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Spectrum of Glomerular Diseases in Biopsy Proven Nephrotic Syndrome in Adults in Tertiary Center of Nepal

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ABSTRACT

Background: Glomerulonephritis (GN) is the important cause of chronic renal disease and had been reported as first common cause of CKD in Nepal after Diabetes and Hypertension. Correct diagnosis of glomerulonephritis requires renal biopsy and correlation with clinical and biochemical parameters.

Methods: This was an observational study conducted in Department of Nephrology, Bir Hospital Kathmandu, during the period of one year. A total of 88 patients were enrolled. Nephrotic syndrome was established by a detailed history, physical examination and investigations including kidney biopsy..

Results: Among the enrolled patients.51.2% were male and 48.8% were female. Almost all patients had hyperlipidemia. IgA Nephropathy was found to be the first commonest cause in 22.8% , second Lupus Nephritis in 9.3%, third Focal Segmental Glomerulosclerosis (FSGS) in 18.2% fourth was Membranous Nephropathy(MN) in 13.6%, Minimal Change Disease (MCD) in 11.4%, 9.1% Diffuse Proliferative Glomerulonephritis (DPGN), 3.4%, Membranous Proliferative Glomerulonephritis (MPGN) in which one was HBsAg positive, 1.1% PSGN,and 1.1% C3 glomerulopathy. Hypertension (HTN) was found in 26%, renal impairment in 28%, hematuria in 16% anemia and oedema in 12%, and 30 % respectively.

Conclusion: According to this study, IgA Nephropathy was the commonest cause 22.7% of Glomerulonephritis among total patients enrolled, whereas lupus nephritis was the second commonest 19.3% followed by focal segmental glomerulonephritis 18.1% and Membranous Nephropathy in 13.6%.

Keywords: Histopathologicalexamination; Immunoflurescence; Kidney biopsy, Nephrotic syndrome; Primary glomerular disease.

INTRODUCTION

Inflammation of glomerular capillaries is called glomerulonephritis.[1] Glomerulonephritis are the third most common cause of ESRD after Diabetes and Hypertension in Europe and the USA. Glomerulonephritis is considered to be an immunologically mediated disorder with involvement of both cellular and humoral immunity .[2] The hall mark of glomerulonephritis is proteinuria. Glomerulonephritis alters the size and charge selectivity of glomeruli with leakage of protein in urine.[3] Glomerular disease is classified into primary and secondary.[4] Histopathologically it can be classified as proliferative and non-proliferative and nephrotic syndrome is the commonest presentation in both which affects all age groups. The proliferative glomerulonephritis like Mesangeal Proliferative (MesPGN), IgA nephropathy, Membrano Proliferative (MPGN) are common in adolescents and young adults.[6]

Hypertension (HTN) is very common once disease progresses The ideal goal for blood pressure is 130/80 mm Hg.[6] In recent reports from different parts of the world the commonest pathologic lesion underlying nephrotic syndrome in adults is FSGS followed by MN and MCD.[7] The prevalence of Membranous Glomerulonephritis (MGN) had not changed in the last 20 yrs and remains the main cause of Nephrotic Syndrome in European adults.[8]

Proteinuria is usually asymptomatic, but heavy proteinuric patient present with generalized anasarca. Minor leakage of albumin may occur transiently after vigorous exercise, during fever or UTI and in heart failure. so tests should be repeated.[9] Complications of NS depends upon the severity of hypoalbuminemia and hyperlipidemia.[10]

Thus the Present study was undertaken to analyze the pattern of glomerulonephritis in patients employing all the diagnostic modalities necessary for a definitive diagnosis. This study also identifies the severity

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of hypoalbuminemia, proteinuria, hyperlipidemia, severity of HTN and renal impairment in various types of glomerulonephritis and to compare our findings with other literature.

METHOD

This was an observational hospital-based study of patients attended Bir Hospital OPD on 88 patients with Nephrotic Syndrome above the age of 8 years. Patients attended in OPD with clinical signs and symptoms suggestive of GN with NS were evaluated. Detailed history, general and systemic examinations done and patients were followed. General examination including pallor, icterus, edema, and JVP, were looked for and recorded accordingly. Vitals including BP, pulse rate, respiratory rate and temperature were also noted. All patients were subjected to kidney functions test serum blood sugar, urine analysis, serum albumin, 24 hours urinary total protein, serum lipid profile, HBsAg, HIV, HCV, ANA and anti-ds,-DNA.Prior to the biopsies coagulation studies CXR and USG were also done. Once patient had fulfilled the inclusion criteria kidney biopsy were done. Two samples of renal tissues were obtained from each patient. Biopsy specimens for LM examinations were fixed in 10% formalin and specimens for DIF microscopy were received in normal saline. Data analysis were done using SPSS 13.0 and Microsoft Excel for words. Results were presented in tables and diagrams.

