British Journal of Medicine & Medical Research
16(2): 1-8, 2016, Article no.BJMMR.24158
ISSN: 2231-0614, NLM ID: 101570965

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A Study of Frequency of Glomerular Diseases (Biopsy Proven) from a Tertiary Care Center of North West Rajasthan

Surendra Kumar[1*], Jitendra Phalodia[2], Zahid Khan[1], Vinod Kumar Aswal[1] and Akhil Gupta[1]

[1]Department of Medicine, S.P. Medical College and A.G. of Hospitals, Bikaner, Rajasthan, India.
[2]S.P. Medical College and A.G. of Hospitals, Bikaner, Rajasthan, India.

Authors' contributions

This work was carried out in collaboration between all authors. Author SK designed the study, wrote the protocol. Author JP analyzed of the study performed the Biopsy analysis. Author ZK wrote the first draft of the manuscript and managed the literature searches. Authors VKA and AG managed the experimental process and wrote the remaining draft of manuscript. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/BJMMR/2016/24158
Editor(s):
(1) Faris Q. B. Alenzi, Department of Medical Laboratories, College of Applied Medical Sciences Salman bin Abdulaziz University (Al-Kharj), Saudi Arabia.
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Complete Peer review History: http://sciencedomain.org/review-history/14831

Original Research Article

Received 6th January 2016
Accepted 29th April 2016
Published 30th May 2016

ABSTRACT

Aims and Objective: Glomerular disease (GD) is one of the most common forms of renal diseases and can have many different clinical presentations and there is a variation in the prevalence of the type of GD according to geographical location and race of the study population, so our aim is to report the frequency of biopsy-proven glomerular disease (GD) in a single center in North-west Rajasthan.
Materials and Methods: Medical records of 48 patients with biopsy-proven GD over a period of 1

**Corresponding author: E-mail: drsurendrakumar@rediffmail.com;*

year from October 2013 to October 2014 were prospectively analyzed. The clinical, laboratory, and histological data were recorded. All biopsy specimens were examined by the same pathologist with light and immunofluorescence microscopy. Electron microscopic analysis was performed only in selected cases.

Results: According to renal biopsies, chronic thrombotic microangiopathy was present in 1 patient and it belonged to secondary glomerular disease, 2 patients had diffuse lupus nephritis class IV and they also had secondary glomerular disease, 17 patients had FSGS and out of them 16 belonged to primary glomerular disease, 9 patients had IgA Nephropathy. We identified 5 patients each had MPGN and MGN and they all belonged to primary glomerular disease. Three patients had mesangioproliferative glomerulonephritis. Minimal change disease was present in 3 patients while 1 patient had renal amyloidosis. Out of total 48 patients, 31 had nephrotic syndrome while 17 patients had nephritic syndrome out of them 28 and 15 patients had primary glomerular disease respectively.

Conclusion: Our study showed that FSGS as most common cause of primary glomerular disease {the most common variant is not otherwise specified (NOS)}, followed by IgA nephropathy in North West Rajasthan. Lupus nephritis was more common in patients who had secondary glomerular disease in our study. The spectrum of GD varies according to the area of study and changes over time.

Keywords: Glomerular disease (GDs); nephrotic syndrome; biopsy; spectrum.

1. INTRODUCTION

Glomerular disease (GD) is one of the most common forms of renal diseases and can have many different clinical presentations. It can present as nephrotic syndrome (NS), nephritic syndrome, rapidly progressive renal disease (RPGN), acute kidney injury (AKI), chronic kidney disease (CKD), microscopic hematuria (MH), recurrent disease in the posttransplant kidney, as well as isolated proteinuria or hematuria [1]. In any case, a kidney biopsy is needed for the correct characterization of various types of GD.

In one of the largest reports of 6469 biopsies with GD from the University of North Carolina, focal segmental glomerulosclerosis (FSGS) was the most common GD (14.22%) followed by membranous nephropathy (MN) (13.09%) [2]. However, there is a variation in the prevalence of the type of GD according to geographical location and race of the study population. IgA nephropathy (IgAN) is the common primary GD is studies from East Asia [3-5], as well as in white Europeans and Americans [6-10]. In contrast, FSGS is the most common GD among African-Americans, South Americans, and in the Middle East [11,12].

