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The Czech registry of renal biopsies. Occurrence of renal diseases in the years 1994–2000

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Abstract

Background. This report describes data collected by the Czech Registry of Renal Biopsies (CRRB).

Methods. Twenty-eight centres provided data on all biopsies of native kidneys performed in the Czech Republic (population 10.3 million) over the period 1994–2000. Data on serum creatinine concentration (sCr), 24 h proteinuria, haematuria, serum albumin level, arterial hypertension, diabetes mellitus, histological diagnosis and complications after renal biopsy were collected.

Results. Altogether 4004 biopsies in 3874 patients were performed (males 57.9%, children ≤15 years 17.7%, elderly >60 years 14.3%). Microhaematuria was present in 65.9%, macrohaematuria in 9.2%, nephrotic proteinuria (≥3.5 g/24 h) in 39.3%, and low-grade proteinuria (<3.5 g/24 h) in 41.4%. Among adults, hypertension was present in 45.2%, mild renal insufficiency in 23% (sCr 111–200 μmol/l) and advanced renal insufficiency in 13.7% (sCr 201–400), while 11.5% of patients had sCr >400 μmol/l. The most frequent renal diseases were primary (59.8%) and secondary (25.4%) glomerulonephritis (GN). Tubulointerstitial nephritis (TIN) was observed in 4.4% and hypertensive nephroangiosclerosis in 3.4%. The samples were non-diagnostic in 4.6%. Among primary GNs, the most frequent diagnoses were: IgA nephropathy (IgAN) 34.5%, minimal change disease (MCD) 12.4%, non-IgA mesangioproliferative GN (MesGN) 11.3%, focal segmental glomerulosclerosis (FSGS) 10.8% and membranous GN (MGN) 9.3%. Among secondary GNs, systemic lupus erythematosus (SLE) represented 23.0%, necrotizing vasculitis (NV) 15.5%, Henoch–Schönlein purpura 5.7%, thin basement membrane glomerulopathy (TBN) 19.3%, Alport syndrome 6.9%, renal amyloidosis 9.9% and myeloma kidney 2.9%. Among children, the most common were IgAN (19.2%), MCD (17.6%) and TBM glomerulopathy (12.3%), while among the elderly the most common were MGN (11.0%), NV (10.7%) and amyloidosis (9.6%). The most common in patients with nephrotic proteinuria were MCD (50.5%) among children, but IgAN (24.6%) in adults aged 16–60 years and MGN (16.8%) among the elderly. IgAN (21.3%) and FSGS (8.3%) were the most common diagnoses among patients with mild renal insufficiency, but TIN (11.6%) and NV (11.3%) were the most common in more advanced renal insufficiency. Since 1999, diabetic patients represented 12.2% of adults, with mean proteinuria 8.9 g/24 h; diabetic glomerulosclerosis was found in 42.4% (with microhaematuria present in 66%) and non-diabetic renal diseases in 47.5% (IgAN in 17.5%, MGN and NAS in 11.1% and NV in 9.5%). The mean annual incidence (per million population) was: primary GN 32.4, secondary GN 13.8, IgAN 11.2, MCD 4.0, MesGN 3.7, FSGS 3.5, SLE 3.2, MGN 3.0, TBM 2.7, TIN 2.4 and NV 2.1. Ultrasound needle guidance was used in 56%, preferably in children (79%). The frequency of serious complications (gross haematuria, symptomatic haematoma, blood transfusion) remained at 3%.

Conclusion. The CRRB provides important data on the epidemiology of GN based on a whole country population.

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Introduction

Glomerulonephritis (GN) is a relatively rare disease with numerous subtypes. Most regional nephrology centres see only a limited number of patients with each type of GN every year. Information about the prevalence and incidence of GN in the general population is rather scarce; comprehensive epidemiological surveys are difficult to undertake, especially since the onset of most cases of GN is 'silent' so the diagnosis is often incidental, made by urine testing during a routine medical examination. Developing a regional and then a national registry gave us the opportunity to learn more about the epidemiology of GN.

Current epidemiological data of renal disease in Europe are available from large national renal biopsy registries from Italy [1], Denmark [2] and Spain [3]. Information derived from local or limited national registries of renal biopsy has been also reported from European [4] and other countries [5–7]. Many other reports have also been published dealing with specific population groups (elderly, native Indians, etc.) or with specific diagnoses (nephrotic syndrome, rapidly progressive GN, vasculitis, etc.) or with local one-centre experience.

In 1993, nephrologists from 12 leading centres in the Czech Republic established a national registry of biopsies of native kidneys recording histopathological, clinical and laboratory data. The Czech Registry of Renal Biopsies (CRRB) has been working continuously since 1994 and the number of participating renal units has risen to 28, representing nearly all Czech renal units currently performing renal biopsy.

The aims of CRRB are: (i) to study the epidemiology of renal disease based on histological diagnosis in the region of Central Europe covered by the Czech Republic; (ii) to identify the most frequent clinical syndromes; and (iii) to evaluate renal function at the time of renal biopsy.

Materials and methods

Over a period of 7 years (1994–2000), renal biopsy records were collected from the Czech renal units. Using a simple questionnaire, the following data were collected at the time of renal biopsy: serum creatinine concentration (sCr), 24 h proteinuria, presence of haematuria (micro or macro), presence of arterial hypertension defined as a blood pressure >140/90 mmHg or permanent treatment with antihypertensive medication, clinical and histological diagnosis, clinical complications after renal biopsy (with serious complications defined as: clinically symptomatic subcapsular or perirenal haematoma, gross haematuria, presence of hypovolaemic shock and need for blood transfusion) and biopsy needle guidance technique [ultrasonography (USG), X-ray, computed tomography (CT), scintigraphy or transjugular route]. Since 1999, the serum albumin level and the presence of diabetes mellitus (DM) have also been recorded. To allow comparison with previous reports, we defined children as ≤15 years, adults as age 16–60 years, and the elderly as age >60 years.

