

Original Article

Incidence of biopsy-proven glomerulonephritis

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Abstract

Background. The reported biopsy-proven glomerulonephritis incidence varies according to population characteristics, the unknown true glomerulonephritis incidence and biopsy rate. Reported glomerulonephritis incidence should be evaluated against the biopsy rate.

Methods. We report here the glomerulonephritis incidence in our University Hospital (UH) consecutive biopsy material. It is compared to those from surrounding central hospitals (CH), previous single-centre studies and European biopsy registries (EBR). Biopsy rate, when reported, has been considered.

Results. The annual biopsy rate/10⁵, median (min–max), at the UHs was 25.4 (15.6–35.1). At the CHs it was 8.7 (5.1–12.6). In previous single-centre studies it has been 18.7–21.5. In the EBRs it has been between 1.0 and 6.9 when reported. The annual incidences (median, min–max) per 10⁵ (1980–2000) at the UH were as follows: proliferative glomerulonephritis (9.5, 6.8–18.1), non-proliferative glomerulonephritis (6.7, 3.4–12.6), the four major glomerulonephritis groups MesGN (7.7, 4.4–15.9), ECGN/FPGN-complex (1.4, 0.5–3.2), MCGP/FSGS-complex (0.9, 0.2–2.7) and MGN (1.4, 0.5–2.4) these which findings were compatible with the single-centre studies and higher than those of the CHs and in the EBRs. Biopsy rate had a major impact on the annual glomerulonephritis incidences explaining 60% of the variation. The relative frequency of MesGN was the highest by all observers, followed by the ECGN/FPGN-complex, MGN and MCGP/FSGS-complex whose frequencies did not differ much. For every patient commencing renal replacement therapy (Finnish Renal Replacement Registry Data) due to glomerulonephritis there were about 11 subjects with biopsy-proven glomerulonephritis, a relationship compatible with previous reports.

Conclusions. The incidence of any glomerulonephritis of 17.6 per 10⁵ population was comparable to those from the single-centre studies, but higher than in

European biopsy registries, a fact largely explained by biopsy rates.

Keywords: biopsy-proven glomerulonephritis; biopsy rate; glomerulonephritis incidence; IgA-glomerulonephritis; renal biopsy; renal pathology

Introduction

The incidence of glomerulonephritis varies according to the population genetic and demographic characteristics, environmental factors like climatology, socio-economics, prevalence of infectious diseases and time period [1,2]. In addition, the incidence varies according to the detection level of urinary findings, the biopsy resources of the community and the biopsy policy which are reflected as the biopsy rate. A universally valid ‘epidemiology’ does not exist. One has to consider race, demography, population, era and biopsy rate. Kidney biopsy reports from single centres do exist, but reports considering biopsy rate are rare. In fact, few reports with control of the background population data, biopsy rate and biopsy policy over time exist. This is a report on the result from our university hospital compared to that of the Western region of Finland served by central hospitals (genetical and environmental equality), and especially to those studies concerned with European populations (socio-economic equality) which have reported biopsy rate and biopsy indication. For details see Table 1.

Subjects and methods

The study was carried out from 1976 to 2000 in Western Finland. One university hospital (UH) and five central hospitals (CH1–5), all of them secondary referral centres, participated, for various lengths of time, the UH and one CH from 1976. The other CHs participated from 1980, 1982, 1990 and 1995, respectively. The common denominator for participating is that the kidney biopsy light microscopy (LM) specimens have been read by a single renal pathologist (H.H.)

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Table 1. Summary of European studies, including one from Australia, concerned with biopsy-proven glomerulonephritis

Centres	Country	Period	Population	Observations	Biopsy rate per 10 ⁵	Glomerulonephritis incidence per 10 ⁵	IgAGN incidence	Reference
National Registry	Denmark	1985–1997	5.2 × 10 ⁶	2380	4.0 calculated	3.9 observed 7.9 estimated	1.1	[13]
National Registry	Italy	1987–1993	Virtually all Centres	13835	NG	3.4	0.8	[14,15]
Torino	Italy	1970–1994	~2 × 10 ⁶	1926	NG	4.7	1.5	[16]
Moldova/Banat	Romania	1995–2004	6.2 × 10 ⁶	635	1.1	3.9	1.0	[17]
Twenty-eight centres	Czech Republic	1994–2000		4004	4.4–6.9	4.6	1.1	[18]
Brittany	France	1976–1990	391 265	942	18.7–20.1–16.3	9.3–8.8–6.7	2.5–3.1	[19,20]
National Registry	Spain	1994–1999	Ninety-three centres	7016	4.8	>3.5	0.8	[21]
Victoria	Australia	1995–1997	4.5 × 10 ⁶	2030	21.5	12.3	10.5	[22]

The definition of glomerulonephritis varies between studies in terms of 'any-, primary-, secondary-'. For details see appropriate reference. NG, not given.

and all of the immunofluorescence (IF) specimens by J.M. or occasionally by H.H.

