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Spectrum of Primary Glomerular Diseases in Patients Presenting with Urinary Abnormalities*

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Abstract

Introduction: Primary Glomerular Diseases are a spectrum of renal disorders of unknown aetiology with distinct characteristics, specific natural history and prognosis. A thorough evaluation is pre-requisite to establish the diagnosis since many systemic diseases and secondary aetiology masquerade as primary diseases. Methods: This prospective observational study was conducted at a tertiary care centre and included 30 patients, with clinical features suggestive of primary glomerular diseases, of which 23 patients (76.6%) were males and 07 patients (23.33%) were females. The mean age at presentation was 37.23 ± 12.89 years. Among the observed spectrum of Primary Glomerular Diseases, IgA Nephropathy (IgA N) was seen in 26.67% patients, Focal Segmental Glomerulosclerosis (FSGS) in 20% patients and Membranous Glomerulopathy (MGN) in 13.33% patients, whereas the incidence of other abnormalities had less percentage contribution. Proteinuria was the commonest presentation seen in 60% patients, followed by Microscopic Haematuria in 20%. Mean Serum Creatinine was 0.99 ± 0.16 mg/dl. Mean Serum Albumin was 2.51 ± 0.76 gm/dl. Overall Nephrotic range proteinuria was observed in 15 (50%) patients. Results: IgA N, FSGS & MGN were the commonest observed Primary Glomerular Diseases. Proteinuria, Haematuria, Anasarca and Pedal Oedema were the commonest observed clinical presentations. Conclusions: In this studied series IgA Nephropathy, FSGS and MGN were the most prevalent diagnoses in the patients presenting with Urinary Abnormality. Nephrotic range Protenuria was the major indication for biopsy, there is a temporal variation in glomerulopathies wherein there is increase in incidence of IgA Nephropathy and decrease in incidence of FSGS.

Keywords

Protenuria, Primary Glomerular Disease, IgA Nephropathy, Creatinine

*Original paper.

1. Introduction

The underlying cause of many glomerular diseases remains unknown, which are classified as Primary Glomerular Diseases, wherein the disease involves kidneys primarily and then there are Secondary Glomerular Diseases where the kidneys get involved secondary to some systemic disorders.

When a patient presents with suspicion of some glomerular disease, all measures must be taken to look for an underlying systemic disease. Evaluation includes assessment for proteinuria, gross/microscopic haematuria and hypertension. Determining the exact underlying aetiology, prognosis and alter the disease progression and severity by timely intervention, if possible. The variable manifestations among glomerular diseases mandate a kidney biopsy for establishing a diagnosis. Urinary abnormality on urinalysis is a common finding in clinical practice. Evaluation of such abnormalities by a renal biopsy helps in identifying an underlying glomerular disease in time.

Data from the western literature depicts IgA Nephropathy (IgA N) as the most common GN in white adults in many studies [1] [2]. Earlier many studies showed Membranous Nephropathy (MGN) as a common cause for adult nephrotic syndrome in US and Europe. However recent studies have shown that frequency of Focal Segmental Glomerulosclerosis (FSGS) is increasing and has become the most common Primary Glomerulopathy in blacks and the Hispanic population [3].

Since most of the data in this respect is from the western literature, this study was carried out to evaluate and identify the pattern and distribution of various Primary Glomerular diseases in Indian adult population, Indians have a relatively heterogenous ethnicity and in addition the rapid urbanization is expected to further result in changing pattern of glomerular disease, which further emphasizes the reason to observe and study the new paradigm.

2. Materials & Methods

This study was performed at a tertiary care hospital and was approved by the Internal Ethical Committee of the hospital vide No. 01/07/MAY/CHWC/2022. A written informed consent was taken from all the patients who were enrolled in this study and also before they were subjected to renal biopsy. A group of 30 patients were included in the study. This study was conducted between Jan 2021 and Dec 2021 (total duration 12 months).

