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Appearance of Primary and Secondary Glomerulonephritis: Single Centre Experience

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Abstract

Introduction. Glomerular disease could lead to chronic kidney disease. The aim of this study is to determine the frequency of kidney biopsy proven glomerulonephritis (GN) to create better database in Turkey.
Methods. We evaluated 1273 native kidney biopsies from 2008 to 2017. Renal disease were divided into five major categories: primary GN, secondary GN, tubulointerstitial nephropathies (TIN), vascular nephropathies (VN) and acute tubular necrosis (ATN).
Results. 756(59.4%) patients had primary GN, 353 (27.7%) patients had secondary GN, 101(7.9%) patients had TIN, 32(2.5%) patients had VN and 31(2.4%) patients had ATN. While, the most frequent pathological diagnosis was focal segmental glomerulosclerosis (FSGS) (31.35%), followed by membranous GN (27.65%) in primary glomerulonephritis, amyloidosis (27.2%) was the most frequent pathological diagnosis followed by systemic lupus erythematosus (SLE) (20.68%) in secondary glomerulonephritis. FSGS is the most common kidney pathology in younger than 50 years old (18-30 years old, 22% and 31-50 years old, 20%). Membranous glomerulonephritis (MGN) is the most common kidney pathology after the ages 50 years old (50-64 years old, 20% and >65 years old, 17%).
Conclusion. FSGS is the most common primary GN in Turkish population and the frequency is gradually increasing.

Keywords: adult, glomerulonephritis, kidney biopsy, registry

Introduction

Chronic kidney disease (CKD) is increasingly prevalent worldwide with high morbidity and mortality [1]. Early diagnosis of CKD, determination and treatment of possible risk factors for progression to end stage kidney disease have prime importance [1,2]. Glomerular diseases can result from many inherited or acquired disorders and could lead to CKD. Glomerular disease frequency varies between countries. National databases such as European Renal Association-European Dialysis and Transplant Association (ERA-EDTA) in Europe, United State Renal Data System (USRDS) and Italian Registry of Renal Biopsies (IRRB) provide comparison of frequency of glomerulonephritis (GN) in these countries. The main causes of CKD in the USA are diabetic nephropathy (46.7%), hypertensive nephropathy (23.8%) and GN (9.4%). On the other hand, the most common cause of CKD in China is GN and the frequency varies between 50% and 68.6% [3,4]. The most common cause of GN vary from country to country in epidemiological studies. While the most common cause of nephropathies is IgA nephropathy (IgAN) in Italy (43.5%) [5], focal segmental glomerulosclerosis (FSGS) in USA [6], IgAN in Japan (%50) [7] and FSGS in Brazil (29.7%) [8]. One of the basic condition to conduct good clinical epidemiological studies is the ability to create databases for specific diseases. National epidemiological studies provide opportunity for determination frequency of specific disease and develop strategies, as well as making it possible to compare with other nations. The aim of this study is to determine the frequency of kidney biopsy proven GN to create better database in Turkey and compare with the data of other countries.

Material and methods

This descriptive study was conducted in Gazi University Nephrology and Pathology departments. We evaluated data relating to 2028 kidney biopsies collected from 2008 to 2017. Patients, who were older than 18 years of age with abnormal urine findings and/or decreased renal function of unknown etiology were evaluated. Data of 114 renal biopsies could not be classified due to inadequate sampling of materials. We analyzed age, gender and biopsy proven diagnosis.
Nephrotic range proteinuria (>3.5 g/d proteinuria), asymptomatic urinary abnormalities (persistent low grade proteinuria with or without microscopic hematu-

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ria), nephritic syndrome (hematuria, arterial hypertension and reduced kidney function), acute kidney failure (sudden increase of serum creatinine and/or reduced urine output) and chronic kidney disease with unexplained reason were kidney biopsy indications. Renal biopsy was not performed if kidney length was below 9 cm. Renal biopsy cores were obtained with ultrasonography accompanied standard procedure by the nephrologist. Fresh biopsy cores were fixed in formaline and evaluated under light microscopy. Paraffin sections were prepared and stained with hematoxylin eosin, Kongo red and Jones silver methenamine stains. Small renal cortical tissue was separated for immunofluorescence study. Immunofluorescence studies on cryostat sections using polyclonal antisera against IgG, IgM, IgA, C3, C1q, C4d, kappa and lambda light chains have been used. Electron microscopy was not used for all biopsy specimens so that reason minimal change disease (MCD) and alport 's syndrome could not be included.

