

Original Article

Clinicopathologic correlations of renal pathology in the adult population of Poland

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*The full list of participants is presented in Appendix 1.

ABSTRACT

Background. This is the first report on the epidemiology of biopsy-proven kidney diseases in Poland.

Methods. The Polish Registry of Renal Biopsies has collected information on all ($n = 9394$) native renal biopsies performed in Poland from 2009 to 2014. Patients' clinical data collected at the time of biopsy, and histopathological diagnoses were used for epidemiological and clinicopathologic analysis.

Results. There was a gradual increase in the number of native renal biopsies performed per million people (PMP) per year in Poland in 2009–14, starting from 36 PMP in 2009 to 44 PMP in 2014. A considerable variability between provinces in the mean number of biopsies performed in the period covered was found, ranging from 5 to 77 PMP/year. The most common renal biopsy diagnoses in adults were immunoglobulin A nephropathy (IgAN) (20%), focal segmental glomerulosclerosis (FSGS) (15%) and membranous glomerulonephritis (MGN) (11%), whereas in children, minimal change disease (22%), IgAN (20%) and FSGS (10%) were dominant. Due to insufficient data on the paediatric population, the clinicopathologic analysis was limited to patients ≥ 18 years of age. At the time of renal biopsy, the majority of adult patients presented nephrotic-range proteinuria (45.2%), followed by urinary abnormalities (38.3%), nephritic syndrome (13.8%) and isolated haematuria (1.7%). Among nephrotic patients, primary glomerulopathies dominated (67.6% in those 18–64 years of age and 62.4% in elderly patients) with leading diagnoses being MGN (17.1%), FSGS (16.2%) and IgAN (13.0%) in the younger cohort and MGN (23.5%), amyloidosis (18.8%) and FSGS (16.8%) in the elderly cohort. Among nephritic patients 18–64 years of age, the majority (55.9%) suffered from primary glomerulopathies, with a predominance of IgAN (31.3%), FSGS (12.7%) and crescentic GN (CGN) (11.1%). Among elderly nephritic patients, primary and secondary glomerulopathies were equally common (41.9% each) and pauci-immune GN (24.7%), CGN (20.4%) and IgAN (14.0%) were predominant. In both adult cohorts, urinary abnormalities were mostly related to primary glomerulopathies (66.8% in younger and 50% in elderly patients) and the leading diagnoses were IgAN (31.4%), FSGS (15.9%), lupus nephritis (10.7%) and FSGS (19.2%), MGN (15.1%) and pauci-immune GN (12.3%), respectively. There were significant differences in clinical characteristics and renal biopsy findings between male and female adult patients.

Conclusions. The registry data focused new light on the epidemiology of kidney diseases in Poland. These data should be used in future follow-up and prospective studies.

Keywords: annual incidence of renal biopsy, epidemiology of kidney diseases, glomerular diseases, renal biopsies registry, renal biopsy diagnoses

INTRODUCTION

Until recently, the epidemiological data on the incidence of kidney diseases in the Polish population were mostly based on the information provided by dialysis centres and Poltransplant, the

central institution responsible for the organization of solid organ transplantation in Poland, which cumulates data on patients awaiting kidney transplantation. Most of the data did not include biopsy-based diagnoses, both due to such information not being covered in clinical charts and because not all patients with end-stage renal failure have had a native kidney biopsy. Consequently, most of the data on the epidemiology of kidney diseases available in Poland have not been verified in studies based on renal biopsy findings. The Polish Registry of Renal Biopsies (PRRB) was founded in 2009, on the initiative of the Polish Society of Nephrology, with the aim of providing access to more reliable, biopsy-based data on the incidence of various types of nephropathies in Poland. The aims of the PRRB are (i) to establish the number of renal biopsies/per million people (PMP) in each of individual regions and in the country as a whole, (ii) to study the epidemiology of renal disease based on renal-biopsy findings and (iii) to analyse clinicopathologic correlations of kidney diseases in Poland.

MATERIALS AND METHODS

Population and variables studied

We recorded one questionnaire filled with clinical and microscopic data for each native kidney biopsy. Each questionnaire had been initially completed by a nephrologist and subsequently sent to a pathologist together with a biopsy sample. The list of variables to be defined in the questionnaire included the name of the medical institution performing the biopsy; patient's date of birth, gender, body weight and height; data on the previous kidney biopsy in this patient; data on familial disease occurrence; the duration of clinical signs suggestive of renal disease, type of clinical syndrome [nephrotic syndrome, nephritic syndrome, haematuria, chronic kidney disease (CKD), acute kidney injury (AKI)]; arterial hypertension (defined as blood pressure $>140/90$ mmHg), serum creatinine concentration, estimated glomerular filtration rate [eGFR; determined using the Modification of Diet in Renal Disease (MDRD) equation]; urine protein loss per day; leukocyturia; diabetes (type, duration) and current pharmacotherapy (immunosuppressants including steroids, antihypertensive treatment and the use of potentially nephrotoxic drugs). Additionally, the questionnaire contained data provided by the pathologist evaluating the biopsy, including histopathological diagnosis and types of microscopic techniques used (light microscopy, immunofluorescence and/or electron microscopy). All 11 pathologists participating in the study used the same agreed-upon list of pathologic recognitions, presented in Table 1.

