Original Article

DOI: https://doi.org/10.70749/ijbr.v2i02.166

INDUS JOURNAL OF BIOSCIENCES RESEARCH
https://induspublisher.com/IJBR
ISSN: 2960-2793/ 2960-2807

The Renal Histopathological Spectrum of Patients with Nephrotic Syndrome Presenting to Nephrology Division Khyber Teaching Hospital, Peshawar, Pakistan

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ARTICLE INFO

Keywords

Histopathological Spectrum, Membranous Glomerulonephritis, Lupus Nephritis, Minimal Change Disease, Nephrotic Syndrome, Khyber Teaching Hospital

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Declaration

Author's Contributions: All authors contributed to the study and approved the final manuscript.
Conflict of Interest: The authors declare no conflict of interest.
Funding: No funding received.

Article History

Received: 20-10-2024
Revised: 28-10-2024
Accepted: 07-11-2024

ABSTRACT

Introduction: This study investigated the renal histopathological patterns in nephrotic syndrome patients who underwent renal biopsy at the Department of Nephrology, Khyber Teaching Hospital, between March 2023 and October 2024. It aimed to identify the underlying glomerulopathies responsible for nephrotic syndrome in these patients.
Methodology: The study included 122 nephrotic syndrome patients, aged 7 to 69 years, categorized into four age groups. Renal biopsies were analyzed using light microscopy and immunofluorescence. The chi-square test assessed the association between histological variants and categorical variables such as gender and age groups.
Results: Out of 122 patients, 80 (65.6%) were male and 42 (34.4%) females, with a mean age of 34.28 ± 14.81 years. Membranous Glomerulonephritis (35.2%) was the most common diagnosis, followed by Focal and Segmental Glomerulosclerosis (18.0%) and Lupus Nephritis (14.8%). Minimal Change Disease affected 10 patients, primarily younger individuals. HIV-Associated Nephropathy (0.8%) and Diabetic Nephropathy (1.6%) were the least frequent. Significant associations were found between histopathological variants and both age and gender (p-values 0.000 and 0.001, respectively), with Lupus Nephritis more common in females and Membranous Glomerulonephritis in males. These findings highlight age- and gender-specific trends.
Conclusion: Membranous Glomerulonephritis is most prevalent, especially in males and younger adults, while Lupus Nephritis is primarily seen in females. Minimal Change Disease is significantly associated with younger individuals, particularly those under 24, with no cases in older patients, suggesting it predominantly affects pediatric or young adult populations.

INTRODUCTION

Nephrotic syndrome, a common kidney disorder, manifests through various histopathological patterns, with notable geographical and demographic variations. In Pakistan, limited data exists on the renal histopathological spectrum, particularly within the Khyber Pakhtunkhwa province. This study, conducted at the Nephrology Division of Khyber Teaching Hospital in Peshawar, aims to fill this knowledge gap by exploring the distribution of histopathological variants in nephrotic syndrome patients.

Nephrotic syndrome is defined by a specific combination of clinical and laboratory manifestations, which include significant proteinuria (exceeding 3.5g in a 24-hour period), low serum albumin levels (less than 3.5g/dl),

increased lipid levels in the blood, and generalized body swelling.[1-7] Glomerular injury frequently presents with this condition. The cause of the glomerular damage may be unclear, classifying it as primary or idiopathic glomerulonephritis (GN), or it could result from a known disorder or systemic disease, referred to as secondary GN. In adults, primary GN accounts for about 60% of all GN cases.[4] Recent reports from various regions worldwide indicate that focal segmental glomerulosclerosis (FSGS) is the most prevalent pathological lesion causing nephrotic syndrome in adults. It is followed by membranous glomerulonephritis (MGN) and minimal change disease (MCD), along with a range of other less common lesions. [8-16]

The aim of this study was to examine the spectrum of pathological lesions in renal biopsies from nephrotic patients in this region, by using all necessary available diagnostic methods to establish a definitive diagnosis for glomerulonephritis (GN), and to compare our results with those documented in global literature.

METHODOLOGY

This study was a retrospective clinico-pathologic analysis in which clinical and histopathological data were gathered by reviewing original renal biopsy reports from patients with nephrotic syndrome who attended the nephrology unit at Khyber Teaching Hospital between 01 March 2023 and 15 October 2024. All patients with unexplained nephrotic syndrome who underwent percutaneous renal biopsy were included. The standard diagnostic criteria for nephrotic syndrome were applied for inclusion. Each of these patients received an ultrasound-guided percutaneous needle biopsy using an automated gun after obtaining informed consent. At our unit, two cores from each native renal biopsy were routinely obtained for comprehensive pathologic evaluation, including light microscopy and immunofluorescence.

