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Original Research Article

A PROFILE OF KIDNEY BIOPSIES IN A TERTIARY CARE HOSPITAL OF SOUTHTAMILNADU: AN OBSERVATIONAL STUDY

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Abstract

Background: The study analysed the geographic distribution of biopsy-proven native kidney disease in Southern Tamil Nadu, India, with a four-year study period from March 2019 to March 2023. There were 407 native kidney biopsies done at a Government Medical college hospital in Madurai, Tamil Nadu. Of the 407 biopsies, 200 were males and 207 were females, with a M: F ratio of 1:1.03. The average age of patients who underwent kidney biopsy was 32.89 years, ranging from 8 to 75 years. The most common indication for renal biopsy was nephrotic syndrome (45.45%), followed by RPGN (21.37%). Primary glomerular diseases (PGD) were the most common, accounting for 64.37% of cases, followed by secondary glomerular diseases (SGD) (26.78%), tubulointerstitial diseases (5.89%), and the least common was vascular disorders, accounting for 2.9%. The most common primary glomerular disease was minimal change disease -MCD(13.51%), followed by infection-related glomerulonephritis (IRGN)13.26%, membranous nephropathy (MN)11.54%, IgA nephropathy-(IgAN)8.1%, Focal segmental glomerulosclerosis -FSGS (6.87%). The predominant secondary glomerular disease was lupus nephritis-LN(18.42%), followed by diabetic nephropathy-DN (6.14%). This study had four cases of lupus-associated thrombotic microangiopathy (TMA). In the diabetic cohort who underwent kidney biopsies(n=45), 15 patients (33%) had diabetic nephropathy with non-diabetic kidney disease (DN with NDKD), and 12(26.6%) had NDKD in the absence of diabetic nephropathy. This study had 4 (0.9%) cases of amyloidosis and 3(0.7%) cases of IgA vasculitis. This study analysed and compared the trends in glomerular disease across different geographical regions in India and globally with our data.

INTRODUCTION

Although many non-invasive biomarkers have come into the field of nephrology, renal biopsy remains crucial in identifying the renal lesion, prognostication, treatment purpose and guiding the physician in a right way.[1] The renal biopsy patterns and trends vary in age, sex, ethnicity, local traditional treatments, and geographical locations. Unfortunately, India lacks a centralized renal biopsy registry. Research on the prevalence of biopsy-proven renal disease in India is sparse.[2-5] This study aimed to explore the prevalence of various native kidney diseases and understand their patterns at our center. It also compared our findings with similar studies from India and around the world. Additionally, the study emphasizes the importance of creating regional, national, and international registries for renal biopsies.

MATERIALS AND METHODS

The study was based on a retrospective analysis of patient biopsy data performed at Madurai Medical College Hospital in Madurai, Southern Tamil Nadu. Data collection took place from March 2019 to March 2023. Patients with insufficient biopsy samples and allograft kidney biopsies were excluded from the study. Ethical committee permission had been obtained. Indications for renal biopsies were Nephrotic Syndrome (N S), Acute Nephritic Syndrome (ANS), Rapidly Progressive Renal Failure (RPRF), acute kidney injury (AKI), and asymptomatic urinary abnormalities (AUA). We classified patients with non-nephrotic proteinuria or isolated microhaematuria as AUA.

The following data were collected for each patient: name, age, sex, indication for renal biopsy, histopathological diagnosis, and laboratory investigations such as serum creatinine, urine spot PCR, 24-hour urinary protein, urine microscopy, virology (HBsAg, anti-HCV, HIV), and serology

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[antinuclear antibody (ANA), C3, C4]. After obtaining written permission, a Bard (18G) Biopsy Gun was used to perform a kidney biopsy under USG guidance. Two tissue samples were submitted for analysis, one for light microscopy (LM) and another specimen for immunofluorescence (IF). The specimens were stained with hematoxylin-eosin, Masson's trichrome, periodic acid–Schiff(PAS), and Jones silver methenamine for LM. In IF, antisera against human immunoglobulin (Ig) G, IgA, IgM, C3, C1q, and kappa and lambda light chains were used. The electron microscopy (EM) investigation was not done due to logistics.

