

# The Spectrum of Glomerular Diseases in Mashhad According to Kidney Biopsy Records

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**Introduction.** Knowing the national statistics of glomerular diseases will help in the management and minimizing their burden in the community. The aim of this study was to assess the overall distribution of subtypes of glomerulonephritis (GN) and the prevalence of renal diseases in a subgroup of diabetic and hypertensive patients.

**Methods.** This cross-sectional study was conducted on 860 patients with different subtypes of GN diagnosed by percutaneous renal biopsy and histological examination.

**Results.** The most common subtype of GN was membranous GN (30.1%) followed by minimal change disease (20.1%), IgA nephropathy (9.5%) and Lupus nephritis (8.8%), as well as membranoproliferative GN (6.4%), focal segmental GN (5.6%), crescent GN (4.3%), and DM nephropathy (3.6%). IgA nephropathy and focal segmental GN were mostly common among males while the most female dominant GN was Lupus nephritis. Lupus nephritis was the most common GN diagnosis among subjects who were younger than 29 years old (50%), while the diabetic nephropathy was the most common GN diagnosis among subjects who were older than 53 years old (44.4%). The most common GN among hypertensive subgroups was focal segmental GN (41.7%) followed by diabetic nephropathy (33.3%) whereas the most common subtypes of GN among diabetics was diabetic nephropathy.

**Conclusion.** The most common type of GN among Iranian population in Mashhad was membranous GN and minimal change disease. The distribution of each subtype of glomerular disease depends on the baseline determinants including age, gender and hypertensive state.

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## INTRODUCTION

Glomerular diseases are a group of kidney diseases, which are mainly characterized by impaired glomerular filtration. In a majority of these patients, disease progression leads to renal failure and even end stage renal disease (ESRD), chronic dialysis or kidney transplantation.<sup>1</sup> Glomerular injury can be due to elemental renal disease, including focal segmental glomerulosclerosis, membranous

nephropathy, and minimal changes disease.<sup>2,3</sup> Glomerular damage can also occur as the result of a systemic disease, including diabetes, hepatitis, or systemic lupus erythematosus (SLE).<sup>4,5</sup> Overall, there has been a change in the epidemiological behavior of various types of glomerular diseases in recent years. Although IgA nephropathy was reported as the most common glomerulopathy worldwide,<sup>6</sup> some reports have shown that the

prevalence of Focal Segmental Glomerulosclerosis (FSGS) is on the rise especially in developed countries.<sup>7</sup> In some other reports, membranous nephropathy was reported as the most common etiology for adulthood nephrotic syndrome.<sup>8</sup> There was a dramatic increase in the prevalence of different stages of chronic kidney diseases during 1999 to 2004 (13.1%), compared to earlier decades (10.0%). Ageing of the population as well as the increase in the trend of diabetes mellitus and hypertension might be the possible causes of this trend.<sup>9-12</sup> Besides the epidemiological aspects of glomerular diseases, the evaluation of socioeconomic burden as well as long-term prognosis have become the basic priority of healthcare systems. The medical cost for ESRD patients in 2001 was about 22.8 million dollars which was mostly due to diabetics.<sup>13</sup> Patients with ESRD have a lower quality of life and life expectancy compared to general population. Regarding the availability of therapeutic methods, including dialysis and kidney transplantation, the quality of dialysis and support for kidney transplant patients mostly depend not only on the patients economic status but also on the socio-economic burden, health care facilities, medical equipment and health care strategies within the community.<sup>14</sup> In these cases, developing countries are fundamentally different from developed countries. Today, in developed countries, the main goal of managing ESRD patients is to provide higher quality of life and increasing the life expectancy, while in developing countries the main goal is to provide minimum treatment needs of ESRD patients with the least economic burden.

Unfortunately, the data on the statistics on the epidemiological aspects and the distribution and spread of glomerular diseases is scarce in developing countries. In Iran, the published reports from different regions suggested various prevalence rates for glomerular impairments and chronic kidney diseases. In a large population-based study on 10063 participants, who were older than 20 years old, from the center of Iran, the overall prevalence of chronic kidney diseases was reported to be 18.9%. The major risk factors for chronic kidney disease were advanced age, female gender, obesity, hypertension, and dyslipidemia.<sup>15</sup> In another study from Kerman, the southern region of Iran, the prevalence of chronic kidney diseases was estimated to be 25.7%, which was higher

than the previously mentioned report, but the risk factors were similar to the previous report.<sup>16</sup> Determining the exact prevalence of glomerular diseases and their risk factors enables health care providers to better plan and establish appropriate management strategies theregion. The present study aimed to assess the prevalence of each subtype of glomerular diseases and the main determinants of the glomerular diseases in a group of Iranian adults.