The Western region of Finland is an area with a high standard of living, a population nearly totally of Caucasian race, an extensive primary health care system and low incidences of chronic infectious diseases like impetigo, hepatitis C and B, and HIV-related conditions. Nephropathia epidemica caused by Puumala hantavirus is endemic (seroprevalence ~5%). It causes acute reversible renal failure with albuminuria and haematuria [3]. Routine urinary screening is carried out in maternity and child health welfare clinics, schools, work-places and some military service health systems (thus, nearly all young males are screened). The recruitment threshold for a kidney biopsy is low.

Population data are electronically available from 1980 onwards. The incidences were calculated from 1980 to 2000 at the UH. The population in the area has been stable in terms of numbers, UH median 423 689, min–max 407 096–447 051 and CH1–5 median 812 275, min–max 790 177–822 376. All paediatric patients in the study area have been studied at the UH. Sixty-eight percent of the biopsies were carried out at the UH. For detailed biopsy rate data at the UH, see Figure 1.

Kidney biopsy at the UH has been carried out in subjects with proteinuria with or without microhaematuria or renal failure or as part of the work-up of known or suspected systemic diseases. A bleeding diathesis, a single functioning kidney, small kidneys, multiple cysts, actual urinary tract infection and non-compliance have been excluded in the procedure. Other exclusions were a presentation suggesting diabetic nephropathy, evident myelomatosis, community-acquired acute renal failure caused by Puumala hantavirus after 1989 and isolated haematuria during the nineties. The same principles have largely been applied at the CHs but the actual decision to carry out a biopsy has been taken locally by an internist or nephrologist. The conduction of this report is retrospect and has not influenced any biopsy decision. Informed consent has been obtained in all subjects. Any applied statistical test is indicated in the text.

The clinical data given in the report and the pathology (LM, IF) have initially been centrally stored at the Department of Pathology at the UH. They have been

re-read and structurally classified by one of the authors (O.W.). The data contain information about the (i) centre, (ii) time of biopsy and (iii) the renal findings (haematuria, proteinuria, nephritic syndrome, nephrotic syndrome, renal failure as biopsy indication), presence or absence of (iv) renal insufficiency (serum creatinine cut-off point 120 µmol/l) or whether the renal disease was (v) acute or not (cut-off point 3 months), (vi) the age and (vii) gender of the subject, the (viii) diseases that are mentioned in the report, the (ix) pathologic anatomy of the specimen by LM and IF. By utilizing criteria (iv) and (v) we defined RPGN as an entity with a <3 months duration and a plasma creatinine level >120 µmol/l, as compared to chronic nephritis with a disease duration >3 months and a plasma creatinine level <120 µmol/l. The indications for the procedure were classified in a hierarchical order according to Table 2. The renal findings were classified according to a combination of clinical and qualitative and quantitative urinalysis data with the aim of clinically delineating certain typical glomerular disease patterns [4].

The kidney biopsy specimen was into cut in three pieces under stereo microscopy, one was fixed in formalin 10% (LM), one in glutaraldehyde 2% (EM) and one submitted in saline (IF) to the laboratory. The latter was immediately processed. It was routinely stained with stains for IgG, IgM and IgA, C3, C1q, light chains kappa and lambda. For light microscopy, paraffin sections were stained with periodic-acid Schiff, haematoxylin–eosin, silver–methenamine and Congo red. The number of glomeruli, a description of the main findings and a morphological diagnosis was given by the pathologist. At the UH the mean was (SD) 13.3 (8.3) glomeruli and at the CH1–5 11.1 (6.9) glomeruli in the samples (excluding samples with no glomeruli) ($P < 0.00001$, *t*-test). At the UH there were optimal, suboptimal, marginal and unsatisfactory samples in 62.2%, 16.8%, 16.1% and 4.9%, respectively. At the CH1–5 the values were 44.5%, 12.5%, 39.0% and 4.0%, respectively ($P < 0.001$, Kolmogorov–Smirnov). An optimal sample contained at least six glomeruli, a suboptimal three to five, and a marginal one to two, on LM while all contained at least one glomeruli on IF. The biopsy specimens were read and classified according to the SNOMED® classification. For abbreviations, further grouping and number of observations, see Table 3.