The clinical and laboratory conditions observed at the time of renal biopsy were reported as follows: (i) *nephrotic proteinuria*: ≥3.5 g/24 h; (ii) *urinary abnormalities*: persistent low-grade proteinuria (< 3.5 g/24 h) with or without microhaematuria; (iii) *isolated haematuria*: presence of micro- or macrohaematuria, without any proteinuria; (iv) *nephritic syndrome*: combination of haematuria, arterial hypertension and reduced renal function (sCr >110 μmol/l); (v) *mild renal insufficiency* was defined as sCr 111–200 μmol/l; and (vi) *advanced renal insufficiency* was sCr >200 μmol/l. More than one of these six syndromes overlapped in some patients.

The indications for renal biopsy varied among centres according to local practice. Histological evaluation by light microscopy and immunofluorescence was performed routinely, combined with electron microscopy in a number of cases. Histological classification of renal diseases used the WHO recommendations (1995), but the slightly modified scheme of Schena [1] was used for statistical analysis. Renal diseases were divided into five groups. (i) Primary GN including minimal change disease (MCD), minor glomerular abnormalities (MGA), focal segmental glomerulosclerosis (FSGS), membranous GN (MGN), IgA nephropathy (IgAN), mesangioproliferative GN (MesGN), membranoproliferative GN (MPGN), crescentic GN (CGN) (defined as CGN not fulfilling the criteria for systemic disease), proliferative endocapillary GN (PEGN), sclerosing GN (ScGN) and unclassified GN. (ii) Secondary GN: (a) immune-mediated GN such as systemic lupus erythematosus (SLE), Henoch–Schönlein purpura (HSP), necrotizing vasculitis (NV) and Goodpasture's syndrome (GPS); (b) GN caused by dysgammaglobulinaemia or paraproteinaemia, such as renal amyloidosis (AM), light-chain deposit disease (LCDD), myeloma kidney (MM) and essential mixed cryoglobulinaemia; (c) GN associated with infectious diseases (non-streptoccocal GN, endocarditis, shunt GN and others); (d) metabolic disorders, particularly diabetic nephropathy (DN); (e) hereditary nephropathies, i.e. Alport syndrome (AS), Fabry disease, thin basement membrane glomerulopathy (TBM) or other hereditary diseases. (iii) Acute and chronic tubulointerstitial nephritis (TIN) and acute tubular necrosis. (iv) Vascular diseases including benign and malignant nephroangiosclerosis (NAS), haemolytic–uraemic syndrome and thrombotic thrombocytopenic purpura (HUS/TTP), renal scleroderma and cortical necrosis. (v) Others, including end-stage renal disease (ESRD) of undetermined cause, miscellaneous (pre-eclampsia, rare nephropathies, etc.), unclassified nephropathies and normal histopathological findings.

Data analysis

One clinician in each participating renal unit was responsible for supplying data to the Registry quarterly by mail. Data were stored on a personal computer, and for statistical analysis, the standard FoxPro2 database and statistics processor was used. The annual incidence was defined as the number of new cases per year related to the mean total population, expressed as per million population (p.m.p) per year.

Results

The total population of the Czech Republic in the years 1994–2000 was ~10.3 million inhabitants, 98% were

Caucasians, with a male/female ratio of 48.7/51.3. The percentage of children (< 15 years) decreased from 18.9% in 1994 to 16.3% in 2000, and the elderly population (≥60 years) increased from 13.1% in 1994 to 14.0% in 2000. Mean age also increased, from 37.0 years in 1994 to 38.8 years in 2000. As far as the urban–rural distribution pattern is concerned, two-thirds lived in cities.

Over the 7 year study, a total of 4004 renal biopsy records were referred to the CRRB; these were performed in 3874 patients. A total of 130 records were identified as re-biopsy, with 40 of these carried out early due to inadequate sampling during the first biopsy, and 90 for therapeutic/diagnostic reasons at different time points of follow-up (range 2–70 months); a third renal biopsy was done in six patients.

During the study, the number of referring centres increased from 19 in 1994 (with five being paediatric nephrology departments) to 28 in 1997 (nine paediatric). Since 1997 the registry has included almost all native kidney renal biopsies performed in the Czech Republic. The number of renal biopsies performed has increased year by year, being 44.1 p.m.p./year in 1994 and 69.3 p.m.p./year in 2000. We observed considerable variation in biopsy rate between centres: 53.9% of adult and 59.4% of paediatric renal biopsies were performed in Prague-based centres.

A total of 3294 biopsies (82.3% of the total) in adults and 710 biopsies in children age ≤15 years (17.7%) were registered. If children are considered to be those aged <18 years, this age group had 1073 biopsies (26.4%). The age distribution is given in Table 1, with mean age being 10 years for children (range 0.5–15) and 42 years for adults (range 16–89). Mean age according to diagnosis was lowest in AS (17 years) and highest in dysgammaglobulinaemias (60 years). Male gender was associated most frequently with most diagnostic categories (Table 8), with only SLE (77.2%) and TBM (55.2%) being more frequent among females.

All biopsy samples were evaluated by light microscopy and immunofluorescence. However, immunofluorescence was not performed in the case of the lack of or poor quality of a tissue sample. The number assessed by electron microscopy varied from 15.0 to 75.5% of all samples; electron microscopy was used at the discretion of the pathologist.

