www.jmscr.igmpublication.org
Index Copernicus Value: 79.54
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossrefDOI: https://dx.doi.org/10.18535/jmscr/v7i1.168

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Spectrum of Nephrotic Syndrome in Adults: Clinicopathological Study in a tertiary health care

Authors
Dr Shwetha Prasad B.S[1*], Dr Sunil R[2], Dr Varun Manjunath[3], Dr Priyanka Venkatesh[4], Dr Shathak S Baikady[5], Dr Vikyath Sathish[6]
[1]Junior Resident, Department of General Medicine, Kempegowda Institute of Medical Sciences and Hospital, Bangalore
[2]Associate Professor, Department of Nephrology, Kempegowda Institute of Medical Sciences and Hospital, Bangalore
[3]Junior Resident, Department of General Medicine, Kempegowda Institute of Medical Sciences and Hospital, Bangalore
*Corresponding Author
Dr Shwetha Prasad B.S
Junior Resident, Department of General Medicine, KIMS Hospital, Bangalore, India
Email: *shwethaspbs@gmail.com*

Abstract
Background: *Nephrotic syndrome is one of the most common, yet, perplexing disease encountered by a nephrologist. The Nephrotic syndrome is now defined in published literature as a pentad of proteinuria more than 3.5 g per 24 h, hypoalbuminemia, edema, hyperlipidemia, and lipiduria Diseases causing the Nephrotic syndrome are generally categorized into those that primarily involve the kidney and those in which kidney involvement is part of a systemic disorder. Limited data from the Indian subcontinent on adult NS also show FSGS as the most common etiology. We present the clinicopathological study on the spectrum of NS in adults presenting to our center.*
Methods: *It is a retrospective study conducted on 50 subject's age more than 16 years who underwent renal biopsy in KIMS hospital, Bengaluru.*
Results: *A total of 50 patients were analysed in our study with the mean age of 41.07 years. 43 (86%) were diagnosed with primary glomerular disease and 7 (14 %) with secondary glomerular disease. Among the patients, focal segmental Glomerulosclerosis was the most common nephropathy seen i.e, in 15(30%) followed by in membranous and membranoproliferative glomerulonephritis in 8 (16%). Among the primary glomerular disease, the most common lesions were FSGS in 30%, membranoproliferative glomerulonephritis (MPGN) and membranous glomerulonephritis (MGN) in 16% each. 31(62%) of patients had deranged Renal function tests.*
Conclusion: *FSGS was the most common cause of nephrotic syndrome in adults.*
Keywords: *nephrotic syndrome, focal segmental glomerulosclerosis, renal biopsy.*

Introduction

Since the description of the clinical presentation as early as in the fifteenth century and its later description as "nephrosis,"[1] nephrotic syndrome (NS) remains one of the most common, yet, perplexing disease encountered by a nephrologist.

Nephrotic Syndrome is defined in published literature as a pentad of proteinuria more than 3.5 g per 24 h, edema, lipiduria, hypoalbuminemia and hyperlipidemia[2] . The prevalence of biopsy-proven glomerulonephritis varies according to the geographic area, socioeconomic condition, race, age, demography and indication of renal biopsy. The most common indications of renal biopsy were nephrotic syndrome, followed by chronic renal failure and rapidly progressive renal failure. The incidence of IgAN and FSGS has been increasing since 1999.[3]

Data compiled during the 1970s and early 1980s indicated membranous nephropathy was the most common cause of unexplained nephrotic syndrome in adults during this period, followed in order of frequency by minimal-change nephropathy and focal segmental glomerulosclerosis (FSGS). The main findings of this study were that, during the 1976 to 1979 period, the relative frequencies of membranous (36%) and minimal-change (23%) nephropathies and of FSGS (15%) as causes of unexplained nephrotic syndrome were similar to those observed in previous studies during the 1970s and early 1980s. In contrast, from 1995 to 1997, FSGS was the most common cause accounting for 35% of cases compared with 33% for membranous nephropathy.[4] In a study conducted retrospectively of the reports of 9,617 renal biopsies, analyzed by the same pathologist, from January 1993 to December 2007 in Brazil the result showed that the most frequent primary glomerular disease was FSGS, followed closely by MN and IgAN. The predominance of FSGS is in accordance with recent studies all over the world that revealed its frequency is increasing. Lupus nephritis predominated among secondary GN in most regions, a finding observed in other studies.[5] A review study was done in India as there is absence of a renal biopsy registry, there is a paucity of data on the renal disease pattern seen in India. This is the largest series of renal biopsy data from India; and therefore, could reflect the demographic picture of renal diseases in this country. It discusses evolving patterns over 30 yrs and highlights differences with the developed world. This report represents the basis for the future of a renal biopsy registry in India.[6]

Methods

The kidney biopsies of 50 patients that were performed in the nephrology unit of KIMS hospital, Bangalore, India, from April 2016 to September 2018 were retrospectively analyzed. The clinical records of these patients were reviewed and Nephrotic syndrome was diagnosed according to the accepted definition. All patients more than 16 years of age with a clinical diagnosis of Nephrotic syndrome and undergoing a kidney biopsy during this period were included for the study. The baseline clinical details along with the relevant laboratory investigations were recorded. Majority of the patients had been satisfactorily worked up for secondary aetiologies depending on the clinical presentation and glomerular histology.