## MATERIALS AND METHODS

The present cross-sectional survey was approved by the Mashhad University of Medical Sciences Ethical Committee and took place in Ghaem and Emam Reza hospitals, Mashhad, Iran within a 2 year (from 2016 to 2018). Patients who had complete hospital records including data regarding the demographic characteristics, underlying comorbidities and diagnostic reports for glomerular diseases were considered eligible to enroll in the present study. All patients gave a written informed consent before conducting any laboratory or pathological tests. The diagnosis of glomerular disease was confirmed based on percutaneous renal biopsy and histological examination with light microscopy and immunofluorescence microscopy. In this regard, different subtypes of glomerular diseases, including membranous glomerulonephritis (MGN), minimal change disease (MCD), IgA nephropathy, lupus nephritis (LN), membranoproliferative glomerulonephritis (MPGN), focal segmental glomerulonephritis (FSGN), crescent glomerulonephritis, and diabetic nephropathy were considered. The main study endpoint was to determine gender and age-related prevalence of each type of glomerular diseases. Furthermore, we aimed to assess the distribution of each category of glomerular diseases in diabetic and hypertensive subgroups.

Data was analyzed using SPSS (IBM Inc, Chicago, Il) version 20. Continuous data was checked for normality using the Shapiro-Wilk test. Normally distributed data were presented using mean and standard deviation (SD) while non-normally distributed data were presented using median and interquartile range (IQR). Categorical variables were presented using frequency and percentage. Distribution pattern of categorical variables between study groups was compared using chi-square or Fisher exact tests while continuous data were

compared using one-way analysis of variance (ANOVA) or Kruskal-Wallis test. Statistical significance was considered as *P* value < .05.

**RESULTS**

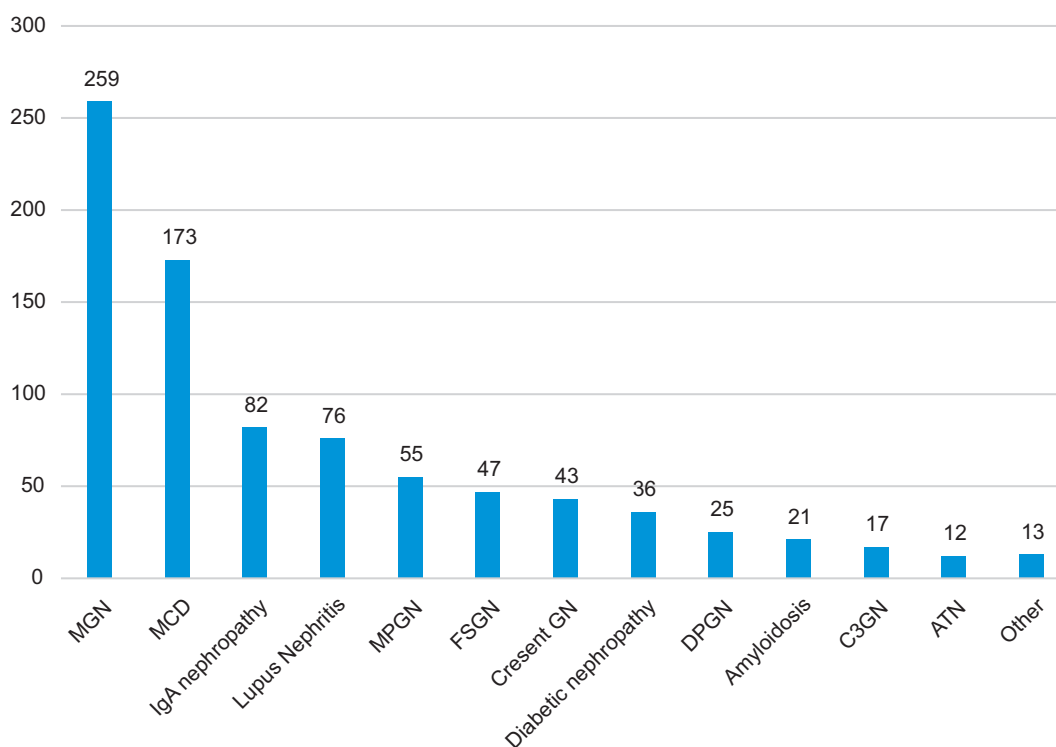
A total of 860 subjects (participated in the study with mean ± standard deviation age of 41.40 ± 16.02 years. Most of the study participants were males (499 patients, 58%). Demographic characteristics of subjects are shown in Table 1. Among the study population, most of the patients were hypertensive and simultaneous hematuria and proteinuria was seen in 7.6% of patients. Among the serologic markers, anti-glomerular basement membrane (anti-GBM) antibody was present in 3 patients, C-antineutrophil cytoplasmic antibodies in 3 patients, P-anti neutrophil cytoplasmic antibodies (C-ANCA) was present in 2 patients, anti-nuclear antibody (ANA) was present in one patient. Among the virology markers, hepatitis B surface antigen (HBSAg) was present in one patient. Secondary GN was present in 120 (13.9%) patients, while primary GN was observed in 640 (86.1%) patients.