RESULTS

In the study of the Spectrum of Glomerular Diseases in Biopsy proven Nephrotic Syndrome in adult in Tertiary Centre of patients who presented during the study period (n=88), various histopathological patterns and clinical as well as biochemical paramenters were observed and compared. In this study among the 88 patients enrolled, 45(51.2%) were males and 43(48.8%) were females. According to age wise dis tribution maximum numbers of patients both in male and female were in the age group 20-29 yearas which is shown in (Figure 2). According to clinical presentations HTN was seen in 28%, anaemia was seen in

Table1. Clinical presentations of patients according to HPE.

Glomerular morphology	Frequency (%)
IgA Nephropathy	20(22.8)
Lupus Nephritis	17(19.3)
FSGS	16(18.2)
MN	12(13.6)
MCD	10(11.4)
DPGN	8(9.1)
MPGN	3(3.4)
PSGN	1(1.1)
C3Nephropathy	1(1.1)

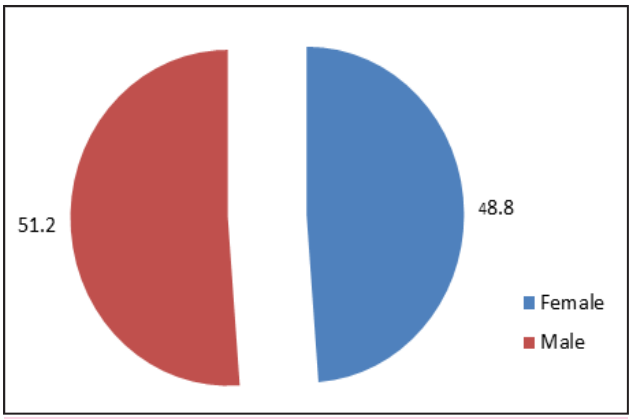

Figure 1. Pie diagram of Sex distribution.

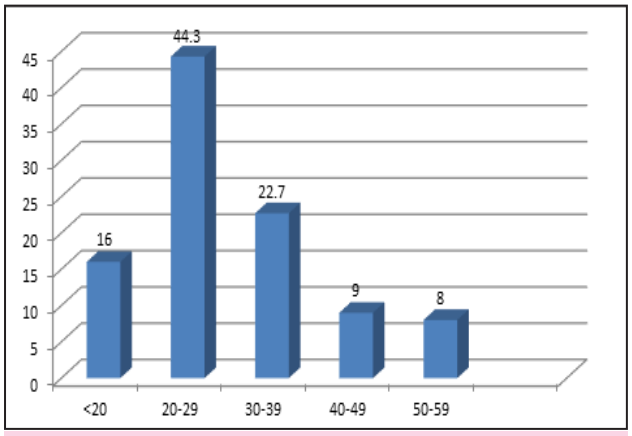

Figure 2. Distribution according to age.

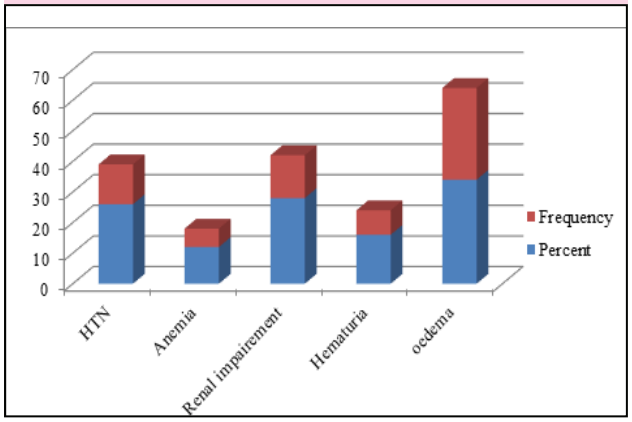

Figure 3. According to clinical presentations

12%, renal impairment was seen in 28% and hematuria in 16% and oedema was found in 26(30%)as shown in (Figure 3).