2.1. Inclusion & Exclusion Criteria

All adult patients (age > 18 years) presenting at the outpatient department with Asymptomatic Urinary Abnormalities (proteinuria, gross/microscopic haematuria, with or without hypertension) were included in the study. Subjects having azotaemia/features of uraemia, previous history of known renal dysfunction or any urinary abnormality were excluded from the study. All patients who were > 60 years age, critically ill, had diagnosed glomerular diseases, hypertension, di-

abetes mellitus, chronic liver disease, HIV infection or any other underlying condition that could lead to secondary glomerular disease were also excluded from the study.

2.2. Study Design & Sample Size

It was a prospective observational study conducted at a tertiary care centre in North-Western India. A sample size of 30 patients was considered based on the prevalence of primary glomerular diseases in patients with no previously known urinary abnormality, renal dysfunction or any glomerular disease.

2.3. Methodology

A group of 30 patients detected to have renal dysfunction in the form of proteinuria, gross/microscopic haematuria, active urinary sediments with or without hypertension during evaluation at the outpatient department of a tertiary care hospital were included in the study. Detailed history was taken regarding presenting complaints, presence of any renal specific complaints or past history of any underlying renal disorders, or other comorbidities that can lead to secondary renal dysfunction, and if found positive such patients were excluded from the study. Baseline blood pressure was measured for all the subjects. A battery of investigations was then done that included baseline serum creatinine (in mg/dl), 24 hours urine protein (in grams), qualitative urine albumin by dipstick method (graded readings: negative, trace, 1+ to 4+), urine routine and microscopic analysis, serum albumin (in gm/dl) and ultrasonography of abdomen. Following this, the study patients were subjected to Percutaneous Renal Biopsy with an 18 Gauge Automated Renal Biopsy Gun after a written informed consent. A written informed consent was pre-requisite for every patient in a predesigned format in the language that patient best understood before inclusion in the study group. This study was approved by the Internal Ethical Committee of the hospital vide No. 01/07/MAY/CHWC/2022.

2.4. Analysis of Data

The data was documented on a pre-designed format, tabulated and was analysed using SPSS (Statistical Packages for Social Sciences) for Windows Version 20.0. The qualitative data variables were expressed using frequency and percentage (%), whereas the quantitative data variables were expressed using mean & SD in nearest two decimal figures.

3. Results

Out of the 30 patients found to have Primary Glomerular Disease, 23 patients (76.6%) were males and 07 patients (23.33%) were females. The mean age at presentation for all patients was 37.23 ± SD 12.89 years, with males having a mean age of 38 ± SD 12.53 years, whereas females had mean age of 34 ± SD 14.61 years (Figure 1).
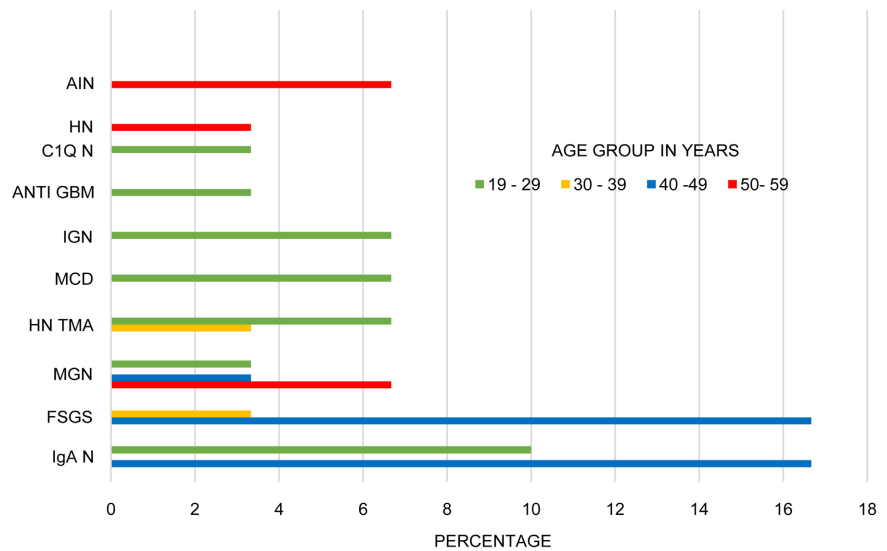
Figure 1. Agewise distribution of primary glomerular diseases. ain-acute interstitial nephritis, hn-hypertensive nephropathy, c1q n-c1q nephropathy, anti gbm-anti glomerular basement membrane nephropathy, ign-immune complex glomerulonephritis, mcd-minimal change disease, hn tma-hypertensive nephropathy with thrombotic microangiopathy, mgn-membranous glomerulonephritis, fsgs-focal segmental glomerulosclerosis, iga n-iga nephropathy.

