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ORIGINAL ARTICLE

Role of kidney biopsy in diagnosis of different patterns of kidney diseases: A single -Center Experience

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ABSTRACT

Background: The diagnosis of kidney diseases still highly depends on kidney biopsies, despite advancements in non-invasive chemical and imaging diagnostics. This research aims to study the frequency of different types of kidney diseases through histopathological findings of kidney biopsies and to evaluate the outcomes of different pathological patterns.

Methods: This prospective observational cohort study involved 56 patients who indicated renal biopsy from January 2022 to June 2022. Percutaneous, ultrasound-guided percutaneous core needle biopsies were performed in the prone position. Two kidney biopsy core specimens were obtained. The biopsy tissues were prepared on routine standard protocols for histopathology using light microscopy and immunohistochemistry. Follow up of patients was done for 6 months regarding response to treatment and disease outcome.

Results:56 patients were included, their mean age was 36.6±14.1 years. 12.5% of patients presented with sub-nephrotic proteinuria, 23% of patients presented with sub-nephrotic proteinuria with renal impairment, 23% presented with nephrotic syndrome, 30% of patients presented with nephrotic proteinuria with renal impairment. The most common pathological findings were focal segmental glomerulosclerosis (FSGS) (25%) followed by lupus nephritis (LN) (19.6%). The most prevalent pathological lesions in the young age group were LN and MCD while in the older age group were hypertensive nephrosclerosis and diabetic nephropathy (DN).

Conclusions:FSGS and LN were the most prevalent patterns. The most common pathological patterns at a young age were MCD followed by LN and FSGS. While the most common pattern in the older age group was DN and hypertensive nephrosclerosis. Partial and complete remission had been seen in 38.3% of all pathological lesions.

Keywords: Kidney biopsy, pathological patterns, kidney diseases.

INTRODUCTION

The diagnosis of kidney diseases still highly depends on kidney biopsies, despite advancements in non-invasive chemical and imaging diagnostics. Kidney biopsies offer prognostic information that may lead to modification of treatment in up to 74% of patients (1). Furthermore, a kidney biopsy is required to determine the extent of active and chronic histological changes, as

well as to decide on the best course of treatment (2). The incidence of renal disease patterns identified by renal biopsy depends on race, age, gender, environmental, nutritional, and socioeconomic factors (3,4). The previous study has suggested that the pattern of incidence of glomerular diseases in different parts of the world is changing (5). Geographical differences affect glomerular disease prevalence. For instance, immunoglobulin A nephropathy (IgAN) is more common in Asia, Australia, and southern Europe (20% to 40%) than it is in the United States (US), the United Kingdom (UK), Canada, South America, and Africa (2% to 10%) (6). Furthermore, age affects the prevalence of the glomerular disease. In contrast to MCD, which is the main cause of glomerulonephritis (GN) and nephrotic syndrome in children, previous research has revealed that membranous nephropathy (MN) is the most frequent cause of nephrotic syndrome in adults. When compared to younger individuals, elder people have a higher relative proportion of crescentic and FSGS (7,8).

Regarding racial differences and the geographic distribution of kidney diseases, epidemiological research on the renal disease is very informative. IgAN is the most prevalent primary glomerular disease in Australia, Finland, southern Europe, and Asia (Japan, Singapore, and Hong Kong) (9,10,11). The Saudi Arabian Registry reports that FSGS is the most common glomerular disease in the Middle East (12). MN is the most prevalent primary cause of nephrotic syndrome in a population of northern European Caucasians (13).

Since the prevalence of kidney diseases varies between regions of the same country as well as between different parts of the world. The current study was conducted at Zagazig University Hospital to demonstrate the current frequency of various types of renal disease through histopathological findings in this area and to evaluate the outcomes of different pathological patterns.