The GN diagnoses frequency among study participants is presented in Figure 1 and Table 2.

**Table 1.** Demographic Characteristics of Study Subjects

Variable	Frequency	Percentage
Gender		
Male	499	58
Female	361	43
Age, y		
< 29	234	27.2
29 to 39	189	21.9
39 to 53	213	24.9
> 53	224	26
Hypertension	131	15.2
Diabetes mellitus	71	8.3
Proteinuria		
Negative	35	4.1
Nephrotic Syndrome	448	52.1
Nephritic Syndrome	210	24.4
Positive	167	19.4
Hematuria	160	18.6
Proteinuria and Hematuria	65	7.6
Creatinine		
Normal	411	47.8
High	283	32.9
Unknown	166	19.3

MGN (259, 30.1%) followed by MCD were the most common and crescent GN following DM nephropathy had the least frequency. Distribution



**Figure 1.** It shows distribution of GN diagnosis among study subjects (MGN, membranous glomerulonephritis; MCD, minimal change disease; MPGN, membranoproliferative glomerulonephritis; FSGN, focal segmental glomerulonephritis; DPGN, diffuse proliferative glomerulonephritis; ATN, acute tubular necrosis).

**Table 2.** Glomerular Disease Diagnoses and Clinical and Laboratory Findings Among Study Subjects

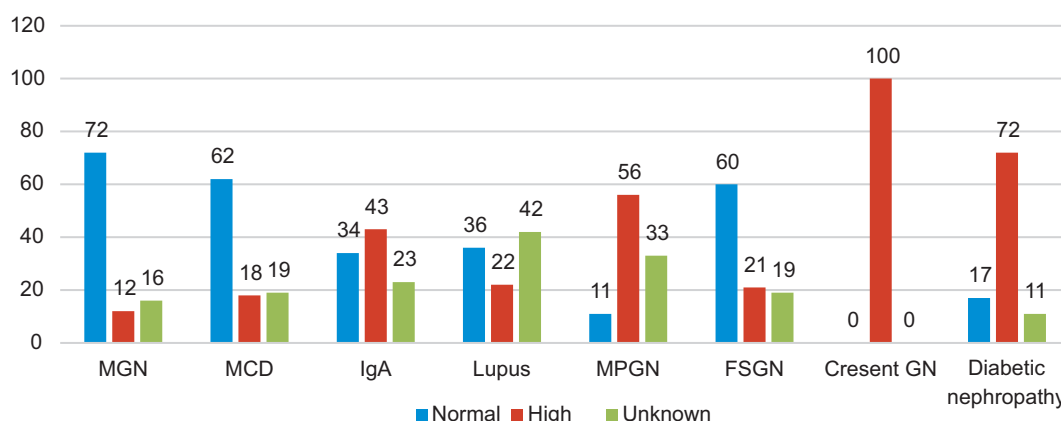
Diagnosis	Total Frequency (%)	Gender (%)		Age (%), y				HTN (%)	DM (%)	Proteinuria (%)			
		Male	Female	< 29	29 to 39	39 to 53	> 53			Nephrotic	Nephritic	Positive	Negative
MGN	259 (30.1)	150 (57.9)	109 (42.1)	40 (15.5)	52 (20.1)	77 (29.8)	89 (34.5)	22 (8.5)	12 (4.6)	159 (61.4)	41 (15.8)	53 (20.5)	6 (2.3)
MCD	173 (20.1)	101 (58.4)	72 (41.6)	55 (31.8)	53 (30.6)	38 (22)	27 (15.6)	17 (9.8)	6 (3.5)	102 (59)	44 (25.4)	21 (12.1)	6 (3.5)
IgA nephropathy	82 (9.5)	59 (71.9)	23 (28.1)	27 (32.9)	22 (26.8)	19 (23.2)	14 (17.1)	16 (19.5)	3 (3.7)	0 (0)	30 (36.6)	34 (41.5)	1 (1.2)
Lupus Nephritis	76 (8.8)	19 (25)	57 (75)	38 (50)	20 (26.3)	16 (21)	2 (2.6)	3 (3.9)	0 (0)	27 (35.5)	23 (30.3)	24 (31.6)	2 (2.6)
MPGN	55 (6.4)	34 (61.8)	21 (38.2)	19 (34.5)	14 (25.4)	8 (14.5)	14 (25.4)	16 (29.1)	5 (9.1)	23 (42.6)	14 (25.9)	14 (25.9)	4 (7.5)
FSGN	48 (5.6)	32 (68.1)	15 (31.9)	21 (45.6)	13 (28.2)	3 (6.5)	9 (19.6)	20 (41.7)	8 (16.7)	27 (56.3)	15 (31.3)	6 (12.5)	0 (0)
Crescent GN	43 (5)	21 (48.8)	22 (51.2)	11 (25.6)	3 (7)	9 (20.9)	20 (46.5)	13 (30.2)	2 (4.6)	14 (32.6)	14 (32.6)	14 (32.6)	1 (2.3)
Diabetic nephropathy	36 (4.2)	24 (66.7)	12 (33.3)	1 (2.8)	3 (8.3)	16 (44.4)	16 (44.4)	12 (33.3)	34 (94.4)	29 (80.6)	0 (0)	5 (13.9)	2 (5.6)

MGN, membranous glomerulonephritis; MCD, minimal change disease; MPGN, membranoproliferative glomerulonephritis; FSGN, focal segmental glomerulonephritis; DPGN, diffuse proliferative glomerulonephritis; ATN, acute tubular necrosis

