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Original research

CLINICAL AND HISTOPATHOLOGICAL STUDY OF GLOMERULAR DISEASES IN CHILDREN

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ABSTRACT

Objective: *To investigate the histopathological and clinical pattern of glomerular diseases in children.*

Method: *A cross - sectional descriptive study was conducted on 71 children with glomerular disease who underwent kidney biopsy from January 2020 to December 2022.*

Results: *Pure nephrotic syndrome was the main diagnosis before kidney biopsy (59.3%), followed by non - pure nephrotic syndrome with 12.7%, Schonlein Henoch nephritis, Lupus nephritis, IgA nephropathy, accounting for 11.2%, 8.4%, 5.6%, respectively. Hemolytic uremic syndrome and Alport syndrome accounted for 1.4% of each type. After being diagnosed by histopathological results, minimal change disease was most common with 36.6% in the primary group, and Lupus nephritis was found mainly with 15.5% in the secondary group. Among the clinical manifestations of glomerular diseases, hematuria, and extrarenal manifestations were significantly different among the glomerular groups ($p < 0.05$). The ratio of change in diagnosis after the renal biopsy was 38%, in which IgA nephropathy had the lowest ratio, and Lupus nephritis and nephrotic syndrome had the highest ratio.*

Conclusions: *Minimal change disease predominated in the group of primary glomerular disease, and Lupus nephritis was the majority in the group of secondary glomerulonephritis. Hematuria and extrarenal manifestations were clinically significant differences among groups of glomerular diseases.*

Keywords: *Renal biopsy, nephrotic syndrome, histopathology, children.*

I. INTRODUCTION

Glomerular disease is the most common cause of kidney disease in children. Its etiology may be the infectious or non - infectious agents. The most known infectious cause is post - streptococcal glomerulonephritis, followed by other bacteria, viruses, fungi, and parasites. Non - infectious causes are often associated with primary glomerular diseases such as IgA nephropathy, membranous proliferative glomerulonephritis, membranous nephropathy, and systemic diseases such as systemic lupus erythematosus, Henoch - Schönlein [1]. Although systemic diseases may have classic symptoms including butterfly rash, purpura on the skin, arthralgia, and abdominal pain... however, the clinical manifestations of acute glomerular diseases at the onset are quite similar, for example edema, hematuria, and hypertension. Besides, many medical centers are not qualified to do advance medical tests. Therefore, it can be easily misdiagnosed, leading to incomplete treatment, making the disease progress, and possibly leading to end - stage kidney disease.

The glomerular diseases in children are diverse, often requiring long - term treatment, and often recurrence [2]. The treatment response as well as progression to end - stage renal disease depends on the pathological lesions [3]. Knowing well the results of renal histopathology

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will help accurately diagnose the etiology, choose the appropriate therapy as well as predict treatment response. However, only a few medical centers can perform kidney biopsy procedures. To understand the relationship between the clinical pattern and the histopathological characteristics of glomerular diseases in children, we carried out this study to describe the results of the renal histopathology of glomerular diseases in children, and investigate the relationship between the renal histopathology with the clinical pattern of glomerular diseases in children.

II. MATERIALS AND METHODS

A cross - sectional descriptive study was carried out in 71 children with glomerular disease who were indicated for kidney biopsy from January 2020 to December 2022 at Pediatric Center of Hue Central Hospital and Pediatrics Department of Hue University of Medicine and Pharmacy Hospital.

Selection criteria were: Children < 16 years old, diagnosed with glomerular diseases and indicated for kidney biopsy, included: (1) Steroid resistant nephrotic syndrome or steroid dependent nephrotic syndrome in a child > 10 years old, or nephrotic syndrome had manifestations of gross hematuria or renal failure. (2) Acute glomerulonephritis with gross hematuria lasting more than 3 weeks or presenting with acute renal failure lasting more than 2 weeks. (3) Persistent proteinuria nephrotic range for more than 3 months. (4) Lupus nephritis, Scholein Henoch nephritis [2 - 5]

Exclusion criteria were parents or caregivers did not consent to participate in the study.

Clinical investigation included: performing clinical examination, and laboratory tests at the time of kidney biopsy. Collecting variables of age, gender, geography, edema, hypertension, gross hematuria, urine volume, serum albumin, serum creatinine, proteinuria, urinary creatinine, dipstick, and diagnosis before performing renal biopsy.

Renal biopsy was conducted by: an ultrasound - guided percutaneous kidney biopsy with a 16G needle, kidney tissue were sent to read at the Histopathology department, Children's Hospital number 1. Diagnosis which were recorded by histopathological results were collected as a variable.

Data were analyzed by using SPSS software

III. RESULTS

3.1. General characteristics of the research group

There were 71 children with glomerular diseases who were indicated for ultrasound - guided percutaneous kidney biopsy, the average age was 9.1 ± 3.9 years, the group 11 - 15 years old predominated with 42,5%. Male children predominated and the majority of children came from rural areas.