The histopathological diagnosis was classified as follows:

1. Primary glomerular disease (PGD) includes minimal change disease (MCD), membranous nephropathy (MN), IgA nephropathy (IgAN), focal segmental glomerulosclerosis (FSGS), membranoproliferative glomerulonephritis (MPGN), mesangioproliferative glomerulonephritis (MesPGN), and infection-related glomerulonephritis (IRGN).
2. Secondary glomerular disease (SGD) includes lupus nephritis (LN), diabetic nephropathy (DN), Amyloidosis (AM), IgA vasculitis, multiple myeloma, and Alport syndrome.
3. Tubulointerstitial lesions: This includes acute interstitial nephritis (AIN), acute tubular necrosis (ATN), acute pyelonephritis, and chronic interstitial nephritis (CIN).
4. Vascular lesions: These diseases include hypertensive nephrosclerosis (HTN) and thrombotic microangiopathy (TMA).

The prevalence of each histological type of renal disease and the clinical syndrome associated was studied. The results obtained were compared with data from other studies conducted in India and worldwide. Quantitative variables are the mean, and qualitative variables are numbers and percentages.

RESULTS

A retrospective examination of 485 renal biopsies was conducted between March 2019 and 2023. Of these, 78 biopsies those with insufficient/inadequate data (n = 45) & renal allograft biopsies (n=33)—were excluded. The study covered the remaining 407 biopsies. The patient group consisted of 200 males (49.14%) and 207 females (50.8%), with an average age of 32.89 years (ranging from 8 to 75 years) as shown in [Figure 2]. The most common indications for performing a biopsy were Nephrotic Syndrome (NS) in 185 cases (45.45%), Rapidly Progressive Glomerulonephritis (RPGN) in 87 cases (21.37%), Acute Kidney Injury (AKI) in 47 cases (11.54%), Rapidly Progressive Renal Failure (RPRF) in 40 cases (9.82%), Acute Nephritic syndrome (ANS) in 37 cases (9.09%), and Asymptomatic Urinary Abnormalities (AUA) in 11 cases (2.7%) as shown in [Figure 1].

Primary glomerular disease (PGD) was the most common diagnosis, affecting 262 people (64.37%), making it the most common type of kidney disease. Secondary glomerular disease (SGD) was detected in 109 patients (26.7%), followed by tubulointerstitial lesions in 24 patients (5.89%) and vascular lesions in 12 cases (2.94%).

Minimal change disease (MCD) was the predominant form of primary glomerular disease in 55 cases (13.51%) with a mean age of 25.89 years. Seven of these individuals had acute tubular damage, and one had acute tubulointerstitial nephritis. One case of non-Hodgkin's lymphoma presented with nephrotic syndrome whom on renal biopsy turned out to be MCD.

Infection-related glomerulonephritis (IRGN) was the second most common PGD, diagnosed in 54 cases (13.26%), with an average age of 35.75 years. IRGN showed a male predominance, M: F cases were 39:15 with ratio (2.6:1). In this cohort, 9(16.6%) patients had both IRGN and diabetic nephropathy, and 12 (22.2%) patients had crescent formation on biopsy.

Membranous nephropathy was found in 47(11.54%) cases, equally distributed between males and females, with an average age of 40.53 years. In this group 14(29.7%) patients tested positive for PLA2R antibodies, and 1(2.1%)tested positive for NELL-1. Due to logistical challenges, PLA2R testing was not performed in 25 cases. 3 (6.38%) patients had membranous nephropathy combined with Global glomerulosclerosis (CKD), and 1case (2.1%) each was associated with acute interstitial nephritis (AIN) and acute tubulointerstitial nephritis (ATIN).2 (4.2%) patients had membranous nephropathy in combination with focal segmental glomerulosclerosis (FSGS).

There were 28 cases (6.87%) of FSGS, with a male predominance (60.7%) and an average age of 29.46. The NOS subtype was the most prevalent variety in 24 cases(85.7%), followed by the tip variant in 3(10.7%) cases and 1 case of the perihilar variant. FSGS was associated with acute tubular injury in 4(14.2%) cases, moderate IFTA & arteriosclerosis in 4(14.2%), and acute tubulointerstitial nephritis in 1(3.5%).

IgA nephropathy was identified in 33 patients (8.1%), with a mean age of 30.03 years. (M: F-17:16). Among these, 11 (33%) had advanced IgA nephropathy.

Crescentic glomerulonephritis (Crescentic GN) was found in 29 cases (7.12%), with an average age of 41.72 years with M: F cases 12:17 {ratio(1:1.4)} . Among these, 10 (34.4%) had anti-glomerular basement membrane (anti-GBM) disease, 7(24.1%) had pauci-immune disease, 10(34.4%) had immune complex-mediated disease, and 2(6.8%) had IgA nephropathy with crescentic transformation as shown in [Figure 4].