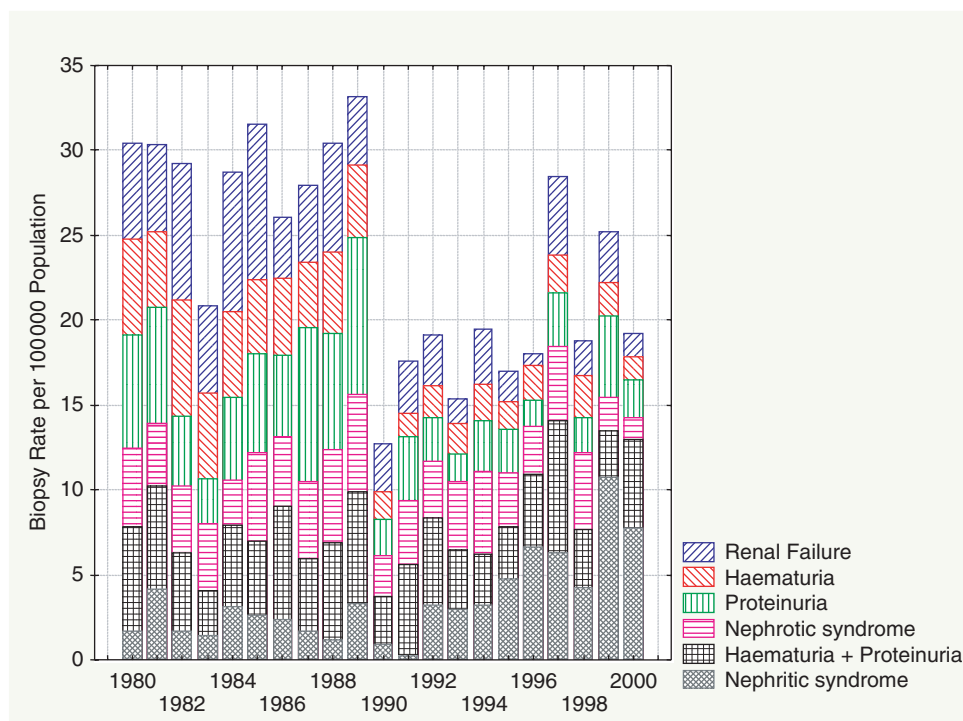


Fig. 1. The biopsy rate per 10^5 population at the University Hospital 1980–2000 stratified for biopsy indications. $N=2465$. Biopsy rate median 25.4, min–max 15.6–35.1, lower quartile–upper quartile 19.4–29.7. The biopsy indications were nephritic syndrome 13.8%, haematuria/proteinuria 19.5%, nephrotic syndrome 16.4%, proteinuria 19.2%, haematuria 13.5% and renal failure 17.6%.

Table 2. Hierarchical classification of kidney biopsy indications based on clinical and laboratory data ($1 > 2 > 3 > 4 > 5 > 6$)

1. Renal failure: The presence of renal failure explicitly stated by the clinician as the cause of a biopsy irrespective of renal findings
2. Nephritic syndrome as stated by the report or either oedema or hypertension and either proteinuria >1.5 g/24 h or urinary albumin (dipstick ++ or +++) and either red cell casts or urinary erythrocytes (dipstick ++ or +++)
3. Proteinuria and haematuria as stated by the report and no statement of oedema or hypertension and either proteinuria 0.3 g/24 h $<$ proteinuria <1.5 g/24 h or urinary albumin (dipstick +) and either red cell casts or urinary erythrocytes (dipstick +)
4. Nephrotic syndrome: Nephrotic syndrome stated in the report or either proteinuria >3.5 g/24 h or urinary albumin (dipstick +++) and no haematuria by statement or dipstick test
5. Proteinuria: Proteinuria stated in the report or either proteinuria <3.5 g/24 h or urinary albumin (dipstick + or ++) and no haematuria by statement
6. Haematuria: Haematuria (macro or micro) stated in the report or urinary erythrocytes either by dipstick test (+, ++, +++) or microscopy