Study Design

Utilizing a cross-sectional study approach, the renal histopathological spectrum of nephrotic syndrome of individuals has been identified.

Study Area

This study was conducted in the Nephrology Department of Khyber Teaching Hospital, Peshawar.

Study Duration

The study spanned a total duration of almost twenty months, from 01 March 2023 to 15 October 2024.

Sample Size

A total of 122 patients, ranging in age from 7 to 69 years with nephrotic syndrome who were biopsied in study time were included in the study.

Inclusion Criteria

Patients diagnosed with nephrotic syndrome on clinical basis (significant proteinuria exceeding 3.5 g in a 24-hour period), serum albumin levels less than 3.5mg/dl) were included in the study. Patients undergone renal biopsy were included in the study.

Exclusion Criteria

Patients with contraindications for biopsy were excluded from the study. Patients previously treated for nephrotic syndrome were excluded from the study.

DATA COLLECTION

Demographic variables: Age and gender of patients at time of biopsy. The patients were stratified into four distinct age groups for analysis: those under 24 years, those aged 25 to 44 years, those aged 45 to 59 years, and those aged 60 years and older.

Histopathological Results: A kidney biopsy was performed, and every patient's histolopathological results were documented**;** Minimal change disease (MCD), Renal amyloidosis, C1q nephropathy ,C3 nephropathy, Diabetic nephropathy, Focal and segmental glomerulosclerosis (FSGS), HIV associated nephropathy(HIVAN), IgA nephropathy, IgM nephropathy, Lupus nephritis, Membranoproliferative glomerulonephritis (MPGN), membranous glomerulonephritis.

Statistical Analysis

Demographic data and histopathological results data sets were examined by using statistical tests such as means, SD and frequencies. The chi-square test was used to evaluate the association between various histopathological variants of nephrotic syndrome and variables like age groups and gender. A p-value of less than 0.05 indicated statistically significant differences.

RESULTS

The study analyzed data from a sample of 122 patients. 80 patients (65.6%) were male, while 42

patients (34.4%) were female. This indicates that the majority of the patients are male, comprising nearly two-thirds of the total population (table 1). The age of the patients ranged from a minimum of 7 years to a maximum of 69 years, with the mean age of 34.28 years. The standard deviation was 14.811, indicating the extent to which individual ages varied from the mean. This standard deviation suggests that there was a moderate spread of ages around the average, reflecting some variability in the age distribution among the patients. The data presented here summarize the age distribution within the patient cohort, revealing a broad age range encompassing both pediatric and elderly patients (Tables 2).

Table 1
Gender of the patients (n=122)

Gender of the Patient		
	Frequency	**Percent**
Male	80	65.6
Female	42	34.4
Total	122	100.0

Table 2
Age groups of the patients (n=122)

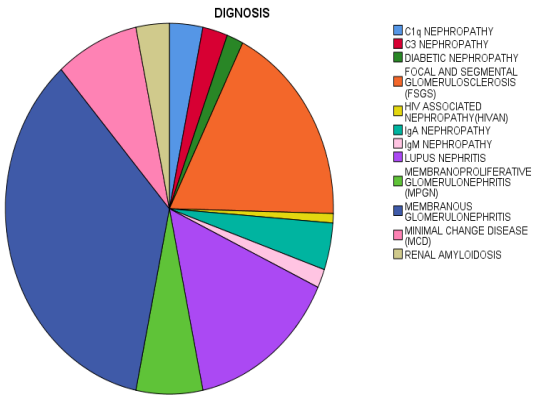
Age Groups		
	Frequency	**Percent**
less than 24	20	16.4
25-44	46	37.7
45-59	44	36.1
60 and above	12	9.8
Total	122	100.0

Of the 122 patients analyzed in this study, Membranous Glomerulonephritis was the most prevalent diagnosis, accounting for 35.2% of cases. Focal and Segmental Glomerulosclerosis was observed in 18% of patients, followed by Lupus Nephritis at 14.8%. Minimal Change Disease and Membranoproliferative Glomerulonephritis were diagnosed in 8.2% and 6.6% of cases, respectively. Less frequent diagnoses included IgA Nephropathy (4.1%), Renal Amyloidosis, and C1q Nephropathy (each at 3.3%), C3 Nephropathy (2.5%), and both Diabetic Nephropathy and IgM Nephropathy (1.6% each). The least common diagnosis was HIV-Associated Nephropathy, found in 0.8% of patients (Table 3 and Figure 1).

Table 3
Histopathological results in renal biopsy (n=122)

	Frequency	**Percent**
C1q Nephropathy	4	3.3
C3 Nephropathy	3	2.5
Diabetic Nephropathy	2	1.6
Focal and Segmental Glomerulosclerosis (FSGS)	22	18.0
HIV Associated Nephropathy(HIVAN)	1	.8
IgA Nephropathy	5	4.1
IgM Nephropathy	2	1.6
Lupus Nephritis	18	14.8
Membranoproliferative Glomerulonephritis(MPGN)	8	6.6
Membranous Glomerulonephritis	43	35.2
Minimal Change Disease(MCD)	10	8.2
Renal Amyloidosis	4	3.3
Total	122	100.0

Figure 1
Histopathological results in renal biopsy (n=122)



The data analysis demonstrated a significant association between age groups and histopathological types, as evidenced by a p-value of 0.000. This suggests that age is an important predictor of histological diagnosis (Table 4 & 5, Figure 2).

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DOI: https://doi.org/10.70749/ijbr.v2i02.166

Table 4

Diagnosis age groups Cross tabulation*

			Age Groups			
			less than 24	25-44	45-59	60 and above
Diagnosis	C1q Nephropathy	Count	0	1	2	1
		Expected Count	.7	1.5	1.4	.4
	C3 Nephropathy	Count	2	0	0	1
		Expected Count	.5	1.1	1.1	.3
	Diabetic Nephropathy	Count	0	0	2	0
		Expected Count	.3	.8	.7	.2
	Focal and Segmental Glomerulosclerosis (FSGS)	Count	4	9	6	3
		Expected Count	3.6	8.3	7.9	2.2
	HIV Associated Nephropathy(HIVAN)	Count	0	1	0	0
		Expected Count	.2	.4	.4	.1
	IgA Nephropathy	Count	1	3	1	0
		Expected Count	.8	1.9	1.8	.5
	IgM Nephropathy	Count	0	1	1	0
		Expected Count	.3	.8	.7	.2
	Lupus Nephritis	Count	3	8	7	0
		Expected Count	3.0	6.8	6.5	1.8
	Membranoproliferatie Glomerulonephritis (MPGN)	Count	0	3	3	2
		Expected Count	1.3	3.0	2.9	.8
	Membranous Glomerulonephritis	Count	0	20	22	1
		Expected Count	7.0	16.2	15.5	4.2
	Minimal Change Disease(MCD)	Count	10	0	0	0
		Expected Count	1.6	3.8	3.6	1.0
	Renal Amyloidosis	Count	0	0	0	4
		Expected Count	.7	1.5	1.4	.4