MATERIAL AND METHODS

This prospective observational cohort study involved 56 patients who indicated renal biopsy from January 2022 to June 2022. Each patient provided informed written consent to participate in this research study, which was authorized by the university hospital's institutional ethics board (ZU-IRB #9134). Every procedure followed the Helsinki Declaration.

Inclusion criteria: The study included patients above 18 years old who indicated renal biopsy.

Exclusion criteria: Patients below 18 years old were not included. We temporarily excluded patients with bleeding disorders or active urinary tract infections until bleeding control or treatment of infection.

Each participant was submitted to history taking (hypertension, diabetes mellitus, smoking, autoimmune diseases, chronic kidney disease (CKD), nephrotoxic drugs), comprehensive physical examination, as well as investigations to establish inclusion and exclusion criteria, including the following: serum creatinine (mg/dl), serum albumin (gm/dl), serum total protein (gm/dl), urine microscopy, 24 hour urinary protein (gm/day), hepatitis C virus antibody (HCV-Ab), hepatitis B surface antigen (HBsAg), Human Immunodeficiency virus antibody (HIV-Ab), serology, antinuclear antibody (ANA), anti-double stranded DNA antibody (Anti-dsDNA), complements levels 3&4 (C3, C4) (mg/dl), ESR, CRP (mg/L), hemoglobin level (gm/dl), and coagulation profile, pelviabdominal sonography.

The indications for kidney biopsy were: sub-nephrotic proteinuria, nephrotic syndrome, sub-nephrotic proteinuria with renal impairment, nephrotic syndrome with renal impairment, RPGN, and unexplained renal impairment.

Percutaneous, ultrasound-guided percutaneous core needle biopsies were performed in the prone position. Two kidney biopsy core specimens were obtained. A pathologist verified the specimen's adequacy based on the number of glomeruli.

Histopathology of renal biopsy tissue was done. The biopsy tissues were prepared on routine standard protocols and light microscopy and immunohistochemistry were done for all biopsies.

The specific treatment was started according to the biopsy results depending on the

KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases (14) and follow up of patients was done for 6 months.

The primary outcomes during the follow up period were kidney disease outcomes which included: disease remission, which will be partial, complete, or resistant to treatment, disease progression to CKD or ESRD, and AKI resolving. According to the Kidney Disease Improving Global Outcomes (KDIGO), treatment effects were classified into complete remission (CR), partial remission (PR), and no response (NR). CR was defined as a urinary protein excretion of <0.3 g/day, accompanied by normal serum concentrations of albumin and serum creatinine. PR was defined as the urinary protein excretion between 0.3 g/day and 3.5 g/day or a proteinuria decline by at least 50% from the initial value, and improvement or normalization of serum albumin concentration, a stable level of serum creatinine. NR was defined as no improvement in urine protein excretion and serum albumin levels (15).

The secondary outcome was the incidence of mortality after the kidney biopsy and starting the specific treatment.

Statistical methods:

The statistical testing was done utilizing the SPSS program (Statistical Package for Social Science version 24 and NCSS 12, LLC, USA). We reported continuous variables as mean (SD) and categorical variables as numbers (%). Age and laboratory data were presented as values at the time of biopsy. Descriptive statistics were used for the analysis.

Results:

Basic patients' characteristics and clinical presentations:

56 patients were included in this study; their age mean was 36.6±14.1 years. 34 (60.72%) patients were males while 22 (39.28%) patients were females. 13% of patients presented with sub-nephrotic proteinuria, 23% of patients presented with sub-nephrotic proteinuria and renal impairment, 23% presented with nephrotic syndrome, 30% of patients presented with nephrotic proteinuria and renal impairment, 4% of patients presented with RPGN while 7% of patients were presented with unexplained renal impairment with mean serum creatinine was 2.7±2.4 mg/dl. For more details, please refer to table 1 and figure1.