of study parameters among major GN types are presented in Table 2. There was a significant difference in gender, age group, hypertension, diabetes, and creatinine level between GN subgroups ( $P < .001$ , for each). The highest male dominance was observed in IgA nephropathy (M/F ratio = 2.6), followed by FSGN (M/F ratio = 2.1), diabetic nephropathy (M/F ratio = 2.0), and MPGN (M/F ratio = 1.6) while the most female dominant GN diagnosis was Lupus nephritis (M/F ratio = 0.3) (Table 2). The most prevalent GN diagnosis among subjects who were younger than 29 years was lupus nephritis (50%) followed by FSGN (45.6%) and the most common GN diagnosis among subjects who aged between 29 and 39 years was MCD (30.6%) followed by FSGN (28.2%). The most prominent GN in hypertensive subgroups was FSGN (41.7%) and the most common subtypes of GN among diabetics included diabetic nephropathy revealed in 94.4% (Table 2). As shown in Figure 2, raised creatinine level was observed in 100% of the subjects with crescent GN, 72% of subjects with diabetic nephropathy and 56% of subjects with MPGN (Figure 2).

### DISCUSSION

The overall gender and age-related distribution of different subtypes of glomerular diseases and the prevalence of these glomerular pathologies among common high-risk individuals, including diabetic and hypertensive patients were presented in the current study. This study revealed that MGN was the most common subtype of glomerular injury, affecting one-third of the patients, followed by MCD (20%). In terms of gender distribution pattern, IgA nephropathy was the most common injury in men while Lupus nephritis was more prominent among women. Furthermore, Lupus nephritis and FSGN were the most prevalent glomerular diseases among young population, while diabetic nephropathy was more prominent in the elderly. Interestingly, the age and gender distribution patterns were different in different regions of our country. In a study by Rahbar *et al.* from western Iran, MCD and membranous glomerulonephritis were the most common findings in children below the age of 16 years.<sup>17</sup> Minimal change disease was also ranked first in adults while membranous glomerular disease and focal segmental glomerulosclerosis were more common in the elderly. In all patients



**Figure 2.** It demonstrates distribution of creatinine categories among the common GN diagnoses (MGN, membranous glomerulonephritis; MCD, minimal change disease; MPGN, membranoproliferative glomerulonephritis; FSGN, focal segmental glomerulonephritis; DPGN, diffuse proliferative glomerulonephritis; ATN, acute tubular necrosis).

