EPIDEMIOLOGICAL DATA ON RENAL BIOPSIES IN SOUTHERN CROATIA – A SINGLE CENTER REPORT OF 22-YEAR EXPERIENCE AT SPLIT UNIVERSITY HOSPITAL CENTER

DIJANA BORIĆ ŠKARO[1], NATALIJA FILIPOVIĆ[2], IVO JELIČIĆ[1], MAJA MIZDRAK[1], IVANA TADIN HADJINA[3], MERICA GLAVINA DURDOV[4,5], MIRNA SARAGA-BABIĆ[2], ADELA ARAPOVIĆ[6], MARIJAN SARAGA[5,6], DRAGAN LJUTIĆ[1,5], KATARINA VUKOJEVIĆ[2]

[1]Department of Nephrology, Split University Hospital Center, Split, Croatia; [2]Department of Anatomy, Histology and Embryology, University of Split School of Medicine, Split, Croatia; [3]Department of Gastroenterology, Split University Hospital Center, Split, Croatia; [4]Department of Pathology, Split University Hospital Center, Split, Croatia; [5]University of Split School of Medicine, Split, Croatia; [6]Department of Pediatrics, Split University Hospital Center, Split, Croatia

The Croatian Registry of Native Renal Biopsy (CRNRB) was established in 2019. Thus, in this study, we present retrospective data on kidney biopsies in adult patients performed at the Split University Hospital Center from 1994 to 2019 before the CRNRB establishment. The aim of the study was to show epidemiological data on glomerular diseases in southern Croatia in order to compare them with others and provide data for the establishment of the CRNRB. During the study period, 110 patients (mean age 46.6±15.4, age range 17-76 years), 68 men and 42 women, underwent renal biopsy at the Department of Internal Medicine, Split University Hospital Center in Split. Data on age, sex, serum creatinine, urinalysis, daily proteinuria, and complications after biopsy were collected and related to indication for biopsy and pathological diagnosis. Light and immunofluorescence analysis was supplemented by electron microscopy in 63.5% of cases. Indications for biopsy were nephrotic syndrome (64.5%), asymptomatic urinary tract abnormalities (12.7%), and acute renal failure of unknown cause (9.1%). The most common diagnosis was IgA nephropathy (IgAN) (20.9%), the prevalence of which decreased during the study period. IgAN was followed by focal segmental glomerulosclerosis (FSGS) (19.1%), membranous nephropathy (13.6%), lupus nephritis and minimal change disease (8.2%), crescentic glomerulonephritis (5.4%), membranoproliferative glomerulonephritis (4.5%), mesangial proliferative glomerulonephritis (3.6%), amyloidosis (3.6%), Henoch-Schönlein nephritis (3.6%), and Alport syndrome (2.7%). Other forms of glomerular diseases were rarely found. IgAN was most frequently found in men (26.5%) and FSGS in women (21.4%). These data can be included in the historical epidemiological observation of glomerular diseases in Southeastern Europe. The guidelines for performing biopsies need to be constantly updated to improve preventive and therapeutic strategies.

Key words: biopsy-proven renal disease, epidemiology, glomerulonephritis, renal biopsy, renal pathology, registry

Address for correspondence: Katarina Vukojević, MD PhD MSc
Department of Anatomy, Histology and Embryology
University of Split School of Medicine
Šoltanska 2
21000 Split, Croatia
E-mail: katarina.vukojevic@mefst.hr

Orcid: 0000-0003-2182-2890

INTRODUCTION

There are more than one million end-stage renal disease (ESRD) patients worldwide (1-3), and the prevalence and incidence of chronic kidney disease and ESRD show a rising trend. The number of patients requiring chronic replacement therapy is expected to increase by 60% by 2030 (4). Renal biopsy remains the gold standard for diagnosis (5), therapeutic management, and outcome prediction in patients with renal parenchymal disease. Unfortunately, there is currently little consensus on the proper indications and clinical utility of this procedure (6), and the decision to perform renal biopsy is usually based on personal opinion and/or individual center policy. Glomerular disease is on the rise and currently ranges from 6.5 to 27 persons/million person/year (p.m.p) (1, 2, 4). In the last report of the ERA-EDTA registry (7), the average

prevalence and incidence of dialysis patients without specific renal diagnosis was 15% to 16%, ranging from 1.5% in Croatia to 38% in Romania. The highest biopsy rates to date have been reported in the Australian database (215 p.m.p./year) (8) and in the experience of individual centers at Helsinki University Hospital, Finland (176 p.m.p./year) (9) and Olmsted County, USA (up to 175 p.m.p./year) (10). In contrast, very low rates have been reported from a regional database in Romania (11.3 p.m.p./year) (11). The lack of clear guidelines for the indication of renal biopsy may hinder the epidemiological classification of kidney disease, as well as the future validation of biomarkers (2).

Therefore, it is necessary to use uniform guidelines for renal biopsies, which will improve regional renal biopsy registries that are an important source for epidemiological studies. These registries would be a useful tool for planning a preventive and therapeutic approach to reduce the burden of patients with chronic kidney disease.

