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Relationship between histopathological patterns with clinical diagnosis in pediatric patients with renal disorders. A single-center observational study, 4-year follow-up

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Abstract

Introduction: Glomerulopathies in children may not be correlated with the degree of glomerular filtration or the intensity of proteinuria as it occurs in adults. The objective of the present study was to describe the histopathological characteristics of renal biopsies performed in a pediatric population with glomerulopathies and to correlate them with the clinical presentation.

Methods: This observational study was carried out at the Baca Ortiz Pediatric Hospital (Quito) from January 2016 to July 2019. Children with glomerulopathies diagnosed with renal biopsy were included. The variables were: clinical diagnosis, histological pattern, age, sex, ethnicity, urea, creatinine, proteinuria, and renal ultrasound. The sample was non-probabilistic. Descriptive statistics were used, and Cramer's V test was used to determine the degree of association.

Results: In 57 cases, 29 (50.9%) were men. The presence of azotemia occurred in 45.6% of the cases. Nephrotic range proteinuria in 47% of cases. The average glomerular filtration rate was 116 ml/min. The most prevalent glomerulonephritis was membranoproliferative (29.8%), with endocapillary and lupus glomerulonephritis accounting for 50% of the sample. Postinfectious glomerulopathy (PGIP) 29 cases (50.9%); Nonproliferative primary glomerulonephritis GMINOP 9 cases (15.8%) and secondary glomerulopathy (GPII) 18 cases (31.6%). There was no association with the presence of clinical syndromes (P>0.05).

Conclusions: There is no relationship between histopathological patterns and clinical diagnosis in the sample analyzed in pediatric patients. Primary proliferative glomerulopathies represent little more than half of the renal pathology biopsied.

Keywords:

MESH: Nephrosis, Lipoid; Glomerular Filtration Rate; Renal Insufficiency, Chronic; Disease Pro-

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The etiology of chronic kidney disease (CKD) in the pediatric population varies according to the area and the continent; for example, in the United States, Japan, and Italy, the leading cause of CKD is congenital anomalies of the kidney and urinary tract, with a prevalence of 34 to 58% [1], while in India and Sudan, the leading cause is chronic glomerulonephritis, with a prevalence ranging between 30 and 60% [2, 3]. In Colombia, malformations of the urinary tract represent more than 50% of the causes of CKD, followed by glomerulopathies, hypoplasia-dysplasia, hereditary nephropathies, and vascular nephropathies [4]. The prevalence of renal lesions is not known locally in children.

On the other hand, the clinical manifestations of renal pathologies in children can be very varied and present as macroscopic hematuria, lumbar pain, nephrotic syndrome (NS), nephritic syndrome (NS) or present nonspecific symptoms: growth retardation or anemia [5]. A limited number of patients progress to end-stage chronic kidney disease (ESRD) in one year, so early diagnosis is of the utmost importance. Ultrasound-guided percutaneous renal biopsy (PRB) is an invasive diagnostic method that must be performed individually, depending on the clinical picture and assessing the risk-benefit in each patient; it helps to assess the therapeutic choice and the prognostic evaluation of kidney diseases, being a fundamental pillar in clinical nephrology and even more so in pediatric nephrology since it allows the precise identification of renal lesions and their nosological classification, the appreciation of the signs of activity and severity, and the evaluation of the importance of the lesions [6, 7]. It has been shown in several studies that it can change clinical diagnosis and treatment by approximately 40% in patients who are at risk of undergoing unnecessary immunosuppression [8].

Glomerulopathies represent a significant cause of CKD in children, thus reducing the quality and years of life of this vulnerable population and the high economic resources that this pathology represents; for these reasons, it is imperative to identify it promptly. The clinical manifestations that the pediatric patient overwhelmed by glomerulonephritis presents and when it will be necessary to carry out a pathological study, without this representing a risk of complications for the patient's health status.