Lupus glomerular disease was the most common secondary glomerular disease.<sup>17</sup> In another study in central Iran by Daneshpajouhnejad *et al.* the three most prevalent diagnoses were FSGS (in about one-fourth of patients), followed by MCD and MGN (in less than 10% of patients).<sup>18</sup> Similar to the findings of the present study, in the study by Ossareh *et al.* on 1407 patients with GN, MGN was reported as the most common GN (26.8%) but IgA nephropathy was the second most prevalent GN.<sup>19</sup> They also reported that IgA nephropathy was more prevalent among men, whereas Lupus nephritis was more prevalent among women. Similarly, in the study on Iranian population by Naini *et al.* MGN was the most common GN followed by IgA nephropathy.<sup>20</sup> This finding was in line with the findings of the current study. Systematic reviewing of the literature revealed a declining trend in overall prevalence of IgA nephropathy in both young and old populations. Al Menawy *et al.*, reported that 2.7% of young adults had IgA nephropathy while IgA nephropathy was reported among 3% of (300 cases) in another study.<sup>21,22</sup> Daneshpajouhnejad *et al.* mentioned that although IgA nephropathy is the least prevalence glomerular disease in Iran and most Asian countries, it is by far the most common GN among European countries.<sup>18</sup> Two reasons have been proposed for the regional variability of the GNs. On the one hand, it is hypothesized that this variation might be due to the genetic differences of the people who live in different regions and the presence of primary GNs, including familial FSGS and IgA nephropathy, while on the other hand, the differences in the socioeconomic status

of different regions of a country, which result in different quality of access to medical and health care, sanitation and social infrastructures, were considered as the prospective reasons for the regional differences in GNs distribution.<sup>23,24</sup>

According to the findings of the current study, FSGN was the most prevalent GN among hypertensive patients. It was previously shown that continued elevation in systemic blood pressure accelerates the decline in kidney function. On the other hand, hypertension is a main systemic finding in a majority of patients suffering from GN, with the self-report prevalence of nearly 86% compared to 29% in the general population.<sup>25,26</sup> There is a direct relationship between the relative risk of developing ESRD and the severity of hypertension.<sup>27,28</sup> Thus, the formation of diffuse glomerular abnormalities and segmental sclerosing lesions are more expected among hypertensive patients compared to normotensive population due to the loss in glomerular function due to ischemia.<sup>29</sup> Among the FSGN subgroup, the presence of severe hypertension was a criterion for aggravated condition. Additionally, Alchi *et al.* and Fukuda *et al.*, showed that hypertension was a unique cause of unilateral FSGN.<sup>30,31</sup> Therefore, hypertension management is the main principle to control and limit hypertensive renal defects.

The prevalence and trend of diabetic nephropathy has been exclusively evaluated within the last decade in parallel with the increasing global trend of diabetes mellitus.<sup>32</sup> According to recent reports, diabetes is the most common cause of ESRD in both Western and Eastern countries.<sup>33,34</sup>

Furthermore, diabetes accounted for one-fifth of chronic dialysis patients and led to a high mortality and morbidity in such patients. The risk factors for diabetic nephropathy include genetic susceptibility, hypertension, race, uncontrolled blood glucose, cigarette smoking, male gender, and dyslipidemia.<sup>35-7</sup> The prevalence of diabetic nephropathy ranged from 16% to 87% in different regions of Iran.<sup>38-42</sup> The increasing trend of this complication is also expected due to the increasing prevalence of diabetes.<sup>42</sup> Therefore, the increasing trend of diabetic nephropathy and its related mortality and morbidity in our society should be considered as a serious warning to our health care managers.

## CONCLUSION

The present report revealed that MGN and MCD were the most common GNs, while FSGN and diabetic nephropathy were the most prevalent GNS among hypertensive and diabetic individuals. The distribution of each subtype of glomerular disease depends on the baseline determinants including age, gender and hypertensive state.

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