The change in the spectrum of GD over the last few decades has been demonstrated in many studies worldwide, with most showing a trend toward increase in FSGS cases [3,6,7,11,12]. There are a limited number of studies from India and most of them are from Southern and Northern Indian centers [13-15]. These studies also demonstrate a trend toward increase in the incidence of FSGS [13-15] and a decrease in membranoproliferative glomerulonephritis (MPGN) [15]. The incidence of non-IgA mesangial proliferative GN (MesPGN) was also quite high (20.2%) in one of these studies [15].

Thus, there is a great variation in the presentation of GD across the globe and the disease spectrum has also been changing over the last few decades. In light of the paucity of data from North-west Rajasthan, we studied the prevalence of GD in a large tertiary care referral center in North-west Rajasthan.

2. MATERIALS AND METHODS

Our study was carried out in Department of Medicine, S.P. Medical College, Bikaner. All the patients fulfilling the criteria attending OPD, Department of Medicine, S.P. Medical College and Associated Group of Hospitals, Bikaner, undergo detailed history and clinical examination. Patients were asked to provide information about their age, marital status, occupation, educational attainment, medical history, smoking, alcohol consumption. The data were collected on a specially designed proforma having baseline demography and participants recieved a detailed physical and laboratory testing. Venous blood samples were collected for the investigations within 24 hours of admission before time of renal biopsy collection.

2.1 Inclusion Criteria

Renal manifestations of systemic disease like isolated hematuria, mild to moderate proteinuria, hypertension, nephritic syndrome, nephritic syndrome, acute renal failure, chronic renal failure and renal tumor in selected patients were included in our study.

2.2 Exclusion Criteria

Uncontrolled hypertension, hypotension, renal abscesses, pyelonephritis, hydronephrosis, marked obesity, severe anemia, uremia, large renal tumors or cysts, solitary kidney, previous technical failure, atrophic kidney(s), bleeding diathesis, anatomic abnormalities, uncooperative behaviour and pregnancy were excluded.

In our center, the kidney biopsy was performed by nephrologists with continuous (real time) ultrasound guidance and disposable automated between needled. We used 16-gauge needles as a compromise between the greater tissue yield of larger needles which resulted a trend of fewer bleeding complications due to the use of smaller needles. For most patients, pre medications or sedation was not required. Local anesthetic (2% lidocaine) was used.

The renal tissue was divided into three samples and placed in formalin for light microscopy; normal saline for subsequent snap; freezing to liquid nitrogen for immuno-fluorescence; and glutaraldehyde for electron microscopy.

All kidney biopsies were performed at our institute from October 2013; and prospectively analyzed. We recorded the following data for each patient: name, age, sex, indication for renal biopsy, histopathological diagnosis and laboratory investigations such as serum creatinine, 24-hour urinary protein, microscopic urine sediment, virology (HBsAg, anti-HCV, HIV) and serology. The microscopic analysis included light microscopy (LM) and immunofluorescence (IF).

In CRF, renal biopsy was performed for unexplained renal failure, if kidney sizes were within normal limit with intact corticomedullary differentiation.

Histological categories were classified [16] as follows: I) primary glomerulonephritis (PGN) which included minimal change disease (MCD), FSGS, membranous nephropathy (MN), IgA nephropathy (IgAN), IgM nephropathy (IgMN), mesangioproliferative glomerulonephritis (MesPGN), membranoproliferative glomerulonephritis (MPGN), crescentic glomerulonephritis (CresGN) diffuse proliferative glomerulonephritis (DPGN) or postinfectious glomerulonephritis (PIGN); II) secondary glomerulonephritis (SGN) included lupus nephritis (LN), diabetic nephropathy (DN), amyloidosis (AM), Henoch–Schönlein purpura (HSP), multiple myeloma (MM), light chain deposit disease (LCDD), systemic vasculitis (VAS), hemolytic–uremic syndrome (HUS)/ thrombotic microangiopathy (TTP) or systemic sclerosis; III) tubulointerstitial nephritis (TIN) included acute TIN, chronic TIN, acute tubular necrosis (ATN); IV) vascular nephropathy (VN) included benign/malignant nephrosclerosis, thrombotic microangiopathy (TMA), acute cortical necrosis or hypertensive changes; V) hereditary; and VI) end-stage renal disease (ESRD) changes.

ESRD changes are characterized by advanced glomerulosclerosis, tubular loss/atrophy, some degree of cystic change and thickened renal blood vessels. The incidence of each type of renal disease was recorded.