6 cases (1.47%) of membranoproliferative glomerulonephritis (MPGN) were documented, 4 of which were Immune-complex(60%) mediated and 2(40%) were complement-mediated.

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Seven cases of global glomerulosclerosis were observed, whereas three cases had mesangioproliferative glomerulonephritis.

Lupus nephritis (LN) was the predominant secondary glomerular disease (SGD), comprising 75 cases (18.42%), with a mean age of 26.98 years with a M: F 6:69{ratio (1:11.4)}. In this group LN class 4 was the most common variant, identified in 27 cases (36%), followed by class 5 in 17 cases (22.6%), class 3 in 10 patients (13.3%), combined class 3 and class 5 in 8 cases (10.6%), and combined class 4 and class 5 in 6 cases (8%). Additionally, there were four cases of lupus thrombotic microangiopathy (TMA), two cases of class 2 lupus nephritis, and one case of lupus podocytopathy. 2 cases of LN were associated with ATN as shown in [Figure 7].

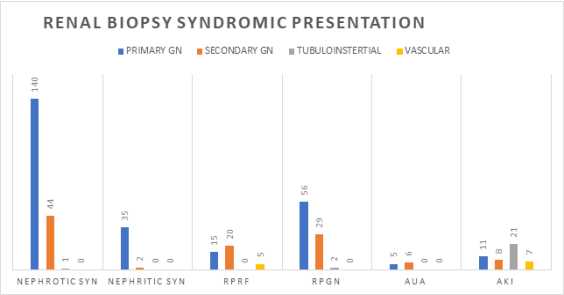

Figure 1: Renal disease with syndromic presentation

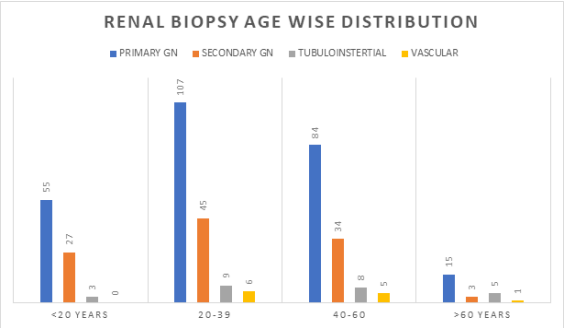

Figure :2 showing renal biospy age wise distribution

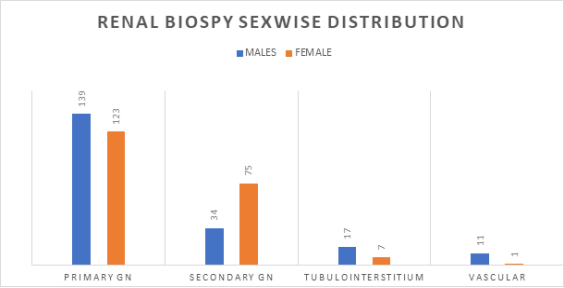

Figure 3 showing renal biopsy SEXWISE distribution

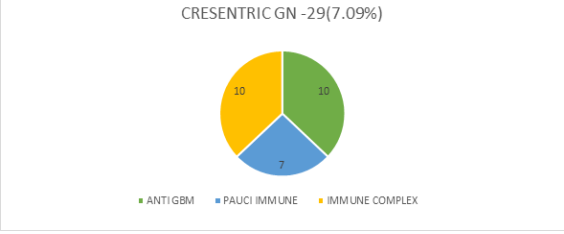

Figure 4: Showing The Cresentric-GN Distribution

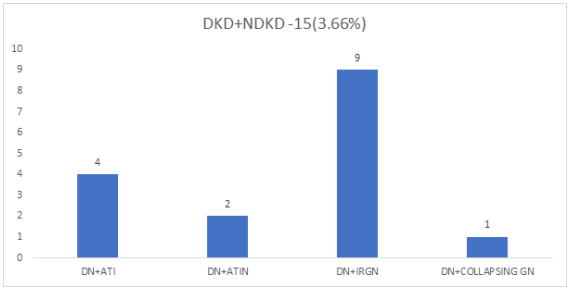

Figure 5: showing distribution of diabetic kidney disease (DKD) and non-diabetic kidney disease (NDKD)