Fifty-nine specimens (1.6%) from the time period 1976–2000 were excluded due to missing clinical and/or pathology data. After that the total material consisted of 3648 specimens (=clinical data). Altogether 338 non-representative (unsatisfactory sample/non-diagnostic equals morphological description without a specific diagnosis) specimens (9.2%) were also excluded from the analysis concerning the pathology (pathology data). Analysis of the pathology data thus included 3310 specimens. The clinical data have mostly been analysed as the UH ($N=2567$) compared with the compiled CH1–5 data ($N=1081$). The age medians were 44.0 and 50.0 years, respectively. The distribution of the age

groups <20 , 20 – 39 , 40 – 59 and >60 years by centre at the UH were 10.2%, 21.6%, 23.1% and 15.4%, respectively and at the CH1–5 were 2.1%, 7.6%, 11.6% and 8.4%, respectively ($P < 0.0001$, ANOVA). The median age of the biopsied subjects at (UH + CH1–5) rose successively from 38, 41, 46, 49 to 52 years from 1976 to 2000 expressed as 5-year intervals ($P < 0.0001$, ANOVA). At the UH the male/female rate was 1512/1055 and at the CH1–5 625/456 ($P = \text{NS}$, χ^2). Of the total sample, 58.6% were males.

The data for renal replacement therapy (RRT) have been provided by The Finnish Registry for Kidney Diseases which contains data for subjects starting dialysis therapy in Finland. Of these data we have included here the frequency per 10^5 population of subjects having commenced RRT between 1980 and 2000 due to glomerulonephritis. The annual incidences, median (min–max), for RRT were at the UH and the CHs 1.4 (0.2–2.3) and 1.3 (0.5–2.2), respectively.

Results

At the UH a proliferative glomerulonephritis was diagnosed in 45.1%, a non-proliferative glomerulonephritis in 21.4%, tubulo-interstitial nephritis in 14.7%, vasculopathy in 1.8% and various other ‘non-specific’ conditions in 17.0%. At the CH1–5 the corresponding findings were 45.8%, 23.0%, 9.0%, 1.6% and 20.7% ($P = \text{NS}$, ANOVA). The defined glomerulonephritides found are shown in Table 3. In addition to the common glomerulonephritides above the following specific diagnoses ($N=153$) were made, but not classified as glomerulonephritides: amyloid

Table 3. The pathologic diagnosis of the glomerulonephritides according to SNOMED[®], abbreviations, observations (total $n = 2057$) and grouping definitions

Name	Abbreviation	Total <i>N</i>	Per cent of specific GN	<15 years <i>N</i> (%)	Grouping includes	Defined as proliferative or non-proliferative GN
Glomerulonephritis, acute exudative	AGN	21	1			
Glomerulonephritis, endocapillary proliferative	EPGN	57	2.9	5 (5)	EPGN/MCGN	Proliferative GN
Glomerulonephritis, extracapillary	ECGN	117	5.7	4 (4)	ECGN/FPGN	Proliferative GN
Glomerulonephritis, membranous	MGN	240	11.6	1 (1)	MGN	Non-proliferative GN
Glomerulonephritis, mesangial proliferative	MesPGN	239	11.6	5 (5)	MesGN	Proliferative GN
Glomerulonephritis, mesangial sclerosing	MesSGN	48	2.4	1 (1)	MesGN	Proliferative GN
Glomerulonephritis, mesangiocapillary I	MCGNI	76	3.7		EPGN/MCGN	Proliferative GN
Glomerulonephritis, mesangiocapillary III	MCGNIII	2	0.1		EPGN/MCGN	Proliferative GN
Glomerulosclerosis, segmental focal	FSGS	81	3.9	3 (3)	MCGP/FSGS	Non-proliferative GN
IgA glomerulonephritis	IgAGN	718	34.9	25 (26)	MesGN	Proliferative GN
IgM glomerulonephritis	IgMGN	108	5.3	25 (26)	MesGN	Proliferative GN
Minimal change nephropathy	MCGP	102	5	21 (22)	MCGP/FSGS	Non-proliferative GN
Glomerulonephritis, proliferative focal	FGN	133	6.4	5 (5)	ECGN/FPGN	Proliferative GN
Glomerulonephritis, NOS	GNNOS	42	2	3 (3)		
Glomerulosclerosis, NOS	GSNOS	73	3.5			

nephropathy, 130; Alport's syndrome, two; thin basement membrane disease, three; thrombotic microangiopathy, five; end-stage renal disease, six; acute lymphocytic leukaemia, one; lupus, six; (lacking a specific glomerular pathology).

Of the four major glomerulonephritis groups (Table 3) we chose for further analysis were found at the UH and CH1–5, respectively, as follows: MesSGN in 64.5% ($n = 799$) and 57.8% ($n = 300$), ECGN/FPGN in 14.2% ($n = 176$) and 14.0% (73), MCGP/FSGS–complex in 9.5% (118) and 11.4% ($n = 59$) and finally MGN in 11.8% (146) and 16.9% (88) ($P = \text{NS}$). Thus 1239 specimens at the UH and 520 at the CH1–5 had one of these four main conditions.

The details of biopsy rate stratified for indications are shown for the UH 1980–2000 in Figure 1. Comparing the pathology in specimens biopsied either due to the nephritic syndrome ($n = 309$) or haematuria/proteinuria ($n = 456$) showed a statistical difference ($P < 0.001$, Kolmogorov–Smirnov test) in that the MCGP/FSGS complex, MGN and ECGN/FPGN were more common in the nephritic syndrome group ($n = 25, 38, 59$, respectively) compared to the haematuria/proteinuria group (3, 20, 67, respectively). Of note is that MesGN still was the most common outcome in both groups ($n = 187$ and 366, respectively). Comparing the pathology in the nephrotic syndrome ($n = 317$) vs non-nephrotic proteinuria ($n = 242$) groups showed that the MCGP/FSGS complex and MGN were more common ($P < 0.001$, Kolmogorov–Smirnov test) in the nephrotic syndrome group ($n = 102, 103$, respectively) compared to the proteinuria group ($n = 29, 44$, respectively). There was no statistical difference in the outcome ECGN/FPGN between the groups ($n = 16$ and 21). MesGN was statistically associated with an outcome of the proteinuria group ($n = 148$), but it was also common in the nephrotic syndrome group ($n = 96$). Comparing the

groups, RPGN ($n = 48$) and 'chronic nephritis' ($n = 579$) showed that ECGN/FPGN was, more common, relatively, in the RPGN than in the chronic nephritis group ($P < 0.001$, Kolmogorov–Smirnov test) ($n = 32$ vs 53). This difference appeared clinically relevant since two thirds of the subjects with RPGN had ECGN/FPGN as compared to one in ten of those with chronic nephritis. There was no difference in the outcomes for MesGN, MCGP/FSGS and MGN among the groups ($n = 12, 2$ and 2 and $n = 451, 25$ and 50, respectively).

The incidences/10⁵ population of the proliferative and non-proliferative glomerulonephritides at the UH from 1980 to 2000 were as follows: median (min–max) 9.5 (6.8–18.1), and 6.7 (3.4–12.6), respectively. The respective values for the CH1–3 were 4.2 (2.4–6.1) and 1.8 (0.9–4.0). The annual biopsy rates and the incidences of the four major glomerulonephritides groups at the UH are given in Figures 1 and 2, respectively. The biopsy rate was the main determinant of the glomerulonephritis incidence ($r = 0.77$, $P = 0.00004$, $r^2 = 0.6$, Spearman's correlation test). The incidence of MesGN was the highest over the entire time period at the UH and the CHs. The incidences of the other three entities were fairly equal at respective centres and over time. The incidence of IgAGN over the period was at the UH median (min–max) 4.8 (2.7–9.8) and at the CH1–3 0.8 (0.2–1.6), respectively. Since IgAGN was the dominant entity in the proliferative glomerulonephritis group the fluctuation in the occurrence of IgAGN determined the fluctuations for the total glomerulonephritides group.

The annual incidence rates for the glomerulonephritides in the total population at the UH are given in detail in Figure 3. The diagnosed glomerulonephritides entities in subjects <15 years of age are given in Table 3. The small number of observations in the paediatric subjects does not permit an analysis on a