Data are available on national registries of biopsy-proven kidney disease established in Italy (12, 13), Denmark (14), Brazil (15), Spain (16, 17), Czech Republic (18, 19) and Saudi Arabia (20). In addition, there are a number of macroregional reports from individual centers and limited national registries for renal biopsies in several other countries (2). The Croatian national registry of native kidney biopsies was established through the efforts of colleagues from all Croatian centers and represents a promising basis for epidemiological data (21).

The aim of this study was to collect epidemiological data on kidney disease in the Dalmatian area of Croatia before establishment of this registry. These data would provide a source of useful information on the prevalent underlying disease and the opportunity to improve protocols for preventive medicine and therapeutic approach. In addition, combining data with renal replacement therapy registries would be a useful strategy for evaluating long-term outcomes of patients with kidney disease in our country, as well as in neighboring parts of Europe.

MATERIALS AND METHODS

The study was performed with the approval of the Ethics Committee of the School of Medicine, University of Split, in accordance with the Declaration of Helsinki. Data were obtained retrospectively from hospital records and pathological data from the Department of Pathology on all biopsies performed at the Department of Nephrology and Dialysis, Split University Hospital Center from 1996 to 2019. During this period, 110 biopsies were performed, 68 in men and 42 in women.

For each case, the following data were collected: age, sex, clinical and histopathologic diagnosis, levels of nitrogen waste products, urinalysis, 24-hour proteinuria, glomerular filtration rate (measured creatinine clearance using a laboratory referral protocol), and relevant clinical data. Renal tissue cylinders were processed according to standardized procedures. Light microscopy (LM) and immunofluorescence (IF) were analyzed at the Department of Pathology, Split University Hospital Center, and electron microscopic analysis (EM) was performed at the Department of Pathology, School of Medicine, University of Zagreb. Glomerular diseases were classified according to the relevant pathological literature (22). The following clinical data were collected: indication for renal biopsy, arterial pressure, presence of nephrotic (NS) or nephritic syndrome (NeS), and complications of renal biopsy.

Biopsies were indicated by a nephrologist and performed under local anesthesia after routine examination had been performed previously. Complete medical history was also obtained and physical examination, including blood pressure measurement, was performed. A series of necessary laboratory tests were performed, such as complete blood count and coagulation parameters. All biopsies were performed using a percutaneous, automated, spring-loaded biopsy instrument (Biopty TM) under real-time ultrasound guidance and a 14-G biopsy needle.

The indications for biopsy were as follows: nephrotic proteinuria (≥3.5 g/dU) (64.5%), asymptomatic urinary abnormalities (AUA) defined with proteinuria of non-nephrotic range with or without hematuria (12.7%), unexplained acute renal failure (ARF) (clinically 'silent' reduction of glomerular filtration rate which lasts for days and weeks, without arterial hypertension and with various urinalysis changes) (9.1%), kidney disorders in patients with diverse clinical presentations of systemic vasculitis (4.5%), nephritic syndrome (NeS) (dysmorphic erythrocyturia, various ranges of proteinuria, arterial hypertension and glomerular filtration rate reduction) (2.7%), kidney biopsy in patients with systemic lupus erythematosus (SLE) in order to adjust therapeutic protocol (2.7%), and isolated hematuria (IH) (0.9%). We took blood pressure ≥140/90 mm Hg as arterial hypertension.

Ethical statement

Split University Hospital Center Ethics Committee, File No. 2181-147-01/06/M.S.-19-2.

Statistical analysis

All analyses were performed with SPSS statistical software package (version 23.0). Continuous variables were expressed as median with interquartile range and categorical variables as frequency and percent.

RESULTS

During the study period, 110 adult Caucasian patients (68 men and 42 women) underwent percutaneous renal biopsy. Their mean age was 46.6±15.4 (range 17-78) years. Mean creatinine at the time of the procedure was 150.5 μmol/L, and mean daily proteinuria 6.58 g/d (Table 1). The most common indication for biopsy was NS in 71 (64.5%) patients. AUA was the indication for biopsy in 14 (12.7%) and ARF in 10 (9.1%) patients. Clinical presentation of systemic vasculitis (4.5%) and acute NeS (2.7%) were the least common reasons for biopsy. Pathological urine findings with or without renal function worsening were the reason for biopsy in 3% of patients with SLE (Figure 1).

