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Histopathological Spectrum among Patients Presenting with Adult Onset Nephrotic Syndrome

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ABSTRACT

Background: Adult nephrotic syndrome is caused by glomerulopathy that manifests differently in Nepal and other nations. Examining the range of glomerulopathy in individuals over 15 with biopsy-proven nephrotic syndrome, estimating its prevalence and age distribution, and connecting its clinical-pathological features using electron microscopy and immunofluorescence are our objectives.

Methods: In our tertiary care hospital, we retrospectively reviewed and analysed 157 renal biopsies of adults with nephrotic syndrome that were performed between January 2021 and August 2024, a period of 3.7 years.

Results: There were 157 patients with nephrotic syndrome, 92 of whom were men and 65 of whom were women (1.4 :1). Nephrotic syndrome was most common in the 15–25 age group (24.84%), and it was least common in the 76–85 age group (3.18%). Minimal change disease was the most frequent histological finding among people with nephrotic syndrome (n = 34), followed by MGN (21.01%; n = 33), FSGS (17.19%) (n = 27), IgA Nephropathy (9.55%; n = 15), and amyloidosis (7%; n = 11). MPGN and SLE were similar in 6.30% (n=10), diabetic nephropathy was similar in 5.09% (n=8), and collageno-proliferative glomerulonephritis, tubulointerstitial nephritis, and fibrillary glomerulonephritis were similar in 0.35% (n=1) of histological findings. MGN and MPGN had the highest male predominances (2.3:1 and 2.3:1, respectively), even though fewer patients had the histological diagnostic of MPGN. In SLE, the female predominance was highest (1:9) (M:F). Primary glomerular disease were 78.34%, and secondary glomerular disease were 21.65%.

Conclusion: Primary glomerular disease, histologically MCD followed by MGN are the most common cause of NS in adults.

Keywords: *nephrotic syndrome; renal biopsy; minimal change disease; glomerulonephritis; electron microscopy.*

INTRODUCTION

Despite significant advancements in healthcare, the major cause of significant morbidity is renal failure due to glomerular diseases.[1] The nephrotic syndrome is defined by a urinary protein level exceeding 3.5 g per 1.73 m^2 of body-surface area per day with several renal and extrarenal features.[2] Annually, there are three fresh cases of NS per 100,000 adults worldwide and two to seven new cases are expected per 100,000/ year globally.[3, 4] Despite its prevalence in pediatric patients, nephrotic syndrome burdens adult health care also.[5] The patterns of glomerular diseases vary between nations and alter over time likely due to improved infection control, changes in environmental pollutants, increasing awareness, and increased life expectancy.[6, 7] Various primary and secondary glomerular disorders (SGD and PGD) are associated with NS with high prevalence of minimal change disease (MCD), membraneous glomerulonephritis (MGN) and lupus nephritis (LN).[8] However, some reports indicate focal segmental glomerulosclerosis (FSGS) predominates both adults and children.[9, 10] Consisting of different histories, therapies, and prognoses, it is critical to identify between these etiologies of the NS using histological analysis. In the current study, we evaluated the histological spectrum of adult nephrotic syndrome in relation to age group, gender, and clinicopathological factors.

METHOD

This descriptive cross sectional study was done at College of Medical Sciences-Teaching Hospital, where medical records of all patients over the age of 15 years with diagnosis of NS kidney biopsy were evaluated. The ethical clearance for conducting the study was taken from the Institutional review committee of the College of

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Medical Science & Teaching Hospital (COMS-TH) (Ref no. 2023/ COMSTH/IRC/182). All adults with features suggestive of nephrotic syndrome were included by using convenient sampling and kidney biopsies throughout the research period (January 2021–July 2024) were performed under ultrasound guidance using Max-Core™ Disposable Core Biopsy Instrument (16 gauge) and reported independently by renal pathologists. Written informed consent was obtained from all the patients. The patient's demographic profile, clinical diagnosis, comorbidities, the reason for hospital admissions. The data were then entered in the MS XP sheet and were transferred to statistical package for social sciences version (SPSS) program for analysis. The data were analysed using mean, number, percentage and ratio.