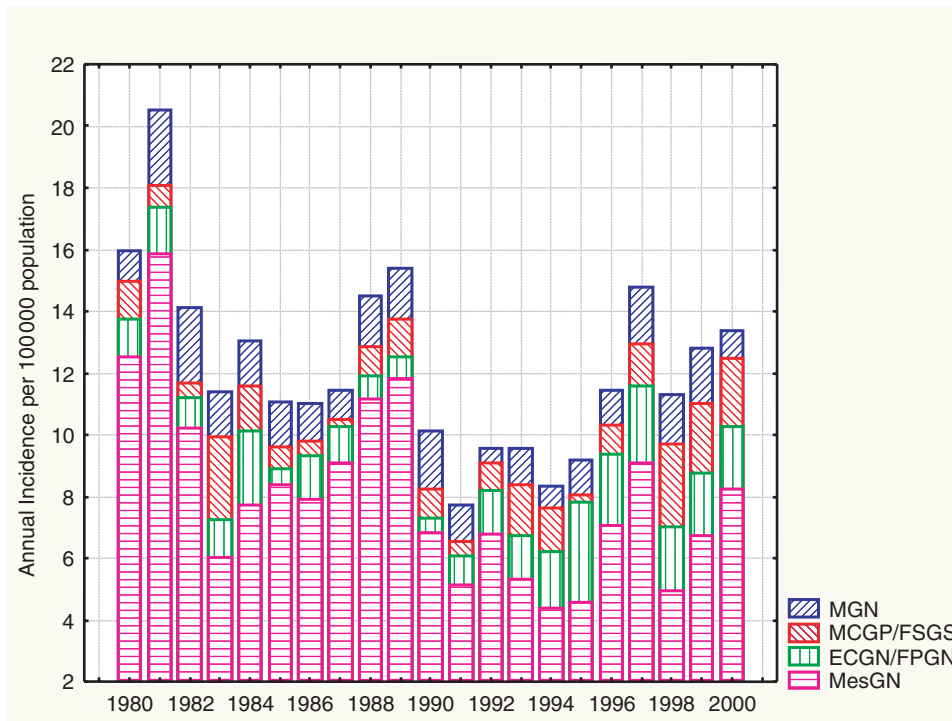


Fig. 2. The annual incidence per 10^5 population of defined glomerulonephritis groups at the University Hospital 1980–2000. $N = 1239$. The relative frequency of the groups were mesangial glomerulonephritis (MesGN) 64.5%, extracapillary/focal proliferative glomerulonephritis complex (ECGN/FPGN) 14.2%, minimal change/focal segmental sclerosis complex (MCGP/FSGS) 9.5% and membranous glomerulonephritis (MGN) 11.8%.

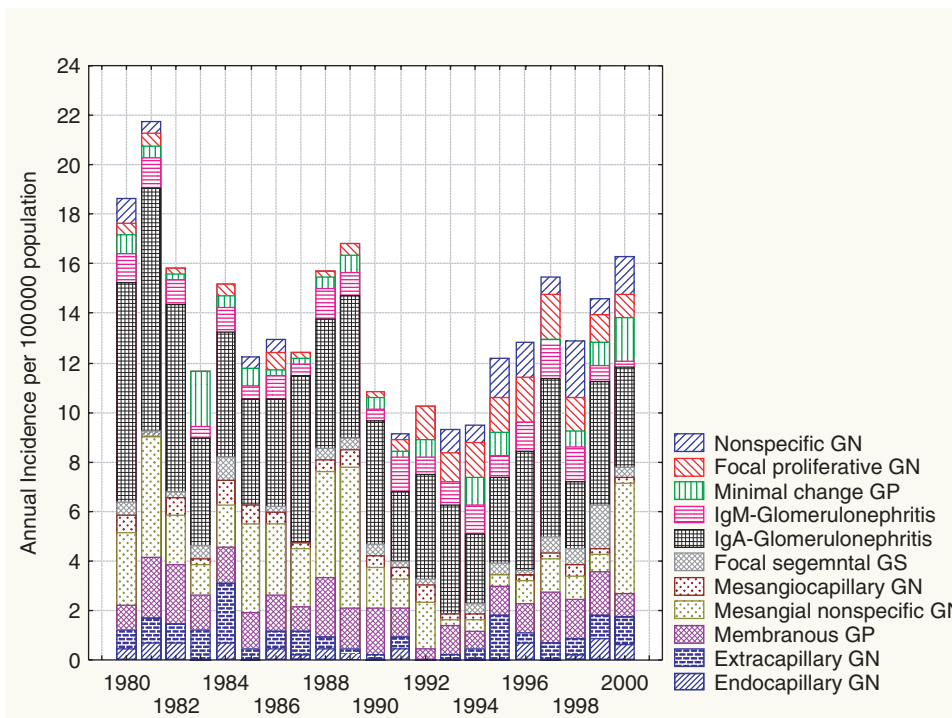


Fig. 3. The annual incidence per 10^5 population of indicated glomerulonephritis groups at the University Hospital 1980–2000. $N = 1489$.

yearly basis. The IgAGN, IgMGN, MCGP and non-specific MesGN were the most common entities, while FSGS, FPGN, MGN and EPGN were rare in paediatric subjects.

