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Clinicopathological Study of Spectrum of Primary Nephrotic Syndrome in Adults

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Abstract

***Background**: Nephrotic syndrome is characterized by the presence of proteinuria, more than 3.5 g per 24 h, hypoalbuminemia, edema, hyperlipidemia, and lipiduria. The spectrum of diseases causing nephrotic syndrome has changed in the past few decades. The current study aimed to study the clinicopathological spectrum of adults presenting with Nephrotic syndrome to our tertiary care teaching Hospital. **Methods**: Based on the inclusion and exclusion criteria details of patients were collected in pretested and validated questionnaires. The data included the sociodemographic profile. Details of clinical history. The selected cases underwent a thorough clinical examination. The investigations included urine microscopic examination, blood sugar levels, renal functions tests, urinary total protein, serum lipid profile, serum total protein, and albumin. **Results**: Out of n=45 cases males were n=33 and females were n=12 40% were hypertensive and 26.67% were diabetic. Dyslipidemia was found in 66.67% cases hematuria was present in 28.89% cases and oliguria in 8.89% cases and anemia in 62.22% cases. In this study minimal change nephropathy (MCN) was common in 16(35.56%) cases, Focal segmental glomerulosclerosis (FSGN) was the second common cause in 10 (22.22%) cases. **Conclusion:** This study found Minimal Change Nephropathy as the predominant microscopic lesion in the spectra of Nephrotic syndrome. Male preponderance was noted, 18-30 years of the age group of patients being affected more commonly presenting facial puffiness as the commonest symptom. 40% of cases were detected with hypertension and hyperlipidemia.*

***Keywords**: Nephrotic Range of Proteinuria, Renal Biopsy, Light Microscopy, Electron Microscopy, Immunofluorescence.*

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Introduction

The term Nephrotic Syndrome (NS) is a clinical complex characterized by renal and extrarenal features, the most prominent of which are proteinuria of >3.5 grams per 1.73 m^2 per 24 h (in practice >3.0 to 3.5 grams Per 24 h), Hypoalbuminemia, Edema, Hyperlipidemia, Lipiduria, and Hypercoagulability. Proteinuria arising from defects in glomerular permeability can result from abnormalities in the charge selective or size-selective barrier. [1-3] Charge-selective barrier defects arise from diffuse biochemical changes in glomerular structure usually not associated with recognizable abnormalities at the level of the light microscope. Protein excretion rates in the nephrotic syndrome vary widely and are influenced considerably by the GFR, the plasma concentration of albumin, and dietary protein intake. [1, 4, 5] The prevalence of biopsy-proven glomerulonephritis varies according to the geographic area, socioeconomic condition, race, age, demography, and an indication of renal

biopsy. The most common indications of the renal biopsy were nephrotic syndrome, followed by chronic renal failure and rapidly progressive renal failure. [6] Studies have shown that membranous glomerulonephritis is the common cause of adult nephrotic syndrome in the USA and Europe. [7] but recent studies have found that focal segmental glomerulosclerosis (FSGN) is the common glomerular disease in African American and Hispanic populations. [7, 8] Few studies from India have shown a declining incidence of mesangiocapillary glomerulonephritis and an increasing trend for focal segmental glomerulosclerosis. [9, 10] Italian, Spanish and Japanese registries have reported membranous nephropathy (MN) as the most common etiological factor in adults for (NS). [11-13] The causes of secondary nephrotic syndrome include hypertension, diabetes mellitus, amyloidosis, and lupus nephritis. Diabetes mellitus is the far more common cause among all the other causes. [14] The usual clinical manifestations of NS in adults include edema of lower limbs, weight gain, and fatigue. In advanced cases, there may be periorbital edema, genital edema, ascites, pleural or pericardial effusions. [15-16] Since there is a paucity of data available for the spectrum of glomerular diseases in our region, we in the current study tried to evaluate the clinicopathological spectrum of nephrotic syndrome cases in adults reporting to our tertiary care teaching hospital.

Materials and Methods

This cross-sectional study was conducted in the Department of General Medicine, Prathima Institute of Medical Sciences, Naganoor, Karimnagar. Institutional Ethical approval was obtained for the study after following the due protocol for human research based on the Helsinki declaration. Written consent was obtained from all the participants of the study.

