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Pathology

HISTOPATHOLOGIC PATTERNS OF NEPHROTIC SYNDROME - A COMPARATIVE ANALYSIS IN PEDIATRIC AND ADULT POPULATION FROM A TERTIARY CARE CENTRE IN CENTRAL TRAVANCORE

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ABSTRACT This was a retrospective cross-sectional study done to understand the spectrum of histopathological patterns of nephrotic syndrome in both adult and pediatric population. We analyzed renal biopsies from 171 patients with nephrotic syndrome at a tertiary care center over five years (2019-2023). The study included patients with nephrotic-range proteinuria (urine albumin >3.5g/day or urine protein-creatinine ratio >3.5). The mean age of the study population was found to be 44.88 ± 17.63 years, with 60.8% males and 39.2% females. Primary nephrotic syndrome constituted 17.5% of cases, while secondary nephrotic syndrome comprised the majority of the cases (82.5%). Among primary cases, membranous nephropathy (33.3%), minimal change disease (MCD) (23.3%), and focal segmental glomerulosclerosis (FSGS) (26.7%) were the predominant lesions. Secondary nephrotic syndrome was mainly attributed to diabetic glomerulosclerosis (33.3%), proliferative glomerulonephritis (27.7%) and IgA nephropathy (22.7%),. The study observed that primary nephrotic syndrome was more common in children as compared to adults in whom secondary causes predominated. Membranous nephropathy was exclusively seen in adults, while MCD and IgM nephropathy were more frequent in pediatric cases.This study provides valuable insights into the histopathological spectrum of nephrotic syndrome in South Kerala, highlighting the importance of renal biopsy as a diagnostic tool,non MCD causes of nephrotic syndrome in pediatric population especially IgM nephropathy and predominance of secondary causes in adults.

KEYWORDS : renal biopsy.nephrotic syndrome, immunofluorescence

INTRODUCTION

Nephrotic syndrome is a common manifestation of many forms of primary and secondary glomerulopathies. Nephrotic syndrome commonly presents as edema, hypoalbuminemia, hypertension, dyslipidemia, the presence of nephrotic-range proteinuria and with a urine protein-creatinine ratio of greater than 3.0 to 3.5. Nephrotic syndrome can have primary or secondary etiologies which varies with age and geography. Primary causes of nephrotic syndrome are MCD, membranous nephropathy, and FSGS.Systemic causes include diabetes mellitus, lupus nephritis, amyloidosis, certain infections like malaria, NSAIDs etc[4].IgA nephropathy, membranoproliferative glomerulonephritis and IgM nephropathy can also present as nephrotic syndrome. Status of IgM nephropathy as a distinct entity of non-proliferative glomerulonephritis still remains debated[3].While MCD is considered the most common cause of nephrotic syndrome in children; membranous nephropathy predominates in older adults. Over the recent years various studies have highlighted a changing trend in the pattern of lesions, according to which FSGS shows a significant increase in proportion making it more common than MCD in pediatric population[1].Steroids remain the mainstay of treatment. Besides steroids newer treatment options like immunomodulators and monoclonal antibodies are available today which are used for steroid resistant cases to achieve remission. An accurate diagnosis is based on the clinical picture and renal biopsy especially in cases with steroid dependence or resistance. Renal biopsy is a safe and low-risk procedure in patients of all ages[3]which plays an important role in the diagnosis and classification of both adult and pediatric medical renal diseases and is invaluable in guiding treatment and assessing the prognosis.[3,4] Various glomerular diseases, both primary and systemic, result in nephrotic syndrome, the incidence of which varies with age and geography. The common histopathologic patterns include MCD, FSGS and membranous nephropathy while IgA nephropathy nephropathy and MPGN constitute the less common lesions. This study was undertaken to get a better outlook on the spectrum of pathological patterns of nephrotic syndrome and to analyse the clinicopathologic differences in pediatric and adult patients thus providing information regarding the pattern of histopathological lesions in cases of nephrotic syndrome in both adult and pediatric population in South Kerala.