The objective of the present study was to describe the main renal pathologies that affect a pediatric population in a reference center in Quito-Ecuador, as well as to describe the clinical diagnoses and sociodemographic characteristics of the patients.

Materials and methods

Study design
The present study is observational, descriptive, and retrospective.

Scenery
The study was carried out in the Baca Ortiz Pediatric Hospital nephrology department of the Ministry of Public Health in Quito-Ecuador from January 01, 2016, to July 31, 2019.

Participants
Pediatric patients between 0 and 17 years old who underwent a renal biopsy due to alterations in renal function were included. Cases with <5 glomeruli in the sample, biopsies in kidney transplant patients, and duplicate biopsies were excluded. Biopsies with results of exclusive tubulointerstitial diseases were excluded. Cases with incomplete data were removed from the analysis.

Variables
The variables were clinical diagnosis, histological pattern, age, sex, ethnicity, edema, urea, creatinine, proteinuria, and renal ultrasound.

Data sources/measurements
The source was indirect; the institutional electronic file was reviewed, and the histopathology record of the pathology service was obtained. Laboratory results were obtained from the electronic laboratory record.

Biases
To avoid possible interviewer, information, and memory biases, the data were guarded at all times by the principal investigator with a guide and records approved in the research protocol. Observation and selection bias was avoided by applying the participant selection criteria. All the clinical and paraclinical variables of the period above were recorded. Two researchers independently analyzed each record in duplicate, and the variables were recorded in the database once their agreement was verified.

Studio size
The sample was nonprobabilistic, census type, where all the analyzable cases of the study period were included.

Quantitative variables
Descriptive statistics were used. Scaled results are expressed as the means and standard deviations. Categorical data such as sex are presented as proportions.

Statistical analysis
Univariate analysis was performed. The chi-square test was used to demonstrate a relationship between the variables; Cramer's V test was used to determine their degree of association. The statistical package used was SPSS 25.0 (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.).

Results

Participants

Fifty-seven cases entered the study.

Baseline characteristics of the study population

In a total of 57 cases, 29 (50.9%) men and 28 (49.1%) women Mestizo ethnic children of school age represented the highest percentage (Table 1). The presence of azotemia occurred in 45.6% of the cases. Nephrotic range proteinuria was observed in 47% of cases (Table 1). The indication and complications of renal biopsy are presented in Table 1. The average glomerular filtration rate was 116 ml/min, 110 ml/min in males, and 123.38 ml/min in females, with a nonsignificant difference between the two groups with a *P value* = 0.869.

Histological diagnosis

The most prevalent glomerulonephritis was the membranoproliferative type (29.8%), which, together with endocapillary and lupus glomerulonephritis, accounted for 50% of the sample (Table 2). Statistical tests of association were as follows: chi-square = 60.34 ($P = 0.001$), likelihood ratio 49.20 ($P = 0.015$), linear by linear association 5.123 ($P = 0.024$).

Histological pattern

Biopsies were grouped by three types of patterns: postinfectious glomerulopathy (PGIP), 29 cases (50.9%); primary nonproliferative glomerulonephritis GMINOP, 9 cases (15.8%); and secondary glomerulopathy (GPII), 18 cases (31.6%) (Table 2). The distributions according to age, sex, and biopsy indication are presented in Table 3. In the same way, when looking for an association between the biopsy indication and the grouped pathology results (seeking to reduce the degrees of freedom of the table), there is no significance in the result with a Pearson chi-square of 11 with 6 degrees of freedom. Moreover, with a significance of 0.087, the chi-square acceptance criteria are not met either, having 75% of expected frequencies with a value less than five and a minimum expected count of 0.8.

Kidney function in pathologies

The average GFR in postinfectious glomerulopathy was 102 ml/min; in primary nonproliferative glomerulopathy, it was 197 ml/min, and in secondary glomerulopathy, it was 98.66 ml/min. The difference between the groups was nonsignificant with a *P value* of 0.145.

The average filtration rate in nephrotic syndrome was 137 ml/min; in unexplained acute kidney injury, it was 24 ml/min; in nephrotic syndrome, it was 75 ml/min; and in hematuria, it was 130 ml/min. The difference between the groups was significant, with a value of $P = 0.0001$.

Corticoresistance

Classifying steroid resistance by syndrome, 46% steroid dependence, 39% steroid resistance, and 7% steroid sensitivity corresponded to nephrotic syndrome. Classified by specific pathology, the data are presented in Table 4.

Table 1. Descriptive variables of the study

Cluster of age	Frequency n=57	Percentage	Percentage accumulated
Scholarship			
Infant	1	1.8	1.8
Preschool	7	12.3	14.0
School	30	52.6	66.7
Teen	19	33.3	100.0
Ethnicity			
Indigenous	12	21.1	21.1
Hispanic	35	61.4	82.5
Afro-Ecuadorian	9	15.8	98.2
White	1	1.8	100.0
Geographical origin			
Saw	23	40.4	40.4
Coast	21	36.8	77.2
Amazon	11	19.3	96.5
Foreign	2	3.5	100.0
Azotemia			
Altered urea	26	45.6	45.6
Creatinine abnormality	18	31.6	31.6
Proteinuria of 24 hours			
<150 mg/24 hours	5	8.8	8.8
150-<1000 mg/24 h	9	15.8	24.6
1000-3500 mg/24 h	16	28.1	52.6
>3500 mg/24 h	27	47.4	100.0
Alterations ultrasound			
presents	4	7	7
Indication of biopsy			
Syndrome nephrotic	35	61.4	61.4
RPGN	5	8.8	70.2
Syndrome Nephritic	9	15.8	86
Hematuria	8	14	100
Complications of biopsy			
Without Fact	2	3.5	3.5
Bleeding	5	8.8	12.3
Pain	6	10.5	22.8
Hypertension	1	1.8	24.6
Infection	1	1.8	26.3
Others	4	7.0	33.3
None	38	66.7	100.0

RPGN: rapidly progressive glomerulonephritis.

Table 2. Histopathological diagnoses in the study group.

Histological Diagnosis	N	%	Sd. nephrotic	RPGN	Sd. Nephritic	Hematuria
GN. Membranoproliferative	17	29.8	12	2	2	1
GN. Endocapillary diffuse	6	10.5	4	0	1	1
GN. Lupus	6	10.5	2	0	4	0
GN. By IgA	6	10.5	1	0	1	4
GN. post strep	5	8.8	4	0	1	0
GN. Changes Minima	4	7.0	3	0	0	1
FSGS	4	7.0	4	0	0	0
GN. Extracapillary	3	5.3	0	2	0	1
GN. Mesangial	3	5.3	3	0	0	0
GN. Membranous	1	1.8	1	0	0	0
Others	1	1.8	0	1	0	0
Sample inadequate	1	1.8	-	-	-	-

GN: glomerulonephritis. FSGS: focal segmental glomerulosclerosis. X^2= 60.34 (*P* =0.001), Likelihood ratio 49.20 (*P* =0.015), Linear by linear association 5.123 (*P* =0.024). RPGN: rapidly progressive glomerulonephritis.

Table 3. Classification of histological patterns by age, sex, and biopsy indication

	PIPG N=29	PNOPG N=9	SG N=18
Age			
Infant	1 (3.45%)	0 (0%)	0 (0%)
Preschool	3 (10.34%)	2 (22.22%)	2 (11.11%)
School	15 (51.72%)	5 (55.56%)	9 (50%)
Teen	10 (34.48%)	2 (22.2%)	7 (3889%)
Sex			
Men	17 (58.62%)	4 (44.44%)	7 (38.89%)
Woman	12 (41.38%)	5 (55.56%)	11 (61.11%)
Biopsy indication*			
Nephrotic Sd.	19 (65.52%)	8 (88.89%)	7 (38.89%)
GNRP	4 (13.79%)	0 (0%)	1 (5.56%)
Sd. Nephritic	3 (10.34%)	0 (0%)	6 (33.33%)
Hematuria	3 (10.34%)	1 (11.11%)	4 (22.22%)
Glomerular Filtration			
GFR mL/min	90 (75-130)	134.5 (77-318)	107.4 (70-127)

PIPG: postinfectious glomerulopathy. PNOPG: primary nonproliferative glomerulopathy. SG: secondary glomerulopathy.
*X2 11.05 *P* =0.087, Likelihood ratio 12.49 *P* =0.052, Linear by linear association 0.38 *P* =0.66.