Additionally, histological diagnoses were divided into five groups and the categorization was based on the approach proposed by others [1, 2]: (i) primary (not associated with systemic diseases) glomerulopathies such as minimal change disease (MCD), focal segmental glomerulosclerosis (FSGS), membranous glomerulonephritis (MGN), minor glomerular abnormality (MGA), immunoglobulin A nephropathy (IgAN), mesangial proliferative glomerulonephritis (MsPGN), membranoproliferative glomerulonephritis (MPGN), crescentic glomerulonephritis (CGN) and diffuse endocapillary

Table 1. The list of kidney biopsy diagnoses^a

Type of nephropathy	Diagnoses
Glomerulopathy	Minor glomerular abnormality (MGA), unclassified glomerular lesions, minimal change disease (MCD), IgM nephropathy, C1q nephropathy, focal segmental glomerulosclerosis (FSGS), nodular glomerulosclerosis, membranous glomerulonephritis (MGN), IgA nephropathy (IgAN), diffuse endocapillary glomerulonephritis (GN), acute post-infectious GN with humps, focal segmental GN (not IgAN, lupus GN, C1q GN, etc), crescentic (crescents in >50% of glomeruli) GN types I, II and III (CGN), membranoproliferative GN (MPGN) types I and III, dense deposits disease, C3 GN, mesangioproliferative GN (not IgAN, lupus GN, C1q GN, etc), thin basement membrane disease (TBMD), glomerulopathy in Alport syndrome, fibrillary GN, immunotactoid glomerulopathy, fibronectin glomerulopathy, Waldenstrom macroglobulinemia, light and/or heavy chain deposition disease (LCDD/HCCDD), collagenofibrotic nephropathy, amyloidosis, diabetic kidney disease (DKD), Fabry disease, lecithin cholesterol acyltransferase deficiency, lipoprotein glomerulopathy, hepatic glomerulosclerosis, sickle cell glomerulopathy, lupus nephritis (LN)
Tubulointerstitial nephropathy	Acute tubular injury/necrosis, light chain tubulopathy, cast nephropathy, myoglobin/hemoglobin cast nephropathy, gout nephropathy, nephrocalcinosis, phosphate nephropathy, oxalosis, cystinosis, acute nondestructive tubulointerstitial nephritis (TIN), chronic non-destructive TIN, acute pyelonephritis, chronic pyelonephritis/reflux nephropathy, xanthogranulomatous or malacoplakia/megalocytic TIN, analgetic nephropathy, granulomatous TIN, nephronophthisis/medullary cystic disease, IgG4-related disease
Vasculopathy	Thrombotic microangiopathy (TMA), arterionephrosclerosis (hypertensive nephrosclerosis and aging nephropathy) (ANS), renal artery stenosis atrophy, atheroembolization (cholesterol embolization), calcineurin inhibitor toxicity, arteritis
Other	Normal kidney morphology (NM), end-stage renal disease (ESRD)

^aThe table contains morphological diagnoses that occurred at least once in the study group.

glomerulonephritis (DEGN); (ii) secondary glomerulopathies: (a) immune-mediated GN such as lupus nephritis (LN), Henoch-Schönlein purpura (HSP), antineutrophil cytoplasmic antibodies (ANCA)-positive vasculitis-related pauci-immune necrotizing focal segmental or crescentic GN, anti-glomerular basement membrane-mediated GN; (b) glomerulopathies related to paraproteinemias such as amyloidosis, light/heavy chain deposition disease, cryoglobulinemic GN; (c) GN related to infectious diseases (acute post-infectious GN, shunt GN and others); (d) glomerulopathies caused by metabolic diseases such as diabetic kidney disease (DKD); (e) hereditary nephropathies such as thin basement membrane disease (TBMD) or glomerulopathy in Alport syndrome; (iii) tubulointerstitial diseases such as various forms of tubulointerstitial nephritis (TIN) and acute tubular injury/necrosis; (iv) vascular diseases such as arterionephrosclerosis (ANS; hypertensive nephrosclerosis and aging nephropathy), arteritis and thrombotic microangiopathy (TMA) in the course of various systemic disorders including haemolytic uraemic syndrome, thrombotic thrombocytopenic purpura, malignant hypertension and scleroderma and (v) others, including unclassified nephropathies, end-stage renal disease (ESRD) of undetermined origin, miscellaneous rare nephropathies and normal kidney morphology (NM).

The study was approved by the Ethical Committee of the Medical University of Warsaw and complied with the provisions of the Good Clinical Practice Guidelines and the Declaration of Helsinki.

Statistical methods

The statistical analysis was performed using the SAS 9.4 software for Windows. Quantitative variables were summarized by medians (ranges), because the parameters did not follow a normal distribution, and they were compared using the Wilcoxon rank-sum test. Qualitative variables were compared using the χ^2 -test and Fisher's exact test, respective to the sample size. P-values <0.05 were considered statistically significant.

RESULTS

In 2009–14, the years covered by the study, a total of 9394 renal biopsy records were referred to the PRRB. Biopsies were performed in 8443 patients. A total of 951 records were identified as re-biopsies (second or third), 542 of which were considered non-diagnostic (lack of sufficient tissue sample for evaluation). Among the non-diagnostic biopsies, 106 were repeated within 3 months. All these 106 biopsies were excluded from clinicopathologic analysis and calculations of the number of biopsies PMP/year. In patients with two (or more) native kidney biopsies that were separated by periods of >3 months, both (all) biopsies were included in the study.

In 2009–14, the total Polish population was ~38.5 million, mostly Caucasians (>98%), with a male:female ratio of 1.2. In 94% of cases, kidney biopsy was carried out for disease identification and in 6% for monitoring of disease evolution or previous diagnosis verification. The mean number of renal biopsies performed PMP per year in Poland for the whole period studied was 40 (36, 40, 39, 41, 43 and 44 in 2009, 2010, 2011, 2012, 2013 and 2014, respectively), ranging from 5 PMP/year in the Subcarpathian Province to 77 PMP/year in the Podlaskie Province (Figure 1).

There were 74 renal centres performing native renal biopsies in Poland in the period studied. In eight of these the number of native kidney biopsies performed in 2009–14 was >300 (maximum 577), in 25 it was between 100 and 300 and there were 13 nephrology units where the number of biopsies was <10.

A total of 1939 (21%) biopsies were performed in patients <18 years of age, 6394 (68.7%) in those 18–64 and 955 (10.3%) in elderly individuals (defined as ≥ 65 years of age [3]). In a high proportion of patients <18 years of age, the clinical and histopathologic data were missing, so in the paediatric cohort the analysis had to be limited and included only 384 individuals. In patients ≥ 18 years of age the quality of data collected allowed for more profound analysis, so the adult cohort was studied as a whole, but also separate analyses in two age groups (18–64 and ≥ 65 years) were performed.