Table 2 shows the annual percentage of each group of nephropathies, Tables 3 and 4 show the annual frequency of different forms of primary GN and secondary GN, respectively. Specimens were inadequate for diagnosis in 185 cases (4.6%). IgAN was the most frequent GN seen (34.5%).

The clinical and laboratory findings are displayed in Table 1. Proteinuria was less often present in children compared with adults: any proteinuria (64.1 *vs* 84.3%) and nephrotic range proteinuria (26.8 *vs* 42.0%). Arterial hypertension was present more commonly in adults (45.2%), and most often among patients suffering with malignant NAS (97.6%) and DN (78.1%), whereas hypertension was least common in patients with hereditary GN (9.6%) and with minor glomerular abnormalities (8.9%).

The sCr distribution pattern in patients with impaired renal function is given in detail in Table 1.

Table 1. Distribution according to age, gender, basic laboratory findings and arterial hypertension: comparison of children and adults (%)

	Total	Children (≤15 years)	Adults
Total number (100%)	4004	710	3294
Age (years)			
0–5	2.7	15.2	–
6–10	5.9	33.1	–
11–15	9.1	51.6	–
16–30	26.7	–	32.5
31–45	19.3	–	23.5
46–60	21.9	–	26.7
61–75	12.6	–	15.3
>75	1.8	–	2.1
Male gender	57.9	53.2	59.0
Macrohaematuria	9.2	13.0	8.3
Microhaematuria	65.9	60.2	67.1
Proteinuria			
Low (<3.5 g/24 h)	41.4	37.3	42.3
Nephrotic (≥3.5 g/24 h)	39.3	26.8	42.0
sCr (μmol/l)			
≤110	59.5	94.2	51.8
111–200	19.4	3.4	23.0
201–400	11.5	1.7	13.7
401–600	4.4	0.1	5.3
>600	5.2	0.6	6.2
Arterial hypertension	38.7	9.1	45.2

Table 2. Annual percentage of major groups of renal diseases ($n = 4004$)

	1994	1995	1996	1997	1998	1999	2000	Total
Primary glomerulonephritis	64.9	65.5	58.2	61.3	58.9	55.5	57.0	59.8
Secondary glomerulonephritis	21.7	24.0	23.5	24.3	24.4	28.0	29.3	25.4
Tubulointerstitial nephritis	4.5	2.0	6.9	3.5	6.2	5.0	2.9	4.4
Hypertensive nephroangiosclerosis	3.4	5.2	3.5	3.1	3.0	2.8	3.0	3.4
End-stage renal disease	2.2	1.0	1.6	1.4	0.4	1.5	0.6	1.2
Miscellaneous	0.4	0.1	0.8	0.9	0.3	0.1	0.1	0.4
Non-diagnostic sample	2.5	1.2	4.6	5.2	5.1	6.4	6.5	4.6
Normal findings	0.7	1.0	0.9	0.3	1.7	0.7	0.6	0.8
Total no. of cases (100%)	454	517	563	586	547	623	714	4004

Table 3. Annual incidence (%) of primary glomerulonephritis ($n = 2333$), re-biopsies excluded

	1994	1995	1996	1997	1998	1999	2000	Total
MCD	10.0	14.2	12.8	10.0	16.9	10.7	12.4	12.5
MGA	3.8	8.3	5.6	8.0	5.7	4.5	4.5	5.8
FSGS	9.3	8.9	11.0	10.7	8.0	17.3	10.0	10.8
MGN	7.2	7.7	9.4	12.0	8.6	9.2	10.3	9.3
MesGN	17.9	10.7	14.1	14.3	13.4	8.3	2.8	11.3
IgAN	33.1	30.5	33.8	29.7	38.0	33.0	41.8	34.5
PEGN	2.4	0.3	1.6	1.4	0.6	1.2	1.8	1.3
MPGN	6.6	8.0	3.1	4.9	2.6	4.8	3.0	4.6
CGN	2.4	3.4	2.5	4.3	1.0	3.3	5.0	3.2
SGN	3.5	1.8	3.5	1.4	2.6	3.9	2.0	2.7
Unclassified GN	3.8	6.2	2.5	3.4	2.6	3.8	6.3	4.1
Total no. of cases (100%)	290	325	319	350	313	336	400	2333

CGN = crescentic glomerulonephritis; FSGS = focal segmental glomerulosclerosis; IgAN = IgA nephropathy; MCD = minimal change disease; MesGN = mesangioproliferative glomerulonephritis; MGA = minor glomerular abnormalities; MGN = membranous glomerulonephritis; MPGN = membranoproliferative glomerulonephritis; PEGN = proliferative endocapillary glomerulonephritis; SGN = secondary glomerulonephritis.