IgA Nephropathy was the most common observed primary glomerulopathy seen in 08 patients (26.67%) of which all were Males, following this 06 patients (20%) had Focal Segmental Glomerulosclerosis (03 Males (10% of total) and 03 Females (10% of total)), 04 patients (13.33%) had Membranous Glomerulopathy (all Males), 03 patients (10%) had Hypertensive Nephropathy with Thrombotic Microangiopathy (02 Males (6.67% of total) and 01 Female (3.33% of total)), 02 patients (6.67%) had Minimal Change Disease (01 Male (3.33% of total) and 01 Female (3.33% of total)), 02 patients (6.67%) had Acute Interstitial Nephritis (01 Male (3.33% of total) and 01 Female (3.33% of total)), 02 patients (6.67%) had Immune Complex Glomerulonephritis (01 Male (3.33% of total) and 01 Female (3.33% of total)), 01 patient (3.33%) had Hypertensive Nephropathy (Male), 01 patient (3.33%) had Anti-GBM Disease (Male) and 01 patient (3.33%) had C1Q Nephropathy (Male) (Figure 2).

All of the subjects in study population had normal size of kidneys on ultrasonography. The commonest presentation was Proteinuria, which was seen in 60% (18 patients), of which 15 (50%) were males and 03 females (10%). Microscopic haematuria was seen in 20% (06 patients), of which all were males and 05 patients had IgA Nephropathy and 01 patient had Anti Glomerular Basement Disease. Anasarca was seen in 13.33% (04 patients), of which 6.67% (02 patients) were males and 6.67% (02 patients) were females. Pedal oedema was seen in 13.33% (04 patients), of which 6.67% (02 patients) were males and 6.67% (02 patients) were females. Accelerated hypertension was seen in 10% (03 patients), of which all were males. Oliguria was seen in 6.67% (02 patients) of which all were males. Visual Blurring was seen in 3.33% (01 patients), who was a male (Table 1).
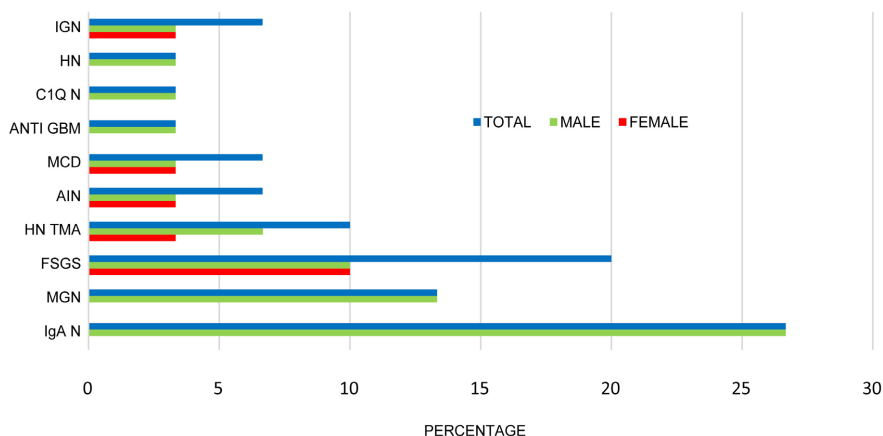
Figure 2. Spectrum of primary glomerular diseases. ign-immune complex glomeruloneph-ropathy, hn-hypertensive nephropathy, c1q n-c1q nephropathy, anti gbm-anti glomerular basement membrane nephropathy, mcd-minimal change disease, ain-acute interstitial nephritis, hn tma-hypertensive nephropathy with thrombotic microangiopathy, fsgs-focal segmental glomerulosclerosis, mgn-membranous glomerulonephropathy, iga n-iga nephropathy.