Sampling Method: Convenient Sampling (total number of samples included were n=45)

Inclusion criteria

1. Patients above the age of 18 years
2. Males and Females
3. diagnosis of nephrotic syndrome (proteinuria ≥ 3gm/24 hours, hypoalbuminemia, edema, hyperlipidemia, and lipiduria)
4. Patients were willing to participate in the study voluntarily.

Exclusion criteria

1. Patients with drug-induced or iatrogenic nephropathy
2. Patients with acute pyelonephritis, unilateral solitary kidney
3. Patients with vesicoureteric reflux and eGFR < 15 ml/min/1.73 m^2
4. Rapidly progressive glomerular nephropathy [RPGN]
5. Secondary nephrotic syndrome like Systemic Lupus Erythematosis, Amyloidosis, Diabetes Mellitus with retinopathy

Based on the inclusion and exclusion criteria details of patients were collected in pretested and validated questionnaires. The data included the sociodemographic profile. Details of clinical history. The selected cases underwent a thorough clinical examination. The investigations included urine microscopic examination, blood sugar levels, renal functions tests, urinary total protein, serum lipid profile, serum total protein, and albumin. Serological tests for syphilis, Hepatitis B, HIV, antinuclear antibody, and anti-ds-DNA in the patients who were suspected of systemic lupus erythematosus were done. Renal biopsy was taken in all the cases. The biopsies were carried out under real-time USG guidance under local anesthesia with a 22-gauge tru-cut needle. The tissue samples were sent to the Department of Pathology for examination and diagnosis by an expert pathologist.

Data Processing: All the available data was uploaded on MS Excel spreadsheet and analyzed by SPSS version 19 on windows format for descriptive statistics such as mean, standard deviation, percentage, and analytical statistics was used to interpret the results p values of <0.05 was considered significant.

Results

In the current study, the majority of patients 15 (33.33%) were from the age group 18 – 30 years followed by 41 – 50 years with 13 (28.89%) cases. Patients in the age group 31 – 40 years and 41 – 50 years were 05 (11.11%). The mean age of the patients in this study was 36.5 ± 7.5 years details depicted in table 1. Out of n=45

cases studied male preponderance is seen with a male to female ratio of 2.75: 1.

Table 1: Age-wise and sex-wise distribution of Nephrotic syndrome patients

Age group in years	*Male*	*Female*	*Total (%)*
18 – 30	12	03	15 (33.33)
31 – 40	03	02	05 (11.11)
41 – 50	09	04	13 (28.89)
51 – 60	04	01	05 (11.11)
61 – 70	04	00	04 (8.89)
> 70	01	02	03 (6.67)
Total	33	12	45 (100)

The predominant clinical presentations of the patients with nephrotic syndrome included pedal edema in 77.78% cases, facial puffiness especially around the eyes in 55.56% cases, weight gain was reported in 73.33% cases fatigue was reported by 55.56% of patients and foamy urine was present in 26.67% cases. Out of n=45 cases, 40% were hypertensive and 26.67% were diabetic. Dyslipidemia was found in 66.67% cases hematuria was present in 28.89% cases and oliguria in 8.89% cases and anemia in 62.22% cases. In this study minimal change nephropathy (MCN) was common in 16(35.56%) cases, Focal segmental glomerulosclerosis (FSGN) was the second common cause in 10 (22.22%) cases the other causes and the percentage has been depicted in table 2.

Table 2: Histopathological diagnosis of Nephrotic syndrome

Histopathological type	Male	Female	Total (%)
Minimal change nephropathy (MCN)	11	5	16 (35.56)
Focal segmental glomerulosclerosis (FSGN)	6	4	10 (22.22)
Membranous Glomerulo Nephropathy (MGN)	2	1	03 (06.67)
Membranoproliferative glomerulonephritis (Memb PGN)	7	2	09 (20.00)
Mesangioproliferative Glomerulonephritis (Mesan PGN)	6	0	06 (13.33)
IgA Glomerulonephropathy	01	0	01 (2.22)

In our study, no patient had abnormal TSH value or reactivity to viral markers like HBsAg, Anti HCV antibody, HIV 1 and 2 antibodies. Proteinuria was 6.31± 2.58 g/24 hr. Mean serum urea was 39.50 ± 15.65 mg/dl. Other parameters were Serum creatinine (1.54± 0.83 mg/dl), mean serum albumin (2.34± 0.75 mg/dl) and mean total cholesterol (320.55± 130.21 mg/dl) given in table 3.