RESULTS

Among the patients who underwent kidney biopsy 157 patients had presented in Nephrotic syndrome where 92 were male and 65 females, with the ratio of 1.4:1. Most common histopathological finding among those with nephrotic syndrome was that of minimal change disease 21.65%(n=34) followed by MGN 21.01%(n=33), FSGS 17.19%(N=27), IgA Nephropathy 9.55%(n=15), Amyloidosis 7%(n=11). MPGN and SLE shared 6.30%(n=10) each, diabetic nephropathy 5.09%(n=8) and least common histopathological finding were shared by collageno-proliferative glomerulonephritis, tubulointerstitial nephritis and fibrillary glomerulonephritis 0.35%(n=1) each. The highest male predominance was seen in MGN(2.3:1) and MPGN(2.3:1) despite lower number of patients having the histological diagnosis of MPGN. The highest female predominance was seen in SLE(1:9)(M:F) (Table 1).

Most common age group presenting with nephrotic syndrome was between (15-25yrs), 24.84% and least common prevalence was among the elderly (76-85yrs), 3.18%. The age group (15-45) consisted 104(66.24%) of the patients (Table 2).

Among the patients presenting with nephrotic syndrome, half(n=79) patients presented with hematuria and 61.14%(n=96) patients presented with hypertension (Table 3).

Table 1. Histopathological types of glomerular lesions among those presenting with Nephrotic syndrome.

Histo-morphological pattern	Total	M	F
MCD	34(21.65%)	21	13
MGN	33(21.01%)	23	10
FSGS	27(17.19%)	17	10
IgA	15(9.55%)	8	7
Amyloid	11(7%)	5	6
SLE	10(6.36)	1	9
MPGN	10(6.36%)	7	3
DN	8(5.09%)	5	3
Myeloma	3(1.91%)	3	0
DPGN	3(1.91%)	2	1
Fibrillary GN	1(0.63%)	0	1
Collageno proliferative GN	1(0.63%)	0	1
TIN	1(0.63%)	0	1
Total	157	92	65

Abbreviation: *MCD: minimal change disease, MPGN: membranoproliferative glomerulonephritis, FSGS: focal segmental glomerulosclerosis, MGN: membranous glomerulonephritis, DN: diabetic nephropathy, SLE: Systemic lupus erythematosis, IgA: IgA nephritis, DPGN: Diffuse proliferative glomerulonephritis, TIN: tubulointersitial nephritis, M: male, F: female, GN: glomerulonephritis.*

Table 3. Clinical characteristics of the patients.

Feature	Present	Absent
Hematuria	79(50.31%)	78(49.67%)
Hypertension	96(61.14%)	61(38.86%)

DISCUSSION

Glomerular disease is the significant contributor to end stage renal disease (ESRD).[11] Histological spectrum of glomerular disease is different in adults than in the children and overall Membranous glomerulonephritis and minimal change disease are the most common primary glomerular diseases causing nephrotic syndrome.[12] Some reports also suggest the FSGS to be most common cause of primary nephrotic syndrome in children and adults.[13] Most common age group presenting with nephrotic syndrome was between (15-25yrs), 24.84% and majority were present in (15-45yrs) age-group and consisted of 66.34%(n=104) patients. This is similar

Table 2. Age and sex wise distribution of various histomorphological patterns of adults nephrotic syndrome.

Histomorphological pattern	15-25 yrs		26-35 yrs		36-45 yr		46-55 yr		56-65 yrs		66-75 yrs		76-85 yrs		Total
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	
MCD	10	5	5	4	4	3	1	0	1	1	0	0	0	0	34(21.65%)
MGN	2	0	5	4	5	2	7	2	1	2	2	0	1	0	33(21.01%)
FSGS	7	4	5	2	3	1	1	1	1	1	0	1	0	0	27(17.19%)
IgA	1	2	3	3	2	1	1	1	1	0	0	0	0	0	15(9.55%)
AMYLOID	0	0	0	0	1	0	1	2	2	2	1	0	0	2	11(7.00%)
MPGN	2	1	1	1	2	1	1	0	0	0	1	0	0	0	10(6.36%)
SLE	1	4	0	2	0	1	0	2	0	0	0	0	0	0	10(6.36)
DN	0	0	0	1	1	0	1	1	1	1	1	0	1	0	8(5.09%)
Myeloma	0	0	0	0	0	0	0	0	1	0	1	0	1	0	3(1.91%)
DPGN	0	0	1	0	0	0	1	0	0	1	0	0	0	0	3(1.91%)
Fibrillary GN	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1(0.63%)
Collageno proliferative GN	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1(0.63%)
TIN	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1(0.63%)
TOTAL(M/F)	23	16	20	17	18	10	14	11	8	8	6	1	3	2	157
Total (%)	39 (24.84%)		37 (23.56%)		28 (17.83%)		25 (15.92%)		16 (10.19%)		7 (4.45%)		5 (3.18%)		