Simple descriptive statistics such as median and mean±SD was used for variables such as age, clinical and laboratory features. The percentages were used for categorical data.

3. RESULTS

The most common age group was $\leq$20 where 14 patients were found and out of them 13 had primary glomerular disease. Mean age of primary glomerular disease patients was 31.14±13.28 years while in secondary glomerular disease, it was 34.20±13.66 years and this difference was statistically insignificant ($p>0.05$) (Fig. 1).

Out of 48 patients there were total 17 females and 31 males. Out of 17 females 15 had primary glomerular while out of total 31 males, 28 had primary glomerular disease and this difference was also statistically insignificant ($p>0.05$) (Fig. 2).

According to renal biopsies, chronic thrombotic microangiopathy was present in 1 patients and it belonged to secondary glomerular disease, 2 patients had diffuse lupus nephritis class IV and they also had secondary glomerular disease, 17 patients had FSGS (Fig. 5) and out of them 16 belonged to primary glomerular disease, 9

patients had IgA Nephropathy. We identified 5 patients each had MPGN and MGN and they all belonged to primary glomerular disease. Three patients had mesangioproliferative glomerulonephritis and also belonged to Primary glomerular disease group. Minimal change disease was present in 3 patients showing primary glomerular disease while 1 patient had renal amyloidosis and it belonged to secondary glomerular disease (Table 1).

Out of total 48 patients, 31 had nephrotic syndrome while 17 patients had nephritic syndrome out of them 28 and 15 patients had primary glomerular disease respectively and this difference was found statistically insignificant ($p>0.05$) (Fig. 3).

The light microscopic view of normal and pathologic kidney was represented as Fig. 4. and Fig. 5. respectively.

4. DISCUSSION

In our study 48 patients were biopsed after routine investigation of CBC (complete bood count), LFT (liver function test), RFT (renal function test), FBS (fasting blood sugar), USG (ultrasonography), PT (prothrombin time), INR (international normalized ratio). Biopsies were examined by light microscopy (x400). Patients were categorized into primary and secondary glomerular disease based on biopsy reports.

Most common indication of biopsy done in our study was found as primary glomerular disease 89.58% (43/48) and secondary glomerular disease was found in 10.42% (5/48).

Golay et al. [17] in 2013, done a study in which a total of 410 kidney biopsies were included for analysis and reported approximately 88.05% of these patients were diagnosed with primary glomerular disease and 11.95% with secondary glomerular disease.

Narasimhan et al. [15] in 2006, in the study of 5415 kidney biopsies showed that most common indication of renal biopsy in their study was nephrotic syndrome (65%), nephritic syndrome (13%) and chronic renal failure (10.2%). Primary glomerular disease accounted for 71% of all biopsies which is more common in their study, similar to our study. In primary glomerular disease mesangioproliferative glomerulonephritis as a group was the predominant pathology (20.2%) followed by idiopathic FSGS (17%), minimal change disease (11.6%), membranous glomerulopathy (9.8%), IgA nephropathy (8.6%) and membrano-proliferative glomerulonephritis (3.7%) of the patients. With secondary kidney disease, lupus nephritis (6.5%), diabetic nephropathy (2.5%), interstitial nephropathy (2.5%) and benign nephrosclerosis (2.2%) were identified. This study also showed that there was a steady increased in prevalence of FSGS ($p<0.001$).

