Received: 7/17/2005 **Accepted: 11/21/2005**

Original Article

The Relative Frequency, Clinical and Laboratory Findings of Adult Glomerulonephritidies in Tehran

A. Emami Naini MD[*], *A. Amini Harandi MD*[*], *S. Ossareh MD*[**], *A. Ghods MD*[**], *B. Bastani MD*[***], *S. Taheri MD*[*]

ABSTRACT

Background: Renal diseases information is population-based and has great geographic variability. Due to the lack of national renal data registry system, there is no information on the prevalence rate, and clinical and laboratory features of various glomerulonephritidies (GNs) in Iran.

Methods: In a retrospective cross sectional study, we analyzed 462 adult renal biopsies in Hashemi Nejad hospital, Tehran, Iran. We determined the prevalence rate and the frequency of different clinical and laboratory findings in patients with different GNs. We also compared our results with the reports from other countries.

Results: There were 267(57.8%) males and 195(42.2%) females. The mean age (± SD) was 33.6 ± 15.7 (range, 13-75) years old. After exclusion of 55 biopsies with pathologies other than GNs and in the remaining 407 biopsies, membranous glomerulopathy (MGN) was the most common GN (23.6%), followed by IgAN (13.5%), membranoproliferative GN (11.5%), systemic lupus nephritis (10.6%), focal segmental glomerulosclerosis (10.3%), and minimal change disease (9.8%). These 6 GNs comprised the majority (79.4%) of all GNs.

Conclusion: MGN is the most common form of GN, followed by IgAN, MPGN, SLE-GN, FSGS and MCD in adult patients in our study. The multi-center studies with a larger sample size are needed for more comprehensive data in Iranian population.

Key words: Glomerulonephritidies, Epidemiology, Renal Biopsy, Glomeulopathy

JRMS 2006; 11(2):87-92

Glomerulonephritidies (GNs) remain the third most common cause of end stage renal failure [1]. Epidemiological data of renal diseases is population-based and has great variability according to the geographic area, socioeconomic condition, race, biopsy indication, and differences in genetic susceptibility and environmental exposure [2-5].

Due to the lack of a nationwide renal data registry system, there is no information on the frequency of different GNs in Iran. Furthermore, the great variability of clinical manifestations confounds the determination of a definitive diagnosis based on the clinical features alone [6], and therefore, kidney biopsy remains the gold standard test for the diagnosis of GNs. However, it is invasive, has some associated morbidity, and in some circumstances may be contraindicated. Due to the great variety of glomerular diseases, approach to the patients heavily relies on the clinical, laboratory and pathologic findings [6]. More analysis of clinical and laboratory findings in these patients could be helpful in developing more definitive criteria for diagnosis, identifying risk factors, prognosis, and predicting the outcome. In this study, we analyzed the clinical and laboratory findings of kidney biopsies from different forms of GNs, and compared our results with the reports from other countries.

* Associated Professor, Division of Nephrology, Isfahan University of Medical Sciences, Isfahan, Iran
** Associated Professor, Division of Nephrology, Iran University of Medical Sciences, Tehran, Iran
*** Associated Professor, Division of Nephrology, Saint Louis University Health Sciences Center, Saint Louis, Missouri, USA
Correspondence to: Dr Afsoon Emami Naini, E-mail:Emaminaini_afsoon@yahoo.com

Materials and Methods

In a retrospective cross sectional study, we analyzed renal biopsies performed from 1998 to 2001 in HashemiNejad hospital as an adult referral university medical center in Tehran, Iran.

Indications for renal biopsy were:
idiopathic nephrotic syndrome in adult before empiric therapy, rapidly progressive renal failure caused by GNs, evaluation and follow up for collagen diseases, predominantly SLE with proteinuria, abnormal urine sedimentation or reduced renal function, glomerular proteinuria with unknown cause accompanied by abnormal urine sedimentation or quantitive persistent proteinuria of urine more than 1gr/d, persistent or recurrent glomerular hematuria with proteinuria more than 500 mg/dl and acute renal failure(ARF) with unknown cause in normal kidney size without obstruction [7].