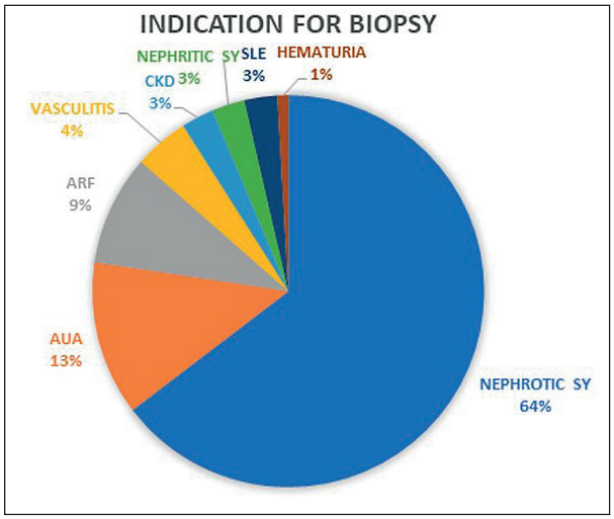

FIGURE 1. *Indication for renal biopsy. The most frequent indication for biopsy was NS, found in 71 patients (64.5%). AUA was the indication for a biopsy in 14 (12.7%) and ARF in 10 patients (9.1%).*

Legend: AUA: Asymptomatic urinary abnormalities; ARF: Acute renal failure; SLE: Systemic lupus erythematosus; SY: syndrome; CKD: chronic kidney disease

Complete pathological analysis was performed on all 110 specimens, with the exception of electron microscopy, which was performed in only 73 (64%) cases. Figure 2 shows relative distribution of renal disease diagnosed on biopsy. The most common renal disease detected by biopsy was IgA nephropathy (IgAN) in 23 (20.9%) cases, followed by focal segmental glomerulosclerosis (FSGS) in 21 (19.1%), membranous nephropathy (MGN) in 15 (13.6%), lupus nephritis (LN) and minimal change disease (MCD) in 9 (8.2%), and membranoproliferative glomerulonephritis (MPGN) in 5 (4.5%) patients. Four patients had mesangial proliferative glomerulonephritis (MePGN) (3.6%) and amyloidosis (AM) (3.6%) in their histopathologic diagnosis. Four (3.6%) patients with clinical signs of systemic vasculitis were diagnosed with Henoch-Schönlein purpura (HSP). Crescentic glomerulonephritis (CGN) (ANCA-related and anti-GBM) accounted for 6 (5.4%) cases. Hereditary nephritis including Alport syndrome (AS) and thin membrane disease (TMD) was detected in 4 (3.6%) cases. Other renal diseases were rarely diagnosed, e.g., IgM glomerulonephritis (IgMGN), endoproliferative glomerulonephritis (EPGN), C1q nephropathy, tubulointerstitial nephritis (TIN), and myeloma kidney (MK), each of which was diagnosed in 1 (0.9%) patient.

Regarding sex, IgAN (78.3% *vs.* 21.7%) and FSGS (57.1% *vs.* 42.9%) were more common in men, in contrast to LN, which was more common in women (88.9%). FSGS was the most common finding in women overall (21.4%) and in men with IgAN (26.5%).

Table 1. *Clinical characteristics of most common glomerulonephritis*

GN	Mean age (years)	Proteinuria (g/dU)	Creatinine clearance (mL/s)	NS (%)	Hypertension (%)	ARF (%)	Male (%)
IgA GN	42.5	5.36	1.01	52.1	90	4.3	78.3
FSGS	51.1	6.48	1.24	85.7	68.4	4.8	57.1
LN	49.3	5.67	1.3	55.5	55	-	11.1
MGN	50.4	9.62	1.49	73.3	57.1	6.7	66.7
MPGN	57.8	10.44	0.79	100	100	-	60
MCD	42.2	11.47	1.37	100	12.5	-	60

IgA GN: IgA glomerulonephritis; FSGS: focal segmental glomerulosclerosis; LN: lupus nephritis; MGN: membranous glomerulonephritis; MPGN: membranoproliferative glomerulonephritis; MCD: minimal change disease; ARF: acute renal failure

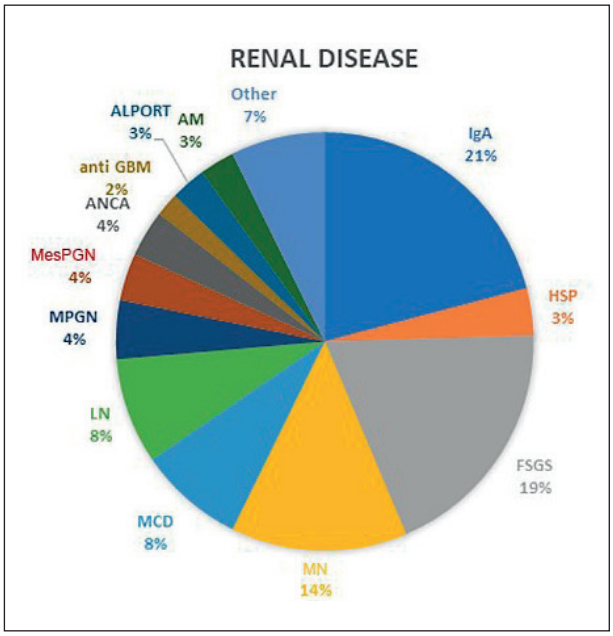

FIGURE 2. *The frequency of certain diagnoses made by kidney biopsy. The most frequently biopsy-proven renal disease was IgAN, found in 23 specimens (20.9%), followed with FSGS in 21 patients (19.1%), MGN in 15 (13.6%), LN and MCD in 9 patients (8.2%), and MPGN in 5 patients (4.5%).*

Legend: IgA: IgA nephropathy; FSGS: focal segmental glomerulosclerosis; MGN: membranous glomerulonephritis; LN: lupus nephritis; MCD: minimal change disease; MPGN: membranoproliferative glomerulonephritis; MePGN mesangial proliferative glomerulonephritis; ANCA: neutrophil cytoplasmic antibody-associated glomerulonephritis; anti GBM: anti-glomerular basement membrane disease.