Distribution of renal Biopsy in patients' populations:

56 Native kidney biopsies were taken with no reported complications. The most common pathological findings were FSGS in 25% of patients followed by LN in 19.6 % of patients more dominant class 3 and 5 in 27.2% of total LN cases. MCD was prevalent in 7.1% of cases, the least pathological findings were small vessels vasculitis, renal amyloidosis, hypertensive nephrosclerosis, and DN (in 1.8% of cases) (table 2).

Demographic distribution of pathological kidney diseases:

The most prevalent pathological lesions in the young age group were LN and MCD while the most common pathological lesions in the older age group were hypertensive nephrosclerosis and DN (table 3).

FSGS and LN were common in female patients (21.4 % and 17.8% respectively) while the most common pathological lesion in male patients was MN in 12.5 % of patients (table 3).

The most common lesions presented with microscopic hematuria were FSGS and Chronic Interstitial nephritis (CIN) (in 16% and 12.5% of cases) (table 3). However, the most common lesions presented with nephrotic proteinuria with renal impairment were MN and FSGS (7.1% for each), while the most common lesions presented with nephrotic syndrome were MN (8.9%) followed by FSGS (7.1%) (table 4).

Outcomes of kidney diseases diagnosed by kidney biopsy:

Complete remission had occurred in 27.6% of patients while partial remission had been seen in 10.7% of pathological lesions. LN was the most common lesion for complete remission followed by FSGS, while MN was the most common lesion for partial remission followed by LN. Progression to ESRD had seen in 27.6% of lesions which had been seen more in patients with FSGS followed by CIN. Progression to CKD had occurred in 19.6% of patients which was more in patients with CIN

followed by MN and acute interstitial nephritis (AIN). The death occurred in only 1 patient with acute cast nephropathy (table 5).
When studying factors may affect the kidney disease outcome, we found Age, smoking, proteinuria, serum creatinine level, and CRP had significant effect on the disease outcome (table 6). Among these factors, age is the only independent risk factor that related to disease outcome (unstandardized β=0.045 p=0.005) (Table 7).

Table1: Basic demographic and laboratory characteristics of the studied group.

	Total Number of patients No 56 (%)
Age (Y)	36.6 ±14.1
Sex Male/female	 34 /22 (60.7/39.2)
BMI (kg/m^2)	24.2±1.3
Smoking	12 (21.4)
Comorbidities: Diabetes Hypertension HCV HBV HIV	 2 (3.6) 10 (17.9) 2 (3.6) 0 (0) 0 (0)
ANA +ve	12 (21.4)
Systolic Blood pressure (mmHg)	145.8 ±21
Diastolic blood pressure (mmHg)	89.3 ±11.5
HB (gm/dl)	10.9 ±2.3
Creatinine (mg/dl)	2.7 ±2.4
Total protein (gm/dl)	6.0 ±1.4
Serum albumin (gm/dl)	3.4 ±1.1
Cholesterol (mg/dl)	246.9 ±107.3
Triglyceride (mg/dl)	213.7102.2 ±560.3
24 h urine protein (gm/day)	4.8 ±4.3
Urine RBC (HPF)	7.3±6.7
C3 (mg/dl)	110.7 ±42.4
C4 (mg/dl)	23.9 ±10.0
ESR 1st H	50.5 ±29.0
ESR 2nd H	82.9 ±34.0
CRP (mg/l)	14.8 ±30.0

Table 2. Pathologic distribution of renal disease

Diagnosis	**Value No 56 (%)**
Biopsy: **1- LN:** - Lupus Nephritis class 3,4 - Lupus nephritis class 3 - Lupus nephritis class 4 - Lupus nephritis class 2 - Lupus Nephritis class 5 2- **FSGS** 3- **CIN**	 11 (19.6) 1 (1.8) 3 (5.4) 2 (3.6) 2 (3.6) 3 (5.4) 14 (25) 7 (12.5)