Renal biopsies were processed for light and immunofluorescence microscopy in all specimens. In all cases, sections were stained for Hematoxylin and Eosin (H&E), Masson's trichrome, periodic acid-Schiff (PAS), and Silver Jone's stain.

Clinical information was obtained from the biopsy requisition forms, and by reviewing the patients' medical records. All data related to the final diagnosis, age, sex, clinical presentation, serum levels of cholesterol, triglyceride, creatinine, complements (C3, C4 and CH50), microscopic hematuria, hypertension (systemic BP>140/90 mmHg), and proteinuria were recorded. Based on diagnostic criteria, clinical presentations were classified as;
a) nephrotic syndromes: proteinuria more than 3.5 gr/1.73m^2/24h;
b) nephritic syndromes: syndrome with hematuria, RBC cast, azotemia, oliguria, edema and HTN;
c) ARF: rapid decline in glomerular filtration rate (GFR) during few days to few weeks;
d) CRF: azotemia for more than 3 months;
e) AUA: syndrome with hematuria, proteinuria less than nephrotic syndrome, sterile pyuria and casts without any symptoms;
f) RPGN: documented recent decline in GFR [8].

The data were analyzed by SPSS, using ANOVA between different clinical or pathological diagnoses, and mean ± SD values of laboratory data were compared.

Results

We reviewed 462 adult renal biopsies, 407 (88%) of which had shown some form of GNs. There were 267 (57.8%) males and 195 (42.2%) females; the mean age was 33.6 ± 15.7 years (ranged from13 to75).

Membranous glomerulopathy (MGN) was the most common GN (23.6%), followed by IgAN (13.5%), membranoproliferative GN (MPGN) (11.5%), systemic lupus nephritis (SLE-GN) (10.6%), focal segmental glomerulosclerosis (FSGS) (10.3%), and minimal change disease (MCD) (9.8%). These 6 GNs comprised the majority (79.4%) of all GNs. More details are shown in Table 1.

The frequency of presenting syndromes in 6 common GNs is presented in Table 2. Proteinuria was present in almost all patients in 6 common GNs. The frequency of hypertension, microscopic hematuria, hypertriglyceridemia, hypercholesterolemia, and serum creatinine > 1.4 mg/dl, at the time of presentation are shown in Table 3.

After using ANOVA test among 6 most common GNs, there was no significant difference in triglyceride concentrations ($p=0.27$) but, the difference was significant in regard to serum cholesterol or creatinine concentration and proteinuria ($p<0.005$).

Table1. Age, male to female ratio and laboratory findings at the time of presentation in 6 most common GNs

Diagnosis	M: F	Age (years)	Proteinuria (mg/24 hr)	Serum cholesterol (mg/dl)	Serum triglyceride (mg/dl)	Serum creatinine (mg/dl)
MGN	1.5:1	43.1±14.8	7268 ± 4003 (1200-25500)	363 ± 110 (130-674)	290 ± 154 (75-842)	1.3 ± 1.8 (0.5-15.0)
IgAN	3.2:1	32.8±12.3	3924 ± 3089 (600-15000)	251 ± 79 (147-484)	242 ± 150 (87-957)	2.2 ± 2.5 (0.6-14.8)
MPGN	1.2:1	28.6±15.9	5470 ± 3455 (86-14300)	278 ± 79 (145-434)	266 ± 231 (69-1550)	1.9 ± 1.4 (0.5-7.9)
SLE-GN	0.1:1	24.4±8.0	5154 ± 3472 (390-12500)	286 ± 109 (123-530)	299 ± 171 (83-864)	2.3 ± 2.2 (0.5-11.3)
FSGS	1.9:1	30.4±13.4	5762 ± 4834 (750-20600)	312 ± 112 (147-646)	304 ± 17 (129-890)	2.8 ± 3.3 (0.5-16.1)
MCD	1.3:1	34.9±15.2	7823 ± 3887 (2200-21000)	398 ± 119 (164-672)	333 ± 175 (91-755)	1.2 ± 1.0 (0.5-6.2)