Abbreviation: *MCD: minimal change disease, MPGN: membranoproliferative glomerulonephritis, FSGS: focal segmental glomerulosclerosis, MGN: membranous glomerulonephritis, DN: diabetic nephropathy, SLE: Systemic lupus erythematosis, IgA: IgA nephritis, DPGN: Diffuse proliferative glomerulonephritis, TIN: tubulointersitial nephritis, M: male, F: female, GN: glomerulonephritis.*

to the study done in eastern India where 33.33% patients were reported in the age group of (18-30yrs).[1] Similarly in a study by Zajjari et al. (15-30yrs) age group consisted highest no of patients and collectively (15-45yrs) of patients constituted 57.97% patients, Kshirsagar et al. also reported the majority 78.72% patients in (15-45yrs) age group.[14, 15] The least number of patients 3.18% were among the elderly(76-85yrs) similar to other studies.[11, 16, 17] Male gender constituted 58.59%(M:F=1.4:1) of the patient with NS that is similar to other studies like by Kshirsagar et al. (M:F=1.7:1), Pradhan SK et al. (2.2:1) 68.75%, Jayaprakash et al. (M:F=1.6:1) 61.5%.[11, 14, 18] Hematuria was present in 49.68% patients as in other studies with higher number of patient with hematuria.[1, 15, 16] This was in contrast to other studies where the characteristics was present in lower percentages.[17, 19] Hypertension was present in 61.14% of our patient which was similar to studies done in India where it was present in higher percentages of patients.[1, 11, 16, 17] Whereas it was lower in studies by Joshi et al. (22.5%), Kshirsagar et al. (26%), Rathi et al. (25%).[14, 19, 20]

The prevalence of MCD was 21.65% that was most common in our study, the result was similar to Golay et al. 23.9%.[21] Similar finding of highest prevalence was seen in another study by Agarwal et al. 38% and Choi Injoon et al. 26.6%.[22, 23] It was most common in age group of 15-25yrs of patients in our study that is similar to other studies 33%(14-24yrs) in a chinese study and >40%(16-30yrs) in a Korean study.[24, 25] However contrasting result of higher prevalence of FSGS(39.87%) and MCD as low as(15.82%) was seen in another study done in Pakistan by Kazi et al.[26] Similar contrasting findings were seen in studies done in Zaire where MCD was prevalent in younger patients in 14% and in Iraq where only 17.1% patients belonged to younger age group.[27, 28] There was higher incidence of MGN(21.01%), and second most common histological finding in our study which is similar to the study by Golay et al. 24.6% and Rathi et al. 24.4%.[19, 21] Other studies having the similar were by Riabov et al. 25%, Medawar et al. 28%.[29, 30] However, a contrasting result was seen in a study by Braden et al. where there was decreasing frequency of the MGN as a diagnosis from 38.3% during (1975-

1979) to 14.5% during (1990-1994).[31] FSGS was present in 17.19% in our study which is similar to the study by Jayaprakash S (12.8%), Aggarwal et al. (17.6%) and Das et al. (15.2%).[8, 11, 32] This was in contrast to the study by Yousuf et al. (28.6%), Rathi et al. (30.6%).[19, 33] The patient with IgA nephropathy associated NS were 9.55% in our study which was similar in the study by Agarwal et al. (11.2%), Golay et al. (8.1%) and Joshi et al. (8.33%).[20-22] The result was however in contrast with the study by Zajjari et al. (2.7%) and Kshirsagar et al. (1.27%).[14, 15]

MPGN was present in 6.36% patients in our study. The other studies like by Golay et al. (6.6%) and Das et al. (5.7%) showed similar results.[8, 21] While the study by Rathi et al. and Aggarwal et al. MPGN accounted for 17.9% and 18.2% each.[19, 32] Secondary glomerular dieases accounted for 21.65% of the cases and the most common among them was amyloidosis 7%, followed by SLE 6.36% and diabetic nephropathy 5.09%. Other pathological findings included myeloma kidney, TIN, and CPGN accounting for 3.2% of cases The weight of overall secondary glomerular diseases is similar in a study done in Mumbai (21.7%).[14] Similarly in other two studies done in Haryana (20.9%) and South India (21.3%).[8, 32] Much higher percentages of patients (35.40%) had secondary glomerular disease in another study done in Morocco.[15] Lower patients with SGD were noticed in studies done at chandigarh by Rathi et al. (11%) and 8% in a study done in eastern India.[1, 19] Most common cause of secondary glomerular lesion were reported to be DN and followed by LN and amyloidosis in studies conducted by several authors.[20, 34, 35] However this trend of report was not present in our study and the commonest SGD was amyloidosis and SLE. The higher trend of amyloidosis in our study could be due to the higher prevalence of tuberculosis as described in the reports from India and Pakistan.[8]