Table 3: Laboratory parameters in patients with nephrotic syndrome

Parameter	*Mean ± SD*
Proteinuria (g/24 hours)	6.31 ± 2.58 g/24 hours
Serum urea mg/dl	39.50 ± 15.65
Serum creatinine mg/dl	1.54 ± 0.83
Serum albumin mg/dl	2.34 ± 0.75
Total cholesterol mg/dl	320.55 ± 130.21

Discussion

In the current study most patients 15(33.33%) were from the age group 18 – 30 years. Out of n=45 cases studied male preponderance is seen with a male to female ratio of 2.75: 1. A similar study by SM Korbet et al., [1] found that age-specific prevalence of nephrotic syndrome as 43 ± 17 years and 57% were male, of which MCN was 14% and FSGS 57%, IgA 2%, in blacks, and for whites MCN 20%, and FSGS 23%. Registry data from India and Pakistan show that glomerular diseases contribute to approximately 14% of cases of chronic kidney diseases. [17] The predominant clinical presentations of the patients with nephrotic syndrome included pedal edema in 77.78% cases, facial puffiness especially around the eyes in 55.56% cases, weight gain was reported in 73.33% cases fatigue was reported by 55.56% of patients and foamy urine was present in 26.67% cases. In this study, the patients did not have any complications of Nephrotic syndrome-like Hypercoagulable state, Thromboembolism, Cardiovascular complications. The patients who had dyslipidemia were proved by fasting Lipid profile in this study. David. C. Wheeler et al., [18] conducted a study on Lipid abnormality in the Nephrotic Syndrome: causes, consequences, and treatment suggested there is a potential long-term benefit of Lipid-lowering agent intervention, in Nephrotic Syndrome, along with the other treatment. There are only a limited number of studies from India on the spectrum of glomerular diseases, and these studies have not investigated the various aspects of NS in adults. 13–15 In this study minimal change nephropathy (MCN) was the most common 16(35.56%) cases, Focal segmental glomerulosclerosis (FSGN) was the second common cause in 10 (22.22%) cases. Dragovic et al., [19] proved that among the increased

incidence of FSGS which constituted 37.8%, 59% were males, but in the current study, MCN was higher 35.56% and males predominantly. From the currently available data, it seems that FSGS is showing an increasing trend over time and is becoming the commonest type of glomerular disease and cause of NS in adults. In another study from India in the pediatric population, FSGS was the commonest histology amongst adolescents (46.3%) compared to MCD in younger children. [20] Kazi et al., [21] in their study also reported FSGS, with an incidence of 39.87% as the commonest lesion seen in adults with NS. Kitiyakara C et al., [8] observed that the commonest lesion in nephrotic syndrome was Focal segmental glomerulosclerosis (FSGN). Hypertension is one of the extrarenal complications of Nephrotic syndrome. [19] The total number of cases of hypertension in this study was 40%. It is a well-known fact that hypoalbuminemia is another complication of proteinuria and the need for an angiotensin-converting enzyme inhibitor to prevent hyperfiltration and increased dietary protein led to a sustained increase in serum albumin. [19] The prognosis for Nephrotic patients is significantly different. With most patients progressing to ESRD after 5-10 years. Since spontaneous remission is rare in Nephrotic syndrome primary FSGS it is in this group of patients that a trial of therapy has been considered. [22-23]

Conclusion

This study found Minimal Change Nephropathy as the predominant microscopic lesion in the spectra of Nephrotic syndrome. Male preponderance was noted, 18-30 years of the age group of patients being affected more commonly presenting facial puffiness as the commonest symptom. 40% of cases were detected with hypertension and hyperlipidemia. The majority of patients of Nephrotic range of proteinuria did not have significant deranged renal function. Renal biopsy is the mandatory investigation for confirmation, initiation of treatment, and deciding the duration of therapy.

***Conflict of Interest*: None**
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