The renal biopsy was done under real-time Ultrasound (USG) guidance using the 18G × 16 cm Bard®Max-Core®Disposable Core Biopsy Instrument. Two cores were obtained and the samples were examined using light microscopy (LM) and immunofluorescence (IF) microscopy in all cases and using electron microscopy (EM) in selected cases or when it could be afforded by the patient. LM was done using hematoxylin & eosin, periodic acid Schiff, Jones silver, and trichrome stains. Additional special stains were used whenever indicated. IF staining was performed on 3-μm cryostat sections using polyclonal fluorescein-isothiocyanate-conjugated antibodies to IgG, IgM, IgA, C3, C1q, kappa, and lambda light chains. The intensity of IF staining was graded on a scale of 0 to 3+.

All the kidney biopsy examinations were confirmed by the same pathologist. Biopsies where a clinical diagnosis was not possible due to paucity of the number of glomeruli in either the LM or IF sample according to the pathologist were excluded from the study.

Results

A total of 50 patients were analysed in our study. The average age of the presentation was 41.07 + 15.61. Out of 50 patients, 36 were male and 14 were female. Among the patients,18 (36%) had hypertension and 13 were diabetics.

Table 1: the various pathological findings of Renal biopsy

	Primary Glomerular Disease	Secondary Glomerular Disease
Membranous glomerulonephritis	8	NA
Minimal change disease	5	NA
Focal Segmental Glomerulosclerosis	15	NA
Membranoproliferative glomerulonephritis	8	NA
Other proliferative Glomerulonephritis	7	NA
Diabetes	NA	4
SLE	NA	3
Total	43	7

Among the 50 patients, 43 (86%) were diagnosed with primary glomerular disease and 7 (14 %) with secondary glomerular disease. Among the patients, focal segmental Glomerulosclerosis was the most common nephropathy seen i.e, in 15(30%) followed by in membranous and membranoproliferative glomerulonephritis in 8 (16%).

Among the primary glomerular disease, the most common lesions were FSGS in 30%, membrano-proliferative glomerulonephritis (MPGN) and membranous glomerulonephritis (MGN) in 16% each.

In this study, 31(62%) of patients had deranged Renal function tests.

Discussion

There are only a limited number of studies from India on the spectrum of glomerular diseases, and in these studies various studies of NS in adults have not been looked into.[3,7,8] In this study, diabetic nephropathy was the leading cause of the primary adult NS and was seen in 30 % of the cases followed by FSGS which seen in 18% of the cases. Kazi et al. from Pakistan reported FSGS, with an incidence of 39.87%, as the commonest lesion seen in adults with NS.[8]

There are several biases regarding demographical, geographical and racial characteristics, differences in indications for renal biopsy, the analyzed clinical syndromes and variations in pathological classification. Hence, comparison with different data and drawing accurate conclusions were difficult. Nephritic syndrome was the most frequent clinical presentation at all age groups. Male predominance was seen in the overall cases except in SGN.[3]

The underlying etiology of NS is variable across the world. PGN was the most predominant renal disease followed by SGN and TIN.[3] MCD has a variable geographic distribution, being more common in some Asian than in the western countries.

In this study, FSGS was the most common PGN seen. Though it is believed that MN is the most common PGD in adults, a review of different literatures reveals that most of the studies have shown MN to be the third or fourth common cause of PGD.[3] Our results also support this.

Minimal change disease was uncommon in this study. IgAN was uncommon in the present study and similar trend has been seen in studies conducted elsewhere.

Conclusion

Thus to conclude, considerable heterogenecity has been seen in the histological spectrum of nephritic syndrome. Recent studies conducted have shown increased incidence of FSGS making it the most common cause of nephrotic syndrome. FSGS was also the most common biopsy diagnosis in our patients with nephrotic syndrome in our study.

Acknowledgement

We extend our gratitude to all the faculty members of the Department of Nephrology and all the other supporting departments and the management for giving their valuable opinion and suggestions during discussion and extending their help in working towards this article. We extend our gratefulness to all the patients. A special thanks goes to Dr Manjunath, Professor and HOD,

department of medicine for giving his support in making this study a success.

Source of support in form of grants: nil
Conflicts of interest: nil

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