Table 4. Classification of sensitivity, dependence, and resistance to steroids.

	Cortico-sensitive N=2	Cortico-dependent N=14	Cortico-resistant N=12
syndromes			
Nephrotic Sd	2 (7%1)	13 (46%)	11 (39%)
Nephritic Sd	0 (0%)	0 (0%)	1 (4%)
Hematuria	0 (0%)	1 (4%)	0 (0%)
Pathology groups			
PIPG	2 (7%)	7 (25%)	7 (25%)
PNPG	0 (0%)	3 (11%)	3 (11%)
SG	0 (0%)	4 (14%)	2 (7%)

PIPG: postinfectious glomerulopathy. PNOPG: primary nonproliferative glomerulopathy. SG: secondary glomerulopathy.

Discussion

In this investigation, 57 kidney biopsies results were analyzed, in which it was observed that there was no significant difference between men and women, at 50.9% and 49.1%, respectively, compared to the REPIR II Project, in which 400 cases were analyzed, 66% were reported in male patients and 34% were female [9].

In the present study, school age was the most prevalent, accounting for 52% of cases, followed by adolescents, with a mean age of 8.66 years, different from the REPIR II study, in which those under two years of age accounted for 59. %, followed by 6 to 12 years with 22% [9].

Concerning ethnicity and its relationship with glomerulopathies, no data were found in the country about the relationship between these variables; in the present study, the mestizo

ethnic group is the most frequent, with 61.4%, followed by indigenous, Afro-Ecuadorian, and white ethnic groups. Glomerulopathies are more frequent in patients from the mountains, followed by those from the coast and finally the Amazon, with 19%.

Regarding changes in complementary tests, we observed that there were changes in urea values adjusted for age in 45.6%, with a mean of 33.6 in preschool children and a median of 31; in schoolchildren, the mean was 62.3 and the median 32.2; in adolescents, the mean was 76, and the median was 56; 31.6% of cases presented altered creatinine values adjusted for age, with a mean in preschool children of 0.27 and a median of 0.3, in schoolchildren the mean was 1.3 and the median of 0.46; in adolescents, the mean was 1.07 and a median of 0.86; 24-hour proteinuria presented as nephrotic range proteinuria in 47.4% followed by proteinuria in moderate significant range, with a mean in preschool children of 383 and a median of 41; in schoolchildren, the mean was 94.6, and the median was 28.11, and in adolescents, the mean was 103.5, and the median was 43.5. The average glomerular filtration rate was 116 ml/min, with 110 ml/min in males and 123.38 ml/min in females, with a nonsignificant difference between the two groups with a p of 0.869. In postinfectious glomerulonephritis, the average GFR was 102 ml/min, while in primary nonproliferative glomerulonephritis, it was 197 ml/min, and in secondary glomerulonephritis, it was 98.66. The difference between the groups was not signed with a P of 0.145; the average glomerular filtration rate in nephrotic syndrome was 137 ml/min, in unjustified acute kidney injury it was 24 ml/min, in nephritic syndrome it was 75 ml/min and in hematuria it was 130 ml/min, and the difference between the two was significant. Groups with a *P* of 0.000, although the data must be taken cautiously as they are tiny groups of analysis. Renal ultrasound: Seven percent of the cases analyzed presented alterations in the ultrasound. Compared with a series that indicates that nephrotic syndrome presents some degree of kidney injury in only 3% [10], while 1% of postinfectious acute glomerulonephritis develop some degree of acute kidney injury [11]: The Italian pediatric registry with 432 biopsies indicates that 31% of cases presented nonnephrotic proteinuria and 34% with nephrotic proteinuria in 34% and 15% due to acute or chronic renal failure [12]. Guillén's study, through univariate analysis, showed that 78% of patients with significant proteinuria had a low GFR, 79% of patients with significant proteinuria had an abnormal renal ultrasound, and 10.4% of patients with normal proteinuria had abnormalities on ultrasound. Kidney [13]. This indicates that the clinical presentation and its clinical and paraclinical manifestations (laboratory and imaging) do not have a statistically significant relationship with the histopathological patterns found in renal histology.