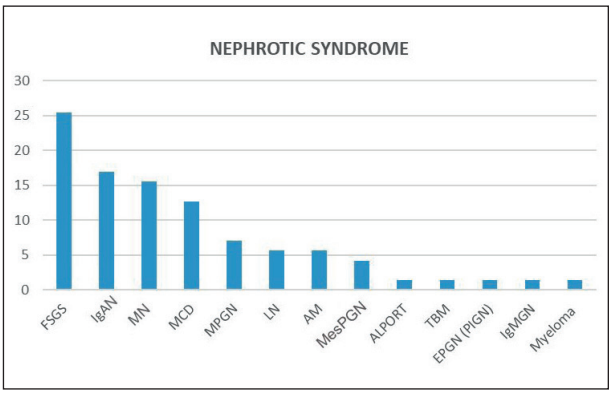

FIGURE 3. *Frequency of nephrotic syndrome in certain entities. Among patients with clinical presentation of nephrotic syndrome, the most often pathohistological finding was FSGS in 18 (25.4%), IgAN in 12 (16.9%), MGN in 11 (15.5%), MCD in 9 (12.7%), MPGN in 5 specimens (7%), followed in decreasing order with LN and AM, each in 4 cases (5.6%).*

Legend: FSGS: Focal segmental glomerulosclerosis; IgA: IgA nephropathy; FSGS: focal segmental glomerulosclerosis; LN: lupus nephritis; MCD: minimal change disease; MesPGN: mesangial proliferative glomerulonephritis; ANCA: neutrophil cytoplasmic antibody-associated glomerulonephritis; anti GBM: anti-glomerular basement membrane disease; IgMGN: IgM glomerulonephritis; Anti-Tubular Basement-Membrane (TBM) nephritis; EPGN (PIGN): proliferative endocapillary glomerulonephritis; MGN: Membranous glomerulonephritis; MCD: Minimal change disease; MPGN: Membranoproliferative glomerulonephritis

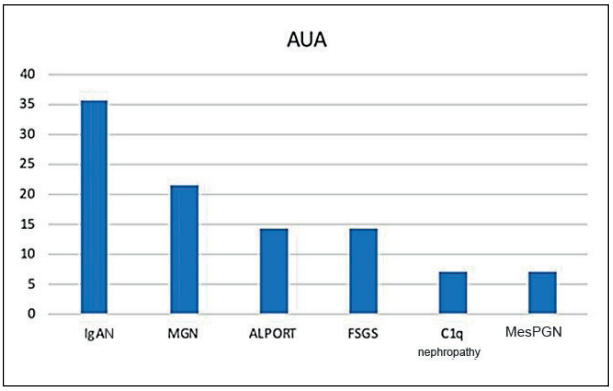

FIGURE 4. *Frequency of certain entities in patients with Asymptomatic urinary abnormalities. AUA were presented in 5 patients with IgAN (35.7%), 3 patients with MGN (21.4%); FSGS and AS were each found in 2 specimens (14.3%).*

Legend: AUA: Asymptomatic urinary abnormalities; IgAN: IgA glomerulonephritis; MGN: Membranous glomerulonephritis; FSGS: Focal segmental glomerulosclerosis; Alport : Alport syndrome; MesPGN: mesangial proliferative glomerulonephritis

In patients with IgAN, the mean age was 42.5 (range 19-66) years, mean proteinuria 5.36 (range 0.92-24.5) g/dU, and mean creatinine clearance 1.01 (range 0.13-2.35) mL/s. The most common clinical presentation was NS (52.1%), followed by AUA (21.7%), chronic renal failure (CRF) (8.7%), ARF, NeS, and isolated hematuria (4.3% each). Arterial hypertension was present in 90% of patients.

Among patients with the clinical picture of nephrotic syndrome (NS), the most common pathohistological finding was FSGS in 18 (25.4%), IgAN in 12 (16.9%), MGN in 11 (15.5%), MCD in 9 (12.7%), MPGN in 5 samples (7%), followed in decreasing order by LN and AM in 4 cases each (5.6%) (Figure 3).

Asymptomatic urine abnormalities were found in 5 (35.7%) patients with IgAN and 3 (21.4%) patients with MGN; FSGS and AS were each found in 2 (14.3%) samples (Figure 4).

The most common histopathologic findings in patients with equivocal ARF, involving 20% each, were anti-GBM and ANCA-related CGN.

Only one serious clinical complication requiring intervention was recorded, i.e., retroperitoneal hemorrhage, which was successfully resolved by an interventional radiological procedure.

