
Research Article

Association of Socioeconomic Status with Glomerular Diseases at a Tertiary Care Hospital in Bangladesh

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Abstract

Background: Social deprivation is a well-known risk factor for chronic kidney disease (CKD), however its association with glomerular diseases is less well understood. This study was aimed to evaluate the association of Socioeconomic Status (SES) with glomerular diseases among patients attending at a tertiary care hospital in Bangladesh.

Methods: This cross sectional study was conducted at Department of Nephrology, Shaheed Sheikh Abu Naser Specialized Hospital, Khulna, Bangladesh from January 2016 to December 2020. A total of 184 diagnosed patients of glomerulonephritis (GN) were enrolled. Patient's socioeconomic status (SES) was assessed using Modified BG Prasad socioeconomic classification. Morphological pattern of glomerular diseases were assessed according to the histopathology report. Relationship of glomerular diseases with particular socioeconomic status (SES) was identified.

Results: Among 184 study patients 99 were male and 85 were female, their mean age was 31.18 ± 13.55 years. It was observed that, in proliferative variety; Mesangial Proliferative Glomerulonephritis (Mes PGN) was the leading morphological variant (34.7%) followed by Membranoproliferative Glomerulonephritis [MPGN (16.8%)], Lupus Nephritis [LN (7.1%)], Focal Segmental Proliferative Glomerulonephritis [FSPGN (7.1%)], IgA Nephropathy (6.5%), IgM Nephropathy (4.3%) and Crescentic Glomerulonephritis [Cres GN (2.2%) serially. In the non-proliferative glomerulonephritis; Membranous Nephropathy (MN) was the commonest form (10.9%) followed by Focal Segmental Glomerulosclerosis [FSGS (7.6%)] and Minimal Change Disease [MCD (2.7%)]. All types of GN were significantly prevalent in the lower socioeconomic classes (Class- III, IV, V), while the frequency of Mes PGN and MPGN were significantly higher in Class- IV and Class- V socioeconomic classes.

Conclusion: Lower socioeconomic classes are associated with a higher incidence of glomerular diseases particularly Messangial Proliferative Glomerulonephritis (Mes PGN) and Membranoproliferative Glomerulonephritis (MPGN) in Bangladesh.

Keywords: Chronic Kidney Disease (CKD); Glomerular Disease; Glomerulonephritis (GN); Socioeconomic Status (SES)

Introduction

Socioeconomic Status (SES) is an important contributory factor for different health problems including chronic kidney disease (CKD) and is a powerful predictor of mortality [1,2]. Socioeconomic status (SES)

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encompasses a number of susceptibilities that may contribute to an individual's disease risk [3]. It was reported that lower socioeconomic status (SES) is constantly associated with CKD but its potential link to glomerular diseases is less clear [1,4]. Despite the improvement of public health measures, sanitization, and quality of life there is a paradoxical increase in allergic and autoimmune diseases, especially in industrialized countries in the last few years [5]. The hygiene hypothesis was originally proposed to explain the mechanism of marked increase in allergies in Westernized societies [6]. This hypothesis proposed that early and frequent exposure to bacterial and other antigens, which is common in developing nations, leads to a normal Th1 response; however, better public hygiene and fewer infections observed in industrialized nations may lead to persistence of the Th2 phenotype and thereby increase the risk for developing allergies [7]. There is a link between this hygiene hypothesis and geographical variation of morphological variants of glomerular diseases [8].