M: F = male to female ratio; Mean ± SD (range)

Table 2. The frequency of presenting syndromes in different GNs

Presenting Syndromes	Diagnosis						
	MGN	**IgA N**	**MPGN**	**SLE-GN**	**FSGS**	**MCD**	**Total**
Nephrotic	81(84.5)	25(45.5%)	31(66%)	28(65%)	24(57%)	38(95%)	226(70%)
Nephritic	10(10.5%)	18(33%)	6(13%)	9(21%)	8(19%)	-	51(16%)
ARF	-	1(2%)	4(8.5%)	3(7%)	4(9.5%)	1(2.5%)	13(4%)
CRF	2(2%)	5(9%)	3(6.5%)	1(2%)	2(5%)	-	13(4%)
AUA	3(3%)	6(11%)	-	2(5%)	3(7%)	1(2.5%)	15(5%)
RPGN	-	-	1(2%)	-	1(2.5%)	-	2(0.5%)
Unknown	-	-	2(4%)	-	-	-	2(0.5%)
Total	96	55	47	43	42	40	322

ARF= acute renal failure; CRF= chronic renal failure; AUA= asymptomatic urinary abnormality; RPGN= rapidly progressive GN.

Table 3. The frequency of hypertension, hematuria, serum creatinine, and hyperlipidemia in different GNs

Diagnosis	Hypertension	Microscopic Hematuria	Hyper-triglyceridemia (mg/dl)	Hyper-cholesterolemia (mg/dl)	Cr >1.4 (mg/dl)
MGN	37(38.5%)	13(13.5%)	62(64.6%)	85(88.5%)	15(15.6%)
IgAN	27(49%)	22(40%)	23(42%)	30(54.5%)	19(34.5%)
MPGN	28(60%)	16(34%)	25(53%)	34(72.5%)	27(57.5%)
SLE-GN	23(53.5%)	15(35%)	25(58%)	29(67.5%)	22(51%)
FSGS	25(59.5%)	8(19%)	23(55%)	29(69%)	23(55%)
MCD	10(25%)	5(12.5%)	27(67.5%)	35(87.5%)	7(17.5%)
Total	150	79	185	242	113

Table 4. The frequency of GNs reported from different countries

	Country [references]	Year	Number	MGN	IgAN	MPGN	SLE-GN	FSGS	MCD
1	**Saudi Arabia** [17,18]	89-94	186	10.8%	10.8%	7.5%	8.6%	32.3%	1.1%
		89-97	166	9.0%	18.9%.	4.5%	-	17.1%	9.9%
2	**United Arab Emirates** [4]	78-96	490	20.1%	6.3%	-	-	18.3%	18.3%
3	**United States** [19]	1996	340	33.0%	7.0%	6.0%	-	34%	16.0%
4	**Italy** [20]	1996	1926	20.0%	26.0%	7.3%	-	7.8%	5.9%
5	**Japan** [20]	1999	1850	10.6%	26.8%	7.1%	-	-	15.7%
6	**China** [20]	79-00	10002	10.5%	39.5%	40.4%		5.2%	1.2%
7	**Denmark** [21]	85-97	2380	11.5%	-	5.1%	-	13.6%	17.5%
8	**Korea** [3]	73-95	3616	11.8%	22.1%	5.9%	6.4%	4.6%	26.6%
9	**Australia** [5]	95-97	1147	10.6%	34.1%	2.2%	13.9%	16.9%	4.4%
10	**Malaysia** [22]	94-00	407	4.4%	9.8%	-	31.0%	4.9%	28.5%
11	**Lima/Peru** [23]	85-95	1263	-	0.9%	14.8%	30.2%	13.9%	-
12	**Macedonia** [24]	75-01	1304	13.5%	11.8%	8.4%	-	9.9%	7.2%
13	**Kuwait** [25]	95-01	584	5%	7.9%	-	-	18.0%	13.0%
14	**Hong Kong** [26]	93-97	1629	8.3%	23.9%	-	20.5%	4.7%	8.8%
15	**Moscow** [27,28]	70-99	4400	13.4%	-	48.9%	-	7.8%	5.6%
		78-83	1031	7.5%	-	-	-	14%	11.7%
16	**Zaire** [29]	86-89	92	10%	-	8%	-	41%	14%
17	**Brazil** [30,31]	79-99	943	14.8%	11.5%	11.5%	-	29.5%	-
		90-93	206	20.4%	10.2%	14.1%	-	43.2%	5.3%
18	**France** [32]	76-90	942	17.7%	33.4%	6.6%	-	10.6%	-
19	**Iran** [33]	81-94	713	15.7%	1.2%	14.8%	12.6%	6.7%	11.3%
20	***Iran*** [present study]	*98-01*	*407*	*23.6*	*13.5*	*11.5*	*10.6*	*10.3*	*9.8*