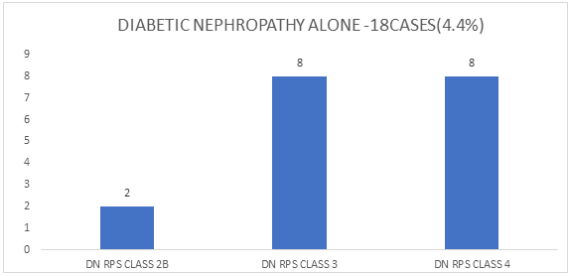

Figure 6: Showing Distribution of Diabetic Nephropathy According to RPS Classification

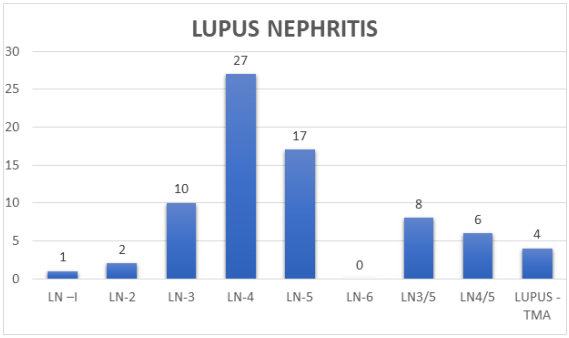

Figure 7: Showing Lupus Nephritis (LN) Distribution

45 diabetic patients underwent kidney biopsy (mean age of 45.88 years). In this group, 18 cases (40%) had diabetic nephropathy alone (DKD), 15 cases (30%) had diabetic kidney disease with non-diabetic kidney disease (NDKD with DKD), and 12 cases (2.94%) had non-diabetic kidney disease without diabetic nephropathy (NDKD without DKD). One diabetic kidney disease patient had collapsing glomerulopathy (CG) as shown in [Figure 5 &6].

There were 4 cases of Amyloidosis, with one being AL type of Amyloidosis, and three cases of IgA vasculitis were identified. One case of hereditary nephritis (Alport syndrome) was reported, presenting as FSGS on light microscopy. A case of heavy and light chain deposition disease was also noted.

Regarding tubulointerstitial diseases, 13 cases (3.19%) involved acute tubular injury (ATI), 9 of which were associated with pigment cast nephropathy. Five cases (1.22%) of acute tubulointerstitial nephritis (ATIN) and 6 cases (1.47%) of acute pyelonephritis were documented.

Ten cases of vascular lesions revealed malignant hypertension changes; all of the patients were men with an average age of 39.5 years. In this group, one

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patient with malignant hypertension exhibited collapsing glomerulopathy.

Two ((0.5%) cases of thrombotic microangiopathy cases were recorded, one of them due to a snake bite.

Table 1: showing promary and secondary glomerular disease -age wise distribution.

Glomerular diseases	<20 years	20-39 years	40-60years	>60 years
Minimal change disease	23	20	10	2
Focal segmental glomerulosclerosis	6	15	7	0
Mesangioproliferative gn	1	1	0	0
Membranoproliferative gn	0	3	3	0
Iga nephropathy	5	20	8	0
Crescentic gn	2	12	12	3
Irgn	13	16	19	5
Membranous nephropathy	4	17	23	4
CKD	1	3	2	1
Diabetic nephropathy	1	4	19	2
Lupus nephritis	23	38	13	0
Amyloidosis	0	2	2	0
Hsp	2	1	0	0
Alport syndrome	1	0	0	0
Multiple myeloma	0	0	0	1