CONCLUSION

Nephrotic syndrome is the common presentation for many primary as well as secondary kidney diseases. Most of the cases in our study had primary kidney disease in the forms of MCD, MGN and FSGS. There were rare diseases like Collagenoproliferative GN, Fibrillary GN and Multiple Myeloma presenting as Nephrotic syndrome where kidney biopsy was necessary for final diagnosis and tailoring the treatment of patients.

Conflict of interest: None

REFERENCE

1. Sarkar A, Haque F. A Study on Clinico Pathological Spectrum of Nephrotic Syndrome in Adult Patients in a Teaching Hospital in Eastern India. IJCMR. 2018;5(5):E55-E8. [DOI]
2. Bradley SE, Tyson CJ. The nephrotic syndrome. New England Journal of Medicine. 1948;238(7):223-7. [DOI]
3. Llach F. Thromboembolic complications in nephrotic syndrome: coagulation abnormalities, renal vein thrombosis, and other conditions. Postgraduate medicine. 1984;76(6):111-23. [DOI]
4. Tapia C, Bashir K. Nephrotic syndrome. 2017. [PubMed]
5. Naicker S. End-stage renal disease in sub-Saharan and South Africa. Kidney International. 2003;63:S119-S22. [DOI]
6. Keddis MT, Karnath BM. Review of Clinical Signs: The Nephrotic Syndrome. Hospital Physician. 2007;43(10):25 [Google Scholar]
7. Kitiyakara C, Kopp JB, Eggers P, editors. Trends in the epidemiology of focal segmental glomerulosclerosis. Seminars in nephrology; 2003 [Google Scholar]
8. Das U, Dakshinamurty K, Prayaga A. Pattern of biopsy-proven renal disease in a single center of south India: 19 years experience. Indian journal of nephrology. 2011;21(4):250-7. [DOI]
9. Hull RP, Goldsmith DJ. Nephrotic syndrome in adults. Bmj. 2008;336(7654):1185-9. [DOI]
10. Singh GK, Singh SN, Niroula D, Debnath K, Sharma RL. Clinicopathological correlation in primary nephrotic syndrome. Journal of Medical Society. 2014;28(3):180-4. [DOI]
11. Jayaprakash S. A Clinico-pathological Study of adult Nephrotic Syndrome. European Journal of Cardiovascular Medicine. 2024;14:917-24.

[DOI]