Glomerulonephritis (GN) literally means "inflammation of the glomeruli" although inflammation is not apparent in all varieties of the disease. Sometimes glomerulopathy is used to mention this entity [9]. Glomerular disease is the commonest cause of end-stage renal disease (ESRD) worldwide [10-12]. It comprises 25-45% cases of ESRD in developing nations, like Bangladesh [11]. While chronic ailments like diabetes and hypertension constitute the major bulk of chronic kidney disease (CKD) [10]. Idiopathic glomerulonephritis (GN) makes a major diagnostic challenge to both nephrologists and pathologists [11-12]. Glomerular disorders constitute one of the major causes of morbidity and mortality [10-12]. It has been suggested that apart from genetic profile, environmental factors and prevalence of infectious diseases, attribute to socioeconomic and demographic differences seen in patterns of glomerulopathy [13-14]. GN epidemiology follows racial and geographical distributions that are affected by a higher overall prevalence of infectious diseases and differences in social and economic statuses [13-14]. Little information exists on the factors leading these underlying changes, and most of the studies have conducted in Western countries [15]. Glomerulonephritis is one of the leading causes of chronic kidney disease (CKD) [10-12]. Timely intervention may limit this number or at least delay this progression which imposes a huge influence on resource limited national economy. In Bangladesh, most of the patients of glomerulonephritis present to the renal physician later and it is often impossible to alter the disease course with treatment. Moreover data is very limited addressing the influence of socioeconomic status (SES) on the pattern of glomerulonephritis. This study was aimed to evaluate the association of socioeconomic status with glomerular diseases among Bangladeshi population.

Methods

This cross sectional study was conducted at the

Department of Nephrology, Shaheed Sheikh Abu Naser Specialized Hospital, Khulna, Bangladesh from January 2016 to June 2020. A total of 184 diagnosed patients of glomerulonephritis were selected purposively following selection criteria. Hospitalized patients age ≥ 12 years, having proteinuria >1 gm/24 hours and hematuria (>3 rbc/hpf) were included. Diabetic patients and patients with proteinuria who meet KDIGO [Kidney Disease Improving Global Outcomes] criteria for chronic kidney disease (CKD), patients having uncontrolled hypertension (HTN) and patients with bleeding diathesis were excluded from the study. Height, weight, blood pressure (BP) of the study patients was measured and body mass index (BMI) was calculated accordingly. Relevant investigations including- urine routine microscopic examination (R/M/E), complete blood count (CBC), serum creatinine, serum electrolytes, 24 hours urinary total protein (24h UTP), random blood sugar (RBS), serum albumin, fasting lipid profile [Total Cholesterol (TC), High Density Lipoprotein- Cholesterol (HDL- C), Low Density Lipoprotein- Cholesterol (LDL- C) and Triglyceride (TG)], serum calcium (S. Ca), serum phosphate (S. PO₄), serological markers [like- antinuclear antibody (ANA), anti-ds DNA antibody, serum levels of complement components (C3 & C4) and antineutrophil cytoplasmic antibodies (ANCA)], HBsAg, Anti-HCV, Anti-HIV and ultrasonogram (USG) of kidneys of all study patients were done.

Study procedure

After admission all patients were evaluated by careful history taking, relevant clinical examination and routine investigations. Patient having suspected glomerulonephritis (GN) were further investigated to rule out primary from secondary GN. Those who had contraindication to kidney biopsy were excluded. After taking informed written consent kidney biopsy was done in each study patient following standard procedure. Then 2 core of renal tissue that obtained during renal biopsy were taken; one for light microscopy and another for direct immunofluorescence (DIF). Patient's socioeconomic status (SES) was assessed using Modified BG Prasad Socioeconomic classification update 2019 [16]. Patient's socioeconomic class was identified converting the Indian rupees into Bangladeshi taka (BDT). After getting biopsy report all the records were reviewed to correlate the variety of specific glomerular disease with different clinical and laboratory reports. Then relationship of glomerular diseases with particular socioeconomic status (SES) was identified. Thereafter each patient was treated accordingly and was advised for follow up as per schedule.