Diagnosis	Value No 56 (%)
4- **MN**	9 (16.1)
5-AIN	4 (7.1)
6-Cresentic GN	2 (3.6)
7- Acute cast nephropathy	1 (1.8)
8- MCD	4 (7.1)
9- Small vessels vasculitis	1 (1.8)
10-Renal amyloidosis	1 (1.8)
11-Hypertensive nephrosclerosis	1 (1.8)
12-DN	1 (1.8)

LN, lupus nephritis, FSGS, focal segmental glomerulosclerosis, MCD, Minimal change disease, CIN, Chronic interstitial nephritis, AIN, acute interstitial nephritis, MN, membranous nephropathy, DN, diabetic nephropathy, GN, Glomerulonephritis

Table 3: Demographic characteristics of different pathological patterns

	Age Mean ±SD	Female No (%)	Male No (%)	BMI kg/m^2	Hematuria No (%)
LN	29.7±12.5	10 (17.8)	1 (1.7)	20.4±2.2	4 (7.1)
FSGS	32.9±15.1	12 (21.4)	2 (3.5)	25.5±4.8	9 (16.0)
CIN	40.7±15.4	2 (3.5)	5 (8.9)	26.7±4.7	7 (12.5)
MN	40.3±11.6	2 (3.5)	7 (12.5)	25.5±2.5	4 (7.1)
AIN	45.7±15.7	1 (1.7)	3 (5.3)	20.8±2.0	3 (5.3)
Crescentic GN	38.5±12.0	0 (0)	2 (3.5)	23.0±0	2 (3.5)
Cast Nephropathy	46±0	1 (1.7)	0 (0)	27.0±0	1 (1.7)
MCD	24.9±1.1	2 (3.5)	2 (3.5)	24±1.8	1 (1.7)
Small Vessels Vasculitis	42.0±0	0 (0)	1(1.7)	26.0±0	1(1.7)
Renal Amyloidosis	47.0±0	1 (1.7)	0 (0)	27±0	0 (0)
Hypertensive nephrosclerosis	64.0±0	0 (0)	1 (1.7)	21	0 (0)
DN	60±0	0 (0)	1(1.7)	28	1 (1.7)
No. (%)		34	22		33

LN, lupus nephritis, FSGS, focal segmental glomerulosclerosis, MCD, Minimal change disease, CIN, Chronic interstitial nephritis, AIN, acute interstitial nephritis, MN, membranous nephropathy, DN, diabetic nephropathy, GN, Glomerulonephritis.

Table 4: Clinical presentation of different pathological pattern

		No (%)
Sub-nephrotic proteinuria No (%) 7 (12.5)		
	LN	4 (7.1)
	FSGS	3 (5.3)
Sub-Nephrotic proteinuria with renal impairment No (%) 13 (23.2)		
	LN	4 (7.1)
	FSGS	3 (5.3)
	CIN	3 (5.3)
	AIN	1 (1.7)
	Cast nephropathy	1 (1.7)
	Hypertensive nephrosclerosis	1 (1.7)
Nephrotic proteinuria with renal impairment No (%) 17 (30.3)		

	No (%)	
	LN	3 (5.3)
	FSGS	4 (7.1)
	CIN	2 (3.5)
	MN	4 (7.1)
	AIN	1 (1.7)
	Crescentic GN	1 (1.7)
	Renal Amyloidosis	1 (1.7)
	DN	1 (1.7)
Nephrotic syndrome No (%) 13 (23.2)		
	FSGS	3 (5.3)
	MN	5 (8.9)
	MCD	4 (7.1)
	AIN	1 (1.7)
Unexplained Renal impairment No (%) 4 (7.1)		
	FSGS	1 (1.7)
	CIN	2 (3.5)
	AIN	1 (1.7)
RPGN No (%) 2 (3.5)		
	Crescentic GN	1 (1.7)
	Small vessels vasculitis	1 (1.7)

LN, lupus nephritis, FSGS, focal segmental glomerulosclerosis, MCD, Minimal change disease, CIN, Chronic interstitial nephritis, AIN, acute interstitial nephritis, MN, membranous nephropathy, DN, diabetic nephropathy, GN, Glomerulonephritis.