DISCUSSION

Numerous reports have been published describing the incidence, correlation of clinical epidemiological data, and histopathologic findings from various renal biopsy databases throughout the world (2, 8-29). Unfortunately, the results are not always easy to compare for several reasons such as inconsistencies in biopsy indications, different time frames for different epidemiological studies, lack of renal biopsy registration due to voluntary data collection, and inconsistencies in the definition of a clinical syndrome and histopathologic classification (2). Some reports included pediatric and adult populations (12, 13, 15-19), whereas others included adults exclusively (11, 20, 21). In addition, some reports collected data exclusively on glomerular biopsy-proven kidney disease (2, 21). In the present paper, we present the results of a 22-year retrospective study of biopsy-proven glomerular and non-glomerular kidney disease in adults older than 18 years because colleagues from the Department of Pediatrics, Split University Hospital Center had previously presented their own data (23, 29). One of the main difficulties in comparing epidemiological data is different approach resulting from different practice of renal biopsy in different countries, as well as in different centers of the same country, partly due to socioeconomic status and availability of biopsy. A wide range of indications for biopsy, ranging from a relatively liberal approach to performing biopsy only when therapy adjustment is required based on histopathologic findings, results in a wide range of biopsy rates, ranging from 215 p.m.p./year, as reported in an Australian database (8) to 176 p.m.p./year at Helsinki University Hospital, Finland (9). Disagreement about the need of biopsy is particularly important in the case of AUA syndrome. In addition, there are different definitions of AUA syndrome, as well as of other clinical renal syndromes used in different epidemiologic reports, which may pose another difficulty for appropriate comparison. In our report, as well as in some other reports (11, 24), the term AUA is used for non-nephrotic proteinuria, isolated or in association with hematuria; in other reports, macroscopic hematuria is considered a separate syndrome (13, 15, 16, 19). AUA syndrome is the most common reason for biopsy reported in two national registries (12, 18, 19), two macroregional reports (9, 15), and in a single-center database (24). In our study, AUA was the second most common reason for biopsy (12.7%). The most common underlying histopathologic finding in the AUA group was IgAN (35.7%), followed by MGN (21.4%), FSGS, and AS (14.3%). IgAN was also diagnosed in single cases of IH (1%). This is consistent with the results of histopathologic findings in two large national registries in the Czech Republic and Italy (12, 18, 19), where IgAN was the most common finding in patients with AUA. IgAN as isolated renal disease or as systemic vasculitis with renal involvement (HSP) was the most common histopathologic finding (24%) in our study. These findings are consistent with 6 of 8 reports from national registries (Italy, Spain, Denmark, Scotland, Czech Republic, and Japan) (12-14, 16-19, 28), 3 macroregional ones (western France, Finland, Victoria-Australia) (8, 9, 27), and in more single-center databases (2). In contrast, FSGS has been reported as the most important histopathologic pattern in African American and Hispanic populations, with an increasing trend in adult Caucasians in the United States (10, 25, 30, 31), and in Brazil and Uruguay (15, 32). Different results have been reported from other European countries; MGN was the predominant histopathologic finding in Macedonia (33), and MPGN in Romania (11). As it is well known, IgAN occurs predominantly in AUA, and in countries with strict biopsy policies, the incidence and prevalence depend largely on biopsy practice. Even in Croatia, different centers have different approaches to the need of renal biopsy, with the two largest centers in northern Croatia taking a more liberal stance. In our center, we have so far accepted the expectation attitude and perform biopsies only in cases where diagnosis is not possible based on clinical data and other relevant tests, e.g., unexplained renal failure, worsening of glomerular filtration rate, and/or worsening of daily proteinuria despite ongoing treatment. This might be a reason for the underestimation of IgAN in our study. Of note, the most common clinical presentation in the group of patients with an underlying pattern of IgAN in our study was NS (52.1%), which is somewhat unexpected and in contrast to most other studies in which AUA was the most common clinical presentation (12, 13, 15-17, 21). This could be due to the fact that performing biopsy earlier in the disease course could change the clinical presentation.

Nephrotic syndrome was the most common indication for performing biopsy in 64.5% of cases. We accept proteinuria above 3.5 g/dU as a sufficient criterion, with or without other clinical manifestations. Our results are consistent with most registry and database reports (2, 34), the results of three national registries (15, 17, 32), three macroregional studies (11, 21, 35), and additional reports from individual centers (2). The most common histopathologic diagnosis underlying nephrotic proteinuria was FSGS (25.4%), followed by IgAN (16.9%), MGN (15.5%), and MCD (12.7%). In the United States, a high prevalence with increasing trend of biopsy-proven primary FSGS has been reported in the African American population (10, 23, 25), and recent data show an increasing trend of incidence in the Caucasian population (10, 25). FSGS, followed by MGN, is the most common histologic pattern reported in Croatia (35). Our findings are in contradiction with most other study reports (MGN as the most common underlying histopathologic pattern of NS (12-14, 26).