Socioeconomic Status (SES)

Socioeconomic status (SES) refers to an individual's position within a hierarchical social structure, which is one of the important determinants of health status. Composite scales are generally used to measure the SES, which has a

combination of social and economic variables. The most commonly used scale for measuring socioeconomic status (SES) is modified BG Prasad scale [16]. B G Prasad's classification was based on per capita monthly income and the scale evolved in 1961. The updated values for the per capita monthly income (Rs/month converted to BDT*/month) for Jan 2019 are given here-

Statistical Analysis

Data were recorded systematically and statistical analysis was performed using windows based software program Statistical Packages for Social Sciences 22 (SPSS- 22). All quantitative data were expressed as mean and standard deviation (SD), while frequency distribution and percentage (%) was used for qualitative data. Simple descriptive statistics was used to analyze the data. Comparison of continuous variables was done by unpaired 't' test. Association between different socioeconomic classes with all varieties of glomerular disease was examined by chi-square test. A p value <0.05 was considered as significant.

Results and observation

A total of 184 patients were enrolled to evaluate the association of socioeconomic status (SES) with glomerular diseases among hospitalized patients at a sub-urban region of Bangladesh. Among 184 patients, majority (54%, n=99) were male and 46% (n=85) were female (Figure 1). Baseline demographic profile shows that, mean age of the patients was 31.18 ± 13.55 years. Youngest patient was 12 years old and the oldest patient was a 66 year old male patient. Their mean height was 154.13 ± 10.39 cm, mean weight was 55.32 ± 10.19 kg, mean body mass index (BMI) was 23.48 ± 4.45 kg/m², mean body surface area (BSA) was 1.55 ± 0.16 m², mean systolic blood pressure was 132.6 ± 24.98 mmHg, mean diastolic blood pressure was 81.84 ± 11.58 mmHg (Table-2). It was observed that, the predominant socioeconomic class of study population was Class- IV which belongs to 45% of the study subjects (n=83). The next major class was Class- V including 64 study subjects (35%). While 13% patients was from Class- III group (n=24) and 5% from Class- II (n=10).

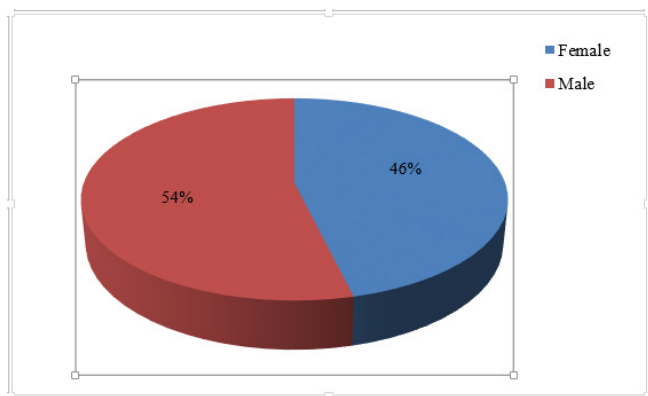


Figure 1: Distribution of the study patients according to gender (n=184).

Table 1: Modified BG Prasad's social classification- update 2019 [16].

Socioeconomic classes	Status	Per capita income limit (Rupees)	BDT* limit
I	Upper class	7533 and Above	8759 and Above
II	Upper-middle class	3766-7532	4379-8758
III	Middle class	2260-3765	2628-4378
IV	Lower middle class	1130-2259	1313-2627
V	Lower class	1129 and Below	1312 and Below

*BDT= Bangladeshi taka

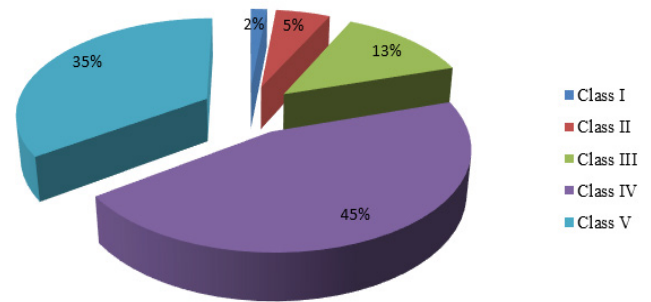


Figure 2: Distribution of the study patients based on socioeconomic status (n=184).