Table 4. Annual incidence (%) of secondary glomerulopathies ($n = 990$), re-biopsies excluded

	1994	1995	1996	1997	1998	1999	2000	Total
Immune-mediated glomerulonephritis	62.3	48.7	46.5	48.2	44.6	41.2	43.2	48.6
Lupus nephritis	24.7	28.6	23.3	23.0	21.5	21.2	21.4	23.0
Necrotizing vasculitides	23.7	13.5	13.9	17.3	14.6	12.3	16.0	15.6
Henoch–Schönlein purpura	10.3	4.2	4.6	6.5	6.9	4.7	4.9	5.7
Goodpasture's syndrome	2.1	0.8	2.3	0	0.8	1.8	1.0	1.2
Dysgammaglobulinaemias	12.4	18.5	17.8	15.8	14.6	13.5	13.1	14.9
Renal amyloidosis	7.2	10.1	10.8	7.9	11.5	10.6	10.2	9.9
Myeloma kidney	4.1	7.6	3.1	3.6	2.3	1.2	1.0	2.9
Light-chain deposit disease	0	0	2.3	2.9	0	0	1.9	1.1
Essential mixed cryoglobulinaemia	1.0	0.8	1.6	1.4	0.8	1.8	0	1.0
Diabetic glomerulosclerosis	9.3	3.4	7.0	10.8	6.9	17.0	14.6	10.6
Hereditary disorders	15.5	29.4	28.7	25.2	33.8	28.2	29.1	27.7
Alport syndrome	2.1	11.8	5.4	4.3	12.3	4.7	7.3	6.9
Thin membrane disease	10.3	16.8	22.5	19.4	20.0	22.3	20.4	19.3
Total no. of cases (100%)	97	119	129	139	130	170	206	990

Data were not available to interpret renal function in children according to size, so we simply report that 5.8% of children had an sCr >110 μmol/l.

Among adults with normal renal function (mean sCr = 70 μmol/l), mean age was 35 years, while 78.8% had proteinuria (mean 6.0 g/24 h), 75.8% also had haematuria at presentation and 28.5% were hypertensive. Among the group with renal insufficiency (sCr >110 μmol/l), a similar percentage had haematuria while mean age (50 years), presence of proteinuria (90.5%) and hypertension (63.4%) were higher. Data concerning dialysis treatment at the time of renal biopsy were not available, but 203 patients (5.2%) had sCr >600 μmol/l. The highest percentage of patients with sCr >600 μmol/l was found in GPS (58.4%), MM (37.9%) and CGN (29.3%). After excluding patients with sCr >600 μmol/l, the highest mean sCr levels were observed in CGN (274 μmol/l), NV (271 μmol/l) and TIN (252 μmol/l). The incidence of GN related to age is shown in Table 5.

More than one clinical syndrome was found in some patients and so a total of 6071 clinical syndromes were registered (Table 6). The most frequent indications for performing renal biopsy in adults were nephrotic range proteinuria (39.3%) and urinary abnormalities (36.2%), but among children it was isolated haematuria.

Nephrotic proteinuria (Figure 1A) was the most common clinical presentation (overall frequency 39.3%) particularly among the elderly (59.0%). The distribution pattern of diagnoses differed with age (Table 7). Those with proteinuria >10 g/24 h comprised 23.5% of all patients and 34.6% of adults. Microhaematuria (66%), hypertension (52%) and renal insufficiency (46%) were found frequently with nephrotic range proteinuria.

Among the patients with urinary abnormalities (Figure 1B), all had low-grade proteinuria, 77.7% also had microhaematuria, with hypertension in 40.5%, and renal insufficiency in 44.5%. Mean age was 36 years. The most common disease was IgAN (23.1%) followed by SLE (7.4%).

Nephritic syndrome (Figure 1C) was observed in 19.1% of all cases. Mean age was 51 years and more than one-third of patients (36%) were in the age range 46–60 years. sCr >600 μmol/l was found in 13.2%.

Table 5. Incidence of glomerulopathies and TIN related to age (given as a percentage of the group, re-biopsies excluded)

Diagnosis	≤15 years	16–30 years	31–45 years	46–60 years	>60 years
Total no. of cases	693	1041	750	851	554
Primary GN	67.0	68.7	60.5	53.2	44.4
MCD	26.2	10.2	9.0	6.4	9.8
MGA	12.0	6.3	5.3	1.3	1.6
FSGS	8.4	9.8	11.0	12.1	15.0
MGN	1.9	3.6	9.3	17.4	24.8
MesGN	11.8	11.9	9.7	6.1	4.1
IgAN	28.6	46.6	38.3	30.0	10.6
PEGN	1.3	0.7	2.0	1.3	2.0
MPGN	3.0	4.1	5.1	6.4	5.3
CGN	0.7	1.7	1.3	5.5	11.8
SGN	0.4	1.1	3.5	4.8	6.1
Unclassified GN	3.4	2.2	4.4	6.4	6.4
Secondary GN	26.4	22.6	21.3	24.8	36.3
Immune mediated	31.1	56.2	57.5	47.9	39.8
Dysgammaglobulinaemia	0.6	2.6	10.6	22.8	38.3
DM	0.0	2.6	9.4	20.3	20.4
Hereditary	68.3	38.7	22.5	9.0	1.5
Hypertensive nephrosclerosis	0.0	0.6	7.3	8.5	6.3
TIN	3.6	3.0	4.9	4.8	6.0

CGN = crescentic glomerulonephritis; DM = diabetes mellitus; FSGS = focal segmental glomerulosclerosis; IgAN = IgA nephropathy; MCD = minimal change disease; MesGN = mesangioproliferative glomerulonephritis; MGA = minor glomerular abnormalities; MGN = membranous glomerulonephritis; MPGN = membranoproliferative glomerulonephritis; PEGN = proliferative endocapillary glomerulonephritis; SGN = secondary glomerulonephritis; TIN = tubulointerstitial nephritis.

Table 6. Clinical syndromes ($n = 6071$) at the time of renal biopsy (given as a percentage of all renal biopsies)

	Total ($n = 4004$)	Children ($n = 710$)	Adults ($n = 3294$)
Nephrotic proteinuria	39.3	26.8	42.0
Urinary abnormalities	36.2	31.7	37.1
Isolated haematuria	16.5	32.7	12.5
Nephritic syndrome	19.1	1.8	22.3
Mild renal insufficiency	19.4	3.4	23.0
Advanced renal insufficiency	21.1	2.4	25.2

In some patients, more than one clinical syndrome was found; for instance, nephrotic proteinuria associated with renal insufficiency.