Discussion

The strength of this report is the way that it has full control of the background population characteristics and the biopsy rate and its determining variables and its uniform evaluation of biopsy indications and pathology.

The major finding in the present study was the much higher annual incidence per 10^5 population of 17.6 of a biopsy-proven glomerulonephritis than in any of the European registries (Table 1). Two single studies, based on a liberal biopsy policy, showed great resemblance to the present study in terms of biopsy rate and reported glomerulonephritis and IgAGN incidence [19,22]. By comparing the biopsy rate and the incidence of glomerulonephritis at the UH of 24.7 and 16.2 respectively, to those at the CH1–3 of 9.1 and 6, respectively, it is evident that the biopsy rate has a major impact on the reported glomerulonephritis incidence found in the identical populations. In the present study, the biopsy rate explained statistically 60% of the annual glomerulonephritis incidence variation at the UH. There is no reason to believe in such a difference in true glomerulonephritis incidence between these two identical populations. Rather, the differences are probably explained by confounding post-screening factors like biopsy resources, i.e. mainly nephrology service utility. Thus, with a liberal biopsy policy there appears to be a relationship between biopsy rate and observed glomerulonephritis incidence in the magnitude of about 3:2.

From Figure 1, it can be seen that there was an abrupt decline in the biopsy rate between 1989 and 1990 at the UH. The same downturn was observed at the CHs. This was most likely due to the most severe economic recession that has occurred in Finland since the thirties, characterized by a collapse in trade, monetary politics resulting in a decline in the gross domestic product of 13% and a rise in national unemployment rate from 3% to 18%. At the UH this was seen as a drop in admission rates of 22% and 38% at the medical and renal out-patient departments, respectively. The recession reached its turning point in 1993. The pre-recession admission rates were achieved gradually by 1997, at which time the biopsy rate had increased to almost pre-recession levels, at least if one considers the change in biopsy indication policy (see subsequently). Consequently, at least at the UH one could speculate whether during the late nineties more subjects were biopsied due to the more serious indication nephritic syndrome than haematuria and proteinuria (Figure 1), i.e. the admission was delayed due to the recession. Furthermore, during 1989 a reliable serological test for nephropathia epidemica became available, which can be seen as a drop in the

biopsy rate due to acute renal failure (Figure 1). Lone haematuria was no longer considered a biopsy indication at the UH (Figure 1) during the nineties. Even considering the above-mentioned three confounding factors the biopsy rate during the entire period would be about 18 per 10^5 population.

Why is there such a large discrepancy in the incidences between our report and the single-centre studies on the one hand and the registries on the other hand? The biopsy rate must be an important confounding factor. The registries with a low reported glomerulonephritis incidence likewise have a low biopsy rate, when given [17,18,21]. By considering the size and number of observations in the background population, the biopsy rate must have been low in those registries where the frequency has not been given [13–15]. Thus the biopsy registries are not reliable considering true glomerulonephritis incidence.

The impact of biopsy policy must evidently also be important. The biopsy rate is high at some Asian and European centres, and low in the United Kingdom, Canada and United States [5]. Some centres obtain a biopsy only when the pathology would alter the therapy [6,7] or in subjects with signs of progressive renal disease [8], while other centres try to establish an early specific diagnosis, whenever there is evidence of kidney disease by urinary analysis [9]. There was no significant difference between the distribution of the indications for biopsy between the UH and the CHs in terms of nephritic syndrome *vs* haematuria/proteinuria or nephrotic syndrome *vs* proteinuria. Moreover, it was demonstrated that over the entire time span subjects had been biopsied at the UH as well as the CHs on all of the above-mentioned indications. Of note, the retrospective nature of the present study had no impact on the biopsy indications. Thus, the difference between the UH and the CHs is not due to major differences in biopsy policy, rather to the biopsy rate. Centres carrying out the biopsy due to the nephritic and nephrotic syndrome and not due to haematuria/proteinuria and haematuria, respectively, will have a result tilted towards extracapillary and focal proliferative glomerulonephritis and minimal change-focal segmental glomerulosclerosis and membranous nephropathy, respectively, in contrast to mesangial nephropathy. Therefore, centres with strict indications will have a spuriously low frequency of mesangial glomerulonephritis, hence a low total reported glomerulonephritis incidence.