Table 5: Outcome of kidney diseases diagnosed by kidney biopsy

	Complete remission	ESRD	Resistant to treatment	CKD	Partial remission	Resolved AKI	Death
LN	7	2	0	0	2	0	0
FSGS	6	8	0	0	0	0	0
CIN	0	3	0	4	0	0	0
MN	1	1	1	3	3	0	0
AIN	0	0	0	2	0	2	0
Crescentic GN	0	1	0	0	0	1	0
Acute cast Nephropathy	0	0	0	0	0	0	1
MCD	3	0	0	0	1	0	0
Small Vessels Vasculitis	0	1	0	0	0	0	0
Renal Amyloidosis	0	0	0	1	0	0	0
Hypertensive nephrosclerosis	0	1	0	0	0	0	0
DN	0	0	0	1	0	0	0
No. (%)	17 (27.6)	17 (27.6)	1 (1.7)	11 (19.6)	6 (10.7)	3 (5.3)	1 (1.7)

LN, lupus nephritis, FSGS, focal segmental glomerulosclerosis, MCD, Minimal change disease, CIN, Chronic interstitial nephritis, AIN, acute interstitial nephritis, MN, membranous nephropathy, DN, diabetic nephropathy, GN, Glomerulonephritis.

Table 6: Risk factors affecting kidney diseases outcome

Variable	Partial remission	Complete remission	Resistant to treatment	CKD	ESRD	Death	Resolved AKI	F-Test	P value
Age	37±12.3	26.1±10.6	55	42.8±15.4	40.1±13.7	46	43.3±14	2.974	0.015*
Sex Male/female	3/3	7/10	1/0	7/4	13/4	0/1	3/0	**(χ^2)** 0.400	0.176
BMI	23.1±2.7	23.3±4.2	29	24.9±3.9	25±4.4	27	22.5±2.2	0.803	0.124
Smoking No/Yes	4/2	17/0	0/1	11/0	9/8	1/0	2/1	**(χ^2)** 0.582	0.004**
Hypertension no/yes	5/1	16/1	1/0	10/1	10/7	1/0	3/0	**(χ^2)** 0.415	0.141
DM No/Yes	6/0	16/1	1/0	10/1	17/0	1/0	3/0	**(χ^2)** 0.201	0.893
Serum creatinine	1.6±0.82	0.73±0.18	0.9±0	2.7±1.4	4.2±2.0	2.5±0	8.7±3.0	16.051	0.000**
Proteinuria	7.1±3.7	4±3.2	15	6.2±4.9	4.4±4.2	0.5	0.3	41.668	0.028*
C3	104±56.5	107.5±40.2	136±0	122.0±30.3	118.1±35.9	156±0	36.0±49.9	2.367	0.44
C4	23.6±12.4	25.3±10.6	13.0±0	23.8±9.3	23.9±9.6	29±0	18.3±12.5	0.422	0.861
ESR 1st H	36.8±9.6	52.2±21.1	80±0	48.7±25.3	56.0±40.8	80.0±0	24.0±7.9	1.1	0.367
ESR 2nd H	63.3±23.1	87.0±22.3	110.0±0	83.6±34.1	86.1±44.6	130.0±0	53.3±25.1	1.2	0.308
CRP	7±1.2	16.9±28.7	8	8.1±2	7.7±3.9	9	73±109	2.666	0.026*
ANA No/Yes	4/2	9/8	1/0	11/0	15/2	1/0	3/0	**(χ^2)** 0.471	0.053
HCV	5/1	16/1	1/0	11/0	5/1	1/0	3/0	**(χ^2)** 0.283	0.613

*p<0.05 is statistically significant **p≤0.001 is statistically highly significant **F** ANOVA test
χ^2 chi square test