Histopathological studies show IgA nephropathy (22.8%), Lupus nephritis (19.3%) FSGS (18.2%) is the leading cause of nephrotic syndrome in adults followed by MN (13.6%), MCD in (11.4%), (9.1%) DPGN.MPGN in (3.4%) in which (1.1%) with hepatitis B positive case and (1.1%) each of PSGN and C3 Glomerulonephropathyas shown in (Figure 4).

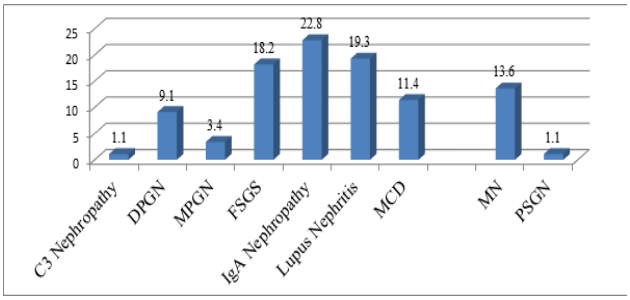

Figure 4. Distribution according to Histopathological examination.

DISCUSSION

Glomerular disorders are one of the major causes of morbidity and mortality. As glomerulonephritis are usually immunologically mediated, immunofluorescence (IF) are must. For exact diagnosis combined analysis of LM and DIF findings and correlation with clinical, biochemical and serological features are needed. The prevalence of glomerular disease is different in various part of the world, according to race, age, geographical, etiological, cultural and economic status.[11] As glomerular diseases being the leading cause of end-stage renal disease globallyand remains the most common cause of end stage renal diseaseso it is important to recognize the pattern of these diseases in any given geographical area.

A total of eighty eight adults above 8 years of age presenting with nephrotic syndrome were included in this study. Among, the total patients, 45 were male and 43 were female. The mean age of the patient was 29.6±11.8 years. It is evident from this study that IgA nephropathy 20 (22.8%) was the commonest histological type of glomerulonephritis leading to adult nephrotic syndrome in our context. This is followed by Lupus nephritis 17(19.3%), MN 12 (13.6%), MCD 10(11.4%), DPGN 8(9.1%) and 3(3.4%) MPGN and 1(1.1%) of PSGN and C3 glomerulopathy each. The male and female ratios were almost near equal. FSGS was mostly seen in adults with age in between 20-39 years where as IgA nephropathy was seen in young adults.

The first most common diagnosis in our study was IgA Nephropathy which represented (22.8%) of the cases. IgA nephropathy is the commonest formsof glomerulonephritis worldwide. Greatest frequency of IgA Nephropathy was seen in Asian countries, accounting for 45–58.2% of primary glomerular disease, while modest frequencyin the USA and Europe and with lower frequencyin Brazil.Many patients with IgA nephropathy, especially those with asymptomatic haematuria and/or proteinuria, are detected on routine urine screening. Prevalence may thereforeappear to be higher in countries with an active urine testing programme.[12] In Italy, Japan, China, Hong Kong, Singapore and Taiwan IgA Nephropathy was the most common of all primary GN followed by MGN and FSGS.[13] In Thailand IgA Nephropathy followed by FSGS and MN represent the most common cause of NS. In Iraq FSGS followed by mesangial glomerular nephritis and MCD represent the most common primary GN.

The second commonest GN is the Lupus Nephritis comprising 19.3% of the total patient, which was similar ‘to that of previous study done by Agrawal et all. All the patients of Lupus nephritis were females of all age groups and among them 12%were Lupus class IV and 4%of Lupus class V. Another study done in Eastern Nepal to determine the clinical profile and patterns of lupus nephritis revealed; class II changes in 1 (5.9%) patients, class III changes in 1(5.9%) patients, class IV changes in 11 (64.7%) patients, class V changes in 4 (23.5%) patients. conclude that class IV was the most common pattern of lupus nephritis encountered in the study.

The third commonest cause according to this study is FSGS comprising 18.2%.This result is similar with that reported from Iraq. Howeverdifferent from what has been reported previously from Jordan,where

MPGN was the most common cause in 35%, followed by FSGS in 27.1%.This results is also similar to those reported from Pakistan where focal segmental glomerulosclerosis (FSGS) (39.87%), followed by membranous GN (MGN) (26.58%), minimal change disease (MCD) (14.82%), mesangiocapillary GN (4.3%), mesangioproliferative GN (4.11%), post-infectious GN (2.84%), IgA nephropathy (2.53%), and other rare lesions.The FSGS was the most common form of GN in Brazil,India,Bahrain,Croatia,and Sudan.In contrast withthese reports, G.Aryalet all revealed FSGS (8%) was the fourth most common disease.