The best option in kidney tissue sample examination is the performance of light microscopy (LM), immunofluorescence (IF) and electron microscopy (EM) evaluation, but not all biopsies were processed that way, depending on the sample adequacy and decisions of individual pathologists. In the majority of cases (58.9%), LM and IF but no EM examination were performed. All three types of microscopic examination (LM + IF + EM) were done in 34.1% of cases. The histological examination was limited to LM in 4.5% of biopsies, whereas other variants (LM + EM, IF + EM, only IF, only EM) accounted for 2.5% of cases. All biopsies in which evaluation was limited to LM were excluded from the analysis with the exception of amyloidosis, whose recognition may be solely based on LM findings.

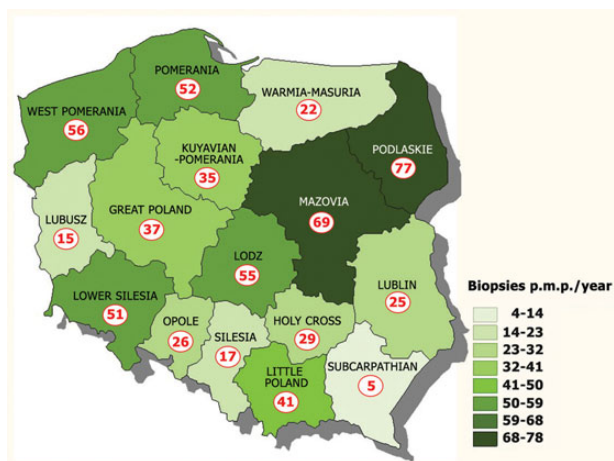


FIGURE 1: Number of native renal biopsies PMP/year in each of 16 Polish provinces (mean values for years 2009–14).

Clinical characteristics and most common renal biopsy diagnoses in adult and paediatric patient populations

The analysis of data retrieved from questionnaires showed a major inconsistency in the way nephrologists define nephrotic and nephritic syndromes, as well as AKI and CKD. Using the clinical and laboratory characteristics provided, we recognized patients with nephrotic range proteinuria (protein loss >3.5 g/day), nephritic syndrome (no proteinuria, or protein loss ≤3.5 g/day accompanied by haematuria, arterial hypertension and GFR <60 mL/min/1.73 m²), urinary abnormalities (persistent non-nephrotic proteinuria with or without haematuria) and isolated haematuria. Among adults the most frequent clinical syndrome at the time of biopsy was nephrotic range proteinuria (45.2%), followed by urinary abnormalities (38.3%), nephritic syndrome (13.8%) and isolated haematuria (1.7%). In the whole adult population studied there were only 60 adult patients with no proteinuria or haematuria and all of these patients were anuric at the time the biopsy was performed.

At the time of biopsy, 67.1% of adult patients had hypertension and 9.3% were diabetic. In 5% of adult patients renal disease in first- and/or second-degree relatives was reported. During the pre-biopsy follow-up, steroid treatment was administered in 21% and other immunosuppressive treatment in 8% of patients. More detailed clinical characteristics in patients 18–64 years of age and in elderly individuals (≥65 years) are presented in Table 2.

In the adult cohort, among the main diagnostic categories, the most prevalent were primary glomerulopathies (63.2%) followed by secondary ones (25.4%), the category of ‘other’ (9.2%), tubulointerstitial (2.4%) and vascular diseases (2.0%). More detail of the diagnostic entities is presented in Figure 2.

Table 2. Clinical characteristics at the time of biopsy in patients 18–64 years of age and in elderly individuals

	Younger adults (18–64 years) (n = 6394)	Elderly (≥65 years) (n = 955)	P-value
Male:female ratio	1.2:1	1.1:1	0.150
Age of disease onset (years), median (range)	38 (1–64)	69 (19–88)	<0.0001
Pre-biopsy follow-up			
<3 months	48.6%	54.6%	0.0005
>3 months	51.5%	45.4%	
Biopsy cause (disease recognition/monitoring of disease evolution)	93.4%/6.6%	97.9%/2.1%	<0.0001
Proteinuria (g/day), median (range)	3.0 (0–40)	4.1 (0–30)	<0.0001
Proteinuria	97.1%	97.4%	
Nephrotic	43.2%	58.7%	<0.0001
Non-nephrotic	53.9%	38.7%	
Haematuria	56.5%	48.0%	<0.0001
eGFR (mL/min/1.73 m ²), median (range)	66.9 (0–272)	38.2 (2.5–171.6)	<0.0001
eGFR ≥60 mL/min/1.73 m ²	55.4%	27.2%	
eGFR 30–59 mL/min/1.73 m ²	24.3%	33.1%	<0.001
eGFR 15–29 mL/min/1.73 m ²	12.1%	21.9%	
eGFR <15 mL/min/1.73 m ²	8.1%	17.8%	
Family history of renal diseases	5.3%	1.3%	<0.0001
The history of previous renal biopsies	15.3%	7.3%	<0.0001
Hypertension	65.0%	80.6%	<0.0001
Diabetes	7.8%	19.5%	<0.0001
Duration of diabetes (years), median (range)	5 (0–41)	8 (0–40)	0.264
Dialysis during pre-biopsy follow-up	4.4%	8.3%	<0.0001
Steroid treatment during pre-biopsy follow-up	20.7%	16.4%	0.004
Other immunosuppressive treatment during pre-biopsy follow-up	8.1%	3.8%	<0.0001

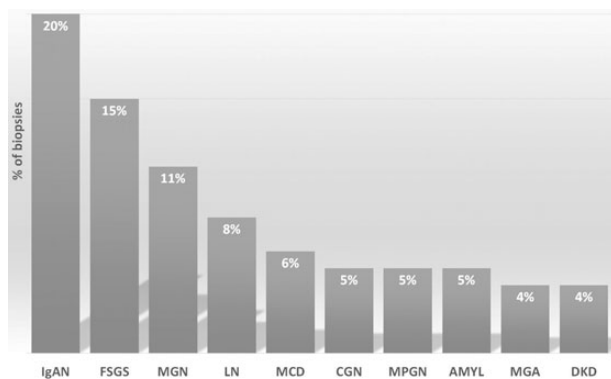


FIGURE 2: Ten most common renal biopsy diagnoses in the adult population studied. Re-biopsies excluded. AMYL, amyloidosis; CGN, crescentic glomerulonephritis; DKD, diabetic kidney disease; FSGS, focal segmental glomerulosclerosis; IgAN, IgA nephropathy; LN, lupus nephritis; MCD, minimal change disease; MGA, minor glomerular abnormalities; MGN; membranous glomerulonephritis; MPGN, membranoproliferative glomerulonephritis.

