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# Assessment of Ten-Year-Long Results of Kidney Biopsies Performed on Children in the Thrace Region of Turkey

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**Background:** Many children with kidney diseases can be diagnosed and treated without a biopsy. However, biopsy is a valuable method for the diagnostic and prognostic evaluation of children with kidney diseases.

**Aims:** To evaluate the clinical and pathological profiles of the kidney biopsies in our department to provide epidemiological data for clinical practice.

**Study Design:** Retrospective cross-sectional study.

**Methods:** Kidney biopsies and patient's charts in pediatric patients performed between May 2005 and February 2015 at the Pediatric Nephrology Department, Trakya University School of Medicine were assessed retrospectively.

**Results:** A total of 100 patients were examined. Their mean age was 9.62±4.26 years (range: 1-17 years); 54% of the patients were girls and 46% were boys. The most frequent indication for kidney biopsy was nephrotic syndrome (33%). The most common kidney disease was primary glomerulonephritis, which was observed in 65% of cases. IgA nephropathy (24%) was the most frequently observed subtype in primary glomerulonephritis groups. Secondary glomerulonephritis was diagnosed in 35% of cases. Systemic lupus erythematosus (51%) was the most frequently observed subtype in the secondary glomerulonephritis groups.

**Conclusion:** IgA nephropathy and systemic lupus erythematosus were the most frequent primary and secondary glomerulonephritis in our region among children, respectively.

**Keywords:** Kidney biopsy, child, histopathological diagnosis, glomerulonephritis

Many children with kidney disease can be diagnosed and treated without a biopsy. However, biopsy is a valuable method for the diagnostic and prognostic evaluation of children with kidney disease (1). Epidemiological studies about kidney diseases, both primary and secondary, may identify the frequency of diseases, their causes, and environmental or genetic factors contributing to disease development.

Valuable epidemiological data are available from studies of children's kidney biopsies in different countries (2-6). Furthermore, some reports dealing with national and regional databases, specific population groups, specific diagnoses or local single-center experiences have been published. The studies investigating epidemiologic, clinical and histopathological findings related to childhood kidney diseases are still scarce in our country (4,7,8).

This study aims to examine the clinical and histopathological profiles of the kidney biopsies from our department.

## MATERIALS AND METHODS

All patients who had undergone kidney biopsy between May 2005 and February 2015 in our department were assessed retrospectively. Patients who had undergone kidney biopsy

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between 2005 and 2015 in our department were assessed retrospectively. Demographic data (age, gender), clinical symptoms at presentation, indications for kidney biopsy, laboratory findings and histopathological diagnosis were collected from the medical record archives.

Informed consent was obtained from parents. After physical examination, complete blood count, prothrombin and partial thromboplastin times and renal function tests were performed on all patients before biopsies. All patients fasted for at least 6 h and were then sedated 30-45 minutes before the procedure. Following premedication and local anesthesia with 1% lidocaine, biopsies were performed on the left kidney of patients. Biopsy was performed using 16-gauge or 18-gauge biopsy needles according to the patient's age with the guidance of ultrasonography by the radiologists; two cores of tissue were taken.

Following the procedure, the patients were kept in the supine position for 24 hours with sandbag compression to the abdomen and intermittent ice pack application to the biopsy region. Vital signs were measured at 15 min. intervals for the first 2h and then hourly. Each urine sample was examined for macroscopic hematuria. Hematocrit values were also monitored. A post-biopsy ultrasound examination of the punctured kidney was performed in all patients on the next day and those patients without complication were discharged after 24 hours. Doppler ultrasonography was used to follow recovery of patient with vascular complications.

All kidney specimens were evaluated by light and immunofluorescent microscopies. Fresh biopsy cores were evaluated on the dissecting microscope. Renal cortical tissue (3-4 mm in length) was separated for immunofluorescence study and kept at -80°C. The remaining biopsy specimen was fixed in 10% buffered formalin for light microscopy. Paraffin sections were stained with hematoxylin and eosin, periodic acid Schiff, Masson's trichrome stain, Congo red and Gomori's methanamine silver. For immunofluorescence studies, cryostat sections were stained using polyclonal antisera against IgA, IgG, IgM, C3, C1q and fibrinogen. Biopsy specimens containing at least eight glomeruli were considered sufficient for a proper diagnosis.

The study was approved by the local ethics committee. Statistical analysis was not used for this study; we only used percentage figures from the data.

## RESULTS

Kidney biopsies were performed in 100 children, 46 boys and 54 girls, aged 1-17 years (mean age=9.62±4.26 years) over a 10-year period. Among these, 24 (24%) were aged under 5 years, 29 (29%) were 6 to 10 years, 30 (30%) were 11 to 14 years and 17 (17%) were 15 to 17 years.