Table 2: Demographic profile of the study patients (n=184).

Variables	Mean ± SD	Minum - Maximum
Age (year)	31.18 ± 13.55	12 – 66
Height (cm)	154.13 ± 10.39	112.5-177.5
Weight (kg)	55.32 ± 10.19	26-81
BMI (kg/m ²)	23.48 ± 4.45	12.8 – 38.8
BSA (m ²)	1.55 ± 0.16	0.96-1.97
Systolic BP (mmHg)	132.6 ± 24.98	90- 210
Diastolic BP (mmHg)	81.84 ± 11.58	50 – 110

BMI= Body Mass Index, BSA= Body Surface Area, BP= Blood Pressure

The minor group was Class- I which includes only 3 of our study patients that covering 2% of the total study subjects (Figure 2).

Among the study population baseline laboratory parameters showed that; mean serum creatinine was 1.68 ± 1.27 mg/dl, mean random blood sugar (RBS) was 6.78 ± 2.6 mmol/l, mean haemoglobin, (Hb) level was 11.59 ± 1.79 gm/dl, mean serum albumin was 3.2 ± 0.83 gm/dl, mean serum calcium was 8.84 ± 1.79 mg/dl, mean serum phosphate was 3.62 ± 0.96 mg/dl, mean serum triglyceride was 305.56 ± 226.7 mg/dl, mean serum cholesterol was 213.6 ± 116.1 mg/dl and mean 24 hour urinary total protein (24h UTP) was 4.6 ± 3.5 gm/24h (Table- 3).

Data analysis revealed that there was no statistically significant difference ($p>0.05$) between male and female in different clinical and laboratory parameters like- age, body mass index (BMI), body surface area (BSA), systolic blood pressure (SBP), serum creatinine, random blood sugar (RBS), haemoglobin, serum albumin, serum cholesterol and 24 hours urinary total protein (24h UTP) (Table- 4).

Histopathological findings showed that, among the proliferative variety; Mesangial Proliferative Glomerulonephritis (Mes PGN) was the leading morphological variant ($n=64$, 34.7%). Membranoproliferative Glomerulonephritis (MPGN) came to the second ($n=31$, 16.8%). While 13(7.1%) patients were in the Lupus Nephritis (LN) group and another 7.1% was in the Focal Segmental Proliferative Glomerulonephritis (FSPGN) group. Thereafter, IgA Nephropathy ($n=12$, 6.5%), IgM Nephropathy ($n=8$, 4.3%) and Crescentic Glomerulonephritis (Cres GN) ($n=4$, 2.2%) serially. In the non-proliferative

glomerulonephritis; Membranous Nephropathy (MN) was the commonest form ($n=20$, 10.9%) followed by Focal Segmental Glomerulosclerosis (FSGS) and Minimal Change Disease (MCD), accounts 7.6% and 2.7% respectively (Table- 5).

Comparison of different morphological pattern of glomerulonephritis among the five socioeconomic classes showed that all varieties of GN were significantly prevalent in the lower socioeconomic classes (Class- III, IV, V), While the frequency of Mesangial Proliferative Glomerulonephritis (Mes PGN) and Membranoproliferative Glomerulonephritis (MPGN) were significantly higher in Class- IV and Class- V socioeconomic groups. The p value was significant ($p<0.005$) in all the instances (Table- 6).

Discussion

Socioeconomic status is a contributory factor to the different health problems and is an important indicator of mortality [5]. Moreover, individual's socioeconomic position encompasses a number of susceptibilities that could contribute to different disease risk [8]. It was reported that lower socioeconomic status has been consistently associated with different chronic disease including chronic kidney disease (CKD) [1-4, 17]. In this background this study was aimed to describe the morphological pattern of primary glomerular diseases and to evaluate this pattern in the light of socioeconomic status of our study population. In this study, out of 184 patients; male sex was slightly predominant (54% versus 46%) which was almost similar to all of the

Table 3: Basic laboratory parameters of the study subjects (N=184).