3.2. The diagnosis before biopsy

Table 1: The diagnosis before the biopsy

The diagnosis before biopsy	Frequency (n)	Percent (%)
Henoch Schonlein purpura nephritis (HSPN)	8	11.2
Lupus nephritis (LN)	6	8.4
Pure nephrotic syndrome (pNS)	42	59.3
Nephritic - nephrotic syndrome (NNS)	9	12.7
IgA nephrology (IgA)	4	5.6
Hemolytic uremic syndrome (HUS)	1	1.4
Alport syndrome (Alport)	1	1.4
Total	71	100

Pure nephrotic syndrome was the main diagnosis before renal biopsy (59.3%), followed by nephritis-nephrotic syndrome with 12.7%, Schonlein Henoch nephritis, Lupus nephritis, IgA nephropathy, accounting for 11.2%, 8.4%, and 5.6%, respectively. Hemolytic uremic anemia and Alport syndrome accounted for 1.4% of each type.

3.3. Histopathological results

Table 2: Histopathological results of glomerular diseases

Group	Histopathological results	Frequency (n)	Percent (%)
Secondary glomerular disease	Henoch Schonlein purpura nephritis (HSPN)	6	8.5
	Lupus nephritis (LN)	11	15.5
	Secondary focal segmental glomerulosclerosis (sFSGS)	1	1.4
Primary glomerular disease	Minimal change disease (MCD)	26	36.6
	Primary Focal segmental glomerulosclerosis (pFSGS)	19	26.8
	IgA nephrology (IgA)	6	8.5
	Membranoproliferative glomerulonephritis (MPGN)	1	1.4
	Membranous nephropathy (MN)	1	1.4
Total		71	100

The group with primary glomerular disease (74.6%) accounted for the majority comparing with the group with secondary glomerular disease (25.4%). In the primary group, minimal change disease was the most common with 36.6%, in the secondary group, Lupus nephritis was found mainly (15.5%).

3.4. Clinical features of glomerular diseases

Table 3: Clinical features of glomerular diseases

Clinical features	Hypertension		Gross hematuria		Oliguria		Extrarenal manifestations	
Causes	Frequency (n)	Percent %	Frequency (n)	Percent %	Frequency (n)	Percent %	Frequency (n)	Percent %
HSP (n=6)	1	16.7	3	50	0	0	6	100
LN (n=11)	6	54.5	5	45.5	2	18.2	4	36.4
sFSGS (n=1)	0	0	1	100	0	0	0	0
MCD (n=26)	3	11.5	0	0	2	7.7	0	0
pFSGS (n=19)	5	26.3	1	5.3	1	5.3	0	0
IgA (n=6)	0	0	5	83.3	0	0	0	0
MPGN (n=1)	1	100	0	0	0	0	0	0
MN (n=1)	0	0	1	100	0	0	0	0
Total (n=71)	16	22.6	16	22.6	5	7.0	10	14.1
p	> 0,05		< 0,05		> 0,05		< 0,05	

In the clinical manifestations of glomerular disease groups, hematuria symptom, and extrarenal manifestations were significantly different between groups of glomerular diseases ($p < 0.05$).

3.5. The rate of the change in diagnosis before and after kidney biopsy

Table 4: The rate of the change in diagnosis before and after kidney biopsy

		Pre - biopsy diagnosis							Total
		HSPN	LN	pNS	NNS	IgA	HUS	Alport	
Post - biopsy diagnosis	HSPN	6	0	0	0	0	0	0	6
	LN	2	5	0	3	0	1	0	11
	MCD	0	0	25	1	0	0	0	26
	pFSGS	0	1	13	4	0	0	1	19
	IgA	0	0	2	0	4	0	0	6
	MPGN	0	0	0	1	0	0	0	1
	MN	0	0	1	0	0	0	0	1
	sFSGS	0	0	1	0	0	0	0	1
Total		8	6	42	9	4	0	1	71

Table 5: The rate of change in diagnosis after renal biopsy

Change in diagnosis	Frequency (n)	Percent (%)
Yes	27	38.0
No	44	62.0
Total	71	100

The rate of change in diagnosis after kidney biopsy was 38%.

IV. DISCUSSION

In Table 1, our study noted that pure nephrotic syndrome was the main diagnosis before kidney biopsy (59.3%), followed by nephritic-nephrotic syndrome with 12.7%, Schonlein Henoch purpura nephritis, Lupus nephritis, IgA nephropathy, accounting for 11.2%, 8.4%, and 5.6%, respectively. Hemolytic uremic anemia and Alport syndrome accounted for 1.4% of each type.