For patients <18 years of age, information on clinical disease presentation, kidney biopsy diagnosis and types of microscopic examination performed was available in only 384 patients. In this paediatric cohort there was a slight male predominance, with a male:female ratio of 1.1. At the time of biopsy, 87.7% of patients had proteinuria, with a median protein loss of 1.8 g/day (range 0–30). The most common clinical disease presentations included urinary abnormalities (55.0%), followed by nephrotic-range proteinuria (30.0%), isolated haematuria (6.0%) and nephritic syndrome (3.0%). Hypertension was present in 23.4% of paediatric patients analysed. Regarding the renal biopsy findings, the most common were primary glomerulopathies (63.3%), followed by secondary ones (22.1%), the category of ‘other’ (10%, due to a relatively high percentage of NM and unknown), tubulointerstitial diseases (3.4%) and vascular diseases (1.0%). The distribution of the most common diagnostic entities in a cohort of 384 paediatric patients is presented in Figure 3.

Selected clinical and laboratory data related to most commonly occurring diagnostic entities in adult patients are shown in Table 3.

In both adult cohorts, primary glomerulopathies were more common than secondary ones. In patients 18–64 years of age, the most frequent biopsy-proven diseases were IgAN, FSGS and MGN, whereas in those ≥65 years of age, MGN, FSGS and amyloidosis were most prevalent. The spectrum of renal biopsy diagnoses in elderly and younger adult patients is shown in Table 4.

In comparison to younger patients, the elderly cohort was characterized by a higher prevalence of secondary glomerulopathies. Among individual diagnostic entities, MGN, amyloidosis, pauci-immune GN, CGN, DKD, TIN and MsPGN were more common in elderly individuals than in those 18–64 years of age. In turn, among younger adult patients (ages 18–64 years) the frequency of primary glomerulopathies was higher than in the elderly group. Among individual biopsy-based diagnoses, IgAN, LN and TBMD occurred more often among patients 18–64 years of age than in elderly patients.

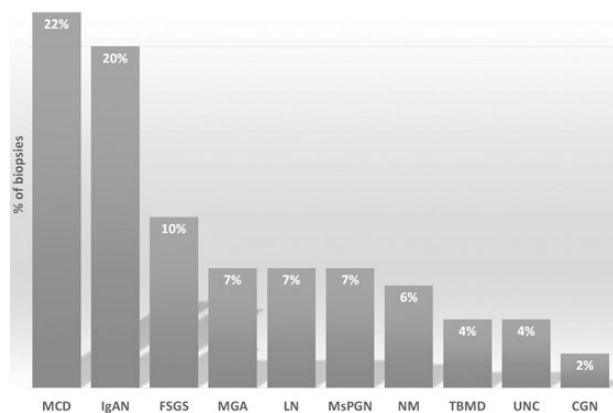


FIGURE 3: Ten most common renal biopsy diagnoses in the paediatric cohort studied. Re-biopsies excluded. CGN, crescentic glomerulonephritis; FSGS, focal segmental glomerulosclerosis; IgAN, IgA nephropathy; LN, lupus nephritis; MCD, minimal change disease; MGA, minor glomerular abnormalities; MGN; membranous glomerulonephritis; MsPGN, mesangioproliferative glomerulonephritis; NM, normal morphology; TBMD, thin basement membrane disease; UNC, unclassified.

Gender differences in clinical characteristics of kidney disease and in the frequency of various renal biopsy diagnoses

Compared with male patients, the female cohort was characterized by longer pre-biopsy follow-up (<3 months in 22.6 versus 30.2%; $P < 0.0001$), lower proteinuria (3.0 versus 3.5 g/day; $P < 0.0001$), less hypertension (60.6 versus 71.9%; $P < 0.0001$), less diabetes (8.4 versus 10.0%; $P = 0.003$), lower eGFR (67.1 versus 59.9 mL/min/1.73 m²; $P < 0.0001$), more steroid (22.6 versus 16.3%; $P < 0.0001$) and other immunosuppressive treatment during pre-biopsy follow-up (8.6 versus 6.6%; $P = 0.003$). Primary glomerulopathies were more common in men, whereas secondary ones prevailed among female patients. Compared with males, the female cohort was characterized by a higher prevalence of LN, amyloidosis and TBMD. Among male individuals, occurrences of IgAN, MGN, CGN, MPGN, DKD and ANS were more common. The distribution of various biopsy-based diagnoses in both sexes is presented in Table 5.

Clinical manifestation of kidney disease in patients 18–64 years of age and in elderly individuals

Proteinuria was present in almost all adult patients (97.4% of the elderly and 97.1% of younger adult patients) in the study. In contrast to the younger adult cohort, in which non-nephrotic proteinuria dominated (53.9%; $P < 0.0001$), a majority among elderly patients presented with nephrotic-range proteinuria (58.6%). In both the younger and elderly adult cohorts, nephrotic-range proteinuria was most commonly associated with primary glomerulopathies (67.6 and 62.4%, respectively). A comparison between both adult cohorts revealed that IgAN, LN and CGN were more common among nephrotic patients 18–64 years of age, whereas MGN and amyloidosis occurred more frequently in nephrotic individuals ≥65 years of age (Table 6).