The fourth commonest cause according to this study was MN comprising 14% of all cases. Hisopathological spectrum of glomerular disease in Nepal: a seven-year retrospective study revealed MN was the most common form of GN (42.3%) followed by MPGN (21.9%), MCD (10.2%), FSGS (8.0%), IgA nephropathy (2.9%), post infectious GN (2.2%), chronic GN (2.2%), tubulointerstitial nephritis (1.5%), lupus nephritis (1.5%), focal proliferative GN (1.5%), C1q nephropathy (1.5%), primary renal amyloidosis (1.5%) and other minor form of glomerular diseases (2.8%),which was similar to the report from Iran at that time but this time it was different.[14]

Other GN in descending orders were MCD (11.4%), DPGN (9.1%), MPGN (3.4%) in which (1.1%) HBsAg positive case and PSGN and C3 glomerulopathy in (1.1%) each. MCD has a variable geographic distribution, being more common in Asia than in North America or Europe. In Korea and Thailand, the MCD comprised 26.6% and 45.8% of total primary glomerular diseases. In contrast, MCD comprised only 11.4% of the total biopsies in our study.Diagnosis of MCD usually made by absence of glomerular alteration in LM and lack of immune deposits in DIF. Pattern of glomerular diseases in Nepal –A single center experience by SudhaKhakurel et all revealedhistopathology findings in the group with IF showed minimal change disease (MCD) in 23.2%, FSGS in 18%, MN in 11.9% and IgA nephropathy in 9.8% of the cases, while histopathology without IF showed mesangial proliferative GN (MesPGN) as the predominant glomerular disease, seen in 21.1% of the patients, followed by MPGN in 18.6% and MN in 14.2% of the patients; IgA nephropathy was undiagnosed.[15]

Study of patients with nephrotic syndrome from Sohag University Hospital byHassan et all revealed 18 patients (30.5%) with membranoproliferative glomerulonephritis, 15 (25.43%) with membranous nephropathy, seven (11.86%) with mesangial proliferative glomerulonephritis, six (10.16%) with amyloidosis, five (8.47%) with focal segmental glomerulosclerosis, three (5.08%) with diffuse proliferative glomerulonephritis, one (1.69%) with focal proliferative, minimal mesangial, sclerosing glomerulonephritides, one patient (1.69%) with crescent glomerulonephritis, andanother one (1.69%) with IgA nephropathy.[16] Vishal Goley et al, Spectrum of NS in adults clinicopathological study from a single center in India where the most common histological lesions were focal segmental glomerulosclerosis (FSGS) (24.63%) followed by minimal change disease (MCD) (23.9%) and membranous nephropathy (MN) (22.44%).FSGS becoming the most common cause of adult NS. This trend in Asia is seen predominantly in countries of the Indian subcontinent.[17]This observational study recommends and emphasizes the importance to have a GN registry. This will definitely help in identifying the patterns and prognosis of GN better so that therapeutic and preventive strategies can be outlined and able to stop or prevent further progression to ESRD.

CONCLUSION

Results from this study indicate that IgA nephropathy (22.8%), Lupus nephritis (19.3%) FSGS (18.2%) is the leading cause of nephrotic syndrome in adults followed by MN (13.6%), MCD in (11.4%), (9.1%) DPGN.MPGN in (3.4%) in which (1.1%) with hepatitis B positive case and (1.1%) each of PSGN and C3 Glomerulonephropathy. Our study has similarities with many of the other studies, like studies done in Italy, Japan, China, Hong Kong, Singapore and Taiwan

where IgA Nephropathy was the most common of all primary GN followed by MGN and FSGS. Among the enrolled patients (51.2%) were male and (48.8%) were females. Agewise, the maximum numbers of patients were in the age group of 20-29 years. The least numbers of patients (8%) were over 50 years. All patients (100%) had hyperlipidaemia and (94%) had hypoalbuminaemia.HTN was found in (26%), renal impairment in (28%),hematuria in (16%) and anaemia in (12%) and edema in (30%).There is a need to establish national registry of glomerular diseases in Nepal and further multicentre studies with large numbers of patients are needed to clearly show the various frequencies of glomerular diseases.

Conflict of interest: None

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