Nguyen Thi Hong Duc's study recorded that pre-biopsy diagnosis were nephrotic syndrome with 46.9%, acute glomerulonephritis with 15.6%, Lupus nephritis with 21.9%, recurrent hematuria with 12.5 %, renal failure of unknown cause with 3.1% [6].

Lee SA's study in 318 cases showed that pre-biopsy clinical diagnosis included 114 patients (35.9%) with asymptomatic urine abnormalities, 44 patients (13.9%) with isolated hematuria, 70 patients (22.0%) hematuria with proteinuria; 93 patients (29.3%) with nephrotic syndrome; 57 patients (18.0%) with acute glomerulonephritis; 38 patients (11.9%) had Henoch Schönlein purpura nephritis; 4 patients (1.2%) with Lupus nephritis; and 12 patients (3.7%) had other diseases, such as acute renal failure, Alport syndrome, hemolytic uremic syndrome…[7]

Thus, the clinical diagnosis of glomerular diseases before renal biopsy is also quite diverse. Among them, nephrotic syndrome is still one of the most common diagnosis.

Regarding the histopathological results of the glomerular group listed in Table 2, we found that primary glomerulonephritis (74.6%) accounted for the majority comparing with the secondary glomerular group (25.4%). In the primary glomerulonephritis, minimal change disease was the most common with 36.6%, in the secondary glomerulonephritis, Lupus nephritis was found mainly (15.5%).

Research by Huynh Thoai Loan from 2008 to 2010 in 262 children showed that the rate of minimal change disease was 24.05%, Lupus nephritis was 23.66%, focal segmental glomerulosclerosis

was 17.94%, IgA nephrology was 11.45%, Henoch schonlein purpura nephritis was 3.44%, membranoproliferative glomerulonephritis was 1.53%, and membranous nephrology was 1.53% [8].

A group of Korean researchers published the results of kidney biopsies in 318 children over 27 years as follows: IgA nephropathy was the most common at 27.9%, followed by minimal change disease at 21.3%, membranoproliferative glomerulonephritis 7.2%, and focal segmental glomerulosclerosis 3.4%. In the group of secondary glomerulonephritis, Schonlein Henoch nephritis accounted for 12.2% while Lupus nephritis accounted for 1.5% [7].

A 16 - year Morroco study in 112 children showed that primary nephropathy accounted for 59.8% of cases, with minimal change disease predominating in 40.2% of cases. Secondary nephropathy accounted for 27.7% of cases, with mainly Lupus nephritis (11.6%), followed by Henoch-Schonlein purpura nephritis (6.2%) and post-infectious glomerulonephritis (3.6%). There was one case of hepatitis B virus-associated membranous nephritis. Chronic glomerulonephritis accounted for 12.5% of cases [9].

These results may be explained by the difference of racial characteristics, regions and medical conditions, however, in general, primary glomerulopathy was the predominant group of glomerular diseases, and minimal change disease was the most common histopathological finding.

When learning about the clinical pattern of glomerular diseases in children, we noted that the overall prevalence of hypertension in the study group was 22.6%. There was no difference in hypertension among glomerular diseases ($p > 0.05$). In the study of Nguyen Thi Hong Duc, the rate of hypertension in renal biopsy patients was 31.3% [6]. Regarding the group of primary glomerular diseases, mainly nephrotic syndrome, we found in Phan Ngoc Hai's study the rate of hypertension was 13.9% [10], and 10.8% of children in Nguyen Van Sang's study showed signs of hypertension [11]. This result was quite similar to our study. In Thai Thien Nam's study on Lupus nephritis in children, the rate of hypertension accounted for 50% [12]. Hypertension is a common symptom of glomerular diseases. Hypertension is result from glomerular damage as well as extraglomerular mechanisms. Renal factors such as hypoalbuminemia lead to a decrease in oncotic pressure, a decrease in glomerular filtration rate, an activation the Renin - Angiotensin - Aldosteron system, which causes salt and water retention, vasoconstriction, and increases blood pressure; or fibrotic lesions in the glomeruli also contribute to hypertension [13, 14]. Recently, the feedback reaction between albuminuria and the glomerular loops has also contributed to hypertension [14]. Extrarenal mechanisms include the use of drugs (corticosteroids, cyclosporine A), genetic factors, diet, and atherosclerotic factors [13]. Therefore, symptoms of hypertension are not specific to any group of glomerular diseases.

In the group of primary glomerular disease, the majority of patients did not have gross hematuria. In the group of secondary glomerular disease, the rate of gross hematuria was higher. There was a significant difference in hematuria among groups of glomerular disease ($p < 0.05$). In clinical evaluation, physician based on gross hematuria to access the cause of primary nephrotic syndrome. Nephrotic syndrome without glomerulonephritis is mostly idiopathic nephrotic syndrome such as minimal change disease, and focal segmental glomerulosclerosis. