The Incidence of Biopsy Proven Primary Glomerulonephritis at the Department of Nephrology, Clinical Centre, Skopje

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Introduction

Primary glomerular diseases are rare in developed countries and because of the large number of sub-classifications most nephrology centers will only meet a small number of patients per year with each type (1, 2, 3, 4). Conversely, glomerulonephritis GN) is one of the commonest causes of end-stage renal failure in underdeveloped countries (5, 6, 7, 8, 9, 10, 11).

There is also a difference among the distribution of different types and subtypes according to different geographical areas (5, 8, 9, 11, 12). Membranous nephropathy and acute GN are more frequent in the tropics and reflect the consequences of exposure to infective agents (1, 5, 6, 7, 13, 14, 15, 16). IgA nephropathy is frequent in the Mediterranean area and the Far East. Membranoproliferative GN as a part of cryoglobulinemic GN may be associated with HCV infection, also widely distributed in the Mediterranean area, but this form may be found worldwide (17, 18, 19, 20).

As a referent center for the area of the Republic of Macedonia (former Yugoslavia), with a two million people population, we would like to present the incidence of biopsy proven primary glomerular diseases in adult patients (age >14) in the past 26 years.

Methods

This is a single center retrospective study. Renal biopsy specimens of adult patients with primary GN were selected from 1,304 percutaneous renal biopsies, performed with Tru-cut needle at the Department of Nephrology, Skopje, R.Macedonia, over a period of 26 years (1975-2001).

All the biopsies were evaluated by light microscopy and immunofluorescence, using standard procedures. A minority were assessed by electron microscopy that was available during the following periods: 1980-83 and 1993-98. The criteria for classifying glomerular lesions as primary were based on the lack of evidence of systemic diseases or underlying abnormality. Churg (WHO) classification was performed for further classification of separated primary forms of GN (21).

Results

Primary glomerular diseases were confirmed in 716 patients (Table 1). Diagnosis of minimal change nephrotic syndrome was confirmed in 52 patients (7.2%), 27 male and 25 female, focal segmental glomerulosclerosis in 72 (9.9%), 43 male, 29 female and membranous nephropathy in 97 (13.5%) patients, 64 male and 33 female. IgA nephropathy (Table 2) was confirmed in 85 (11.8%) 61 male, 24 female, diffuse mesangial GN without IgA in 32 (4.4%) 24 male, 8 female, and focal mesangial GN in 97 patients (13.5%), 66 male and 31 female.

Table 1: Incidence of non-proliferative forms of GN

Year	Minimal change		FSGS		Membranous nephropathy	
	M	F	M	F	M	F
1975	1	1	0	0	6	5
1976	0	2	3	3	1	0
1977	0	0	0	0	3	0
1978	1	1	0	1	1	0
1979	1	0	0	0	1	2
1980	0	1	1	1	3	1
1981	1	1	1	0	5	3
1982	0	1	0	1	2	0
1983	1	1	0	0	2	0
1984	0	0	1	2	3	1
1985	3	1	1	1	2	0
1986	3	1	0	0	4	3
1987	0	2	1	2	1	1
1988	2	1	1	0	3	1
1989	2	0	1	0	0	1
1990	1	1	2	1	2	0
1991	1	1	0	2	3	0
1992	2	1	2	2	1	0
1993	2	1	4	1	2	0
1994	1	2	1	1	2	1
1995	3	1	4	1	1	1
1996	0	0	3	0	3	5
1997	1	1	5	3	1	0
1998	1	0	3	1	1	2
1999	0	0	6	3	2	1
2000	0	4	3	3	4	3
2001	1	0	1	0	3	2
	27	25	43	29	64	33
total	52		72		97	

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Table 2: Incidence of mesangial forms of GN

Year	IgAN		Diffuse mesangial GN		Focal mesangial GN	
	M	F	M	F	M	F
1975	3	0	0	0	0	0
1976	3	2	2	1	1	0
1977	3	0	1	0	0	0
1978	3	0	1	0	4	0
1979	2	0	1	0	1	0
1980	4	1	0	1	2	0
1981	1	0	0	0	2	0
1982	1	2	0	0	0	1
1983	1	1	2	0	6	1
1984	3	1	1	0	1	2
1985	1	3	4	1	1	1
1986	4	5	1	1	7	4
1987	1	1	1	1	5	3
1988	0	1	0	0	7	3
1989	5	1	0	0	4	6
1990	2	0	2	1	5	1
1991	0	0	1	0	5	0
1992	1	2	1	0	6	1
1993	2	0	3	1	0	0
1994	0	0	0	0	1	1
1995	2	0	1	0	1	1
1996	2	0	0	1	1	1
1997	1	1	1	0	0	2
1998	2	0	0	0	1	0
1999	1	1	2	0	0	1
2000	8	1	1	0	3	2
2001	5	1	0	0	0	0
	61	24	24	8	66	31
total	85		32		97	

Membranoproliferative GN (Table 3) was found in 59 patients (8.4%), 34 male and 25 female, acute GN in 88 (12.3%), 60 male and 28 female, crescentic GN in 53 (7.4%), 38 male and 15 female, and sclerosing GN in 46 (6.4%), 35 male and 11 female. Analyzing presented data it can be seen that males are predominant in all groups of glomerular diseases. Looking at Fig.1 we can see the incidence of non-proliferative forms of primary glomerulonephritides during the follow-up. The incidence of minimal change nephrotic syndrome was relatively stable, with a slight increase in the period 1985-86. Incidence of focal segmental glomerulosclerosis presented a slow increase from 1978 to 1999, when it was the highest. Membranous nephropathy was more frequent in some periods of time, for example, in 1975, 1981, 1987, 1996 and 2000. We were not able to confirm the presence of some environmental antigens in those periods of time as these "peaks" of membranous nephropathy suggested. The incidence of IgA nephropathy (Fig. 2) was higher during the follow-up on two occasions, in 1986 and 1999, while the incidence of diffuse mesangial glomerulonephritis without IgA was stable.

Table 3 Incidence of the other forms of primary GN

Year	Membrano proliferative GN		Acute GN		Crescentic GN		Sclerosing GN	
	M	F	M	F	M	F	M	F
1975	0	0	3	1	1	0	0	0
1976	4	1	2	0	1	0	0	0
1977	3	0	3	1	1	0	0	0
1978	2	0	1	1	4	0	0	0
1979	1	1	2	0	2	1	0	0
1980	0	1	1	0	2	0	0	0
1981	2	1	4	0	1	0	0	0
1982	1	1	1	0	3	1	0	0
1983	0	0	1	2	1	0	0	0
1984	0	0	1	1	0	0	1	0
1985	0	4	3	4	0	0	1	0
1986	3	1	5	1	2	1	2	0
1987	2	2	3	4	1	0	5	1
1988	2	1	5	0	5	1	1	0
1989	0	0	2	1	1	2	0	1
1990	3	0	3	2	2	2	1	2
1991	1	2	11	1	2	1	4	2
1992	3	2	1	0	5	1	5	2
1993	1	0	0	0	0	0	0	0
1994	0	0	0	0	0	0	0	0
1995	0	1	0	0	0	0	0	0
1996	0	2	1	2	3	0	1	1
1997	2	0	3	2	0	0	2	0
1998	1	2	3	2	2	1	3	2
1999	0	0	1	1	0	2	4	0
2000	1	3	0	1	1	2	2	0
2001	2	0	0	1	3	0	3	0
	34	25	60	28	38	15	35	11
total	59		88		53		46	

Focal mesangial glomerulonephritis (without IgA) presented a high incidence over a longer period of time (1986-1993). The incidence of membranoproliferative glomerulonephritis (Fig. 3) during the follow-up was stable, without decreasing, as was reported in the other studies. Our group of patients with this form of diseases consisted of all histological forms (type 1, 2 (dense-deposit disease) and 3). The incidence of crescentic and sclerosing glomerulonephritis was also stable. The highest incidence of acute poststreptococcal glomerulonephritis was registered in 1991. As can be seen, the incidence of primary glomerular diseases is very similar in the age groups 15-20, 21-30 and 31-40, decreasing in the older groups. Several clinical features could be found in the same patient; for example, a patient with nephrotic syndrome could complain of chronic renal failure or hematuria as well (Fig. 4).

Figure 1: Incidence of non-proliferative forms of GN during follow-up

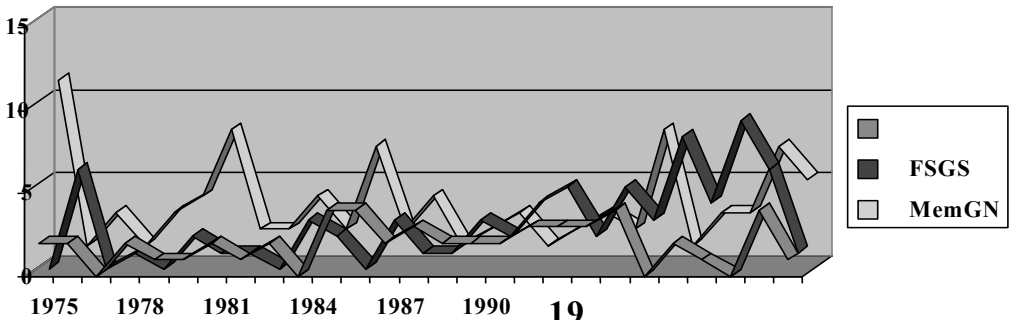

Figure 2: Incidence of mesangial forms of primary GN during follow-up

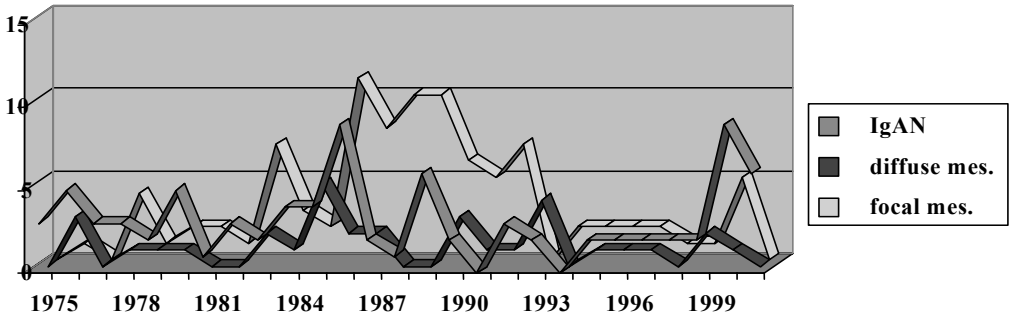

Figure 3: Incidence of other forms of primary GN during follow-up

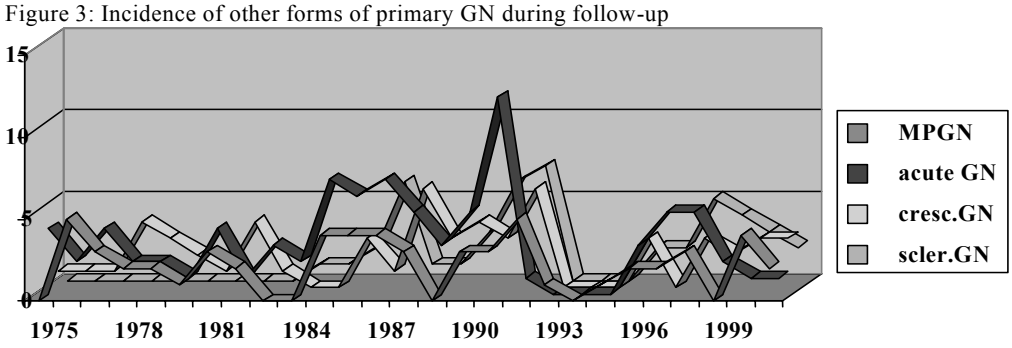

Figure 4: Clinical features-indications for renal biopsy

Discussion

We report on the age- and sex-specific incidence of biopsy proven glomerulonephritis in R. Macedonia during a period of time of 25 years. Indicators for renal biopsy include non-urological hematuria, proteinuria and renal impairment, as well as the more specific presentations of glomerulonephritides such as nephrotic and nephritic syndrome. We have to take into consideration that the rates for biopsy-proven renal diseases underestimate the true rate of disease. Many patients with slight clinical features and slow-progressive forms of GN are not biopsied. Some of them consult nephrologists in the phase of end-stage chronic renal failure, after one or two decades of "silent" disease. Notable patterns of disease identified in this review included the male predominance of biopsy-proven primary glomerulonephritis for all histological categories. The incidence of all histological forms is higher in younger adult groups and the incidence is different at different periods of time, especially for patients with membranous and IgA nephropathy. This finding suggests the potential role of age-specific environmental exposures, such as infective, dietary or occupational, in the etiology of these renal diseases. The most frequent histological forms in this study were membranous nephropathy (13.5%) and focal mesangial GN (13.5%). The high incidence of membranous nephropathy may be associated with high prevalence of HbS antigen among the population of R.Macedonia. The incidence of focal mesangial glomerulonephritis is high because we did not subdivide this histological form into subclasses such as: IgM nephropathy, C3 nephritis, C1q nephropathy (22, 23). Only IgA nephropathy is separated, and its incidence is high, as in the studies from other Mediterranean

countries (Italy, Spain, Greece, France) as well as studies form countries located on the same geographical latitude (Korea, Japan) (3, 4, 10, 15). We still have a high incidence of acute glomerulonephritis, and the incidence of membranoprolipherative glomerulonephritis is not significantly decreasing.