MATERIALS AND METHODS

This was a retrospective cross-sectional study which included renal biopsies received in the Department of Pathology in Pushpagiri Institute of Medical Sciences & Research Centre over a period of five years from January 2019 to December 2023.All renal biopsies with a clinical diagnosis of nephrotic syndrome were included.Sample size based on 1-year statistics was calculated with the formula $N= 4pq/d^2$ and was determined as 121 for a period of 5 years.

Inclusion Criteria:

1. Cases with a clinical diagnosis of nephrotic syndrome
2. Cases with nephrotic range of proteinuria (urine albumin 3+ / urine albumin >3.5g/day)
3. Cases with high urine protein creatinine ratio (>3.5)

Cases with inadequate clinical data and insufficient laboratory investigations were excluded from the study. Based on the inclusion and exclusion criteria 171 cases were evaluated for their demographic data, clinical, histopathological and immunofluorescence features. All renal biopsy specimens were processed, cut and stained, and evaluated under light microscopy based on H and E staining including special stainsImmunofluorescence staining was performed on 4 µm thick cryostat sections obtained from snap-frozen sections. The sections were tested with antibodies and complement components including immunoglobulin G (IgG), IgM, IgA, C3, C1q, and kappa and lambda light chains. Statistical Package for Social Sciences (SPSS) version 19.0 (IBM Corp. San Francisco) was used for statistical analysis.

The frequency of lesions was studied separately in pediatric and adult patients. All the data collected were entered in a specific proforma and statistically analysed using appropriate tools. Categorical variables are reported as frequencies and percentages and continuous variables as mean ± standard deviation. For descriptive purposes, data was stratified according to age and sex and entered in tabulated and graphical form.

RESULTS

The study population included 171 patients, with a mean age of 44.88 ± 17.63 years. The age distribution showed a wide range, with 1.8% of patients aged 0-10 years and 5.3% older than 70 years. The majority, (91.2%) were adults, while 8.8% were pediatric cases. The gender distribution was 60.8% (104 cases) males and 39.2% (67 cases) females.

Table:1 Gender Distribution Of The Study Population

Gender	Frequency	Percentage
Males	104	60.8
Females	67	39.2

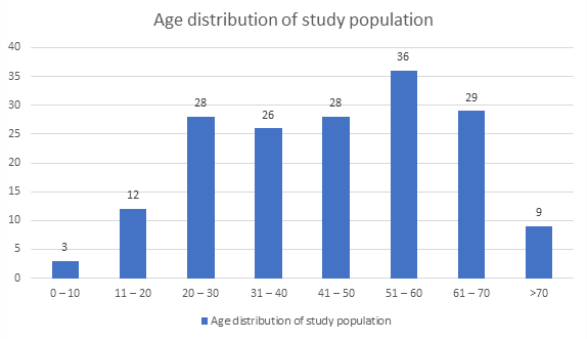

Figure 1: Age Distribution Of The Study Population

Table: 2 Frequency Of Adult And Pediatric Cases

Age group	Frequency	Percentage
Paediatric (<16 years)	8	8.8
Adult	163	91.2
Total	171	100.0

Primary nephrotic syndrome accounted for 17.5% of cases, and secondary nephrotic syndrome predominated with 82.5%. Among primary nephrotic syndrome cases, 26.7% were pediatric and 73.3% were adult. All the pediatric cases were of primary nephrotic syndrome. The primary lesions included membranous nephropathy (33.3%), MCD (23.3%), FSGS (26.7%), and IgM nephropathy (16.7%). Membranous nephropathy was exclusively observed in adults, while MCD and IgM nephropathy were more frequent in pediatric cases.