In our study, MGN was the third most common histopathologic finding, accounting for 14% of cases. In the literature, reports on MGN are generally inconsistent. Although MGN is the most common GN in the elderly population, and considering the increase in life expectancy and aging of the population, there are reports on a lower proportion of MGN in primary GN, for unclear reasons (30). In contrast, MGN was the second most common primary GN in the Italian national registry (13), and an increase in the proportion of MGN among primary GN has been reported in the Spanish national registry (17).

Uniformity in the use of IF and EM in confirming the histopathologic diagnosis is another difficulty in comparing the results of particular epidemiological studies. These techniques, especially EM, are limited, mainly because of the low economic resources in some countries (2). It is known that IF is important for confirming the histopathologic diagnosis and some clinical entities, such as IgAN and pauci-immune glomerulonephritis. It could be speculated that an increase in the incidence of IgAN may be due to an increase in the IF technique. On the other hand, EM is an important technique to confirm the correct diagnosis of MCD and inherited diseases and to distinguish primary from secondary FSGS. As previously reported, ultrastructural analysis using EM was required in 21% of cases to confirm the correct diagnosis, in addition to LM and IF. Thus, the availability of a particular technique could influence the histopathologic pattern. Reports on the use of IF are incomplete in most studies, with few exceptions, i.e., Spain 90% (17), Denmark 78% (14), and a regional report in Croatia 100% (35). According to the available data, EM is used even less frequently, e.g., in Italy 38% (13), Brazil 9% (15), Spain 23% (17) and Croatia 100% (35). We routinely performed IF in all samples, in contrast to EM, which was performed in 66% of cases, although EM could not be performed in our center so far. The missing data from EM were mainly due to technical problems. The most common histopathologic findings in patients presenting with ARF were CGN, ANCA, and anti-GBM (5.4%). Of note, unusual histopathologic findings such as FSGS and MGN were found in a certain percentage of patients. The other primary GN were found less frequently in our study. We found combined histopathologic patterns in seven patients; FSGS was combined with TMD in three cases, and we found renal vasculitis and TMD in one sample; HSP, MCD, and MGN were combined with acute TIN in one case each. LN was the most common secondary GN, found in 8% of cases, predominantly in women (88.9%). Similar results have been reported in larger national and macroregional registries and in single-center registries (8, 11, 13, 16, 18, 25). In Czech Republic, Japan, and Scotland, diabetic nephropathy has been reported as the predominant secondary form of biopsy-proven glomerular disease (2). Only one clinically serious complication of biopsy was recorded (0.9%); the frequency is consistent with reports (5).

We found that the pattern of distribution in our study was largely similar to that reported from other European countries (2, 9, 16, 17, 19, 33). We might even suspect more differences due to our overly restrictive biopsy practice and low biopsy rate, with the possibility that some histopathologic patterns are underestimated. Therefore, it was necessary to expand the spectrum of indications for diagnosis in order to establish a Croatian national registry of biopsy-proven kidney disease comparable to others in Europe and worldwide. Different data observed in different studies could be due to geographic heterogeneity, changes in environmental and lifestyle factors, and biopsy practice.

CONCLUSION

In conclusion, longitudinal follow-up, observing changes in the clinicopathologic pattern of kidney disease in separate centers/national registries, and combining these data with registries of renal replacement therapies would be a particularly useful tool to assess long-term outcomes in our patients and potential outcomes after renal transplantation. Our data can contribute to the guidelines for performing kidney biopsies because these inputs can help improving preventive and therapeutic strategies, as well as testing appropriate preventive and therapeutic measures to reduce the burden of chronic kidney disease.

REFERENCES

1. Collins AJ, Foley RN, Gilbertson DT, Chen SC. United States Renal Data System public health surveillance of chronic kidney disease and end-stage renal disease. Kidney Int Suppl (2011). 2015;5(1):2-7.

2. Fiorentino M, Bolignano D, Tesar V *et al.* Renal Biopsy in 2015 – from epidemiology to evidence-based indications. Am J Nephrol 2016;43(1):1-19.

3. Gonzalez Suarez ML, Thomas DB, Barisoni L, Fornoni A. Diabetic nephropathy: is it time yet for routine kidney biopsy? World J Diabetes 2013;4(6):245-55.

4. Wetmore JB, Liu J, Li S *et al.* The healthy people 2020 objectives for kidney disease: how far have we come, and where do we need to go? Clin J Am Soc Nephrol 2017;12(1):200-9.

5. Hogan JJ, Mocanu M, Berns JS. The native kidney biopsy: update and evidence for best practice. Clin J Am Soc Nephrol 2016;11(2):354-62.

6. Dhaun N, Bellamy CO, Cattran DC, Kluth DC. Utility of renal biopsy in the clinical management of renal disease. Kidney Int 2014;85(5):1039-48.

7. ERA-EDTA. ERA-EDTA registry annual report 2012. 2012.

8. Briganti EM, Dowling J, Finlay M *et al*. The incidence of biopsy-proven glomerulonephritis in Australia. Nephrol Dial Transplant 2001;16(7):1364-7.