Renal disease were divided into five major categories: (1) primary GN; (2) secondary GN; (3) tubulointerstitial nephropathies (TIN); (4) vascular nephropathies (VN); and (5) acute tubular necrosis (ATN). Primary GN were classified as IgA nephropathy, FSGS, membranous GN (MGN), MCD, membranoproliferative GN (MPGN), diffuse proliferative GN (DPGN), mesangioproliferative GN (MePGN) and acute poststreptococcal GN (APSGN). Systemic lupus erythematosus, Hench-Schönlein purpura, amyloidosis, Goodpasture's syndrome, vasculitis, diabetes mellitus, Alport's syndrome and dysgammaglobulinemia associated GN (Waldenstrom's macroglobulinemia, monoclonal gammopathy and light chain disease) were considered as secondary GN. Acute and chronic TIN evaluated in TIN. While thrombotic microangiopathy, malignant nephrosclerosis, cortical necrosis and preeclampsia were considered among VN, acute tubular necrosis considered among ATN.

Categorical variables are expressed as percentage. Data distribution was determined by using Kolmogorov-Smirnov test. Homogenity of variables were determined by using one way anova homogenity of variance test. Chi-square test was used to compare categorical variables. The Kruskal-Wallis one way analysis of variance was used if more than two groups were being compared. Analyses were performed with Statistical Package for the Social Science (SPSS version 20.0.0, IBM) software for Windows.

Results

We examined 2028 kidney biopsies which were performed between 2008 and 2017 in Gazi University, department of Nephrology. Biopsies, which were non-diagnostic (n=114), non-specific (n=128) and transplant kidney (n=126), were excluded from the study. Also, biopsies reported as CKD and patients who were younger than 18 years old were excluded (Figure 1). Finally, 1273 native kidney biopsies were examined. Among all adults, 756(59.4%) patients had primary GN, 353 (27.7%) patients had secondary GN, 101(7.9%) patients had tubulointerstitial nephropathies, 32(2.5%) patients had vascular nephropathies and 31 patients (2.4%) had ATN.