The most frequent diagnosis was IgAN, but it is of interest that NAS and FSGS were also found frequently.

Finally, IgAN was also found most frequently (26.1%) in patients with isolated haematuria (Figure 1D) followed by hereditary nephropathies (23.4%). Most patients in this group had normal sCr (93.6%), normotension (87.7%); mean age (25 years) was the lowest of all evaluated groups.

IgAN (21.3%) and FSGS (8.3%) were the most frequent diagnosis in mild renal insufficiency (Figure 1E), while TIN (11.6%) and NV (11.3%) were the most frequent in advanced renal insufficiencies (Figure 1F). Nephrotic proteinuria was common in both groups with renal insufficiency, 58.5 and 52.3%, respectively.

Since 1999, the presence of DM was registered, and diabetic patients represented 12.2% of adult renal biopsies in 1999–2000 with a mean age of 58 years (range 18–80). Only five patients (3.6%) were younger than 30 years, but none of them was in the paediatric age group. DN was found in 42.4% and non-diabetic renal diseases (NDRD) in 47.5%. It is also of interest that a large number of samples were non-diagnostic (10.1%). Mean proteinuria was 8.9 g/24 h. Comparing the DN and NDRD groups, there were no significant differences in predominance of male gender (61/69%), hypertension (83/79.8%), microhaematuria (66/62%), low-grade proteinuria (28/36%) or nephrotic proteinuria (68/62.5%). Mean sCr was 244/207 μmol/l (range 54–1002). Normal renal function was reported in 18.5/33.0% and sCr 111–200 μmol/l in 27.8/27.3%. However, more advanced renal insufficiency was more common in DN compared with NDRD: sCr 201–400 μmol/l in 33.4/24.2% and sCr >400 μmol/l in 19.0/7.5%. Among NDRD, the most frequent diagnoses were IgAN in 17.5%, MGN and NAS in 11.1%, and NV in 9.5%.

The most important clinical and laboratory data related to each diagnostic entity are summarized in Table 8.

USG needle guidance was used most commonly (56.4%), followed by X-ray guidance (35.7%). The other modalities were used rarely: CT in 2.4%, scintigraphy in 4.5% and transjugular biopsy in 0.8%. USG was used more among children (78.9%). The biopsy gun has been used since 1994 with an increasing frequency, from 2.0% in 1994 to 50.3% in 2000. The use of USG compared with X-ray was likewise increasing over the years, being 40.6/51.2% in 1994 and 58.4/35.5% in 2000. Ninety-four clinically serious complications (Table 9) were recorded (3.12% of all biopsies), being more frequent in children (4.37%) than in adults (2.85%). Serious complications were observed most frequently in CT (5.15%) and least frequently in USG without a gun (2.33%). Use of the biopsy gun was not associated with a lower complication rate (2.80 *vs* 2.88%).

Discussion

This report provides information about the occurrence of renal diseases diagnosed by renal biopsy during a period of 7 years covering the population of a whole country. Our preliminary results have been presented elsewhere [8–10]. To our knowledge, only three papers have been published dealing systematically with renal biopsy data for a whole country with a population exceeding 10 million [1,3,6]. Since a national registry may fail particularly due to incomplete data collection, we decided to minimize the required data set to achieve a high response rate and ensure it was truly nationally representative.

Records collected by the CRRB showed that males were over-represented in biopsy-proven renal diseases, with the exception of SLE and TBM.