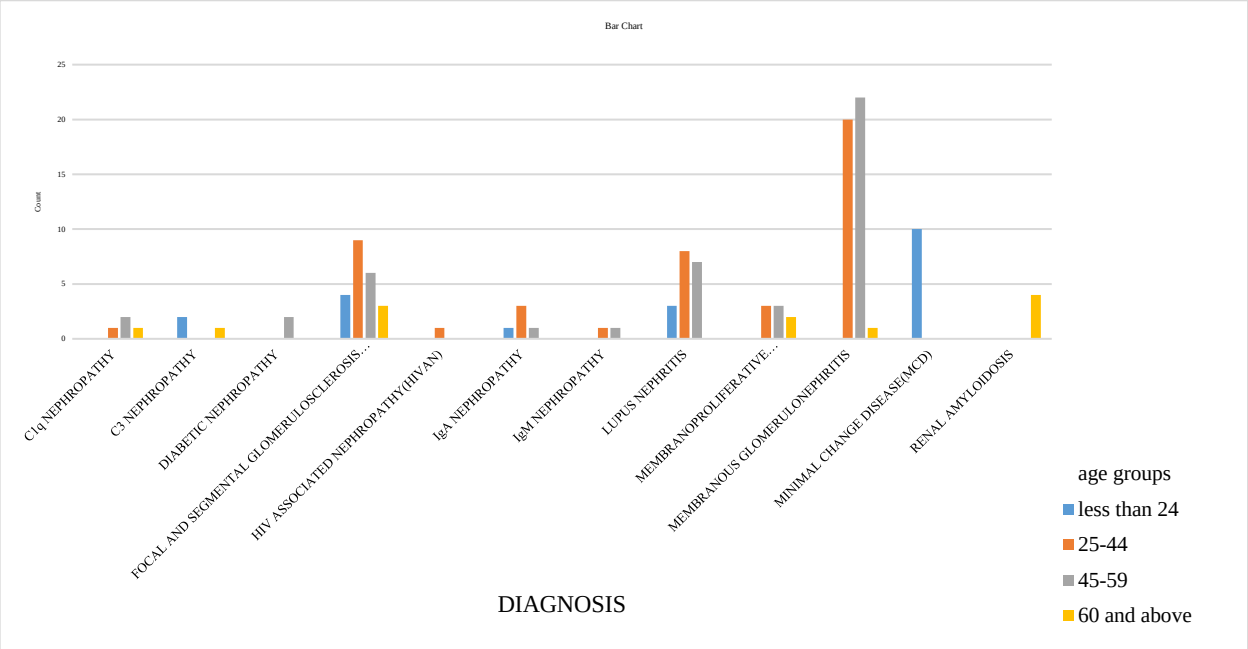
Table 5

Chi-square tests

	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	124.854	33	.000
Likelihood Ratio	103.894	33	.000

Figure 2

Association between age groups and histopathological types



The data analysis also demonstrated a significant association between gender and histopathological types, as evidenced by a p-value of 0.001. This suggests that gender is also an important predictor of histological diagnosis (Table 6 & 7, Figure 3)

Table 6

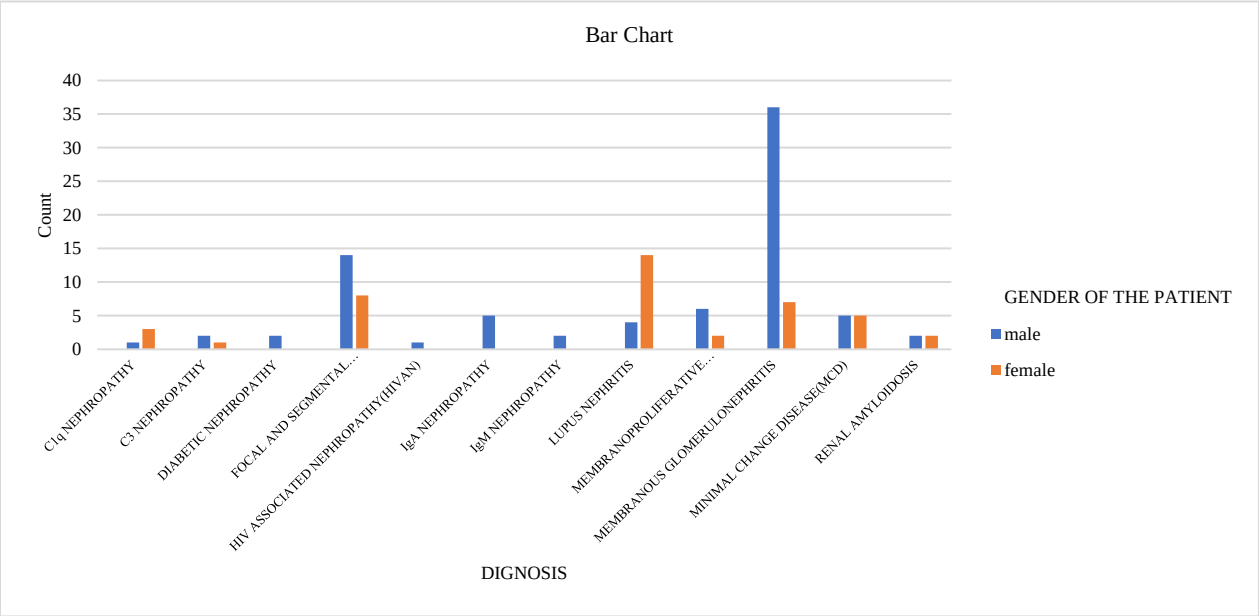
*Diagnosis * Gender of the patient Crosstabulation*

