. History of kidney disease in relatives

17. Known associated systemic disease

Diabetes HTN HIV SLE Lymphoma Carcinoma

Others specify.....

18. Previous history of:

Intravenous drug use blood transfusion antihypertensive drugs
Consumption of alcohol smoking

19. Within the past 6 months has there been:

Exposure to skin chemicals, agro or industrial chemicals
Treatment with steroids penicillamine
Treatment with immunosuppressive agents gold

Treatment with other drugs specify-----

Other possible aetiological factors Specify.....

PHYSICAL FINDINGS

20. Blood Pressure (mmHg)

21. Temp (°C).....

22. Pallor Present 1 Absent 2

23. Oedema Present 1 Absent 2

Other findings Specify

LABORATORY RESULTS

- 24. Urine microscopy.....
- 25. Serum albumin (g/l)
- 26. Urea (mmol/l).....
- 27. Serum creatinine (umol/l).....
- 28. GFR (ml/min).....
- 29. RBS (mmol/l).....
- 30. Total cholesterol (mmol/l).....
- 31. Hb (g/dl).....

Positive=1, Negative=2, Not done=X

- 32. HBV HCV HIV ASOT
- 36. Blood slide for malaria parasites
- 37. ANA VDRL

Other tests

Indication for renal biopsy.....

Renal histology findings.....

APPENDIX II: CLINICAL/LABORATORY METHODS

Blood pressure measurements: Blood pressure was measured using a validated sphygmomanometer. It was taken on the right arm with the patient lying supine and propped up in bed with arms at the same horizontal level as the trunk. An average of 2 readings was recorded at least 15 minutes apart.

Oedema was assessed by inspecting for any generalized body, periorbital, or localized swelling and then applying sustained finger pressure on dependent areas e.g. ankles or over sacrum in recumbent patients.

The skin and its appendages were examined for features of systemic illnesses.

Abdominal examination to look for organomegaly was done.

Laboratory methods

Serum urea, creatinine, electrolytes, total protein, urinalysis and hemoglobin assays was performed at the renal unit, KNH.

Urine dipstick- fresh sample of midstream urine was collected in a clean bottle. A reagent strip was inserted into the unspun specimen using multistix from Bayer Diagnostics within 1 hour of urine collection. The reagent strips were stored as per the manufacturer's instructions.

Urine microscopy- a drop of urine was placed on a glass slide, covered with a cover strip and examined under a light microscope.

Urine Albumin Creatinine Ratio -1ml of urine was collected from each patient in a clean bottle and analyzed at Nairobi Hospital laboratory using Abbot Aeroset machine.

Serum creatinine, urea and electrolytes- 2ml of blood was taken from each patient in a biochemically clean bottle and analyzed using the Technicon RA-1000 automatic analyzer, from Bayer.

Full blood count and ESR - 2ml of venous blood was taken in a citrated bottle and sent to KNH haematology Laboratory. The blood was analyzed using a Coulter Counter Model S-Plus IV made by Coulter Education Centre.

Total cholesterol- 2ml of blood was taken in a biochemically clean bottle and the test done at the KNH biochemistry laboratory.

Hepatitis B surface antigen- 2ml of venous blood was taken in a clean bottle and the test done in the KNH immunology laboratory by ELISA method using an ImmunoComb kit manufactured by Orgenics.

Hepatitis C virus antibodies-2ml of venous blood was taken in a clean bottle and the test done in the KNH immunology laboratory by ELISA method using 4TH generation HCV antibody kit from Innogenetics

HIV-2ml of venous blood was taken in a clean bottle and the test done in the KNH immunology laboratory by ELISA method.

ANA- 2ml of blood was taken in a clean bottle and the test done in the KNH immunology laboratory.

Blood slide for malaria parasite was be done at the KNH microbiology laboratory.

VDRL-1ml of blood shall be taken and the slide test done at KNH immunology laboratory. This is a non treponemal antibody test for syphilis

Antistreptolysin O titers (ASOT), RBS -2ml of was taken in a clean bottle and the test done in the KNH biochemistry laboratory.

PTI/INR-2.7 ml of venous blood was collected in a bottle with 0.3ml of sodium citrate. The sample was analyzed at the KNH hematology laboratory using an Instrumentation Laboratory Coagulation machine from Techno med.

APPENDIX III: PROCESSING SCHEDULE FOR RENAL BIOPSY

1. 10% buffered formal saline	1hr	37 ⁰ C
2. 10% buffered formal saline	1hr	37 ⁰ C
3. 95% ethyl alcohol	1hr	37 ⁰ C
4. 95% ethyl alcohol	1hr	37 ⁰ C
5. 95% ethyl alcohol	1hr	37 ⁰ C
6. Absolute ethyl alcohol	1hr	37 ⁰ C
7. Absolute ethyl alcohol	1hr	37 ⁰ C
8. Absolute ethyl alcohol	1hr	37 ⁰ C
9. Xylol	1hr	37 ⁰ C
10. Xylol	1hr	37 ⁰ C
11. Paraffin wax	1hr	60 ⁰ C
12. Paraffin wax	1hr	60 ⁰ C
13. Paraffin wax	1hr	60 ⁰ C
14. Paraffin wax	1hr	60 ⁰ C

APPENDIX IV: STAINING OF SLIDES

H & E STAIN

1. De-paraffinise slides and hydrate in water.
2. Mayer's haematoxylin (5min)
3. Wash in running tap water (10min)/blue nuclei in ammonia water.
4. Rinse in water
5. Rinse in 95% alcohol
6. Stain in eosin (5min)
7. Dehydrate and clear through 2 changes each of 95% ethyl alcohol. Absolute alcohol and xylene (2min each)
8. Mount