Discussion

In our series, MGN was the most common form of GN (23.6%), followed by IgAN, MPGN, SLE-GN, FSGS and MCD. They comprised 79.4% of our total native kidney biopsies.

MGN is the most common cause (25%) of idiopathic nephrotic syndrome in adults, world wide [1,6], with male to female ratio as 2:1, peak incidence in 4th and 5th decades of life and significant geographic variation in its clinical manifestations. Patients from Australia and Japan have a lower frequency of nephrotic syndrome, as compared to patients from Europe or North America[6]. We found a high incidence of nephrotic syndrome (84.5%) at the time of presentation (mean protein excretion rate, 7.3 grams/24 hours), that may be due to severity of disease in patients at the time of admission to our hospital as a referral center for renal disease in Tehran, Iran.

IgAN is now regarded as the most common form of GN in the world [6, 10, 11]. Its prevalence rate varies in different geographic regions [8]; most prevalent in Asia (30-40%), also quite prevalent in Europe (20%), but less common in North America (10%) [10, 11]. Its incidence varies from 2 per 10,000 populations in France and Germany to 2.0%-4.8% of population in Singapore [6, 11], and its male to female ratio is 2:1 [6]. In our series, low IgAN prevalence may be related to our late stage criteria for renal biopsy such as excluding the patients with isolated hematuria and proteinuria <1gr/dl. we haven't screening plan for early stage of disease for example in school age children, and we only evaluate patients with proteinuria more than 500 mg/dl or raising in serum creatinine level whereas isolated hematuria contains many new IgAN cases that may be missed.

FSGS comprises 2-41% of primary GNs in the world [2]. In the past 20 years, prevalence rate of primary FSGS has risen from < 10% to 25% of adult primary GNs [6]. FSGS comprises 6-15% of GNs in Europe and 2-11% of GNs in Asia [2]. FSGS is slightly more common in males (M:F ratio, 1.4 : 1). In Cattran report, half of adult patients had nephrotic syndrome at presentation [1]. In our series, mean protein excretion rate was 5.8 gram/24 hours, and 57% of FSGS patients presented with nephrotic syndrome.

MCD is responsible for 10-15% of primary nephrotic syndromes in adults [6]. It has a variable geographic distribution, being more common in Asia than North America or Europe [12], and is equally distributed between two sexes [6].

Recent studies have focused on the significance of epidemiologic and clinical features of SLE-GN, and report a female to male ratio of 8-13:1 [13]. In our series, SLE-GN accounted for 10.6% of all GNs; the patients were the youngest (average age, 24.4 years) among all GNs, 10 times more females than males, 65% with nephrotic syndrome, and only 21% with a nephritic picture.

MPGN accounts for a wide range (2% to 49%; average, 12.5%) of GNs worldwide; 50% with nephrotic syndrome, and 30% with mild and asymptomatic proteinuria [6]. In our series, MPGN accounted for 11.5% of all GNs, with average age of 28.6 years. There were slightly more males (M: F ratio 1.2:1), and almost all patients presented with proteinuria (average of 5.5 gr/day). In Iran, hepatitis B prevalence is reported low (1.07%) and high (8.96%) in different provinces [14, 15], and a ten-time higher incidence of hepatitis C was noted in Iranian MPGN patients in comparison with normal population [16]. In our study, we haven't any available information on the hepatitis B or C status of the MGN or MPGN patients and consequently related result could be influenced by this fact.