Table (7): Linear stepwise regression analysis of factors significantly associated with kidney diseases outcome

	Unstandardized Coefficients		Standardized Coefficients	T	P	95.0% Confidence Interval	
	B	Std. Error	Beta			Lower	Upper
Constant	0.711	0.699		1.030	0.308	-0.673	2.095
Age	0.045	0.015	0.379	2.959	**0.005***	.014	.075
Smoking	0.235	.558	.057	.421	.675	-0.884	1.353
CRP	.012	0.007	0.211	1.605	0.115	-.003	.027
Proteinuria	0.044	0.051	0.111	0.854	0.397	-.059	.146

*p<0.05 is statistically significant

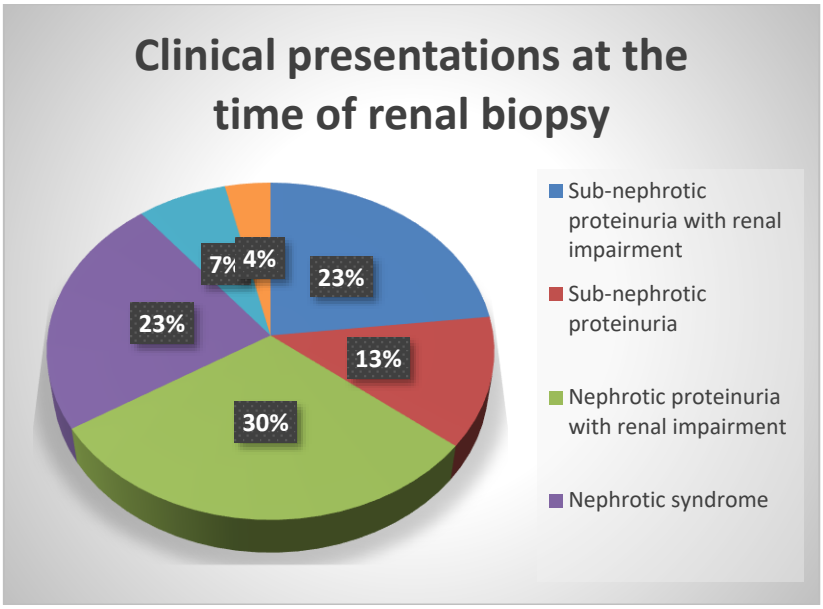

Figure 1: Clinical presentations at the time of renal biopsy

DISCUSSION

In this study, we evaluated the clinical and pathological features of renal disease in 56 patients who presented to Zagazig university hospital aiming to study the pathological patterns of kidney diseases in this geographic region. Moreover, we studied the outcome of treatment of the different pathological renal patterns.

In this descriptive study, we have found that patients who underwent kidney biopsies were at young middle age. In our study, the mean age was 36.6±14.1 years. It is consistence with a previous report which has been done in South Korea (16) and showed that the mean age of the participant was 37.7 ± 16.5 years. However, the mean age of our study was lower than those in other studies. The average age of Japanese patients in the Japan renal biopsy registry was 44.4 ± 21 years (17). In our cohort, the male sex group was predominated with almost 60% of patients being males. This result is compatible with another previous report (16) which showed that the main sex predominant was the male gender. According to earlier cohorts, males typically predominate in glomerular diseases or the sex ratio is equal in cases of MCD, FSGS, MN, MPGN, IgAN, and HSP nephritis (18).

In this study, we have found that the main indication for kidney biopsy was a nephrotic syndrome with abnormal renal function which was present in 30% of patients followed by patients with sub-nephrotic range proteinuria with abnormal renal function in 23% of cases while patients with nephrotic syndrome with normal kidney function were found in 23% of cases. In a previous report (19), the nephrotic syndrome was the most prevalent manifestation in patients who had a biopsy, followed by glomerulonephritis, CKD, and AKI. In our cohort, the most common pathological findings were FSGS in 25% followed by lupus nephritis in 19.6%. This result was consistent with another previous report from Brazil 2021 (22) when they confirmed that for primary glomerulonephritis, FSGS was the prevalent histological finding followed by IgAN, MN, MCD, and MPGN.