Table 2: Comparison of renal biopsy with various parts of India and worldwide

Diagnosis (%)	Our study	Jeyaprakash et al,[5]	Varun et al,[15]	Das et al,[19]	Balakrishnan et al,[13]	Golay et al,[4]	Lingaraju U et al,[23]	Mubarak et al,[3]	Le-shi-li et al,[20]	Chang et al,[21]
	Madurai, South India	Chennai, South India	Vijayawada, South India	Hyderabad, South India	Vellore, south India	Kolkata, India	Bangalore,India	Pakistan	China	korea
	4 years (2019-2023)	1 year (2014)	2004–2018	1990–2008	1990–2001	2010-2012	2013-2015	1995–2008	1979 - 2000	1987 to 2006
Primary glomerular disease	64.37	37.74	66.8	69.1	-	79.13	57.45	73	71	74
Minimal change disease	13.51	8.89	15.4	15.1	10.8	20.12	7.37	5.8	0.93	15.5
Membranous nephropathy	11.54	8.41	11	7	9.5	12.01	7.70	17.2	9.89	12.3
Infection related glomerulonephritis	13.26	9.81	6.3	5.6	13.5	4.95	5.69	-	2.75	-
IgA nephropathy	8.11	7.69	14.3	4.4	8.4	8.1	13.40	1.5	40	28.3
Focal and segmental glomerulosclerosis	7.12	6.49	10.6	10.5	16.8	18.02	17.08	21.2	6	5.6
Membranoproliferative glomerulonephritis	1.4	2.16	2.4	3.9	2.9	5.25	5.36	1.1	3.38	4.0
Cresentric GN	7.1	1.44	1.9	0.7	-	7.51	11.89	0.3	1.9	-
Mesangial proliferation	0.73	0.72	1.7	5.2	7.3	0.6	0.50	1.9	25.62	-
Diffuse proliferative glomerulonephritis	-	0.72	0.6	4.7	-	-	-	-	-	-
CGN	1.71	-	1.9	6.7	4.62	3	4.18	11.6	-	-
Secondary glomerular disease	26.78	32.21	12.1	18.2	-	20.87	42.54	10.9	23	11.8
Lupus nephritis	18.42	15.14	4.9	14.6	6.9	15.32	7.03	4.9	54.3	8.7
Diabetic nephropathy	6.14	6	2.6	1.2	2.8	0.15	14.90	0.9	7.3	2.0
Amyloidosis	0.98	1.2	1.8	1.5	1	1.2	1.84	4.6	2.2	-
Alport	0.24	-	-	-		0.15	-	0.4		-
Multiple myeloma	0.24	0.72	1.1	0.4	0.57	0.45	-	-	0.89	-
HSP	0.73	-	-	0.37	-	0.3	-	-		1.0
TIN	5.89	18.51	17.5	6.7	-	-	-	11.6	3.2	-
Vascular	2.94	1.92	3.5	3.2	2.1	1.5	2.84	3.9	-	-

DISCUSSION

This study was conducted as an in-depth analysis of the demographics, renal syndromes, and various biopsy-proven renal pathologies over four years (2019-2023) at a tertiary care government hospital in southern Tamil Nadu, India. The study findings reveal distinct patterns of renal diseases that differ from those reported in Western studies and some other Asian research.[6-12] In our study, Nephrotic syndrome was the most frequent manifestation, accounting for 45.45% of all renal biopsies, consistent with many other studies worldwide.[8-13] Only a few research from Italy and Japan,[6,9] have identified AUA as the main presentation. This increased AUA could be attributed to more aggressive screening programs for universal urine screening for asymptomatic proteinuria &/or

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Microhematuria. This study also revealed a male predominance in all kinds of renal biopsy diseases, except LN, which is consistent with the majority of published research.[6-12]

Our study's most frequent cause of NS was MCD, followed by MN, FSGS, and IgAN. This aligns with research conducted by Varun et al,[15] and other Asian studies. MCD was the most frequent cause of NS in Korea and Japan,[6,16] followed by MN and IgAN. On the other hand, MN and IgAN were the most frequent causes of NS in the Czech registry, whereas in Brazil, FSGS was the most common cause, followed by MCD and MN.[8,10]

In this study, PGD was the most prevalent renal disease followed by SGD and TIN & it concurs with other trials.[6-10,15]

Among the PGDs, MCD, IRGN, MN, IgAN, and FSGS were the most common causes of PGD, accounting for up to 82.82% of cases.

MCD was the most prevalent PGD in this series, accounting for 13.51% of all cases, consistent with other studies (2,4). It had a female Preponderance (male: female 1:1.29) and was more prevalent in the second and third decades.[17,18]

In this study, IRGN ranks second among all PGDs, accounting for 13.26% of cases, with a male preponderance. This finding aligns with the study by Balakrishnan et al,[13] which reported a similar rate of 13.5%. However, it contrasts with the results from various studies across India by Varun et al. (6.3%)., Das et al. (5.6%)., lingaraju U et al. (5.69%), and Golay et al. (4.95%)., as well as studies from China by Chang et al., which observed different patterns.[4,19,20]

Although MN is considered the most prevalent cause of PGD in adults,[7,9,17,22] a survey of several pieces of literature indicates that most studies classify MN as the third or fourth most common cause.[6,8,13,16,18] Our results also demonstrate comparable findings (3rd most common PGD), accounting for 11.54% of cases overall. Among the 22 patients who underwent PLA2R testing, 14 were positive & 1 patient had NELL-1 positive.