**TABLE 1.** Indications of kidney biopsy

| | n (%) |
|---|---|
| Nephrotic syndrome | 33 (33) |
| Acute nephritic syndrome | 24 (24) |
| Nephrotic-nephritic syndrome | 18 (18) |
| Rapidly progressive glomerulonephritis | 3 (3) |
| Acute kidney injury | 3 (3) |
| Chronic kidney disease | 2 (2) |
| Asymptomatic urinary abnormalities | 17 (17) |
| Total | 100 (100) |

The main indication for performing a biopsy was nephrotic syndrome (NS) in 33/100 (33%) children. Other indications were acute nephritic syndrome (ANS) in 24 cases (24%), nephrotic-nephritic syndrome in 18 cases (18%), rapidly progressive glomerulonephritis (RPGN) in 3 cases (3%), acute kidney injury (AKI) in 3 cases (3%), chronic kidney disease (CKD) in 2 cases (2%), and asymptomatic urinary abnormalities in 17 cases (17%) (Table 1). Of the 17 asymptomatic urinary abnormalities, 6 cases presented with isolated hematuria and 11 cases with isolated proteinuria.

None of the patients presented sedation-related complications during or after the procedure. Two out of 100 patients (2%) presented macroscopic hematuria, and were evaluated with Doppler ultrasonography. Because there were no vascular complications, the patients were followed up until bleeding stopped and recovered without any blood transfusion.

Kidney biopsies with insufficient specimen were excluded from further analysis and a total of 91 kidney biopsies were included in the present study.

The histopathological diagnosis according to the clinical indications are shown in Table 2. The most frequent types of kidney diseases were systemic lupus erythematosus (SLE) nephritis in 14/91 patients (15%), IgA nephropathy (IgAN) and Henoch-Schonlein Purpura (HSP) nephritis both in 12/91 (13%), followed by focal segmental glomerulosclerosis (FSGS), diffuse proliferative glomerulonephritis (DPGN), and minimal change disease (MCD) each in 8/91 patients (9%), normal findings in 6/91 patients (7%), nonspecific findings in 6/91 patients (7%), membranous glomerulonephritis (MGN) in 4/91 patients (4%), mesangioproliferative glomerulonephritis (MesGN) in 3/91 (3%), membranoproliferative glomerulonephritis (MPGN) in 2/91 (2%), congenital nephrotic syndrome (CNS) in 2/91 (2%), and others each in 1/91 patients (1%) (acute tubulointerstitial nephritis (ATIN), Alport syndrome, crescentic glomerulonephritis, nodular glomerulosclerosis, secondary amyloidosis, end-stage renal disease).

The most common diagnosis in the biopsies was glomerulonephritis in 77/91 patients (84%). Primary glomerulonephritis (GN) accounted for 65% (50/77) and secondary glomerulonephritis for

**TABLE 2**. Comparison of histopathological findings according to clinical indications

| Histopathological findings | Clinical Indications | | | | | | | TOTAL n (100) |
|---|---|---|---|---|---|---|---|---|
| | NS | ANS | NS+ANS | RPGN | AKI | CKD | Asymptomatic urinary abnormalities | |
| Primary glomerulonephritis | | | | | | | | |
| Membranous GN | 2 | 1 | - | - | - | - | 1 | 4 (5) |
| FSGS | 8 | - | - | - | - | - | - | 8 (9) |
| IgA nephropathy | - | 8 | 2 | - | - | 1 | 1 | 12 (13) |
| Mesangioproliferative GN | - | 1 | 1 | - | 1 | - | - | 3 (3) |
| Membranoproliferative GN | - | - | 2 | - | - | - | - | 2 (2) |
| Crescentic GN | - | - | - | 1 | - | - | - | 1 (1) |
| Minimal change disease | 7 | - | - | - | - | - | 1 | 8 (9) |
| Nodular glomerulosclerosis | 1 | - | - | - | - | - | - | 1 (1) |
| Alport syndrome | - | - | - | - | - | - | 1 | 1 (1) |
| Diffuse proliferative GN | - | - | 6 | 2 | - | - | - | 8 (9) |
| Congenital nephrotic syndrome | 2 | - | - | - | - | - | - | 2 (2) |
| Secondary glomerulonephritis | | | | | | | | |
| Secondary amyloidosis | - | - | - | - | - | - | 1 | 1 (1) |
| SLE nephritis | 4 | 5 | 1 | - | - | - | 4 | 14 (15) |
| HSP nephritis | 4 | 3 | 4 | - | 1 | - | - | 12 (13) |
| Tubulointerstitial disease | | | | | | | | |
| Acute tubulointerstitial nephritis | - | - | - | - | - | - | 1 | 1 (1) |
| End-stage renal disease | - | - | - | - | - | 1 | - | 1 (1) |
| Nonspecific findings | 2 | 1 | 1 | - | 1 | - | 1 | 6 (7) |
| Normal findings | - | 2 | - | - | - | - | 4 | 6 (7) |
| TOTAL n (%) | 30 (33) | 21 (23) | 17 (19) | 3 (3) | 3 (3) | 2 (2) | 15 (17) | 91 (100) |