Table: 3 Distribution Of Nephrotic Syndrome As Primary And Secondary Among The Study Population

Nephrotic syndrome	Frequency	Percentage
Primary	30	17.5
Secondary	141	82.5
Total	171	100.0

Table:4 Distribution Of Primary Nephrotic Syndrome In Adult And Pediatric Population

Primary nephrotic syndrome	Frequency	Percentage
Paediatric	8	26.7
Adult	22	73.3
Total	30	100.0

Table5: Distribution Of Types Of Primary Nephrotic Syndrome

Primary nephrotic syndrome	Frequency	Percentage
Membranous nephropathy	10	33.3
MCD	7	23.3
FSGS	8	26.7
IgM N	5	16.7
Total	30	100.0

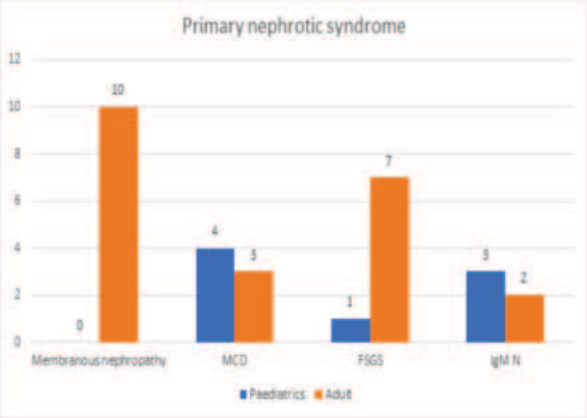

Figure 2 : Distribution Of Primary Nephrotic Syndrome

Secondary nephrotic syndrome lesions were observed as dominant lesion in adult population and comprised IgA nephropathy (22.7%), diabetic glomerulosclerosis (33.3%), crescentic glomerulonephritis (0.7%), lupus nephritis (1.4%), renal amyloidosis (1.4%), arterionephrosclerosis (9.2%), chronic interstitial nephritis (3.6%), and proliferative glomerulonephritis (27.7%).

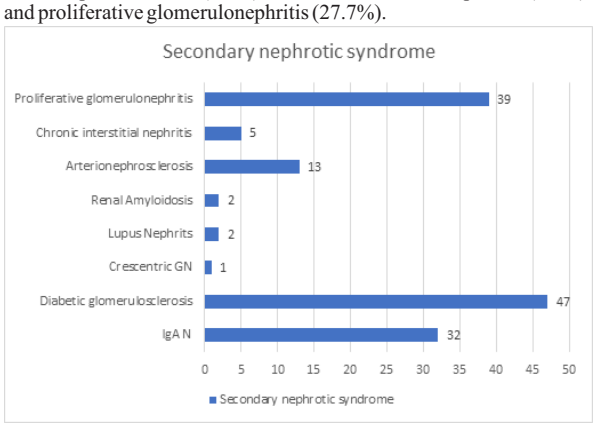

Fig 3 Distribution Of Secondary Nephrotic Syndrome

Comorbidities were common, with hypertension present in 32.7% of patients, diabetes mellitus in 4.1%, and both conditions in 29.9%.

Table :6 Distribution Of Comorbidities Among The Study Participants

Comorbidities	Frequency	Percentage
Hypertension	56	32.7
Diabetes mellitus (DM)	7	4.1
Both DM and hypertension	51	29.9

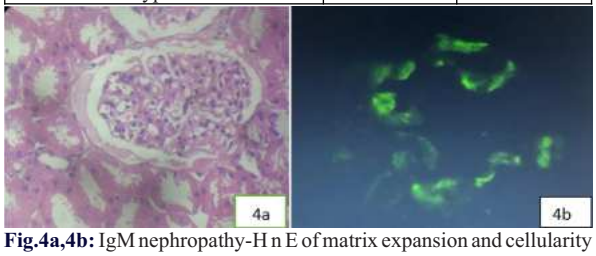

Fig.4a,4b: IgM nephropathy-H n E of matrix expansion and cellularity and IF showing IgM deposits

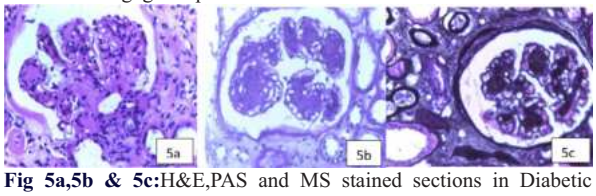

Fig 5a,5b & 5c:H&E,PAS and MS stained sections in Diabetic nephropathy showing KW nodules