Table 1. Clinical profile of study population.

PRESENTATION	MALES	FEMALES	TOTAL
Age At Presentation (Mean ± SD years)	38 ± 12.53	34 ± 14.61	37.23 ± 12.89
Proteinuria	15 (50%)	03 (10%)	18 (60%)
Microscopic Hematuria	05 (16.67%)	01 (3.33%)	06 (20%)
Pedal Oedema	02 (6.67%)	02 (6.67%)	04 (13.33%)
Anasarca	02 (6.67%)	02 (6.67%)	04 (13.33%)
Accelerated Hypertension	03 (10%)	-	03 (10%)
Oliguria	02 (6.67%)	-	02 (6.67%)
Visual Blurring	01 (3.33%)	-	01 (3.33%)
Systolic BP (Mean ± SD mm Hg)	155.04 ± 17.70	150 ± 13.66	153.87 ± 16.77
Diastolic BP (Mean ± SD mm Hg)	93.65 ± 8.83	92 ± 6.85	93.38 ± 8.40
Serum Creatinine (Mean ± SD mg/dl)	1.0 ± 0.17	0.92 ± 0.17	0.99 ± 0.16
Serum Albumin (Mean ± SD gm/dl)	2.5 ± 0.75	2.56 ± 0.87	2.51 ± 0.76
Nephrotic Range Proteinuria	11 (36.67%)	04 (13.33%)	15 (50%)
Massive Proteinuria	03 (10%)	02 (6.67%)	05 (16.67%)
Urine Albumin By Dipstick:-			
4+	02 (6.67%)	02 (6.67%)	04 (13.33%)
3+	06 (20%)	02 (6.67%)	08 (26.67%)
2+	08 (26.67%)	03 (10%)	11 (36.67%)
1+	05 (16.67%)	01 (3.33%)	07 (23.34%)
Trace	01 (3.33%)	-	01 (3.33%)

The overall Mean Systolic Blood Pressure observed was 153.87 mm Hg SD 16.77 mm Hg, which was 155.04 mm Hg SD 17.70 mm Hg in males and 150 mm Hg SD 13.66 mm Hg in females. The overall Mean Diastolic Blood Pressure observed was 93.38 mm Hg SD 8.40 mm Hg, which was 93.65 mm Hg SD 8.83 mm Hg in males and 92 mm Hg SD 6.85 mm Hg in females. The overall Mean Serum Creatinine was 0.99 mg/dl SD 0.16 mg/dl, which was 1.0 mg/dl SD 0.17 mg/dl in males and 0.92 mg/dl SD 0.17 mg/dl in females. The overall Mean Serum Albumin was 2.51 gm/dl SD 0.76 gm/dl, which was 2.5 gm/dl SD 0.75 gm/dl in males and 2.56 gm/dl SD 0.87 gm/dl in females. Overall Nephrotic range proteinuria was observed in 15 (50%) patients, of which 11 (36.67%) were males and 4 (13.33%) were females.

Qualitative urine albumin by dipstick was found to be 4+ in 04 (13.34%) patients who had either underlying Minimal Change Disease, Membranous Glomerulo-nephropathy or C1Q Nephropathy, 3+ albuminuria seen in 08 (26.67%) patients who had underlying IgA Nephropathy, Focal Segmental Glomerulosclerosis, Hypertensive Nephropathy with Thrombotic Microangiopathy, Immune complex Glomerulonephritis or Membranous Glomerulonephritis, 11 patients (36.67%) had 2+ urine albumin, 07 patients (23.34%) had 1+ urine albumin, whereas trace urine albumin was seen in 01 patient (3.33%) who had Hypertensive Nephropathy on kidney biopsy.