Variables	Mean ± SD	Minum – Maximum
S.Creatinine (mg/dl)	1.68 ± 1.27	0.6 - 8.3
RBS (mmol/l)	6.78 ± 2.6	4.0 - 8.8
Hb (g/dl)	11.59 ± 1.79	10.7 - 16.2
S. Albumin (g/dl)	3.2 ± 0.83	1.4 - 5.7
S. Ca (mg/dl)	8.84 ± 1.39	8.6– 10.0
S. PO ₄ (mg/dl)	3.62 ± 0.96	3.2-4.3
S. TG (mg/dl)	305.56 ± 126.7	205.0 - 1027.10
S. Cholesterol (mg/dl)	213.6 ± 116.1	151.30 - 723.40
24h UTP (gm/24h)	4.63 ± 2.52	1.38 - 7.20

RBS=Random Blood Sugar, Hb= Haemoglobin, S. Ca= Serum Calcium, S. PO₄= Serum phosphate, S. TG= Serum Triglyceride, 24h UTP= 24 hours Urinary Total Protein

Table 4: Comparison of clinical and laboratory parameters of the study population among different gender (N=184).

Variables	Male (n=99)	Female (n=85)	p-value
Age (years)	31.68 ± 14.43	30.56 ± 12.52	0.581
BMI (kg/m ²)	22.95 ± 4.14	24.09 ± 4.74	0.084
BSA (m ²)	1.58 ± 0.168	1.48 ± 0.15	0.309
SBP (mmHg)	132.93 ± 24.17	132.35 ± 26.03	0.877
S. Creatinine (mg/dl)	1.39 ± 1.39	1.52 ± 1.09	0.093
RBS (mmol/l)	6.97 ± 2.36	6.57 ± 2.97	0.314
Hb (gm/dl)	11.83 ± 1.79	11.33 ± 1.75	0.060
S. Albumin (gm/dl)	3.33 ± 0.86	3.18 ± 0.81	0.248
S. Cholesterol (mg/dl)	219.3 ± 121.7	206.93 ± 109.6	0.469
24h UTP (gm/24h)	4.54 ± 2.52	4.76 ± 2.56	0.668

BMI= Body Mass Index, BSA= Body Surface area, SBP= Systolic Blood pressure, RBS=Random Blood Sugar, Hb= Haemoglobin, 24h UTP= 24 hours Urinary Total Protein

Table 5: Distribution of study population according to the morphological pattern of Glomerulonephritis (N=184).

Variables	Number (n)	Percentage (%)
Proliferative Glomerulonephritis (78.7%)		
Mes PGN	64	34.7
MPGN	31	16.8
FSPGN	13	7.1
LN	13	7.1
IgA Nephropathy	12	6.5
IgM Nephropathy	8	4.3
Cres GN	4	2.2
Non Proliferative Glomerulonephritis (21.3%)		
MN	20	10.9
FSGS	14	7.6
MCD	5	2.7

Mes PGN= Messangial proliferative Glomerulonephritis, MPGN= Membranoproliferative Glomerulonephritis, MN= Membranous Nephropathy, MCD= Minimal Change Disease, LN= Lupus Nephritis, IgM Nephropathy= Immunoglobulin M Nephropathy, IgA Nephropathy= Immunoglobulin A Nephropathy, FSPGN= Focal Segmental Proliferative Glomerulonephritis, FSGS= Focal and Segmental Glomerulosclerosis, Cres GN= Crescentic Glomerulonephritis

Table 6: Association of different varieties of Glomerulonephritis with all five socioeconomic classes (N=184).