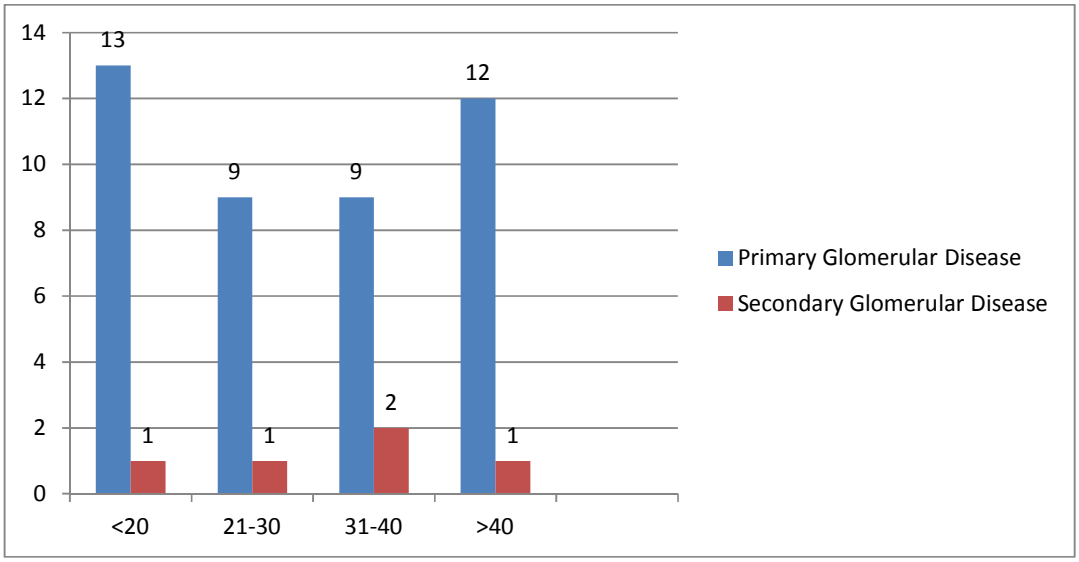

Fig. 1. Distribution of cases according to age group in relation to glomerular disease

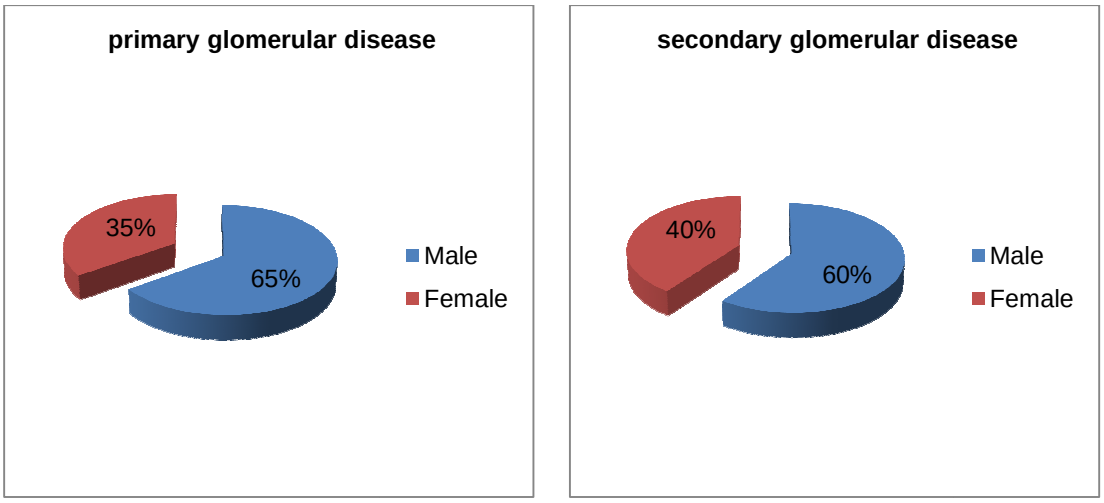

Fig. 2. Distribution of cases according to sex in relation to glomerular disease

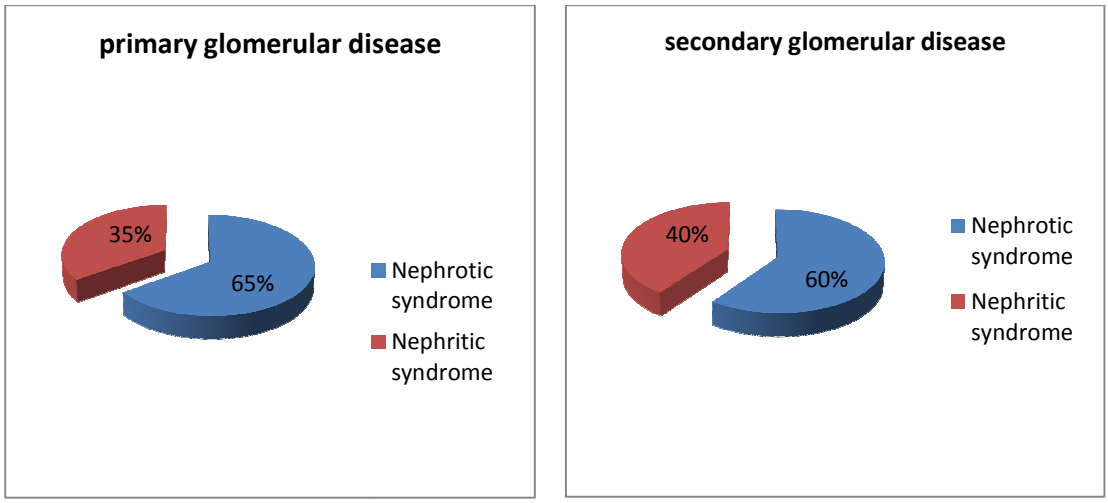

Fig. 3. Distribution of cases according to syndrome in relation to glomerular disease