			Gender of the Patient	
			Male	**Female**
Diagnosis	C1q Nephropathy	Count	1	3
		Expected Count	2.6	1.4
	C3 Nephropathy	Count	2	1
		Expected Count	2.0	1.0
	Diabetic Nephropathy	Count	2	0
		Expected Count	1.3	.7
	Focal and Segmental Glomerulosclerosis (FSGS)	Count	14	8
		Expected count	14.4	7.6
	Hiv Associated Nephropathy (HIVAN)	Count	1	0
		Expected count	.7	.3
	Iga Nephropathy	Count	5	0
		Expected count	3.3	1.7
	Igm Nephropathy	Count	2	0
		Expected count	1.3	.7
	Lupus Nephritis	Count	4	14
		Expected count	11.8	6.2
	Membranoproliferate Glomerulonephritis (MPGN)	Count	6	2
		Expected count	5.2	2.8
	Membranous Glomerulonephritis	Count	36	7
		Expected count	28.2	14.8
	Minimal Change Disease(MCD)	Count	5	5
		Expected count	6.6	3.4
	Renal Amyloidosis	Count	2	2
		Expected Count	2.6	1.4

Table 7
Chi-square tests

	Value	df	p-value
Pearson Chi-Square	31.282	11	.001
Likelihood Ratio	34.252	11	.000

Figure 3
Association between gender and histopathological types



DISCUSSION

An accurate diagnosis of nephrotic syndrome requires integrating clinical and laboratory data with light microscopy, complemented by immunofluorescence microscopy (IMF) and serological testing. [1-7] The actual frequencies of various pathological lesions underlying nephrotic syndrome within our Khyber Teaching Hospital (KTH) were previously unknown. Occasional papers previously published in Pakistan have primarily focused on light microscopic features, often representing only morphological patterns rather than specific disease entities.[17-20] This study represents the first from KTH to employ light microscopy, immunofluorescence microscopy (IMF), and serology in examining the range of pathological lesions associated with nephrotic syndrome. As a single-center investigation, it encompasses both adult and pediatric patients from the Peshawar facility. This study shows that the distribution of nephrotic syndrome histopathological spectrum across four age groups. Membranous Glomerulonephritis was most common, particularly in the 25-44 and 45-59 age ranges. Minimal Change Disease was predominantly seen in patients under 24, while Renal Amyloidosis was exclusive to those 60 and above. Focal and Segmental Glomerulosclerosis, Lupus Nephritis, and Membranoproliferative-related patterns were noted across different diagnoses. Additionally, the cross-tabulation analysis of nephrotic syndrome diagnoses revealed notable gender differences among the 122 patients studied. Lupus Nephritis was predominantly observed in females, while Focal and Segmental Glomerulosclerosis (FSGS) and Membranous Glomerulonephritis were more frequently diagnosed in males. Conditions such as Minimal Change Disease (MCD) and Renal Amyloidosis displayed an even distribution between genders. Additionally, Diabetic Nephropathy and IgA Nephropathy were either exclusively or primarily found in males. These findings indicate significant gender-based patterns in the occurrence of various nephrotic syndrome subtypes.

The spectrum of pathological lesions in the adult nephrotic population demonstrated in another study in Pakistan conducted at adult nephrology clinic of SIUT from July 1996 till July 2006 considerable diversity, with focal segmental glomerulosclerosis (FSGS) accounting for 39.87% of cases, followed by membranous glomerulonephritis (MGN) at 26.58%. Minimal change disease (MCD) represented 14.82%, while mesangiocapillary glomerulonephritis (4.3%), mesangioproliferative glomerulonephritis (4.11%), post-infectious glomerulonephritis (2.84%), IgA nephropathy (2.53%), and other rare lesions constituted the remaining cases.[21] In another analysis among the 1523 Chinese patients, the most common cause of nephrotic syndrome was idiopathic membranous nephropathy (IMN) (20.7%), followed by minimal change disease (MCD) (20.4%). Among the patients aged 14–24, 25–44, 45–59 and above 60 years, the most common cause of nephrotic syndrome was MCD (33.0%), lupus nephritis (LN) (23.0%), IMN (37.9%) and IMN (42.3%), respectively. Among the female patients aged 14–24 and 25–44 years, LN was the leading cause of nephrotic syndrome (35.8 and 36.2%, respectively).[22]

CONCLUSION

The renal histopathological spectrum of nephrotic syndrome exhibits variations based on age and gender. Notably, Membranous Glomerulonephritis was identified as the most prevalent diagnosis, particularly among individuals aged 25 to 59, while Minimal Change Disease was predominantly seen in those under 24. Additionally, Lupus Nephritis was diagnosed more frequently in females, whereas Focal and Segmental Glomerulosclerosis and Membranous Glomerulonephritis were more common in males. These findings underscore the significance of demographic factors in the clinical assessment of nephrotic syndrome. Understanding these associations can enhance diagnostic strategies and facilitate the development of tailored management plans for patients, ultimately improving patient outcomes.

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