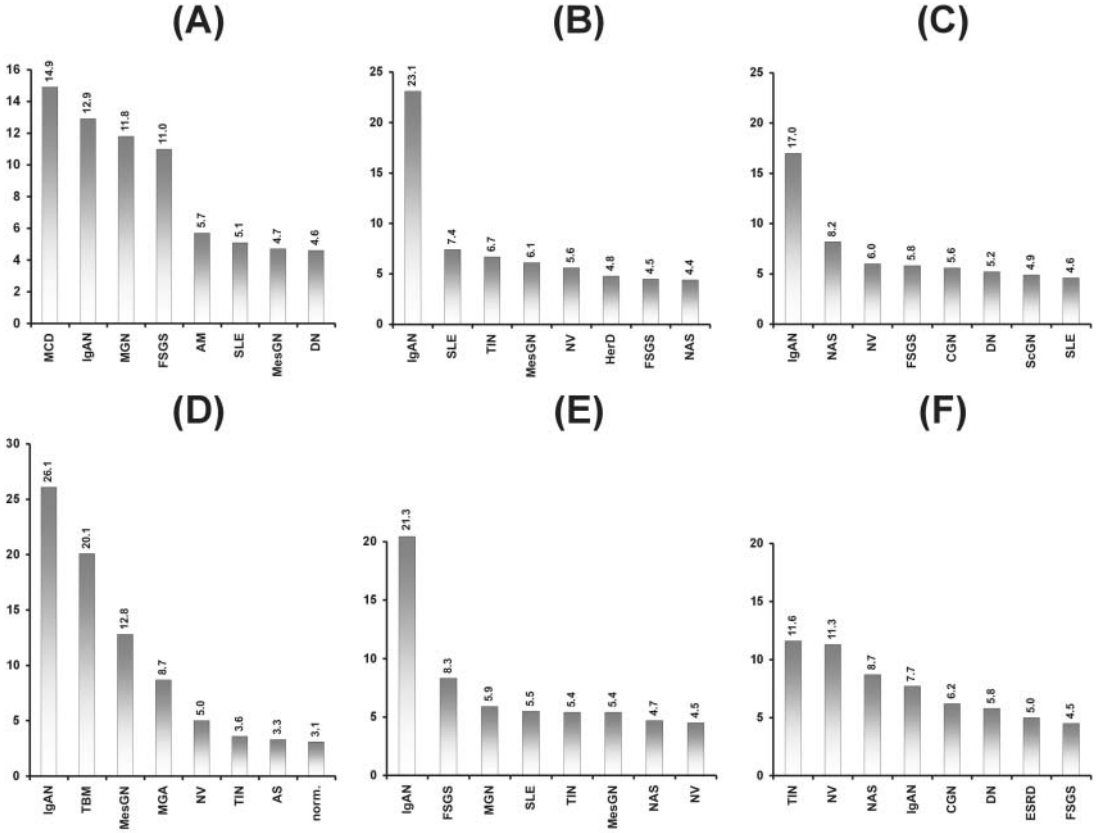

Fig. 1. Percentage of different forms of renal diseases according to clinical presentations: (**A**) patients with nephrotic proteinuria ($n = 1557$); (**B**) patients with urinary abnormalities ($n = 1451$); (**C**) patients with nephritic syndrome ($n = 747$); (**D**) patients with isolated haematuria ($n = 643$); (**E**) patients with mild renal insufficiency ($n = 762$); (**F**) patients with advanced renal insufficiency ($n = 829$). For abbreviations see text.

Table 7. Distribution of nephrotic proteinuria according to selected diagnosis and age (given as a percentage of all patients with nephrotic proteinuria in each age group)

Diagnosis	All	Children (≤15 years)	Adults				
			16–30 years	31–45 years	46–60 years	>60 years	All
MCD	14.9	50.5	17.0	9.7	5.7	6.7	9.4
IgAN	12.9	7.8	21.7	18.1	10.5	3.7	13.1
MGN	11.8	2.1	4.7	11.3	16.3	16.8	12.7
FSGS	11.0	12.5	13.0	11.3	8.9	8.9	10.3
AM	5.7	0.5	0.7	3.8	5.5	14.4	6.2
SLE	5.1	3.6	9.3	5.6	3.6	2.5	5.1
MesGN	4.7	6.8	7.0	4.4	4.1	1.8	4.3
DM	4.6	0.0	0.7	2.8	6.9	8.9	5.1
MPGN	4.1	1.6	5.3	4.7	4.5	2.5	4.3
NAS	3.4	0.0	0.7	5.0	5.0	3.7	3.7
CGN	2.4	0.0	2.0	0.6	3.1	4.6	2.6
% of all cases	39.3	26.8	28.8	42.6	49.1	59.0	42.0

AM = amyloidosis; CGN = crescentic glomerulonephritis; DM = diabetes mellitus; FSGS = focal segmental glomerulosclerosis; IgAN = IgA nephropathy; MCD = minimal change disease; MesGN = mesangioproliferative glomerulonephritis; MGN = membranous glomerulonephritis; MPGN = membranoproliferative glomerulonephritis; NAS = hypertensive nephroangiosclerosis SLE = systemic lupus erythematosus.

Other investigators have also observed this finding in 65 [1] and 66% [3], respectively.

More than a quarter of renal biopsies were performed in paediatric units. We used an age limit for children of 15 years to allow comparison with other studies. There are few epidemiological data concerning renal biopsy in children in European registries. Coppo *et al.* [11] reported 432 children ≤15 years old undergoing renal biopsy in 1992–1994, representing only 5.7% of the all-Italian Registry

Table 8. The epidemiology of selected glomerulopathies and TIN, ranked by frequency showing the incidence of different parameters at the time of biopsy, re-biopsies excluded

Diagnosis	No. of cases	% of CRRB	% of group	Incidence (p.m.p./year)	Mean age (years)	Gender (% male)	Hypertension (%)	Mean sCr (μmol/l) (HD excluded)	% of RI (sCr >110 μmol/l)	% of HD (sCr >600 μmol/l)	Nephrotic proteinuria (%)	Nephritic syndrome (%)
Primary GN	2333	59.8	100.0	32.4	33	61.9	35.4	114	30.4	2.0	43.4	9.9
MCD	289	7.5	12.7	4.0	25	56.7	20.4	83	10.7	0.0	77.8	3.8
MGA	135	3.5	6.4	1.9	21	43.7	8.9	80	7.4	0.7	3.7	0.7
FSGS	251	6.5	9.5	3.5	37	60.2	45.4	127	39.8	0.4	65.7	17.1
MGN	217	5.6	9.0	3.0	49	58.5	49.8	115	30.4	0.0	81.6	12.0
MesGN	260	6.9	12.3	3.7	28	61.9	21.5	94	21.9	1.4	26.8	7.2
IgAN	804	20.8	32.9	11.2	30	67.7	32.1	112	28.1	0.5	24.1	15.8
PEGN	31	0.8	1.3	0.4	38	61.3	41.9	146	54.8	0.0	48.4	32.3
MPGN	111	2.9	5.1	1.5	37	67.6	45.9	130	40.5	3.6	55.0	18.9
CGN	75	1.9	2.8	1.0	52	60.0	69.3	274	86.7	29.3	48.0	56.0
SGN	63	1.6	2.5	0.9	47	68.2	74.6	243	87.3	15.9	42.9	58.7
Unclassified GN	97	2.5	3.8	1.3	40	45.4	45.4	135	38.1	1.0	30.9	11.3
Secondary GN	990	25.6	100.0	13.8	39	46.8	36.5	–	41.4	8.3	34.7	18.3
SLE	228	5.9	23.0	3.2	34	22.8	35.5	113	27.6	5.3	33.3	14.9
HSP	57	1.5	5.7	0.8	19	63.2	26.3	88	10.5	0.0	31.6	5.3
NV	154	4.0	15.5	2.1	54	56.5	44.8	271	83.1	20.8	22.7	31.2
AM	98	2.5	9.9	1.4	59	52.0	43.9	174	53.1	6.1	86.7	25.5
MM	29	0.8	2.9	0.4	60	65.5	41.4	274	86.2	37.9	34.5	13.8
DN	105	2.7	10.5	1.5	56	63.8	78.1	199	77.1	8.6	65.7	37.1
AS	68	1.8	6.9	0.9	17	55.9	8.8	82	14.7	0.0	27.9	5.9
TBM	192	5.0	19.3	2.7	22	44.8	9.9	72	2.6	0.0	7.3	0.5
NAS benign	91	2.3	68.9	1.3	51	74.7	84.1	237	78.0	5.5	45.0	45.0
NAS malignant	41	1.1	31.1	0.6	48	75.6	97.6	309	90.2	31.7	24.3	48.6
TIN	170	4.4	100.0	2.4	41	57.6	40.0	252	80.6	16.5	15.3	20.6