Regarding FSGS, studies by Balakrishnan et al. and Mubarak et al,[3,13] found that FSGS was identified as the most common histological finding. At the same time, research by Golay et al. and Das et al,[4,19] ranked second. However, our study presents a contrasting observation: FSGS ranks fourth, accounting for 7.12% of cases. These results align with findings from studies conducted in Korea and China,[20,21] highlighting regional variations in the prevalence of FSGS. In this study, MCD was the most common; however, in those with MCD, the possibility of unsampled FSGS couldn't be ruled out. Serial sectioning is required to detect segmental sclerosis, which is most common in juxtamedullary glomeruli. Sections of segmentally sclerotic glomeruli may appear normal if the plane of the section does not include segmental sclerosis. The probability of detecting glomerular lesion (P) is a function of % of glomeruli affected in the kidney(p) & number of glomeruli in biopsy. P= (1-p)^n. Several features can favour the diagnosis of FSGS, such as glomerulomegaly and the presence of tubular atrophy.

Crescentic GN is histopathologically defined by crescents in 50% or more of the glomeruli. In our study, Crescentic GN accounts for 7.1% of cases, with a noticeable female predominance. This finding is consistent with similar studies by Lingaraj et al. (11.89%) and Golay et al. (7.51%). However, it contrasts with the results from studies conducted by Jeyaprakash et al., Varun et al., and Das et al. and studies from Brazil, where Crescentic GN contributed to only 0.7% of cases. The higher incidence observed in our study could be attributed to the post-COVID era, where underlying health conditions may have exacerbated the disease's prevalence; it could also be due to referral bias as this government medical college caters to nine adjoining districts.

In this study, MPGN accounted for 1.47% of all cases, primarily affecting the adolescent age group, which is slightly lower than the findings from studies conducted by Golay et al. (5.25%) and Lingaraju U et al. (5.36%).[4,23] Numerous studies worldwide have reported a decline in the incidence of MPGN, often attributed to improved hygiene, widespread use of universal precautions, and vaccinations, which have significantly reduced infection rates.[24] An exception to this trend is seen in Romania,[11] where MPGN remains the most common primary glomerular disease.

This study had a low prevalence of MesPGN (0.73% of all cases) and concurs with the other studies.[4] This pattern can be associated with several types of glomerulonephritis, such as IgA nephropathy, the resolution phase of postinfectious glomerulonephritis, and GN related to systemic lupus erythematosus (SLE).

Lupus nephritis (LN) was the most common SGD in the study, accounting for 18.42% of cases. This data aligns with global trends, where LN is consistently reported as the leading cause of SGD, particularly with a female predominance.[3,4,5,19] However, this finding contrasts with the study by Lingaraj et al., where diabetic nephropathy (DN) was the most common SGD.[23]

Diabetic Nephropathy (DN) is the second most common type of secondary glomerular disease, making up 6.14% of cases, with a clear male predominance. This finding aligns with most existing studies.[4,5,13,14,15,20,21] except for the research by Mubarak et al., where DN was reported at a significantly lower rate of only 0.9%.[3]

Regarding Amyloidosis, the prevalence of Amyloidosis was much lower at 0.98%, which is consistent with findings from other centers in India,[4,5,13,14,23] except for Das et al.[19] In contrast, the study by Mubarack et al. from Pakistan reported a notably high prevalence of Amyloidosis (4.6% of all glomerular diseases), mostly secondary.[3] The

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authors attributed this to the high rates of tuberculosis in their study population.

Many studies indicate that Tubulointerstitial Nephritis (TIN) is relatively uncommon in renal biopsies.[9,10,19,20] Our study also reflected this trend, with TIN accounting for just 5.89% of cases. In contrast, we observed a higher incidence of Acute Tubular Injury (ATI), followed by acute pyelonephritis and acute tubulointerstitial nephritis.

Vascular lesions were the least common type of biopsy-proven renal disease, representing 2.94% of cases, and showed a male predominance. This low prevalence of vascular lesions aligns with findings from other studies conducted in India and worldwide.[3-5,13,14,21,23]

CONCLUSION

In conclusion, minimal change disease is the most common primary glomerular disease we observed, while infection-related glomerulonephritis (IRGN) is emerging as a significant concern in our area. Lupus nephritis remains the most prevalent secondary glomerular disease, with class 4 being the most frequently seen. Diabetic kidney disease patients mostly defer biopsy, but the emergence of non-diabetic kidney disease necessitates renal biopsy in these patients, which has therapeutic and prognostic importance. Establishing a renal biopsy registry is essential to identify patterns and trends in our region, which will help guide preventive measures and treatment policies.

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