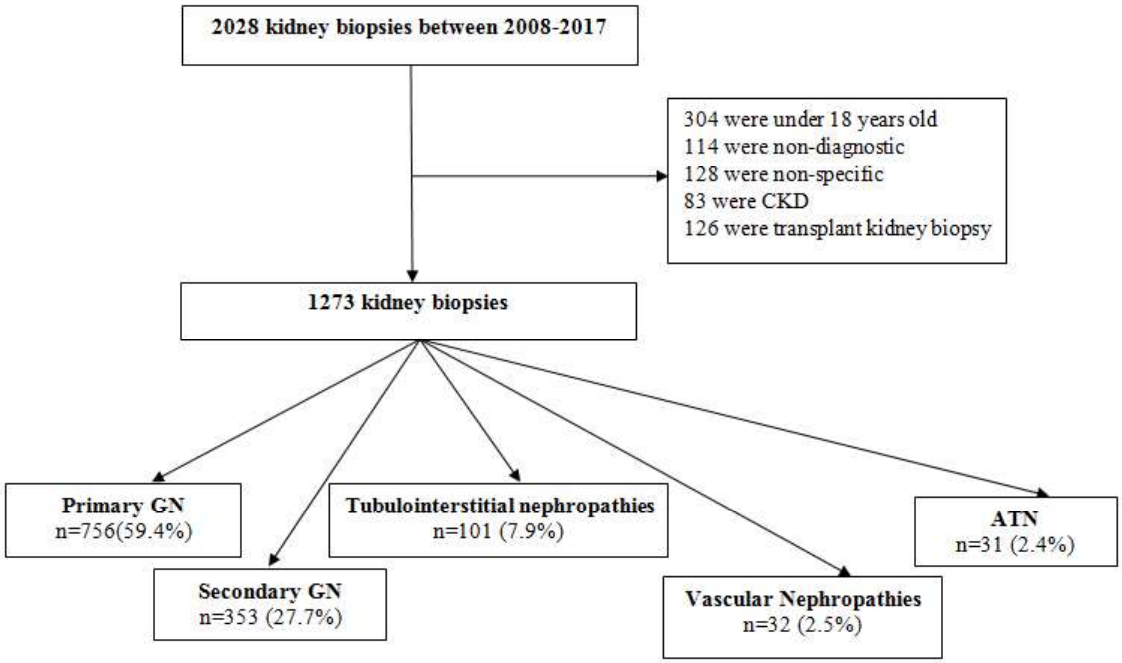

Fig. 1. Distribution of kidney biopsies between 2008 and 2017

While, the most frequent pathological diagnosis was FSGS (31.35%), followed by membranous GN (27.65%) and IgAN (22.09%) in primary glomerulonephritis, amyloidosis (27.2%) was the most frequent pathological diagnosis followed by SLE (20.68%) and diabetic nephropathy (15.01%) in secondary glomerulonephritis (Figure 2). About 53% (n=679) of total patients who had done kidney biopsy were male. Primary GN were more frequent in males (54%), when compared to females (46%); similarly, secondary GN (males 55% and females 45%) and ATN (males 61% and females 39%) were more frequent in males. On the contrary, TIN (females 54% and males 46%) and VN (females 69% and males 31%) were more frequent in females. Glomerular diseases, whose frequency was significantly higher in males, were IgAN (p<0.001), amyloidosis (p=0.02) and diabetic nephropathy (p=0.03).

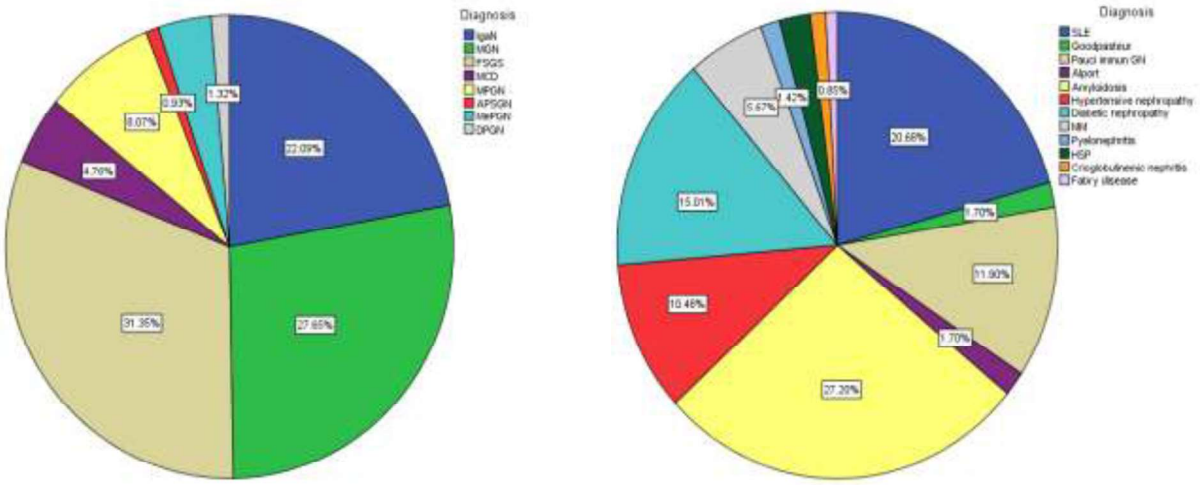

Fig. 2. Frequency of histological diagnosis of primary and secondary nephropathies: Abbreviations are: IgAN, IgA nephropathy; MGN, membranous glomerulonephritis; FSGS, focal segmental glomerulosclerosis; MCD, minimal change disease; MPGN, mesengioproliferative glomerulonephritis; APSGN, acute poststreptococcal glomerulonephritis; MePGN, mesengioproliferative glomerulonephritis; DPGN, diffuse proliferative glomerulonephritis; HSP, Hench-Schönlein purpura; SLE, systemic lupus erythematosus; MM, multiple myelom