9. Wirta O, Mustonen J, Helin H, Pasternack A. Incidence of biopsy-proven glomerulonephritis. Nephrol Dial Transplant 2008;23(1):193-200.

10. Swaminathan S, Leung N, Lager DJ *et al*. Changing incidence of glomerular disease in Olmsted County, Minnesota: a 30-year renal biopsy study. Clin J Am Soc Nephrol 2006;1(3):483-7.

11. Covic A, Schiller A, Volovat CI. Epidemiology of renal disease in Romania: a 10 year review of two regional renal biopsy databases. Nephrol Dial Transplant 2006;21(2):419-24.

12. Gesualdo L, Di Palma AM, Morrone LF, Strippoli GF, Schena FP, Italian Immunopathology Group ISoN. The Italian experience of the national registry of renal biopsies. Kidney Int 2004;66(3):890-4.

13. Schena FP. Survey of the Italian Registry of Renal Biopsies. Frequency of the renal diseases for 7 consecutive years. The Italian Group of Renal Immunopathology. Nephrol Dial Transplant 1997;12(3):418-26.

14. Heaf J, Lokkegaard H, Larsen S. The epidemiology and prognosis of glomerulonephritis in Denmark 1985-1997. Nephrol Dial Transplant 1999;14(8):1889-97.

15. Polito MG, de Moura LA, Kirsztajn GM. An overview on frequency of renal biopsy diagnosis in Brazil: clinical and pathological patterns based on 9,617 native kidney biopsies. Nephrol Dial Transplant 2010;25(2):490-6.

16. Rivera F, Lopez-Gomez JM, Perez-Garcia R, Spanish Registry of Glomerulonephritis. Clinicopathologic correlations of renal pathology in Spain. Kidney Int 2004;66(3):898-904.

17. Rivera F, Lopez-Gomez JM, Perez-Garcia R, Spanish Registry of Gomerulonephritis. Frequency of renal pathology in Spain 1994-1999. Nephrol Dial Transplant 2002;17(9):1594-602.

18. Maixnerova D, Jancova E, Skibova J *et al.* Nationwide biopsy survey of renal diseases in the Czech Republic during the years 1994-2011. J Nephrol 2015;28(1):39-49.

19. Rychlik I, Jancova E, Tesar V *et al*. The Czech Registry of Renal Biopsies. Occurrence of renal diseases in the years 1994-2000. Nephrol Dial Transplant 2004;19(12):3040-9.

20. Huraib S, Al Khader A, Shaheen FA *et al.* The spectrum of glomerulonephritis in Saudi Arabia: the results of the Saudi Registry. Saudi J Kidney Dis Transpl 2000;11(3):434-41.

21. Laganović M, Gellineo L, Bulimbašić S *et al.* Report of the Croatian registry of native kidney biopsies for year 2019. Acta Clin Croat 2019;60(2021):173-80.

22. Haas M, Rastaldi MP, Fervenza FC. Histologic classification of glomerular diseases: clinicopathologic correlations, limitations exposed by validation studies, and suggestions for modification. Kidney Int 2014;85(4):779-93.

23. Bazina M, Glavina-Durdov M, Scukanec-Spoljar M *et al*. Epidemiology of renal disease in children in the region of southern Croatia: a 10-year review of regional renal biopsy databases. Med Sci Monit 2007;13(4):CR172-6.

24. Chan KW, Chan TM, Cheng IK. Clinical and pathological characteristics of patients with glomerular diseases at a university teaching hospital: 5-year prospective review. Hong Kong Med J 1999;5(3):240-4.

25. Dragovic D, Rosenstock JL, Wahl SJ, Panagopoulos G, DeVita MV, Michelis MF. Increasing incidence of focal segmental glomerulosclerosis and an examination of demographic patterns. Clin Nephrol 2005;63(1):1-7.

26. Naini AE, Harandi AA, Ossareh S, Ghods A, Bastani B. Prevalence and clinical findings of biopsy-proven glomerulonephritidis in Iran. Saudi J Kidney Dis Transpl 2007;18(4):556-64. Epub 2007/10/24.

27. Simon P, Ramee MP, Autuly V *et al.* Epidemiology of primary glomerular diseases in a French region. Variations according to period and age. Kidney Int 1994;46(4):1192-8.

28. Sugiyama H, Yokoyama H, Sato H *et al*. Japan Renal Biopsy Registry and Japan Kidney Disease Registry: Committee Report for 2009 and 2010. Clin Exp Nephrol 2013;17(2):155-73.

29. Arapovic A, Vukojevic K, Filipovic N *et al*. Epidemiology of 10-year paediatric renal biopsies in the region of southern Croatia. BMC Nephrol 2020;21(1):65.

30. Braden GL, Mulhern JG, O'Shea MH, Nash SV, Ucci AA, Jr, Germain MJ. Changing incidence of glomerular diseases in adults. Am J Kidney Dis 2000;35(5):878-83.