The frequency of different GNs in other geographic regions of the world is presented in Table 4. Unfortunately, many reports lack detailed information about clinical and laboratory indices. MGN, which is the most common GN in our series, has also been reported as the most common GN in United Arab Emirates, and Macedonia, and among the top in USA.

Recent data points to the genetic and biologic, as well as, socioeconomic factors that may be contributing to these findings [34]. The contribution of clinical epidemiology to evidence-based nephrology is not limited to randomized controlled trials [35]. Epidemiological studies on the prevalence rate, and clinical and laboratory findings can lead to a higher index of suspicion to a particular diagnosis that may lead to a therapeutic intervention at a more timely fashion. Whether racial and socioeconomic data should be used in treating individual patients, and how, remains controversial. Moreover, like other fields in medical research, epidemiology has some methodological limitations that must be taken into account [35].

Our study has several shortcomings. We did not elaborate on the remaining variants of GNs, sub-types of MPGN (I or II), or associated conditions such as malignancy or drug consumption. Further studies with larger sample size and survival analysis of patients are needed for better understanding of the epidemiologic features of GNs in the Iranian population.

References

1. Cattran DC. Outcomes research in glomerulonephritidies. Semin Nephrol 2003; 23: 340-54.
2. Kitiyakara C, Kopp JB, Eggers P. Trends in the epidemiology of focal segmental glomerulosclerosis. Semin Nephrol 2003; 23: 172-82.
3. Choi IJ, Jeong HJ, Han DS, et al. An analysis of 4,514 cases of renal biopsy in Korea. Yonsei Med J 2001; 42: 247-54.
4. Yahya TM, Pingle A, Boobes Y, Pingle S. Analysis of 490 kidney biopsies: Data from the United Arab Emirates renal diseases Registry. J Nephrol 1998; 11: 148-50.