AM = amyloidosis; AS = Alport syndrome; CGN = crescentic glomerulonephritis; DN = diabetic nephropathy; FSGS = focal segmental glomerulosclerosis; HD = haemodialysis; HSP = Henoch–Schönlein purpura; IgAN = IgA nephropathy; MCD = minimal change disease; MesGN = mesangioproliferative glomerulonephritis; MGA = minor glomerular abnormalities; MGN = membranous glomerulonephritis; MM = myeloma kidney; MPGN = membranoproliferative glomerulonephritis; NAS = hypertensive nephroangiosclerosis; NV = necrotizing vasculitis; PEGN = proliferative endocapillary glomerulonephritis; RI = renal insufficiency; SGN = secondary glomerulonephritis; TBM = thin basement membrane glomerulopathy; TIN = tubulointerstitial nephritis.

Table 9. Clinically significant complications after renal biopsy

Type	No of cases	% of all renal biopsis	Concomitant co-morbidity (%)			
			Renal insufficiency	Hypertension	Both	Total
Haemorrhage and hypotension	35	0.87	20.0	13.3	28.6	65.7
Gross haematuria	45	1.12	17.8	8.9	31.1	57.8
Symptomatic haematoma	45	1.12	6.7	8.9	26.7	42.3
Total	125	3.12	14.4	11.2	28.8	53.6
Children	31	4.37				
Adults	94	2.85				

of renal biopsy. Rivera *et al*. [3] and Briganti *et al*. [7] reported 487 and 104 renal biopsies performed among children <15 years old, which represented 7.0 and 5.2% of all biopsies, respectively. Our registry reports almost twice the total number of paediatric renal biopsies ($n = 710$, i.e. 17.7% of all biopsies), apparently indicating more liberal criteria for renal biopsy among our paediatric nephrologists. Higher proportions of paediatric biopsies have also been reported in Asia, with 40.5% out of all renal biopsies, in Korea [5] and in Japan with 20% [6].

It is rather difficult to report definitive epidemiological data on the frequency of the various forms of GN for several reasons. First, the renal biopsy indication policy varies from centre to centre. Secondly, renal biopsy is often not performed when the likelihood of a therapeutic consequence is low (e.g. steroid-sensitive nephrotic syndrome in children, intermittent haematuria without proteinuria, bilateral small kidneys, post-infection GN). For this reason, the true incidence of MCD, PEGN and IgAN will be underrepresented. Using the experience of biopsy registries with a similar design [2], we estimate that the CRRB includes up to 70–85% of these patients. Thirdly, insufficient tissue did not always allow complete evaluation, i.e. by immunofluorescence, so that a correct histological diagnosis could not be established (e.g. IgAN). Other reports are similarly incomplete; for example, only 78% out of all samples were evaluated by immunofluorescence in a Danish study [2] and 56.5% in Japan [6], where 42.5% cases of MesGN were not evaluated by immunofluorescence. During the 7 year survey, we could observe a 'crossover' phenomenon with decreasing incidence of MesGN and increasing incidence of IgAN, suggesting increasingly complete evaluation by immunofluorescence. Electron microscopy is rather expensive and was not used in this study for all biopsies, although it is a crucial diagnostic tool in some circumstances, e.g. establishing the diagnosis of MCD and TBM. The frequency of electron microscopy did not differ compared with other reports worldwide (~30% of all samples). Newer techniques, e.g. polymerase chain reaction (PCR) or *in situ* hybridization, would seem to be helpful in the future [12], but certainly their routine use is not intended.

Our report showed that renal biopsy was predominantly performed in patients with primary and secondary GN. Despite any possible local influence of renal biopsy policy, the incidence of GN (47 p.m.p./year) was comparable with that seen in other European countries: 34, 39, 63 and 86 cases p.m.p./year [2–4,11]. The distribution pattern of renal diagnosis also corresponded to other European series. IgAN was the most frequent disease among all biopsied patients as well as among primary GN, reaching an incidence of 11.2 p.m.p./year. A similar frequency has been also reported from Italy, 8.4 p.m.p./year [1], but is higher in France at 25–31 p.m.p./year [4], and lower in Spain at 7.9 p.m.p./year [3], Denmark at 1.8 p.m.p./year [2] and Central Kentucky, USA at 5.4 p.m.p./year [13]. The true incidence of IgAN is probably higher since another 11.3% of primary GN was diagnosed as MesGN, and not all these cases were evaluated by immunofluorescence.