Table 3. Clinical characteristics of selected nephropathies in adult individuals, re-biopsies excluded

	<i>n</i> (%)	Age (years) at recognition, median (range)	Gender (% male)	HT (%)	eGFR (mL/min/1.73 m ²), median (range)	eGFR <60 mL/min/1.73 m ² (%)	eGFR ≥60 mL/min/1.73 m ² (%)	HD (%)	Steroid treatment (%)	Other IS (%)	Nephrotic syndrome (%)	Nephritic syndrome (%)	UAB (%)	IH (%)
IgAN	1330 (20.0)	38 (19–84)	62.4	67.0	67.1 (0.4–245.0)	43.3	56.7	1.2	7.8	2.3	26.4	18.9	52.9	1.8
FSGS	997 (15.0)	47 (19–87)	55.1	71.5	62.7 (3.0–272.0)	45.6	54.4	1.9	16.5	7.6	47.7	11.2	40.6	0.5
MGN	744 (11.2)	53 (19–86)	63.5	71.4	84.8 (8.6–272.0)	22.1	77.9	0.5	14.4	6.7	73.4	1.6	25.3	0
LN	559 (8.4)	34 (19–86)	21.0	59.0	77.5 (4.5–198.0)	39.0	61.0	2.7	59.9	24.1	41.1	11.2	46.0	1.5
MCD	368 (5.5)	35 (19–87)	51.5	49.6	94.1 (6.3–252.0)	21.5	78.5	11.3	22.2	5.7	80.3	1.8	16.9	0
Pauci-immune GN	366 (5.5)	58 (19–82)	55.1	71.4	16.6 (2.5–156.6)	87.5	12.5	23.2	37.3	12.0	24.2	36.3	36.3	0.8
CGN	359 (5.4)	57 (19–82)	60.7	68.2	13.7 (2.5–156.0)	93.6	6.4	29.4	29.4	9.1	31.6	37.4	29.6	0.5
MPGN	306 (4.6)	50 (19–80)	57.4	75.1	53.7 (2.7–224.0)	55.5	44.5	3.7	13.1	6.4	64.2	11.6	22.6	0.5
AMYL	299 (4.5)	61 (22–85)	43.8	53.2	62.5 (5.7–250.0)	47.7	52.3	4.0	29.9	7.1	76.5	4.0	19.5	0
UNC	299 (4.5)	48 (19–86)	48.7	71.2	50.0 (3.0–219.2)	58.3	41.7	8.3	15.8	5.1	39.2	20.3	39.6	2.7
MGA	253 (3.8)	43 (19–82)	48.5	52.6	85.8 (7.3–182.6)	27.8	72.2	0.4	13.2	3.7	27.6	7.3	53.3	11.5
DKD	246 (3.7)	58 (22–88)	61.1	91.5	44.1 (6.4–152.0)	68.0	32.0	2.7	5.2	1.0	76.4	6.7	17.4	0
MsPGN	180 (2.7)	42 (19–77)	57.0	59.6	70.0 (6.0–182.0)	42.0	58.0	4.5	14.0	1.3	36.5	19.8	43.7	0
TIN	126 (1.9)	52 (19–84)	54.3	61.2	18.0 (3.1–219.0)	96.9	3.1	17.0	12.1	1.0	14.5	28.8	47.5	0
NM	96 (1.5)	36 (19–77)	43.8	40.9	88.5 (6.8–185.6)	23.6	76.4	2.6	15.3	9.7	13.0	9.5	54.8	21.4
TMA	67 (1.0)	42 (20–88)	42.9	75.4	24.6 (2.1–107.0)	82.1	17.9	23.3	29.8	10.7	42.9	22.2	33.3	0
ANS	47 (0.7)	49 (30–80)	75.0	80.1	38.1 (5.8–125)	84.9	15.1	7.7	8.6	2.9	41.9	22.2	29.6	0
Primary GP	4009 (60.3)	44 (19–87)	58.8	66.9	711.2 (0.4–272.3)	38.9	61.1	2.0	13.0	4.9	48.0	11.7	38.8	1.5
Secondary GP	1609 (24.2)	52 (19–88)	41.8	66.0	49.4 (2.5–250.4)	57.5	42.5	8.7	36.2	12.5	48.2	15.4	34.4	1.5
TI diseases	153 (2.3)	52 (19–85)	56.9	61.1	18 (3.1–218.9)	95.9	4.1	20.9	12.5	1.6	14.0	27.8	47.2	0
Vascular diseases	134 (2.0)	45 (20–88)	56.1	76.6	34.1 (2.1–124.6)	83.2	16.8	15.9	21.5	7.5	42.1	22.4	31.8	0

AMYL, amyloidosis; ANS, angioneurotic edema; CGN, crescentic glomerulonephritis; DKD, diabetic kidney disease; FSGS, focal segmental glomerulosclerosis; GN, glomerulonephritis; GP, glomerulopathy; HD, hemodialysis; HT, hypertension; IgAN, IgA nephropathy; IH, isolated haematuria; IS, immunosuppression; LN, lupus nephritis; MCD, minimal change disease; MGN, membranous glomerulonephritis; MPGN, membranoproliferative glomerulonephritis; MsPGN, mesangiocapillary glomerulonephritis; NM, normal morphology; TI, tubulointerstitial; TMA, thrombotic microangiopathy; UAB, urinary abnormalities; UNC, unclassified lesions.

Table 4. Renal biopsy diagnoses by age (the table encompasses only diagnoses that were made in at least 1% of biopsies in any of the two cohorts studied)

Diagnosis	Younger adults (18–64 years) (n = 5785)	Elderly (≥65 years) (n = 864)	P-value
IgAN	21.8%	8.3%	<0.0001
FSGS	15.1%	14.6%	0.657
MGN	10.3%	16.9%	<0.0001
LN	9.3%	2.3%	<0.0001
MCD	5.6%	4.8%	0.365
CGN (types I, II, III)	4.9%	8.3%	0.001
Pauci-immune GN	4.9%	9.4%	<0.0001
CGN (type III)	3.1%	6.2%	<0.0001
Focal segmental GN	1.8%	3.2%	0.014
MGA	4.0%	2.6%	0.492
MPGN	4.6%	4.5%	1.000
Unclassified lesions	4.5%	4.8%	0.651
Diabetic kidney disease	3.4%	6.1%	0.0003
Pure DKD	3.0%	5.0%	0.0002
DKD associated with NDKD	0.4%	1.1%	
AMYL	3.2%	12.8%	<0.0001
MsPGN	2.8%	1.7%	0.079
TIN	1.8%	2.7%	0.073
ESRD	1.7%	2.2%	0.315
TBMD	1.0%	0.1%	0.007
TMA	1.1%	0.6%	0.263
ANS	0.7%	1.0%	0.368
NM	1.5%	1.0%	0.272
Primary glomerulopathies	64.7%	53.6%	<0.0001
Secondary glomerulopathies	24.1%	34.0%	<0.0001
Tubulointerstitial diseases	2.2%	3.7%	0.013
Vascular diseases	2.0%	2.1%	0.893
Other	8.2%	8.2%	0.539

Re-biopsies excluded.