RESULTS:	Nuclei-	blue
	Cytoplasm-	pink
	Other tissues-	pink

PERIODIC ACID SCHIFF

1. Hydrate sections
2. Periodic acid 1% (10min)
3. Rinse in water
4. Schiff's reagent (15min)
5. Wash in running tap water (5-10min)
6. Mayer's haematoxylin (2min)
7. Blue nuclei in running water
8. Counter stain with orange G, quick dip (optional)
9. Wash in tap water
10. Dehydrate, clear and mount

RESULTS:	Nuclei-	blue black
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Basement membrane- PAS positive magenta

MASSON'S TRICHROME

1. De-paraffinise and hydrate in water
2. Insert in Bouin's for 1hr at 56⁰C
3. Wash in running water until yellow colour disappears
4. Wash in Weigert's iron haematoxylin (10min)
5. Rinse in 1% acid alcohol
6. Rinse in distilled water
7. Stain in Biebrich scarlet (2min)
8. Rinse in distilled water
9. Insert on 5% phosphotungstic acid (15min)
10. Counter stain in 1% light green
11. Rinse in distilled water
12. Dehydrate, clear and mount

RESULTS Nuclei-	blue black
Muscle-	red
Collagen-	green
Red blood cells-	red

JONE'S SILVER METHALAMINE

1. De-paraffinise and hydrate with distilled water
2. Lugol's iodine (5min)
3. Rinse in distilled water
4. 2.5% sodium thiosulphate
5. Leave sections for 30min in a solution made of 48ml 95% alcohol and 2ml concentrated ammonium. This enhances silver impregnation.
6. Wash well in running tap water then distilled water.
7. Leave in 1% periodic acid
8. Preheat methenamine silver solution at this stage
9. 0.5% thiosemicarbazide

10. Rinse in distilled water
11. Incubate sections in preheated methenamine silver solution at 60⁰C for 60-75min but check microscopically after 45min to assess staining of basement membranes.
12. Rinse in distilled water
13. Tone in 1% gold chloride
14. Rinse in distilled water
15. 2.5% sodium thiosulphate (2min)
16. Wash in distilled water
17. Mayer's haematoxylin (5min)
18. Wash in running tap water
19. Eosin (3min)
20. Dehydrate, clear and mount

RESULTS: Basement membrane-	black
Other tissue	as for H & E

CONGO RED STAIN

1. De-paraffinise in xylene for 5min and hydrate in water.
2. Wash in tap water
3. Stain with hematoxylin (5min)
4. Dip briefly in 1% acid alcohol to differentiate
5. Rinse in water
6. Blue in Scotts tap water
7. Rinse in tap water
8. Flood slide with Congo red stain (10-20min)
9. Wash in 0.2% aqueous NaOH
10. Wash in water
11. Dehydrate, clear in xylene and mount.

APPENDIX V: CONSENT FORMS

Consent Explanation before Recruitment

I am Dr. Muthui Beatrice, a postgraduate student in Internal Medicine at the University Of Nairobi. I would like to inform you / your next of kin that I am conducting a study on ‘The clinicopathological profile of glomerular diseases at the Kenyatta National Hospital’. I would also like to inform you that:

Joining the study is voluntary and no payments will be charged to you due to participation in the study.

Participation in the study will not delay your treatment in any way and will be beneficial to you.

You may decline to participate in the study or drop out at will and this will not lead to any denial of treatment or any form of care in the hospital.

The clinical pathological profile will entail that once you agree to participate in the study, you will answer questions of personal nature as laid in the study proforma, I will carry out a full physical examination and take some blood for laboratory tests. You will feel a little pain as is normal with standard phlebotomy and the amount of blood drawn will not affect your health.

Any results obtained will be communicated to your primary physician for the appropriate therapy to be instituted.

The information obtained from you will be treated with utmost confidentiality. Any publications arising out of the study will not identify you or your next of kin in person.

If you have understood the information that we have given you and you are willing to participate in the study, you will be required to sign a form indicating your willingness to be recruited.

If you have any questions about this study, you may contact Dr. Muthui B.N at the following contact addresses: Tel: 0721 278 036

STATEMENT OF CONSENT BY THE PATIENT OR NEXT OF KIN / GUARDIAN

The purposes of this study, procedure, study benefits and my rights / patients' rights have been fully explained to me. I hereby give my written consent to allow myself / my to participate in the study.

NAME:..... SIGNATURE:

DATE:

WITNESS SIGNATURE:

DATE:

STATEMENT OF ASSENT FOR MINORS

The purposes of this study, procedure, study benefits and my rights have been fully explained to me. I hereby give my written assent to allow myself to participate in the study.

NAME:..... SIGNATURE:

DATE:

WITNESS SIGNATURE:

DATE:

INTERVIEWER'S STATEMENT

I have explained the purpose and benefits of this study to the respondent. To the best of my knowledge and conviction, he / she has understood and has given consent.

INTERVIEWER: SIGNATURE:

DATE:

CONSENT FOR RENAL BIOPSY

Iofhereby consent to undergo a renal biopsy. I have understood the importance of a renal biopsy in the management of my condition and that the information obtained will be used in the study on 'Clinicopathological profile of glomerular diseases at The Kenyatta National Hospital' being undertaken by Dr. Beatrice Muthui. The procedure and its complications have been explained to me. I therefore willingly agree to have the procedure and for the information obtained to be used in the study.

SIGNED..... WITNESS.....

DATE