Table 1. Distribution of cases according to renal biopsy in relation to glomerular disease

Renal biopsy	Glomerular disease				Total	
	Primary		Secondary			
	No.	%	No.	%	No.	%
Chronic thrombotic microangiopathy	0	-	1	20.0	1	2.1
Diffuse Lupus Nephritis Class IV	0	-	2	40.0	2	4.2
FSGS	16	37.2	1	20.0	17	35.4
Ig A. Nephropathy	9	20.9	0	-	9	18.8
MPGN	5	11.6	0	-	5	10.4
MGN	5	12.1	0	-	5	10.5
Mesangioproliferative Glomerulonephritis	3	7.0	0	-	3	6.3
Minimal Change Disease	3	7.0	0	-	3	6.3
Renal amylodosis	0	-	1	20.0	1	2.1
Total	43	100	5	100	48	100

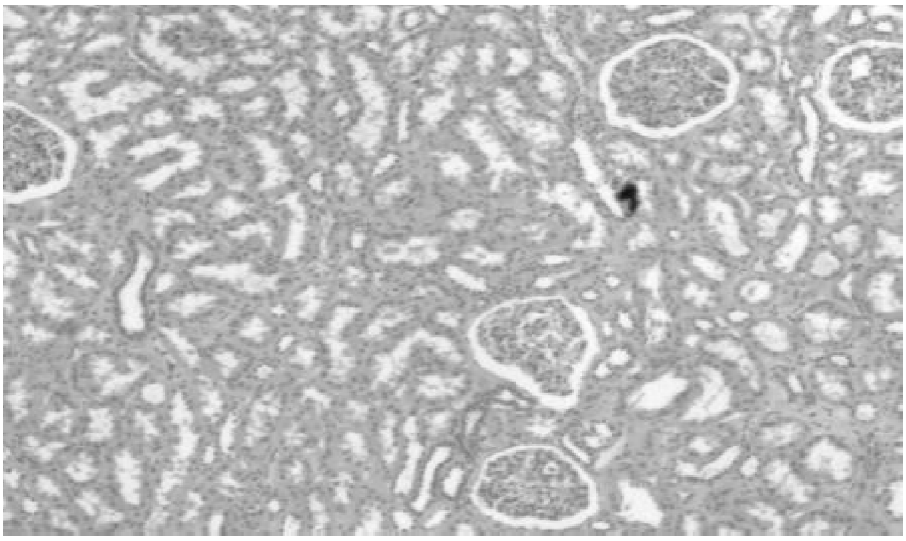

Fig. 4. Normal renal histology by light microscopic view (×400)

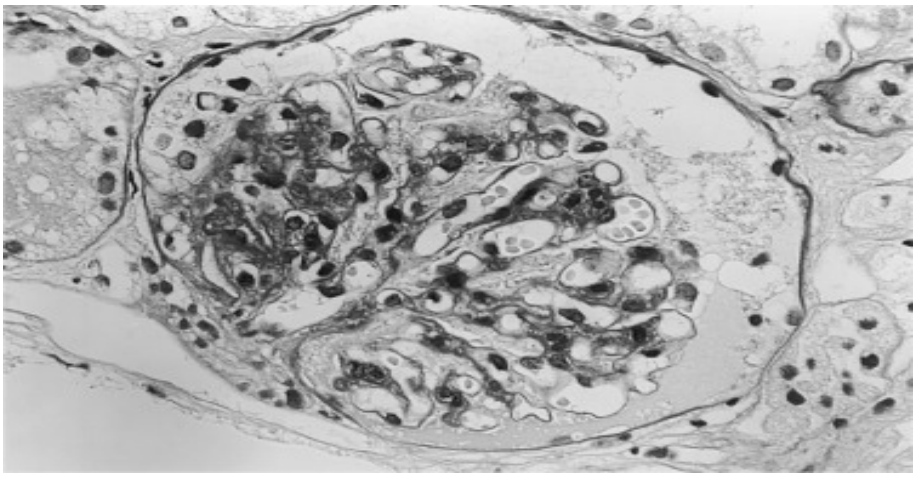

Fig. 5. Light microscopic view of a kidney biopsy specimen obtained from patient revealing a segmentally sclerotic lesion (×400)

The primary glomerular disease phenotypes found to be more common in our study were 65.10% of patients with nephrotic syndrome and 34.90% of patients with primary glomerular disease had nephritic syndrome. This suggests that nephrotic syndrome was the most common presentation of primary glomerular disease while in secondary glomerular disease in 60% of patients had nephrotic syndrome and 40% of patients had nephritic syndrome.