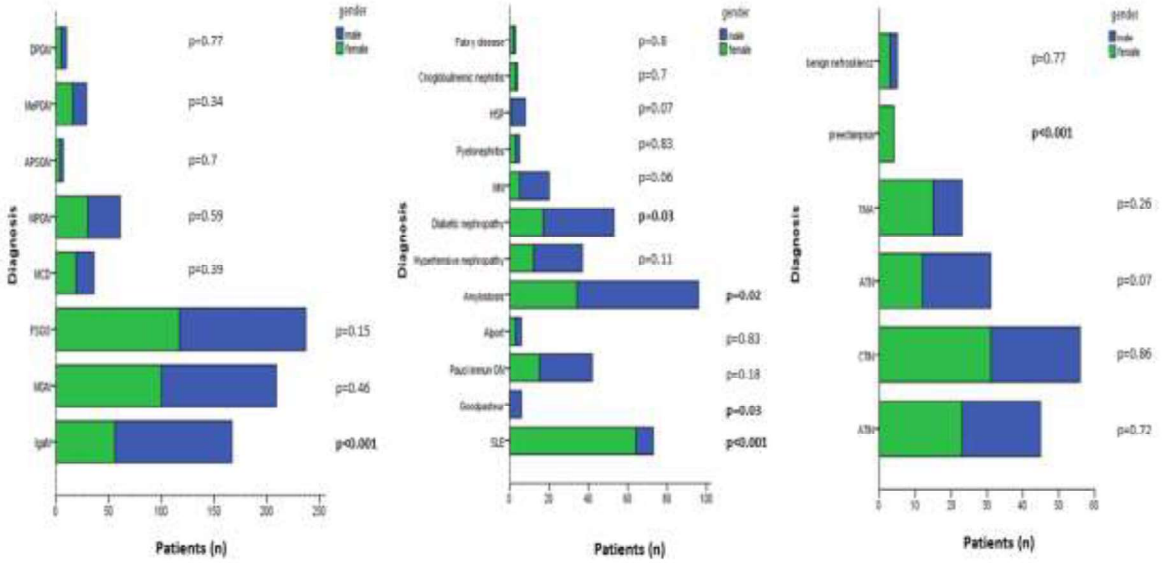

Fig. 3. Gender distribution of patients in kidney diseases: Abbreviations are: IgAN, IgA nephropathy; MGN, membranous glomerulonephritis; FSGS, focal segmental glomerulosclerosis; MCD, minimal change disease; MPGN, mesengioproliferative glomerulonephritis; APSGN, acute poststreptococcal glomerulonephritis; MePGN, mesengioproliferative glomerulonephritis; DPGN, diffuse proliferative glomerulonephritis; HSP, Hench-Schönlein purpura; SLE, systemic lupus erythematosus; MM, multiple myelom; ATIN, acute tubuinterstitial nephritis; CTIN, chronic tubulointerstitial nephritis; ATN, acute tubular necrosis; TMA, thrombotic microangiopahty

Besides, SLE (p<0.001) was significantly higher in females (Figure 3). When the age distribution of primary glomerulonephritis was examined, it was observed that frequency of MGN increased significantly with age and frequency of IgAN decreased after the age of 50 (p<0.001 and p=0.01, respectively). While, the frequency of SLE and Goodpasture Sy, decreased significantly with the age (p<0.001 and p=0.009), frequency of amyloidosis, hypertensive nephropathy, diabetic nephropathy and MM increased significantly with the age (p=0.01, p=0.002, p=0.007 and p=0.02, respectively) (Figure 4). When the age distribution of primary and secondary GN is examined within themselves; FSGS is the most common primary GN between the ages of 18-30 and 31-50 [35% (n=78) and 30% (n=109) respectively]. On the contrary, MGN is the most common primary GN in patients who are 50 years and older [37% (n=41) and 42% (n=25]. And also frequency of IgAN decreases with the age. SLE is the most common secondary GN in the age of 30 [42% (n=37)], whereas amyloidosis is the most common secondary GN after the age of 30 [31-50 years old, 28% (n=36), 50-64 years old, 33% (n=22) and >65 years old, 36% (n=25)]. When the frequency of kidney pathology is examined in all biopsy population; we showed that FSGS is the most common kidney pathology until 50 years old [18-30 years old, 22% (n=78) and 31-50 years old, 20% (n=109)]. While MGN is the most common kidney pathology between the ages 50-64 years old [20% (n=41)], MGN and amyloidosis are the most common glomerular pathology after the age of 65 [17% (n=25) and 17% (n=25) respectively] (Table 1). When the prevalence of diabetic nephropathy is examined among the secondary GN, the prevalence gradually increases until the age 65, but it decreases slightly after this age. When we analyzed the frequency of primary GN according to years, we showed that MGN is the most common primary GN until the end of 2013, whereas FSGS became the most common primary GN with a marked increase in the frequency after 2013 (Figure 5).