In this study, the most frequently observed is membranoproliferative glomerulopathy, followed by diffuse endocapillary glomerulopathy. It is also evident that proliferative glomerulopathy constitutes the primary histology in all age groups, compared with the study by Fidan et al. or Printz, which reports focal glomerulosclerosis as the most frequent [14, 15]. Other studies, such as that of Román or the clinical practice guidelines of Mexico, report a minimal change in nephropathy as the most frequent histology of idiopathic NS [10].

Nephrotic syndrome is the first indication for biopsy, as in the study by Printza and the study by Mayor et al., followed by nephritic syndrome, hematuria, and unexplained acute kidney injury. Within nephrotic syndrome, steroid-dependent patients represent the main indication for renal biopsy, followed by steroid-resistant patients. This differs from the study by Printza and Mayor, which indicates that steroid resistance is the most frequent indication for biopsy. In addition, it was observed that a nonnegligible percentage of patients with primary proliferative glomerulopathy were corticoresistant (44.81%).

In this study, there were no significant complications. Among the minor complications, the main postbiopsy complication was pain followed by bleeding, which is related to other studies in which small-sized perirenal hematoma and macroscopic hematuria with 10% were the main complications, while limited infection, arteriovenous fistula, and significant bleeding had a frequency of <1%. For another study by Whittier and Korbet, they found 13% of complications, 6.4% being primary, and only 0.1% (1 patient) died secondary to a massive perirenal hematoma. In Argentina, a small series of ultrasound-guided PRBs found that all patients presented with microscopic hematuria within the first 24 hours postbiopsy, macroscopic hematuria, and perirenal hematoma in 2.9% of patients [16, 17], indicating that renal biopsy, despite being a safe procedure, can have complications that can become serious in extremely low percentages.

Conclusions

There was no relationship between histopathological patterns and clinical diagnosis in the sample analyzed in pediatric patients. Primary proliferative glomerulopathies represent little more than half of the renal pathology biopsied.

Abbreviations

PIPG: postinfectious glomerulopathy.
GMINOP: primary nonproliferative glomerulopathy.
GPII: secondary glomerulopathy.
RPGN: rapidly progressive glomerulonephritis.

Supplementary information

Supplementary materials have not been declared.

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Does not apply.

Author contributions

Wilmer Stalin Sanango Reinoso: Conceptualization, Data Curation, Formal Analysis, Fundraising, Research, Methodology, Project Management, Resources, Software, Writing – original draft.
Junior Rafael Gahona Villegas: Conceptualization, supervision, validation, visualization, and writing: review and editing.
Jorge Manuel Pérez Galarza: Methodology, validation, supervision, writing: Review and editing.
All authors read and approved the final version of the manuscript.

Financing

The authors provided research expenses.

Availability of data or materials

The data sets generated and analyzed during the current study are not publicly available due to participant confidentiality but are available from the corresponding author upon reasonable academic request.

Statements

Ethics committee approval and consent to participate

This study was approved by the ethics and research committee of the Baca Ortiz Pediatric Hospital.

Consent to publication

It does not apply when images or photographs of the physical examination or X-rays/tomographies/MRIs of patients are not published.

Conflicts of interest

The authors report having no conflicts of interest.

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