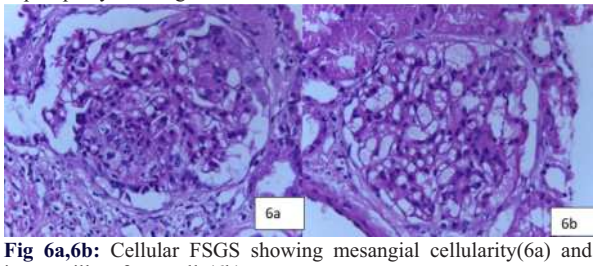

Fig 6a,6b: Cellular FSGS showing mesangial cellularity(6a) and intracapillary foam cells(6b)

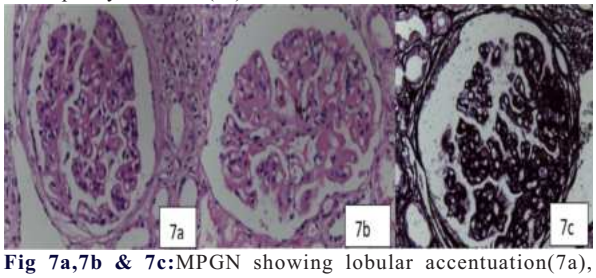

Fig 7a,7b & 7c:MPGN showing lobular accentuation(7a), endocapillary hypercellularity(7b) and wire loop lesions(7c)

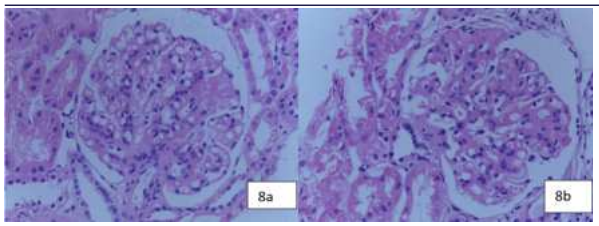

Fig 8a & 8b: Mesangioproliferative glomerulonephritis with matrix expansion(8a) and segmental sclerosis(8b)

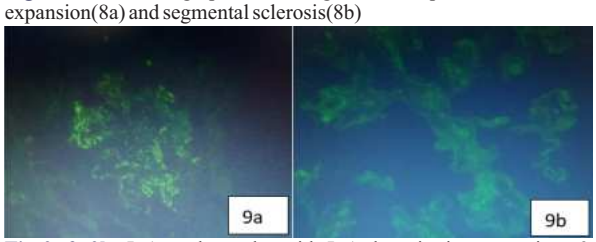

Fig 9a& 9b: IgA nephropathy with IgA deposits in mesangium & capillary wall in IF

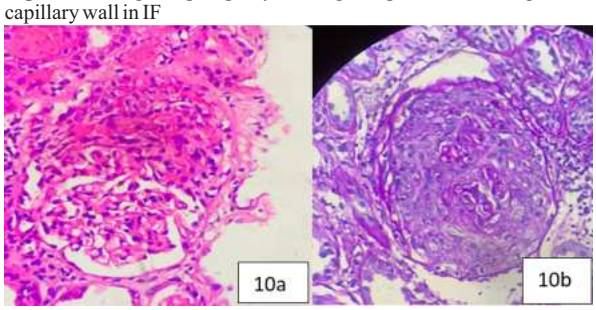

Fig 10a & 10 b: cellular crescents(a),PAS(b)

DISCUSSION

This study provides a comprehensive analysis of the histopathologic patterns of nephrotic syndrome in a tertiary care center in South Kerala. The findings are consistent with few of the published studies though there are differences with other researches which highlights regional variations and evolving trends in the histopathologic patterns of nephrotic syndrome The study highlight the predominance of secondary nephrotic syndrome (82.5%) over primary forms (17.5%), which may be attributed to the increasing prevalence of systemic diseases like diabetes mellitus and hypertension in the population.

The mean age of the study population (44.88 ± 17.63 years) indicates that nephrotic syndrome is more prevalent in adults, which is supported by the observation that 91.2% of the cases were adults. This is consistent with previous studies that have reported a higher incidence of nephrotic syndrome in the adult population.