12. Broyer M, Meyrier A, Niaudet P, Habib R. Minimal changes and focal segmental glomerular sclerosis. Oxford textbook of clinical nephrology. 1998;1:493-535.[Google Scholar]
13. Burton C, Harris K. The role of proteinuria in the progression of chronic renal failure. American journal of kidney diseases. 1996;27(6):765-75. [DOI]
14. Kshirsagar GR, Gadgil N, Margam S, Chaudhari C, Kumavat PV, Pagare S. Histopathological spectrum of adult nephrotic syndrome over 16 years at a tertiary care center in Mumbai with clinicopathological electron microscopy and immunoflurescence correlation of renal biopsies. Ann Pathol Lab Med. 2017;4(6):705-13.[DOI]
15. Zajjari Y, Aatif T, Kawtar H, Benbria S, Montasser D, El Kabbaj D. Histopathological study of nephrotic syndrome in adults: A Moroccan report. Saudi Journal of Kidney Diseases and Transplantation. 2018;29(3):643-8. [DOI]
16. Rajesh NJ, Swaraj CI. Clinicopathological Study of Spectrum of Primary Nephrotic Syndrome in Adults. Journal of Contemporary Medicine and Dentistry. 2021;9(3):27-31. [Link]
17. Sheikh Zubair JA, Nissar SM, Pala MR, Hussain A, Pala MR, Latief M. Clinicopathologic Spectrum of Nephrotic Syndrome in the Elderly. Journal of Renal and Hepatic Disorders. 2023;7(1):34-7. [DOI]
18. Satpathy SK, Pradhan SK, Bhat S, Krishnamoorthy A. Single-center Experience of Histopathological Spectrum and Treatment Profile in Adolescent-onset Nephrotic Syndrome in India. Journal of Pediatric Nephrology. 2018;6(1). [DOI]
19. Rathi M, Bhagat R, Mukhopadhyay P, Kohli H, Jha V, Gupta K, et al. Changing histologic spectrum of adult nephrotic syndrome over five decades in north India: A single center experience. Indian journal of nephrology. 2014;24(2):86-91. [DOI]
20. Joshi A, Gajare L, Mahore S. Changing spectrum of nephrotic syndrome: A clinicpathology study. World J Pharm Res. 2019;8:885-96. [DOI]
21. Golay V, Trivedi M, Kurien AA, Sarkar D, Roychowdhary A, Pandey R. Spectrum of nephrotic syndrome in adults: Clinicopathological study from a single center in India. Renal Failure. 2013;35(4):487-91. [DOI]
22. Agarwal S, Dash S. Spectrum of renal diseases in Indian adults. The Journal of the Association of Physicians of India. 2000;48(6):594-600. [PubMed]
23. Choi IJ, Jeong HJ, Han DS, Lee JS, Choi KH, Kang SW, et al. An analysis of 4,514 cases of renal biopsy in Korea. Yonsei medical journal. 2001;42(2):247-54. [PubMed]
24. Chang JH, Kim DK, Kim HW, Park SY, Yoo T-H, Kim BS, et al. Changing prevalence of glomerular diseases in Korean adults: a review of 20 years of experience. Nephrology Dialysis Transplantation. 2009;24(8):2406-10. [DOI]
25. Zhou F-d, Shen H-y, Chen M, Liu G, Zou W-z, Zhao M-h, et al. The renal histopathological spectrum of patients with nephrotic syndrome: an analysis of 1523 patients in a single Chinese centre. Nephrology Dialysis Transplantation. 2011;26(12):3993-7. [DOI]
26. Kazi JI, Mubarak M, Ahmed E, Akhter F, Naqvi SAA, Rizvi SAH. Spectrum of glomerulonephritides in adults with nephrotic syndrome in Pakistan. Clinical and experimental nephrology. 2009;13:38-43. [DOI]
27. Pakasa M, Mangani N, Dikassa L. Focal and segmental glomerulosclerosis in nephrotic syndrome: a new profile of adult nephrotic syndrome in Zaire. Modern Pathology: an Official Journal of the United States and Canadian Academy of Pathology, Inc. 1993;6(2):125-8. [PubMed]
28. Shaker IK, Al-Saedi AJ, Al-Salam S, Saleem MS, Al-Shamma IA. Spectrum of glomerular disease in Iraqi patients from a single center. Saudi Journal of Kidney Diseases and Transplantation. 2002;13(4):515-9. [PubMed]
29. Medawar W, Green A, Campbell E, Carmody M, Donohoe J, Doyle G, et al. Clinical and histopathologic findings in adults with the

nephrotic syndrome. Irish journal of medical science. 1990;159:137-40. [DOI]

30. Riabov S, VIa P, Klemina I. Nephrotic syndrome in primary glomerulonephritis. Terapevticheskii Arkhiv. 1986;58(8):65-71. [DOI]
31. Braden GL, Mulhern JG, O'Shea MH, Nash SV, Ucci Jr AA, Germain MJ. Changing incidence of glomerular diseases in adults. American journal of kidney diseases. 2000;35(5):878-83. [DOI]
32. Aggarwal H, Yashodara B, Nand N, Chakrabarti D, Bharti K. Spectrum of renal disorders in a tertiary care hospital in Haryana. The Journal of the Association of Physicians of India. 2007;55:198-202. [PubMed]
33. Nath MY, Dar MA, Wani FD. Changing histological spectrum of adult nephrotic syndrome in comparison to previous study: single centre analysis. International Journal of Research in Medical Sciences. 2023;11(2):551-7. [DOI] [Link]
34. Agarwal S, Sethi S, Dinda A. Basics of kidney biopsy: A nephrologist's perspective. Indian journal of nephrology. 2013;23(4):243-52. [DOI]
35. Reshi A, Bhat M, Najar M, Banday K, Naik M, Singh D, et al. Etiological profile of nephrotic syndrome in Kashmir. Indian Journal of nephrology. 2008;18(1):9-12. [DOI]

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