GN: glomerulonephritis; FSGS: focal segmental glomerulosclerosis; SLE: systemic lupus erythematosus; HSP: Henoch-Schonlein Purpura; NS: nephrotic syndrome; ANS: acute nephritic syndrome; RPGN: rapidly progressing glomerulonephritis; AKI: acute kidney injury; CKD: chronic kidney disease

35% (27/77). Common causes of primary GN were IgAN in 12/50 (24%), FSGS, DPGN and MCD each in 8/50 patients (16%). SLE nephritis and HSP nephritis were the most common causes of secondary GN [14/27 (51%) and 12/27 (45%) respectively].

The histopathological findings in 6 cases of isolated hematuria were: SLE nephritis in 3/6 (50%), IgAN, MGN and Alport syndrome each in 1/6 patients (~17%). Nine children with isolated proteinuria had the following histopathological findings: normal findings in 4/9 (45%) followed by MCD, secondary amyloidosis, SLE nephritis, ATIN and nonspecific findings each in 1/9 patients (11%).

## DISCUSSION

Our study provides data regarding kidney disease pattern from a pediatric population in our region over a ten-year period. Our hospital is a tertiary referral hospital in our region, playing a major role in healthcare management. At present, there is no national database of kidney biopsies in the country and this is the first reported kidney biopsy data from our population in this region.

We performed biopsies on 100 children with a success rate of 91% (insufficient specimen in 9 patients) and a complication rate of 2% over ten-year period. Complications seen in 2 patients were macroscopic hematuria and all recovered spontaneously.

The sufficient biopsy material rate has a range of 69% to 100% in the different studies (9,10). The complication rates in different series may be as low as 2.6% or as high as 43% (9-15). In our biopsy series, the success and complication rates did not differ from most of the studies on children.

In our study, NS (33%) was the most common indication for kidney biopsy, in accordance with other studies in children (2,4,16,17). Other common indications were ANS (24%) and nephrotic-nephritic syndrome (18%). FSGS was the most

common histopathological diagnosis in 26% of biopsies of NS. MCD is known as the most common cause of NS in children (18). However, recent studies from different countries have reported an increased frequency of FSGS in children (17,19,20).

The most common diagnosis in the biopsies was primary GN as a group (53%), as in the studies by Ergin and Altuntaş (7,21). The distribution of types of primary GN varies from one center to another depending on age, ethnicity, geographical region, patient characteristics and the indication for biopsy. Chang et al. (22) reported that IgAN was the most common histopathological diagnosis in primary GN, while Printza et al. (1) defined FSGS as the most common primary GN. In our study, IgAN was the most common histopathological diagnosis in children with primary GN (24%). Consistent with a local study, it was also the most common histopathological diagnosis in children presenting with ANS (38%) (4).

However, SLE nephritis was the leading the histopathological diagnosis and contributed 15% of cases in overall biopsies. Since renal involvement is more frequent in children with SLE than in adults and represent 15-20% of all SLE patients, kidney biopsy is very important for prognostic and therapeutic approaches (1,23).

Systemic lupus erythematosus nephritis was also the most common diagnosis (51%) among secondary GN. The high proportion of SLE nephritis in our study is consistent with studies from Hong Kong (71%) and Pakistan (54%), but not consistent with the studies from other regions of our country (2,5). In a study of 614 children, Demircin et al. (4) found that amyloidosis was the most frequent histopathology in secondary GN.

There were several limitations to our study. The population size was a relatively small sample from a single center even though it is a tertiary referral hospital. Additionally, data were collected retrospectively. Biopsy specimens were not evaluated by electron microscopy.

The pattern of kidney diseases in children is quite different among countries, even the regions of the country (1-8). Many differences in specific incidences of glomerulopathies can also be explained by confounding factors including genetic or environmental factors, race, frequency of infections, referral bias, the non-availability of the necessary facilities (e.g., electron microscopy) or biopsy rate. We suggest that small numbers of our study population and the fact that as a tertiary centre, admitting mostly difficult cases might have affected our results.

In conclusion, our study presents the first epidemiological data regarding kidney disease pattern of kidney biopsies from the pediatric population of our region. IgAN as primary glomerulonephritis and SLE as secondary glomerulonephritis were the most common kidney diseases among children in our region. Despite its limitations, this study may provide an insight into the spectrum of kidney diseases within the region, as there is no national registry. The histopathological diagnosis of kidney disease is very important to predict the prognosis.

**Ethics Committee Approval:** Ethics committee approval was received for this study from the ethics committee of Trakya University School of Medicine.

**Informed Consent:** Written informed consent was obtained from the parents of the patients who participated in this study.

**Peer-review:** Externally peer-reviewed.

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