Among primary nephrotic syndrome cases, membranous nephropathy, MCD, and FSGS were the most common lesions. Membranous nephropathy was exclusively seen in adults, which was concordant with the established pattern in older adults. MCD, traditionally considered the most common cause of nephrotic syndrome in children, was also observed in this study, although FSGS also had a significant proportion (26.7%) in primary cases[3]. This observation supports the changing trend noted in recent studies, where FSGS is increasingly becoming a common cause of nephrotic syndrome in children.

Arif MK et al.[1] (2016) observed FSGS as the most common subtype (46.8%) in children, followed by membranous glomerulonephritis (14.7%) and MCD (25.3%). This is partially consistent with our findings, which also showed FSGS as a significant primary lesion though MCD predominated. They also found that FSGS was the main underlying cause of steroid resistant NS. The study highlighted the emergence of non-MCD as the common cause of nephrotic syndrome in the pediatric population and signifies the importance of renal biopsies in children.

A study by Ibrahim Seif E et al[2]. (2013) in Egyptian children reported FSGS as the most common histopathological pattern (30.2%), followed by MCD (24.5%) and IgA nephropathy (13.2%). In contrast, our study found membranous nephropathy to be the most common primary lesion, followed by FSGS and MCD. This difference could be attributed to variations in study populations, age groups, and geographical locations.

Secondary nephrotic syndrome in this study was mainly attributed to diabetic glomerulosclerosis, IgA nephropathy, and proliferative glomerulonephritis. Diabetic glomerulosclerosis, the leading cause, reflects the high prevalence of diabetes mellitus in the study population (34%). This finding underscores the importance of screening for and managing systemic diseases that can lead to nephrotic syndrome.

Yusuf et al. [13](2016) reported membranoproliferative glomerulonephritis (MPGN) as the most common cause (36.8%) in adults, followed by mesangial proliferative glomerulonephritis (31%) and membranous glomerulonephritis (18.4%). Our study, while including MPGN in secondary lesions, found diabetic glomerulosclerosis and IgA nephropathy to be more prevalent.

A study conducted by Chae Y et al.,[19]2021compared renal outcomes of IgMN patients with those of patients with minimal change disease (MCD), focal segmental glomerulosclerosis (FSGS), or mesangial proliferative glomerulonephritis (MsPGN) from a prospective observational cohort and indicated that IgMN would have a clinical course and renal prognosis similar to MCD, FSGS, and MsPGN.

Tarik H et al.,[21]2007 showed Mesangioproliferative GN as the commonest underlying cause which was found in 36 (40%) cases followed by minimal change disease in 22 (24.44%), membranous GN 16 (17.77%), membranoproliferative glomerulonephritis 12 (13.33%), Focal segmental glomerulosclerosis 3 (3.34%) and IgA nephropathy 1 (1.12%) cases.

Our findings differ, with diabetic glomerulosclerosis being the predominant secondary lesion. These differences highlight the variability in histopathologic patterns across different regions and time periods and also reflect differences in the prevalence of diabetes and other systemic diseases between the study populations.

The distribution of comorbidities in this study further emphasizes the role of systemic diseases in nephrotic syndrome. Hypertension and diabetes mellitus, both significant risk factors for renal disease, were highly prevalent in the study population. This highlights the need for a comprehensive approach to managing nephrotic syndrome, including addressing underlying systemic conditions.

CONCLUSION

Histopathological spectrum of nephrotic syndrome is wide and varies among age groups and geographical areas. This study provides valuable insights into the histopathologic patterns of nephrotic syndrome with reference to the particular study population in South Kerala. The findings highlight the predominance of secondary nephrotic syndrome, particularly diabetic glomerulosclerosis, and the changing trends in primary lesions such as FSGS. The study also underscores the importance of considering age-specific variations in the histopathologic patterns. Further research, including prospective studies with larger and more diverse populations, is needed to validate these findings and explore the long-term clinical implications of the different histopathologic lesions.

ABBREVIATIONS

NS-nephrotic syndrome
MCD-minimal change disease
FSGS-focal segmental glomerulosclerosis
MPGN-membranoproliferative glomerulonephritis
DM-diabetes mellitus
INS-idiopathic nephrotic syndrome
IgMN-IgM nephropathy
MsPGN-mesangioproliferative glomerulonephritis

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