5. Briganti EM, Dowling J, Finlay M,et al. The incidence of biopsy-proven glomerulonephritidies. Australia. Nephrol Dial Transplant 2001; 16: 1364-7.
6. Falk RJ, Jennette JC, Nachman PH. Primary Glomerular Disease. In: Brenner BM. Brenner and Rector's. The Kidney. Philadelphia: WB Saunders 2004, pp 1293-380.
7. Denker BM, Brenner Bm. Azotemia and urinary abnormalities. In: Kasper DL, Braunwald E, Fauci A, Hauser S, Longo D, Jameson JL (editors). Harrison's Principles of Internal Medicine: 16th edition: New York: McGraw-Hill 2005: pp 247.
8. Massry SG, Glassock RJ (editors). Massry and Glassock's Textbook of Nephrology (4th Edition). Lippincott Williams and Wilkins, Philadelphia; 2001: pp1743.
9. Forland M, Spargo BH. Clinicopathological correlations in idiopathic nephrotic syndrome with membranous nephropathy. Nephron 1969; 6: 498-525.
10. D'amico G. the commonest glomerulonephritidies in the world: IgA nephropathy. Q J Med 1987; 64:709-27.
11. Clarkson AR, Woodroffe AJ, Faull RJ. Immunoglobulin A Nephropathy and Henöch-Schonlein purpura. In: Schrier RW. Disease of the kidney and urinary tract. Philadelphia: Lippincot, 2001, pp 1691-716.
12. Sharples PM, Poulton J, White RH. Steroid responsive nephrotic syndrome is more common in Asians. Arch Dis Child 1985; 60: 1014-7.
13. Appel GB, Radhakrishnan J, D'Agati VD. Secondary Glomerular Disease. In: Brenner BM. Brenner and Rector's The Kidney. Philadelphia: WB Saunders Company, 2004, pp1381-481.
14. Zali MR, Mohammad K, Farhadi A, Masjedi MR, Zargar A, Nowroozi A. Epidemiology of hepatitis B in the Islamic Republic of Iran. East Mediterr Health J 1996; 2: 290-8.
15. Merat S. Malekzadeh R. Rezvan H. Khatibian M. Hepatitis B in Iran. Archives of Iranian Medicine 2000; 3: 192-201.
16. Broumand B, Ghaleh-Baghi B, Abbasi M, Bonabi NB. The association between hepatitis C and membranoprolifrative glomerulonephritis. Nephrology 1997; 3(Suppl): S-365.
17. Mitwalli AH, Al Wakeel JS, Al Mohaya SS, Malik HG. Pattern of glomerular disease in Saudi Arabia. Am J Kidney Dis 1996; 27: 797-802.
18. Al-Homrany MA. Pattern of renal diseases among adults in Saudi Arabia. Ethn Dis 1999; 9: 463-7.
19. Korbet SM, Genchi RM, Borok RZ, Shwartz MM. The racial prevalence of glomerular lesions in nephritic adults. Am J Kidney Dis 1996; 27:647-51.
20. Chen H, Tang Z, Zeng C, et al. Pathological demography of native patients in a nephrology center in China. Chin Med J (Engl) 2003; 116:1377-81.
21. Heaf J, Lokkegaard H, Larsen S. The epidemiology and prognosis of glomerulonephritidies in Denmark 1985-1997. Nephrol Dial Transplant 1999; 14:1889-97.
22. Khoo JJ. Renal biopsies in Johor: A 7-years study. Malays J Pathol 2001; 23:101-4.
23. Hurtado A, Escudero E, Stromquist CS. Distinct pattern of glomerular disease in Peru. Clin Nephrol 2000; 53: 325-32.
24. Polenakovic MH, Grcevska L, Dzikova S: The incidence of biopsy-proven primary glomerulonephritidies in the Republic of Macedonia-long-term follow-up. Nephrol Dial Transplant 2003; 18 (Suppl 5): 26-7.
25. El-Reshaid W, El-Reshaid K, Kapoor MM, Madda JP. Glomerulopathy in Kuwait: The spectrum over the past 7 years. Ren Fail 2003; 25:619-30.
26. Chan KW, Chan TM, Ceng IKP. Clinical and pathological characteristics of patients with glomerular diseases at a university teaching hospital: 5-years prospective review. Hong Kong Med J 1999; 5: 240-4.
27. Dzhanaliev BR, Varshavskii VA, Laurinavichus AA. Primary glomerulopathies: incidence, dynamics and clinical manifestations of morphological variants. Arkh Patol 2002; 64:32-5.
28. Serov VV, Varshavsky VA, Schill H, Nizze H. Incidence of glomerular diseases in kidney biopsy materials using WHO classification. Zentralbl Allg Pathol 1986; 132: 471-5.
29. Pakasa M, Mangani N, Dikassa L. Focal and segmental glomerulosclerosis in nephrotic syndrome: a new profile of adult nephrotic syndrome in Zaire. Mod Pathol 1993; 6: 125-8.
30. Bahiense-Oliveira M, Saldanha LB, Mota EL, Penna DO, Barros RT, Romao-Junior JE. Primary glomerular diseases in Brazil (1979-1999): Is the frequency of focal and segmental glomerulosclerosis increasing?. Clin Nephrol 2004; 61:90-7.
31. Mazzarolo Cruz HM, Cruz J, Silva AL Jr, Saldanha LB, de Oliveira Penna D. Prevalence of adult primary glomerular diseases: Retrospective analysis of 206 kidney biopsies (1990-1993). Rev Hosp Clin Fac Med Sao Paulo 1996; 51: 3-6.
32. Simon P, Ramee AP, Autuly V, et al. Epidemiology of primary glomerular diseases in a French region. Variations according to period and age. Kidney International 1994; 4:1192-8.
33. Antonovych TT, Sabins SG, Broumand BB. A study of membranoprolifrative glomerulonephrotis in Iran. An Saudi Med 1999; 19(6); 505-10.
34. Halevy D, Radhakvishnan J, Appel GB. Racial and socioeconomic factors in glomerular disease. Semin Nephrol 2001; 21: 403-10.
35. Frimat L. Contribution of clinical epidemiology to evidence-based nephrology. Nephrologie 2001; 22:199-203.