AMYL, amyloidosis; ANS, arterionephrosclerosis (hypertensive nephrosclerosis and aging nephropathy); CGN, crescentic glomerulonephritis; DKD, diabetic kidney disease; ESRD, end-stage renal disease; FSGS, focal segmental glomerulosclerosis; IgAN, IgA nephropathy; LN, lupus nephritis; MCD, minimal change disease; MGA, minor glomerular abnormalities; MGN, membranous glomerulonephritis; MPGN, membranoproliferative glomerulonephritis; MsPGN, mesangioproliferative GN; NM, normal morphology; TIN, tubulointerstitial nephritis; NDKD, non-diabetic kidney disease; TMA, thrombotic microangiopathy; TBMD, thin basement membrane disease.

Nephritic syndrome was present in 13.6% of patients ages 18–64 years and in 15.3% of elderly individuals. In patients 18–64 years of age, nephritic syndrome was most commonly related to primary glomerulopathies (55.9%), whereas among nephritic individuals ≥65 years of age the proportions of primary and secondary glomerulopathies were the same (41.9%). A comparison between both adult cohorts revealed that IgAN was more common among nephritic patients 18–64 years of age, whereas MGN and CGN occurred more frequently in nephrotic individuals ≥65 years of age (Table 7).

At the time of renal biopsy, urinary abnormalities were present in 40.4% of patients 18–64 years of age and in 24.0% of those ≥65 years. In a majority of patients 18–64 years of age and in a half of elderly individuals, urinary abnormalities were associated with primary glomerulopathies. IgAN, FSGS and LN were most prevalent among younger adults presenting

Table 5. Renal biopsy diagnoses by gender

Diagnosis	Females (n = 3085)	Males (n = 3564)	P-value
IgAN	16.3%	23.3%	<0.0001
LN	14.3%	3.3%	<0.0001
MGN	8.8%	13.2%	<0.0001
FSGS	14.6%	15.4%	0.390
Pauci-immune GN	5.3%	5.6%	0.653
CGN (type III)	3.4%	3.6%	0.727
Focal segmental GN	1.9%	2.0%	0.855
Unclassified lesions	5.0%	4.1%	0.096
AMYL	5.3%	3.6%	0.001
CGN (types I, II, III)	4.6%	6.1%	0.009
MPGN	4.3%	4.9%	0.223
Diabetic kidney disease	3.1%	4.2%	0.256
Pure DKD	2.8%	3.7%	0.064
DKD associated with NDKD	0.4%	0.6%	
TBMD	1.4%	0.4%	<0.0001
ANS	0.4%	1.0%	0.006
Primary glomerulopathies	56.2%	69.2%	<0.0001
Secondary glomerulopathies	31.9%	19.7%	<0.0001
Tubulointerstitial diseases	2.2%	2.5%	0.451
Vascular diseases	1.9%	2.2%	0.467
Other	8.7%	7.9%	0.286

Re-biopsies excluded.

AMYL, amyloidosis; ANS, arterionephrosclerosis (hypertensive nephrosclerosis and aging nephropathy); CGN, crescentic glomerulonephritis; DKD, diabetic kidney disease; FSGS, focal segmental glomerulosclerosis; GN, glomerulonephritis; IgAN, IgA nephropathy; LN, lupus nephritis; MGN, membranous glomerulonephritis; MPGN, membranoproliferative glomerulonephritis; NDKD, non-diabetic kidney disease; TBMD, thin basement membrane disease.

urinary abnormalities, whereas in elderly patients with this clinical syndrome the most common diagnoses were FSGS, MGN and pauci-immune GN (12.3%) (Table 8).

Isolated haematuria was seen in only 1.8% of patients 18–64 years of age and was most commonly related to MGA (25.0%), IgAN (24.0%) and TBMD (13.0%). Only 0.7% of elderly individuals presented isolated haematuria, which was mainly associated with non-specific microscopic lesions best defined as MGAs.

Types of kidney disease in diabetic individuals

The percentage of diabetics among adult patients subjected to native kidney biopsy in Poland rose from 10.8% in 2009 to 17.5% in 2014. Among all 766 adult there were 267 (34.9%) patients with microscopic lesions typical of DKD (pure DKD in 30.3% and DKD associated with another type of kidney injury in 4.6% of cases). Among 35 patients whose renal biopsy revealed DKD associated with another form of kidney injury, the most common types of non-diabetic kidney disease (NDKD) were IgAN (25.7%), MGN (14.3%) and MPGN (14.3%). In 499 diabetic patients with no DKD, the most prevalent renal biopsy diagnoses were FSGS (17.4%), MGN (11.4%) and IgAN (10.7%).

DISCUSSION

We believe that we have a complete list of renal biopsies performed in Poland in 2009–14, so we were able to calculate the

Table 6. Distribution of renal biopsy diagnoses among elderly and younger adult patients with nephrotic-range proteinuria

Renal pathology	Nephrotic range proteinuria		<i>P</i> -value
	18–64 years (<i>n</i> = 2762)	≥65 years (<i>n</i> = 560)	
MGN	17.1%	23.5%	0.003
FSGS	16.2%	16.8%	0.767
IgAN	13.0%	6.4%	<0.0001
MCD	9.3%	6.7%	0.102
LN	9.1%	1.2%	<0.0001
MPGN	6.6%	5.5%	0.436
DKD	6.0%	8.7%	0.057
Pure DKD	5.2%	6.7%	0.050
DKD associated with NDKD	0.8%	2.0%	
AMYL	5.3%	18.8%	<0.0001
Unclassified lesions	4.1%	3.5%	0.675
CGN (types I, II, III)	3.7%	1.5%	0.022
Pauci-immune GN	3.1%	2.2%	0.421
CGN (type III)	1.9%	1.0%	0.297
Focal segmental GN	1.2%	1.2%	0.803
MGA	2.5%	1.5%	0.278
MsPGN	2.2%	1.7%	0.705
ESRD	1.7%	1.2%	0.665
TMA	1.0%	0.3%	0.236
ANS	0.4%	1.2%	0.054
Primary glomerulopathies	67.6%	62.4%	0.043
Secondary glomerulopathies	26.0%	32.4%	0.010
Tubulointerstitial diseases	0.6%	0.5%	1.000
Vascular diseases	1.4%	1.7%	0.649
Other	6.0%	6.0%	1.000

AMYL, amyloidosis; ANS, arterionephrosclerosis (hypertensive nephrosclerosis and aging nephropathy); CGN, crescentic glomerulonephritis; DKD, diabetic kidney disease; ESRD, end-stage renal disease; FSGS, focal segmental glomerulosclerosis; GN, glomerulonephritis; IgAN, IgA nephropathy; LN, lupus nephritis; MGA, minor glomerular abnormalities; MGA, minor glomerular abnormalities; MGN, membranous glomerulonephritis; MPGN, membranoproliferative glomerulonephritis; MsPGN, mesangioproliferative glomerulonephritis; NDKD, non-diabetic kidney disease; TMA, thrombotic microangiopathy.

number of biopsies PMP for the whole country and for each of its 16 provinces in the period studied. We were not able to count the incidence of different forms of renal biopsy diagnoses, as we did not have a complete list of histopathological findings in the paediatric cohort. The clinical description of paediatric patients was also insufficient, and we had to narrow the clinicopathologic analysis to the adult population.

The mean number of renal biopsies performed PMP per year in Poland rose from 36 in 2009 to 44 in 2014. This is comparable to annual renal biopsy rates reported in three other European national registries—Spain, Italy and Denmark—but it is lower than in the Czech Republic (61.6 in year 2011) and Scotland (126.3 in year 2006) [1, 2, 4–7]. We found considerable variability in renal biopsy rates among Polish provinces, with the lowest value of 5 PMP/year in the Subcarpathian Province and the highest (77 PMP/year) in the Podlaskie Province. In total, there were six provinces with annual biopsy rates of ≥50 and three with a rate <20. This discrepancy among provinces with regard to the number of native renal biopsies performed is possibly related to divergent opinions on indications for this procedure, but it might be also explained by patients being commonly relocated from small nephrology units to

Table 7. Distribution of renal biopsy diagnoses among elderly and younger adult patients with nephritic syndrome

Renal pathology	Nephritic syndrome		<i>P</i> -value
	18–64 years (<i>n</i> = 870)	≥65 years (<i>n</i> = 146)	
IgAN	31.3%	14.0%	0.0005
Pauci-immune GN	12.9	24.7%	0.006
CGN (type III)	8.4%	16.1%	0.032
Focal segmental GN	4.5%	8.6%	0.121
FSGS	12.7%	12.9%	1.000
CGN (types I, II, III)	11.1%	20.4%	0.017
LN	6.8%	5.4%	0.820
Unclassified lesions	6.6%	6.5%	1.000
MPGN	4.5%	2.2%	0.403
ESRD	3.7%	3.2%	1.000
MsPGN	3.3%	3.2%	1.000
DKD	2.1%	1.1%	0.703
Pure DKD	1.9%	1.1%	1.000
DKD associated with NDKD	0.2%	0	
TMA	1.8%	1.1%	1.000
MGA	1.6%	4.3%	0.097
ANS	1.2%	0	0.598
DEGN	1.2%	0	0.598
AMYL	1.0%	3.2%	0.110
MGN	0.6%	5.4%	0.003
LCDD/HCDD	0.6%	2.2%	0.171
Primary glomerulopathies	55.9%	41.9%	0.017
Secondary glomerulopathies	26.6%	41.9%	0.004
Tubulointerstitial diseases	3.1%	5.4%	0.349
Vascular diseases	3.1%	1.1%	0.492
Other	12.3%	10.8%	0.863

AMYL, amyloidosis; ANS, arterionephrosclerosis (hypertensive nephrosclerosis and aging nephropathy); CGN, crescentic glomerulonephritis; DKD, diabetic kidney disease; DEGN, diffuse endocapillary GN; ESRD, end-stage renal disease; FSGS, focal segmental glomerulosclerosis; GN, glomerulonephritis; IgAN, IgA nephropathy; LCDD/HCDD, light and/or heavy chain deposition disease; LN, lupus nephritis; MGN, membranous glomerulonephritis; MPGN, membranoproliferative glomerulonephritis; MsPGN, mesangioproliferative glomerulonephritis; NDKD, non-diabetic kidney disease; TMA, thrombotic microangiopathy.

the closest specialist hospital, which may be in a neighbouring province.

The majority of paediatric patients as well as those 18–64 years of age in the study presented with non-nephrotic proteinuria (57.7 and 53.9%, respectively), whereas nephrotic-range proteinuria was seen in 30.0 and 43.2% of these cohorts. Among elderly patients the most common clinical syndrome was nephrotic-range proteinuria (58.7%), which is concordant with other reports indicating nephrotic syndrome as the leading clinical syndrome in patients ≥65 years of age subjected to native kidney biopsy, or the second most common after AKI [7–14]. Unfortunately, the estimation of AKI prevalence among patients studied was found to be problematic. This is partly due to the fact that the clinical picture of AKI is very heterogeneous, which is reflected in the existence of various classification systems based on different diagnostic criteria, with the most recent one announced by Kidney Disease: Improving Global Outcomes in 2012 [15]. Our study covered the period between 2009 and 2014, the clinical data were provided by different renal centres and the descriptions of disease courses were not uniform and precise enough to allow for a reliable distinction between AKI, AKI superimposed on CKD and ‘pure’ CKD.