The main pathological lesions in the younger age group were LN followed by MCD while the most common pathological lesions in the older age group were hypertensive nephrosclerosis and DN. In a previous descriptive report (16), they found that IgAN was the most prevalent primary glomerular disease (37.4%), while LN was the most prevalent secondary form (4.6%). The difference between both studies can be explained by the small number of patients included in our cohort compared with the previous study and the difference in ethnic populations between the two studies.

DN and hypertensive nephrosclerosis were predominate in the older age group and this was consistence with previous studies (19,20)

which showed that DN was the main pathological finding in elderly patients. Moreover, another previous study (22) showed that DN was prevalent at the age of 60 years, and systemic vasculitis and monoclonal gammopathies in those over 65 years of age. Compared to earlier studies, the incidence of DN in older individuals has greatly increased in recent years due to improvements in people's living conditions (21).

In this cohort, the most common lesions presented with nephrotic proteinuria with renal impairment were MN and FSGS. It is consistence with the result of a previous study (22) which showed that nephrotic proteinuria and hypoalbuminemia were the most common clinical presentations in patients with MCD, FSGS, MN, and MPGN, while in patients with IgAN and MPGN, the prevalence of sub nephrotic proteinuria was more frequent.

Renal biopsies help in identifying an accurate histopathological diagnosis and the optimum treatment plan. In a previous study (19), they retrospectively analyzed the renal disease spectrum in 7,122 patients and they noted that 79.9% of primary glomerulonephritis patients who received immunosuppressive therapy showed a remission rate of 83.5%. In our study, the complete remission rate was 27.6% while partial remission occurred in 10.7% for all pathological patterns of kidney disease. However, progression to ESRD was 27.6% and this indicated the importance of kidney biopsy in diagnostic approaches and early treatment intervention to achieve a high percentage of complete remission and to delay the progression to ESRD.

In recent Chinese study on 375 patients, 25% of patients achieved complete remission, 63% achieved partial remission (23). However,, in another recent large cohort study which was done on elderly Chinese patients, 79.9% of primary glomerulonephritis patients who received immunosuppressive therapy showed a remission rate of 83.5% (19). The higher rate of remission in this study can be explained by the different glomerular pathological lesions, different ethnic populations and more populations included in that study.

Our study has some limitations: First, it was of a small sample size which could have a drawback effect on the conclusion of the study. Second, because it was a single center study, the findings might not accurately reflect the prevalence of glomerular diseases at other centers. The third one is that we did not do electron microscopy due to unavailability at our center. Fourth, we did not do a second kidney biopsy to see the effect of treatment response as we relied only on clinical and laboratory responses. Finally, the short sex months follow period up could have limitations in full disease outcomes, especially for patients with partial remissions.

CONCLUSIONS

FSGS and LN were the most prevalent patterns in patients with primary glomerulonephritis. The most common pathological patterns at a young age were MCD followed by LN and FSGS. While the most common pattern in the older age group was DN and hypertensive nephrosclerosis. Partial and complete remission has been seen in 38.3% of all pathological lesions, while only one case expired during follow up period. Renal biopsy is a relatively safe procedure and can help in deciding the choice of treatment and hence, can improve the prognosis. Further prospective studies with bigger numbers of patients and longer follow up periods are recommended to confirm the results.

Declaration of interest and Funding information:

The authors report no conflicts of interest.

Authors' contributions: A.A. and E.A. formulated and designed the study; T.G. was a major contributor in writing the manuscript; A.A, S.S. and T.G. analyzed the data; E.A. and A.A. revised the paper. All authors read and approved the final manuscript.

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