We have no precise registry for renal biopsy and this study is retrospective, but we are the referent center for R.Macedonia and our data can contribute to the epidemiological knowledge about glomerulonephritis incidence, sex- and age-distribution

References

1. Briganti EM, Dowling J, Finlay M et al: The incidence of biopsy-proven glomerulonephritis in Australia. Nephrol Dial Transplant 16:1364-1367, 2001.
2. Heaf J, Løkkegaard H, Larsen S: The epidemiology and prognosis of glomerulonephritis in Denmark 1985-1997. Nephrol Dial Transplant 14:1889-1897, 1999.
3. Simon P, Ramée MP, Autuly V et al: Epidemiology of primary glomerular diseases in a French region. Variations according to period and age. Kidney Int 46:1192-1198, 1994.
4. Zuccala A, Zucchelli P: A renal disease frequently found at postmortem, but rarely diagnosed in vivo. Nephrol Dial Transplant 12:1762-1767, 1997.
5. Ghnaimat M, Akash N, El-Lozi M: Kidney biopsy in Jordan: Complications and histological findings. Saudi J Kidney Dis Transplant 10(2): 152-156, 1999.
6. Mitwalli AH, Al Wakeel JS, Al Mohaya SS et al: Pattern of glomerular disease in Saudi Arabia. Am J Kid Dis 27:797-802, 1996.
7. Chugh KS: Renal disease in India. Am J Kid Dis 31:ivii-iix, 1998.
8. Bailey RR, Hannan SF, Neale TJ, Williams LC: The New Zealand glomerulonephritis study: introductory report. Clin Nephrol 31: 239-246, 1989.
9. Hoy WE, Mathews JD, McCredie DA et al: The multidimensional nature of renal disease: rates and associations of albuminuria in an Australian Aboriginal community. Kidney Int 54:1296-1304, 1998.
10. Shin JH, Pyo HJ. Kwon YJ et al: Renal biopsy in elderly patients: clinicopathological correlation in 117 Korean patients. Clin Nephrol 56:19-26, 2001.
11. Albitar S, Bourgeon B, Genin R et al: Epidemiology of end-stage renal failure in Reunion Island (results from the registry of the Indian Ocean Society of Nephrology). Nephrol Dial Transplant 13: 1143-1145, 1998.
12. Haas M, Spargo BH, Coventry S: Increasing incidence of focal-segmental glomerulosclerosis among adult nephropathies: A 20-year renal biopsy study. Am J Kid Dis 26:74-750, 1995.
13. Wakai K, Nakai S, Matsuo S et al: Risk factors for IgA nephropathy: A case-control study with incident cases in Japan. Nephron 90:16-23, 2002.
14. Wakai K, Kawamura T, Matsuo S, Hotta N, Ohno Y: Risk factors for IgA nephropathy: A case-control study in Japan. Am J Kid Dis 33:738-745, 1999.
15. Nussenzveig I, Saldanha LB, Marconides M: Primary mesangial IgA nephropathy in São Paulo, Brazil. Nephron 52: 198-199, 1989.
16. Yap HK, Chia KS, Murugasu B et al: Acute glomerulonephritis – changing patterns in Singapore children. Pediatr Nephrol 4: 482-484, 1990.
17. Hattori M, Kim Y, Steffes MW, Mauer SM: Structural-functional relationships in type I mesangiocapillary glomerulonephritis. Kidney Int 43:381-386, 1993.
18. Strife CF, Jackson EC, McAdams AJ: Type III membranoproliferative glomerulonephritis. Clin Nephrol 21:323-334, 1984.
19. Klein M, Poucell S, Arbus GS et al: Characteristics of a benign subtype of dense deposit disease: comparison with the progressive form of this disease. Clin Nephrol 2): 163-171, 1983.
20. Strife CF, McAdams AJ, West CD: Membranoproliferative glomerulonephritis characterized by focal, segmental proliferative lesions. Clin Nephrol 18: 9-16, 1982.
21. Churg J, Sobin LH: Renal disease: Classification and atlas of glomerular disease. Igaku Shoin, Tokyo, New York, 1982.
22. Hirszel P, Yamase HT, Carney WR et al: Mesangial proliferative glomerulonephritis with IgM deposits, Nephron 38:100-108, 1984.
23. Calls Ginesta J, Almirall J, Torras A, Darnell A, Revert L: Long-term evolution of patients with isolated C3 mesangial glomerulonephritis. Clin Nephrol 43: 221-225, 1995.