Our incidence of unclassified GN is also higher (4.1%) than reported in other studies, e.g. 0.9% in Korea [5] and 1.2% in Japan [6]; data are not available in European registries.

GN induced by immunological factors was the most frequent among secondary GNs. The incidence of SLE was relatively high, and comparable data have been reported from Italy [1] with 2.6 p.m.p./year and Spain [3] with 5.6 p.m.p./year. AM was the most frequent dysgammaglobulinaemia-associated GN, especially in the elderly, as has been repeatedly reported by other investigators [17].

Among those with nephrotic proteinuria, MGN, IgAN, MCD and FSGS were the most frequent diagnoses in CRRB. With the exception of IgAN, this is in accordance with other experience [1–4]. IgAN was present in a similar percentage of adult nephrotic syndrome patients (14%) in the report of Haas *et al*. [14], while others found lower frequencies, 8 [15] and 2.4% [1]. Since 1999 when the serum albumin level was recorded, the incidence of nephrotic syndrome among IgAN patients decreased to only 6.5%, indicating a large proportion of IgAN patients with nephrotic range proteinuria but without frank nephrosis. This figure is very similar to that (6.0%) reported from Korea [5]. This may be because IgAN patients often undergo renal biopsy at a more advanced stage of disease.

Persistent urinary abnormalities represented the second most frequent clinical syndrome (36.2%), rather higher than that observed in Italy (30.8%) [1] but much lower than reported from Japan (48.1%) [6].

IgAN was the disease diagnosed predominantly in this group (23.1%), similar to data from Italy (29.8%); however, in our study, the next most common was SLE (7.4%), which was quite different from the Italian experience (28.2%).

The presence of nephritic syndrome is usually taken as a sign of acute renal inflammation. It is therefore not surprising that IgAN, NV and CGN were found commonly among those with nephritic symdrome. However, it is of interest that NAS, FSGS and also DN were recorded frequently among those with nephritic syndrome even though haematuria is not usually regarded as a typical feature of these diseases. The experience from Italy [1] was quite different, IgAN representing 14.0% of patients presenting with nephritic syndrome but SLE 20.1 and PEGN 16.1%.

IgAN and TBM glomerulopathy were the most frequent diagnoses in patients with isolated haematuria, which is not significantly different from other reports in Europe [1–3] and elsewhere [5,6].

Concerning diabetic patients, it is not surprising that the incidence of DN was low, since isolated proteinuria in patients with long-standing diabetes is not an indication for renal biopsy, and those diabetics who have a renal biopsy are likely to have atypical clinical features suggesting a cause other than DN. However, since 1999, we observed an apparent doubling of the incidence of DN [10], which we ascribe to local policies on the indications for renal biopsy. Recently, the influence of varying renal biopsy policies has been stressed by Mazzucco *et al*. [16]. Since 1999, diabetic patients represented 12.2% of all adult biopsies but about half had non-diabetic renal disease. In this group, the percentages of low-grade proteinuria, normal renal function, the number of patients on haemodialysis and mean age were significantly higher compared with those with DN. There was a surprisingly high number of diabetic patients with renal vasculitis (9.5%). On the other hand, in 1999–2000, a high percentage of microhaematuria (66%) was also found among patients with DN; comparable data from other registries in this respect are not available.

With regard to post-biopsy complications, we recorded lower rates of clinically serious complications compared with the experience of other authors [17] who reported gross haematuria in 5–7% or severe perirenal haemorrhage in 0.2–1.4%. The presence of hypertension and renal insufficiency was related to the occurrence of haemorrhage with hypotension. Contrary to other reports [18], we did not observe a significant decrease in complication rate when the biopsy gun was used, but we are not aware whether a thinner needle gauge was used in the gun. Although some authors [19] did not observe any serious complications using the biopsy gun, we believe that despite these newer devices, the risk of renal biopsy as an invasive procedure remains. USG-guided biopsy was predominant in our series, particularly among children, but still a large number biopsies were performed under X-ray guidance despite the wide availability of USG. This may be the result of local policy, perhaps influenced by good personal experience with particular techniques. USG guidance was also reported as predominant (~85%) in Europe [20].

CRRB continues to collect data, and a number of new features are planned: (i) the CRRB records are now available on the Internet (www.nefrol.cz); (ii) 10 year follow-up data are being collected, particularly in patients with GN; and (iii) comparison of CRRB records is being made with the Czech Registry of Renal Replacement Therapy, which uses ESRD as the identifier.

In conclusion, CRRB, which includes renal biopsies of the native kidney performed in almost all Czech renal units over a period of 7 years, represents an important contribution to the epidemiology of renal diseases in the Czech Republic, and permits a valuable comparison with other renal biopsy registries worldwide. Our results show that the frequency of the main groups of renal diseases and the distribution pattern of different forms of GN change only slightly over a long period. Two groups of disease were particularly frequent: primary GN (59.8%) and secondary GN (25.6%) which showed incidences of 32.4 and 13.8 p.m.p./year, respectively. Particular attention should also be paid to TIN and vascular diseases, in which a significant percentage of patients showed renal insufficiency. This report is intended to serve as a source for nephrologists, researchers and health care providers to stimulate new analysis and investigation, to improve treatment of renal diseases, to design nationwide trials, and to help national and regional governments to develop protocols for preventive medicine.

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