The most common primary glomerular disease in our study was FSGS (Fig. 5) at 37.2%, followed by IgA nephropathy at 20.9%, MGN at 12.10%, MPGN at 11.60% mesangioproliferative glomerulonephritis at 7% and minimal change disease at 7%. In secondary glomerular disease, diffuse lupus nephritis, accounted for 40% of all secondary glomerular disease; and was followed by renal amyloidosis at 20%, chronic thormboitic microangiopathy at 20% and secondary FSGS at 20%.

Chang et al. [4] in 2009, reported in patients at age 16 years or older which generated a total 1818 kidney biopsy. The most common primary glomerular disease was IgA Nephropathy (28.3%), which was followed by minimal change disease (15.5%), membranous glomerulonephritis (12.3%) and focal segmental glomerulosclerosis (5.6%) and membranoproliferative glomerulonephritis (4%).

The most common secondary glomerulonephritis was lupus nephritis (8.7%) and most common idiopathic nephrotic syndrome was minimal change disease (38.5%), these incidences were followed by membranous glomerulonephritis (25.7) and IgA Nephropathy (11.1). This difference in prevalence of glomerular disease may be due to patients that were HbsAg positive.

Das et al. [13] in 2011, analyzed the distribution of biopsy proven glomerular disease in a tertiary care hospital in South India and 1849 biopsies were analysed. The most common indication of renal biopsy was nephrotic syndrome (49%), followed by chronic renal failure (13.6%). Rapidly progressive renal disease (12%). Primary glomerulonephritis comprised 69.1% of total patients. Among primary glomerulonephritis minimal change disease (21.8%) most common followed by FSGS (15.3%), membranous glomerulonephritis 10%, chronic glomerulo-neprhitis (9.7%), post infectious glomerulonephritis (8.1%), mesangio-proliferative glomerulonephritis (6.7%), IgA Nephropathy 6.3%, membranoproliferative glomerulonephritis 5.7% and FSGS 1.6%. The most common secondary glomerulonephritis was lupus nephritis (80.1%) followed by amyloidosis 8%. This difference in prevalence may be due to a large number of patients in this study group, age 10-80 years included and diabetic patient included in this study group.

Golay et al. [18] in 2013, reported 666 patients with biopsy proven glomerular disease. Among the nephrotic syndrome most common glomerular disease was MCD 31.46%, followed by FSGS 25.6%, membranous glmerulonephritis (15.58%), IgA Nephropathy 6.09% and membranoproliferative glomerulonephritis 4.88%. In secondary glomerular disease, lupus nephritis was most common (73.38%), MCD was more common in this study (31.46%) in children while FSGS was more common primary glomerular disease in adults in this study.

Kazi et al. [19] in 2009, studied 316 patients for percutaneous renal biopsy. The spectrum of pathological lesion in adult comprised focal segmental glomerulosclerosis (39.87%) followed by membranous glomerulonephritis (26.58%), minimal change disease (14.82%), mesangiocapillary glomerulonephritis (4.3%), mesangioproliferative glomerulonephritis (4.11%), post infectious glomerulonephritis (2.84%), IgA Nephropathy (2.53%) indicated that FSGS was the single most common cause of nephrotic syndrome in this adult population similar to our study. Other differences may be due to the prevalence and geographical variation in that population.

5. CONCLUSION

Our study was carried out among patients with glomerular disease, which upon biopsy showed, that FSGS as the commonest cause of primary glomerular disease followed by IgA nephropathy in North-West Rajasthan. Lupus nephritis was more common in patients with secondary glomerular disease in our study. Further studies may help us to diagnose glomerular disease early in its course so that appropriate measure can be taken to halt its progression early.

CONSENT

All authors declare that 'written informed consent was obtained from the patients for publication of this paper and accompanying images.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
http://sciencedomain.org/review-history/14831