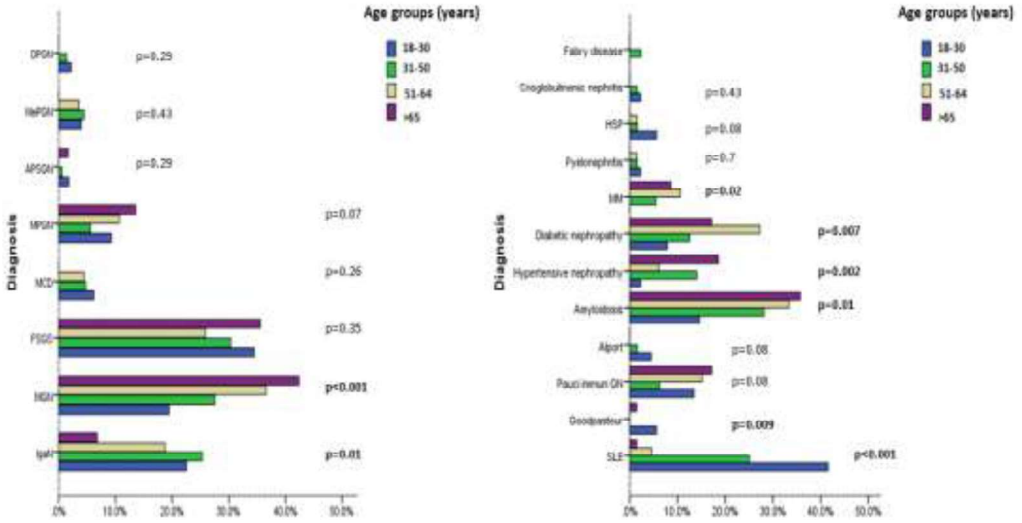

Fig. 4. Age distribution of primary and secondary glomerulonephritis

Table 1: The frequency of glomerulonephritis among age groups

	Primary Glomerulonephritis			Secondary Glomerulonephritis		
	IgAN	**MGN**	**FSGS**	**Amyloidosis**	**SLE**	**DN**
Age (years)	37(18-75)	44(18-84)	38(18-84)	50(21-81)	30(18-48)	53(22-79)
Age groups(years)						
18-30	23%(51)	20%(44)	35%(78)	15%(13)	42%(37)	8%(7)
31-50	25%(91)	28%(99)	30%(109)	28%(36)	25%(32)	13%(16)
50-64	19%(21)	37%(41)	26%(29)	33%(22)	5%(3)	27%(18)
>65	7%(4)	42%(25)	36%(21)	36%(25)	1%(1)	17%(12)
Total	22.1%(167)	27.6%(209)	31.3%(237)	27.2%(96)	20.7%(73)	15%(53)
	General Biopsy Population					
	IgAN	**MGN**	**FSGS**	**Amyloidosis**	**SLE**	**DN**
Age groups(years)						
18-30	14%(51)	12%(44)	22%(78)	4%(13)	10%(37)	2%(7)
31-50	16%(91)	18%(99)	20%(109)	6%(36)	5%(32)	3%(16)
50-64	10%(21)	20%(41)	14%(29)	11%(22)	2%(3)	9%(18)
>65	3%(4)	17%(25)	15%(21)	17%(25)	1%(1)	8%(12)
Total	13%(167)	16%(209)	19%(237)	8%(96)	6%(73)	4%(53)

IgAN: IgA nephropathy; MGN: membranous glomerulonephritis; FSGS: focal segmental glomerulosclerosis; DPGN: diffuse proliferative glomerulonephritis; SLE: systemic lupus erythematosus; DN: diabetic nephropathy