Varieties of Glomerulonephritis	Number (n)	Class- I (n=3)	Class- II (n=10)	Class- III (n=24)	Class- IV (n=83)	Class- V (n=64)	p-value
Mes PGN	64	1(1.6)	1(1.6)	4(6.3)	29(45.3)	29(45.3)	<0.05
MPGN	31	0(0.0)	1(3.2)	5(16.1)	16(51.6)	9(29.0)	<0.05
FSPGN	13	0(0.0)	0(0.0)	0(0.0)	7(53.8)	6(46.2)	<0.05
IgA Nephropathy	12	2(16.7)	0(0.0)	2(16.7)	4(33.3)	4(33.3)	<0.05
LN	13	0(0.0)	0(0.0)	1(7.7)	8(30.8)	4(30.8)	<0.05
MN	20	0(0.0)	5(25.0)	4(20.0)	5(30.0)	6(30.0)	<0.05
IgM Nephropathy	8	0(0.0)	0(0.0)	3(37.5)	4(12.5)	1(12.5)	<0.05
FSGS	14	0(0.0)	2(14.3)	2(14.3)	6(28.6)	4(28.6)	<0.05
MCD	5	0(0.0)	1(20.0)	2(40.0)	2(40.0)	0(0.0)	<0.05
Cres GN	4	0(0.0)	0(0.0)	1(25.0)	2(25.0)	1(25.0)	<0.05

Values within the parenthesis denote corresponding percentage, Mes PGN= Mesangial Proliferative Glomerulonephritis, MPGN= Membranoproliferative Glomerulonephritis, MN= Membranous Nephropathy, MCD= Minimal Change Disease, LN= Lupus Nephritis, IgM Nephropathy= Immunoglobulin M Nephropathy, IgA Nephropathy= Immunoglobulin A Nephropathy, FSPGN= Focal Segmental Proliferative Glomerulonephritis, FSGS= Focal and Segmental Glomerulosclerosis, Cres GN= Crescentic Glomerulonephritis

studies depicting male predominance [18-19]. Although Habib *et al.* from Bangladesh found female predominance [18]. The mean age of the study subjects was 31.18 ± 13.55 years. A related study observed that the mean patient's age was 31.9 ± 15.9 years which was also similar to this study [19]. Most of the participants of this study were hailing from lower socioeconomic status (80% belongs to Class IV and Class V- lower middle class and lower class respectively) reflecting the overall socioeconomic status in a sub-urban region of the Bangladeshi population. This finding was similar to a previous study where 80.1% of the studied patients were from lower socio-economic classes [20]. In both developing and developed countries, glomerular disease is a common cause of end stage renal disease (ESRD) [10-12]. The histological spectrum of glomerulonephritis (GN) varies widely between decades and nations, reflecting the possible effects of socio-economic, genetic and environmental factors [21]. IgA Nephropathy is the common primary glomerular disease from East Asia, as well as in white Europeans and Americans [5]. In contrast, Focal Segmental Glomerulosclerosis (FSGS) is the most common glomerular disease among African Americans, South Americans and in Middle East [5]. Proliferative glomerular disease was the most prominent renal disease in our biopsy cohort (78.7% versus 21.3%). This finding was supported by all recent studies [10, 18-20, 22]. In this current study Mesangial proliferative Glomerulonephritis (Mes PGN) was the commonest primary GN seen. Mes PGN was found as the commonest primary and proliferative GN in several other studies from different area of Bangladesh [23]. Although it was the second most common GN reported by Ahmed *et al.* (11.50%) [19]. Tabssum *et al.* conducted a cross sectional study on 67 cases and found that Mes PGN was the second most common primary glomerulonephritis (30.95%) after Membranoproliferative Glomerulonephritis