31. O'Shaughnessy MM, Hogan SL, Poulton CJ *et al.* Temporal and demographic trends in glomerular disease epidemiology in the southeastern United States, 1986-2015. Clin J Am Soc Nephrol 2017;12(4):614-23.

32. Mazzuchi N, Acosta N, Caorsi H *et al*. [Frequency of diagnosis and clinic presentation of glomerulopathies in Uruguay]. Nefrologia. 2005;25(2):113-20.

33. Polenakovic MH, Grcevska L, Dzikova S. The incidence of biopsy-proven primary glomerulonephritis in the Republic of Macedonia – long-term follow-up. Nephrol Dial Transplant 2003;18 Suppl 5:v26-7.

34. Cagnoli L, Italian Society of Nephrology. [Instructions and implementations for percutaneous renal biopsy. Guidelines for the therapy of glomerular nephropaties]. G Ital Nefrol 2003;20 Suppl 24:S3-47.

35. Horvatic I, Tisljar M, Bulimbasic S, Bozic B, Galesic Ljubanovic D, Galesic K. Epidemiologic data of adult native biopsy-proven renal diseases in Croatia. Int Urol Nephrol 2013;45(6):1577-87.

S A Ž E T A K

EPIDEMIOLOŠKI PODATCI BUBREŽNIH BIOPSIJA U JUŽNOJ HRVATSKOJ – IZVJEŠTAJ O 22-GODIŠNJEM ISKUSTVU KBC-A SPLIT

D. BORIĆ ŠKARO[1], N. FILIPOVIĆ[2], I. JELIČIĆ[1], M. MIZDRAK[1], I. TADIN HADJINA[3], M. GLAVINA DURDOV[4,5], M. SARAGA-BABIĆ[2], A. ARAPOVIĆ[6], M. SARAGA[5,6], D. LJUTIĆ[1,5], K. VUKOJEVIĆ[2]

[1]Klinički zavod za nefrologiju, KBC Split, Split, Hrvatska; [2]Zavod za anatomiju, histologiju i embriologiju, Sveučilište u Splitu, Medicinski fakultet, Split, Hrvatska; [3]Klinički zavod za gastroenterologiju, KBC Split, Split, Hrvatska; [4]Klinički zavod za patologiju, KBC Split, Split, Hrvatska; [5]Sveučilište u Splitu, Medicinski fakultet, Split, Hrvatska; [6]Klinički zavod za pedijatriju, KBC Split, Split, Hrvatska

Hrvatski registar nativne bubrežne biopsije (CRNRB) uspostavljen je 2019. godine. Stoga u ovom istraživanju prikazujemo retrospektivne podatke biopsija bubrega odraslih bolesnika KBC-a Split obavljenih od 1994. do 2019. godine prije uspostave CRNRB-a. *Cilj rada* bio je prikazati epidemiološke podatke o glomerularnim bolestima u južnoj Hrvatskoj radi usporedbe s drugima i dobivanja podataka za uspostavu CRNRB-a. U promatranom razdoblju 110 bolesnika (raspon dobi 17-76 godina, srednja dob 46,6±15,4 godina), 68 muškaraca i 42 žene, bilo je podvrgnuto biopsiji bubrega na Klinici za unutarnje bolesti KBC-a Split. Podatci o dobi, spolu, kreatininu u serumu, analizi mokraće, dnevnoj proteinuriji i komplikacijama nakon biopsije prikupljeni su i povezani s indikacijom za biopsiju i patološkom dijagnozom. Analiza svjetlosnom mikroskopijom i imunofluorescencijom dopunjena je elektronskom mikroskopijom u 63,5 % slučajeva. Indikacije za biopsiju bile su nefrotski sindrom (64,5 %), asimptomatske abnormalnosti mokraćnog sustava (12,7 %) i akutno zatajenje bubrega nepoznatog uzroka (9,1 %). Najčešća dijagnoza bila je IgA nefropatija (IgAN) (20,9 %), učestalost koje se smanjila tijekom promatranog razdoblja. Nakon IgAN-a slijede žarišna segmentna glomeruloskleroza (FSGS) (19,1 %), membranska nefropatija (13,6 %), lupusni nefritis i bolest minimalnih promjena (8,2 %), polumjesečasti glomerulonefritis (5,4 %), membranoproliferativni glomerulonefritis (4,5 %), mezangijski proliferativni glomerulonefritis (3,6 %), amiloidoza (3,6 %), Henoch-Schönleinov nefritis (3,6 %) i Alportov sindrom (2,7 %). Drugi oblici glomerularnih bolesti rijetko su nađeni. IgAN je najčešće nađen u muškaraca (26,5 %), a FSGS u žena (21,4 %). Ti se podatci mogu uključiti u povijesno epidemiološko promatranje glomerularnih bolesti u jugoistočnoj Europi. Smjernice za izvođenje biopsije bubrega potrebno je stalno ažurirati kako bi se poboljšale preventivne i terapijske strategije.

Ključne riječi: biopsijom dokazana bubrežna bolest, epidemiologija, glomerulonefritis, biopsija bubrega, patologija bubrega, registar