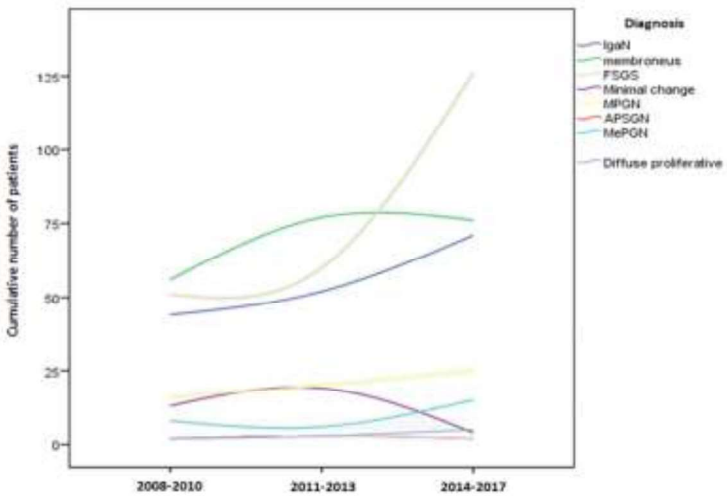

Fig. 5. Changes in the frequency of primary glomerulonephritis over the years

Discussion

Renal biopsy registries can provide very important information about epidemiology of renal diseases. Our observational study showed that FSGS is the most common GN in Turkey and it is followed by MGN and IgAN. The frequency of FSGS has increased during the last 5 years period. It has also been demonstrated in our study that FSGS is a type of GN that can be seen similar in both genders and every age groups.

Ozturk *et al*. demonstrated that MGN is the most frequent primary GN in Turkey in 2014 [2]. In subgroup analysis of age they showed that FSGS is the most common primary GN in patients who are younger than 40 years old. Similar to their study, we showed that MGN is the most leading cause of primary GN until 2014. But, we also demonstrated that the frequency of FSGS has increased steadily and became the most leading cause of primary GN after 2014. Many factors may have contributed to increase in FSGS frequency. Development in biopsy techniques and increased number of glomeruli colected by biopsy may have facilitated the diagnosis. On the other hand, Borges FF *et al*. showed that the frequency of FSGS is increasingly high and the obesity may be the cause of this rise [9]. We can also hypothesize that epidemic of obesity can facilitate the disease occurrence. Secondary forms of FSGS are potentially preventable, through promoting healthy lifestyle choices and reducing obesity [10]. The latest observational study, which is conducted with 264 patients, in Turkish population was published by Ayar Y *et al*. in 2016 to our knowledge [11]. They showed that MGN is the most common cause of primary GN in Turkey. Although the study was published in 2016, they have reviewed the medical records of their Clinics until 2014. On the other hand, Hur *et al*. reported that FSGS is the most common primary GN in Turkey and followed by MGN and IgAN [12]. Similar to our study, they showed that amyloidosis is the most common secondary GN followed by SLE. The frequency of GN varies regional. In a review, which was published in 2017, they showed that the most common GN was IgAN in Asia and Europe; FSGS in USA and Latin America [10]. Braden GL *et al*. showed that there was a significant increase in the percentage of Afircan-american, Hispanics and Caucasions with FSGS [13]. Similar to our result, Sim JJ *et al*. demonstrated that FSGS frequency has increased steadily between 2000 and 2011 and it is the most common primary GN in USA [14].

It is known that, diabetic nephropathy is the most common cause of CKD, but it is usually found low in kidney biopsy specimens. In our series, diabetic nephropathy prevalence was found to be low. The most important reason is that clinical diagnosis is still important in diabetic nephropathy and renal biopsy is usually not performed unless there is evidence of the presence of accompanying primary GN in these cases.

In conclusion, FSGS is the most common primary GN in Turkish population and the frequency is gradually increasing. Among the secondary GN, SLE in early ages and amyloidosis in middle and older ages are more frequent. The reason for the less frequent observation of diabetic nephropathy in secondary GN is the small number of biopsy cases.

Conflict of interest statement. None declared.
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