In most European studies like in ours, the mesangial glomerulonephritides, reflecting mainly IgAGN, are the most common with percentages between 30 and 60 typically found. The two studies with a high biopsy rate showed IgAGN incidences comparable to ours [19,22]. The annual incidence of IgAGN, when given, was about 0.8–1.0, compared to that in the UH of $5/10^5$. Again the incidences found are explained largely by the biopsy indications with a low incidence in strict criteria centres.

The incidences per 10^5 population of ECGN/FPGN, MCGP/FSGS and MGN at the UH and the CH1–3 in

this study, and the Danish Registry of (UH) 1.5, 1.2 and 1.4 and (CH) 0.7, 0.6 and 0.8 and (DR) of 0.6, 0.7 and 0.5 are comparable, especially if one considers biopsy rate and indications. The incidence data for the above-mentioned entities in the other registries are fragmentary but for ECGN/FPGN, MCGP/FSGS and MGN they were usually about 0.2–0.3, 0.1–0.8 and 0.5–0.6 respectively, when given. A further comparison to other centres must be on a percentage basis. Usually the frequencies of ECGN/FPGN, MCGP/FSGS and MGN have been about 5–10%, 10–20% and 10–22% in these registries, which corresponds to the findings here. Any differences, if real, between these series could be explained by different biopsy rates, and indications.

When comparing the incidence data for the UH here with the registry data for commencing renal replacement therapy (RRT) in the same region it appears that for every one subject commencing RRT there were about 11 subjects with biopsy-proven glomerulonephritis. This would agree with the Danish registry data with 13% of the subjects with glomerulonephritis reaching end-stage disease in a 10-year follow-up, and with another study showing that the incidence rate in 17 years of ESRD was 17%, and that the biopsy rate had been 12% in those subjects on RRT with a glomerulonephritis [10]. The Australian study showed a 6-fold relation between IgAGN incidence and RRT incidence. Apart from yearly fluctuations, there was no trend in this relationship in the present study over the years. Another study from Kentucky showed that in IgAGN, the incidence of ESRD was similar to European reports, although the biopsy-proven incidence of IgAGN was lower, i.e. about 0.5 per 10^5 [11]. One could thus assume that there is at least a 10-fold true incidence of IgAGN in a population with respect to the RRT rate, assuming an unrestricted access to replacement therapy.

What would the relation between true and reported glomerulonephritis incidence be if it was known? One could anticipate that some completely healthy or some incapacitated and/or elderly subjects would not be recruited or not considered suitable for biopsy, respectively. Studies in army conscripts show that about 0.3–0.5% have haematuria and/or proteinuria, and that about 50% of those would have IgAGN on biopsy [12]. From these figures, assuming a point prevalence of IgAGN of 0.4% in army conscripts of about 20 years of age, would give an annual incidence of unreported IgAGN in the present study of 15 per 10^5 population. Also, in autopsy series clinically completely silent IgA-deposits fulfilling IgAGN nephropathy can be found. Thus, a speculative relation between true and reported glomerulonephritis incidence would be greater than 3:1 based on studies in IgAGN.

We have focused here on European studies, including an important one from Australia, in recent years. Many reports with quite different results exist worldwide (relatively less MesGN), which probably is due to very different population genetics, race, climatology, environmental exposure to pathogens, frequency of

chronic skin and other infections, viral hepatitis and HIV-related conditions, as well as biopsy rate. In those populations, the incidences of acute exudative GN, mesangiocapillary glomerulonephritides, FSGS and collapsing nephropathy as well as HIV-AN are more frequent. Our results are, thus not relevant to such populations.

To summarise, the incidence of reported glomerulonephritis, provided the biopsy rate is sufficiently high, in European populations in recent years would be about 18 per 10^5 population. The true glomerulonephritis incidence is probably at least three times higher but really unknown. The mesangial glomerulonephritides, especially the IgAGN, are the most frequent ones and their reported incidences are mainly responsible for the variations between reports. No important large-scale time trends in the eighties and nineties were found here for the glomerulonephritides.

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Conflict of interest statement. None declared.

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