(MPGN) [12]. Another study also showed that Mes PGN is the predominant form of GN in the Southwestern region of Bangladesh (36.48%) [24]. A study done in Singapore on the spectrum and trends of glomerulonephritis for three decades showed that, in the 1st decade most Asians countries had MPGN and Mes PGN as the most common form of primary GN [25]. The similar trend was reported from some Asians countries like China, Japan and Thailand [26-28]. A recent study also found high prevalence of Mes PGN in India [29]. Hurtado *et al.* proposed that this variation in the morphological pattern of glomerulonephritis between regions can be explained by hygiene hypothesis [8]. Some types of human GN have Th1-predominant immune responses, including Crescentic Glomerulonephritis and MPGN. Other types of GN have predominant Th2 immune response, including Membranous Nephropathy (MN), Minimal Change Disease (MCD), and IgA nephropathy [7]. In developing countries, over stimulation of the immune system with numerous bacterial and other antigens may lead to a Th1 predominance and susceptibility to MPGN and other proliferative types of GN; in contrast, in Westernized nations fewer exposures to infections and better public hygiene may lead to a Th2-dominant phenotype and an increased risk for developing allergies with consequent IgA Nephropathy and MCD [8]. That may be possible explanation for higher prevalence of Mes PGN and MPGN in this study (34.7% and 16.8% respectively) as well as similar other studies from this region [25-28]. IgA Nephropathy is the most common form of primary GN as reported from different part of the globe, accounting for up to 30-40% of all biopsies from Asia, for 20% in Europe and for 10% in North America [5]. Although Asian studies showed variable result regarding the prevalence of IgA Nephropathy [25-29]. In comparison to the other Asian countries IgA Nephropathy is less common in Bangladesh (4.67%-7%)

[20]. In this current study IgA Nephropathy constitute only 6.5% of the total GN. This finding was consistent with some other Asian studies reported from India and Pakistan [29-30]. The lower prevalence of IgA Nephropathy in our study may be explained by the benign presentation of this disease. As asymptomatic urinary abnormalities mostly go undetected and varying approaches for using renal biopsy. Another factor is that proteinuria less than 1 gm without having renal failure was not considered for renal biopsy in our biopsy protocol. Indeed, the cases of IgA Nephropathy detected in our patients probably represented the tip of the iceberg. It is likely that the vast majority of these cases go undetected as a result of the current indicative criteria for renal biopsy [12]. Membranous Nephropathy (MN) accounts for 10.9% and Focal Segmental Glomerulosclerosis (FSGS) 7.6% in our study. The finding slightly differs with similar previous studies as reported, MN (7.34%) and FSGS (2.8%) [19], while MN 7.37 % but FSGS was 11.58% [18] in two different studies. The incidence of IgM Nephropathy in our study was 4.3%. Most of the studies did not mention IgM nephropathy as a distinct category. We have only 5 cases of MCD (2.7%). Several studies have shown a decline in the relative frequency of MCD [27-30]. A study from China also reported a very low incidence of MCD [26]. In this study, we compared different morphological pattern of glomerulonephritis among the five socioeconomic classes according to the modified BG Prasad scale [16]. It was found that different types of glomerulonephritis were significantly ($p < 0.05$) more frequent in the lower socioeconomic classes, particularly Mes PGN and MPGN were significantly higher in Class- IV and Class- V socioeconomic groups. This result was supported by a couple of previous study as reported that there is an inverse association between socioeconomic position and the incidence of glomerulonephritis [17, 31]. Glomerular diseases are complex conditions that require specialized care and expensive therapies, which may be more challenging for patients with a low socioeconomic status [17].

Conclusion

This study demonstrated that primary glomerulonephritis (GN) are more common in Bangladesh; Mesangial Proliferative Glomerulonephritis (Mes PGN) is the leading variety (accounts for 34.7%) of all morphological variant of glomerular disease followed by Membranoproliferative Glomerulonephritis [MPGN (16.8%)], other varieties are not very prevalent. Most of the study population belongs to Class- IV and Class- V socioeconomic groups (45% and 35% respectively). All varieties of GN are significantly prevalent in the lower socioeconomic classes particularly Mes PGN and MPGN follow relatively higher prevalence in the lower socioeconomic classes.

Limitation of the Study

It was a single center study with a relatively small sample size.

Recommendation

A large-scale multi-centered study should be conducted to see the reliability of the results.

Conflicts of Interest

The authors declare that they have no conflicts of interest regarding the publication of this article.

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