Table 8. Distribution of renal biopsy diagnoses among elderly and younger adult patients with urinary abnormalities

Renal pathology	Urinary abnormalities		P-value
	18–64 years (n = 2583)	≥65 years (n = 229)	
IgAN	31.4%	8.2%	<0.0001
FSGS	15.9%	19.2%	0.346
LN	10.7%	3.4%	0.004
MGN	7.2%	15.1%	0.002
MGA	5.9%	1.4%	0.023
Pauci-immune GN	4.8%	12.3%	0.001
CGN (type III)	2.7%	6.8%	0.011
Focal segmental GN	2.1%	5.5%	0.020
UNC	4.6%	4.8%	0.838
CGN	3.2%	8.2%	0.009
MPGN	2.8%	2.7%	1.0000
MsPGN	2.8%	0.7%	0.173
MCD	2.2%	4.1%	0.147
AMYL	1.9%	7.5%	0.0004
TBMD	1.7%	0.7%	0.507
DKD	1.7%	4.1%	0.048
Pure DKD	1.6%	3.4%	0.033
DKD associated with NDKD	0.1%	0.7%	
NM	1.5%	0.7%	0.450
ESRD	1.1%	4.1%	0.012
LCDD/HCDD	0.1%	1.4%	0.041
Primary glomerulopathies	66.8%	50.0%	<0.0001
Secondary glomerulopathies	23.1%	32.2%	0.019
Tubulointerstitial diseases	1.7%	7.5%	0.0001
Vascular diseases	1.8%	2.1%	0.810
Other	1.8%	2.1%	0.743

AMYL, amyloidosis; CGN, crescentic glomerulonephritis; DKD, diabetic kidney disease; ESRD, end-stage renal disease; FSGS, focal segmental glomerulosclerosis; GN, glomerulonephritis; IgAN, IgA nephropathy; LCDD/HCDD, light and/or heavy chain deposition disease; LN, lupus nephritis; MCD, minimal change disease; MGA, minor glomerular abnormalities; MGN, membranous glomerulonephritis; MPGN, membranoproliferative glomerulonephritis; MsPGN, mesangioproliferative glomerulonephritis; NDKD, non-diabetic kidney disease; NM, normal morphology; TBMD, thin basement membrane disease; UNC, unclassified lesions.

The most common renal biopsy diagnoses in the whole adult population studied were IgAN, FSGS and MGN, which is similar to the data collected by other European registries [1, 2, 4–6, 14]. Although the spectrum of diseases affecting people ≥65 years of age is the same as in the younger population, there are some distinct differences in the frequency of certain nephropathies between these two age groups. We found a higher prevalence of MGN, amyloidosis, pauci-immune GN, CGN, DKD, TIN and MsPGN in the elderly compared with individuals aged 18–64 years of age. In the younger adult cohort (ages 18–64 years), IgAN, LN and TBMD were more common. These observations are in line with other reports [13, 16–19].

In the group of 384 paediatric patients (<18 years of age) studied, the most common biopsy-based diagnoses were MCD (22%), IgAN (20%) and FSGS (10%), which is a distribution pattern quite similar to other European reports [2, 4, 6].

Amyloidosis was found to be the third most common histological diagnosis in elderly patients, with a prevalence of 12.8% compared with 3.2% in younger adult individuals ($P < 0.001$). These findings are in line with the reports of others [1, 12, 13, 17]. At the time of biopsy amyloidosis was typically manifested by nephrotic-range proteinuria (Table 6), but in as many as

19.5% of cases it presented with non-nephrotic proteinuria, fulfilling the criteria for urinary abnormalities (Table 8). This finding should be emphasized since many nephrologists would refrain from kidney biopsy in an elderly patient with mild proteinuria in whom concomitant amyloidosis-related cardiomyopathy can be easily misinterpreted as ischaemic heart disease.

In several published studies that analysed the prevalence of kidney biopsy-based diagnoses in elderly individuals, the percentage of cases in which age- and/or hypertension-related lesions were dominant was 1.6% in Chinese patients to 6.2% in a Japanese cohort [18–20]. The proportion of in our elderly group was 1.0% (Table 4), despite the fact that as many as 80.6% of patients ≥65 years of age suffered from hypertension (Table 2).

Our study revealed the predominance of males in biopsy-proven renal diseases in the adult population of Poland (Table 5), with the exception of LN, TBMD and, surprisingly, amyloidosis (4.7 versus 3.2% in males). The data reported were not complete with regard to the type of amyloidosis recognized, but we speculate that more common amyloid A amyloidosis occurring in a course of autoimmune diseases could be an explanation. Similar trends with regard to male predominance in most renal diseases have been reported by others [1, 4, 6, 21]. Clinically, females had lower proteinuria, less hypertension and less diabetes, but were more commonly treated with immunosuppression, which might also be related to the more prevalent occurrence of autoimmune diseases.

DKD is one of the most common renal biopsy diagnoses in the Polish adult population, with a prevalence of 4%. The reported proportion of DKD in renal biopsy registries ranges from 2.2 to 10% [6, 22, 23]. The percentage of diabetics among adult patients subjected to native kidney biopsy in Poland rose from 10.8% in 2009 to 17.5% in 2014. Almost 2/3 of them did not have DKD, but another type of kidney disease (NDKD). According to current policy, only those diabetic patients whose clinical symptoms are not typical for DKD are subjected to renal biopsy, so the cohort studied is not representative for the whole population of diabetics. Similar to other registries, the most common type of NDKD found to coexist with DKD was IgAN and the leading biopsy diagnosis among diabetic patients with no DKD was FSGS [2, 24, 25].

The PRRB is one of the largest native renal biopsy registries in Europe. We gathered information on all native renal biopsies performed in the years covered by the study, which allowed us to calculate the annual incidence of this procedure in Poland. The value of the study is attenuated by the fact that both clinical and histopathological data on the paediatric population were sparse.

There is not a single registry that includes all the medical and epidemiological information needed to fully describe the population of patients with kidney diseases. Our registry includes information on patients who have a kidney disease but whose renal function was preserved or only slightly decreased, as 50% of individuals 18–64 years of age and almost 30% of elderly patients had an eGFR ≥60 mL/min/1.73 m² at the time of biopsy. A merger of the PRRB with a registry encompassing patients at more advanced stages of CKD evolution who never had

a kidney biopsy would broaden our potential for further epidemiologic as well as follow-up and prospective studies.

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CONFLICT OF INTEREST STATEMENT

None declared.

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APPENDIX 1. PARTICIPATING RENAL UNITS

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