4. Discussion

Primary glomerular disease in patients with asymptomatic urinary abnormalities were found to be more common in males (76.67%) than females (23.33%). However, females presented at an earlier age as compared to males. The three most common Primary Glomerular Disorders observed were IgA Nephropathy (26.67%), FSGS (20%) and MGN (13.33%). Study by Jay Hyun Chang et al and Thome' GG et al in Korea and Brazil respectively in 2009 and 2021 reported similar observation with most common being IgA N (28.3%) [2] [4], followed by MCD (15.5%), MGN (12.3%), FSGS (5.6%) and Membranoproliferative GN (MPGN) (4.0%) [4]. However, MCD comprised only 10.2% of the total biopsies in a study in Nepal [5], MCD shows a variable geographic distribution and is more common in Asia than in North America or Europe [6] In Korea [7] and Thailand [8], MCD amounted to 26.6% and 45.8% of all primary glomerular diseases, respectively, FSGS was observed to be the most common Primary Glomerulo-nephropathy in Brazil [9], India [10], Bahrain [11], Croatia [12] and Sudan [13], 34.5% in Czech Republic [14], whereas 18.8% in Italy [15]. However, MCD was the most common biopsy proven Primary glomerular disease with wide age of presentation in a study by Shalini Bhalla et al in Uttar Pradesh in India [16].

Proteinuria (60%), microscopic haematuria (13.33%), pedal oedema (13.33%) and anasarca (13.33%) were among the most common presentations seen in majority of study subjects. The patients with IgA Nephropathy, FSGS, Hypertensive Nephropathy with TMA and Acute Interstitial Nephritis commonly pre-

sented with hypertension, even to the extent of accelerated hypertension 10% patients who had underlying IgA Nephropathy. Microscopic haematuria was most commonly seen in IgA Nephropathy (16.67%), followed by Anti GBM disease (3.33%).

Nephrotic range proteinuria was seen in 50% patients and they had underlying MCD, MGN, Immune Complex GN, C1Q disease, FSGS, IgA Nephropathy or Hypertensive Nephropathy with TMA. Massive proteinuria (>10 gm/day) was seen in 16.66% patients who had underlying MCD (6.67%), Immune Complex GN (6.67%) or MGN (3.33%). In a study by Ho Sik Shin et al in South Korea (2017) it was observed that adults in age group of 18 - 59 years who underwent kidney biopsy most commonly presented with asymptomatic urinary abnormalities (75.3%), followed by nephrotic syndrome (19.8%) and acute kidney injury (3.4%) [16]. Almost all of the patients had hypoalbuminemia with a mean serum level of 2.51 ± 0.76 gm/dl. The baseline creatinine was normal (<1.3 mg/dl) in all of the subjects with a mean of 0.99 ± 0.16 mg dl.

Limitations

It being an observational study, the tendency towards bias and confounding inherent to this study model owing to the lack of randomization and process of selection of subjects cannot be ruled out despite best of efforts. This may have effect on the observations and thus during interpretation of outcome this factor needs to be considered to so as to appreciate the results in a more realistic fashion.

5. Conclusion

This study was unique in the form that it studied the distribution of only the primary glomerular diseases in individuals presenting with asymptomatic urinary abnormality, all the systemic/secondary causes were excluded. Most of the other studies report about the spectrum of primary glomerular diseases in all patients evaluated, whether asymptomatic or not, who were subjected to renal biopsy. Unlike other studies, subjects having any previous old renal complaint/ disorder or any co-morbidity known to cause secondary glomerular diseases, like hypertension, diabetes mellitus, chronic liver disease, HIV infection or SLE, were excluded from this study. IgA N, FSGS & MGN were among the commonest observed Primary Glomerular Diseases, whereas Proteinuria, Haematuria, Anasarca and Pedal Oedema were the commonest observed clinical presentations. This study was one of its kind and elaborates upon not only the observed spectrum of primary glomerular diseases in individuals with asymptomatic urinary abnormality, but also provides an insight about their complete clinical profile with distribution individually in both males and females.

Conflicts of Interest

There has been no interest whatsoever of any third party or firm pertaining to

this article and also no disputes involved as ethical committee clearance was taken for this study.

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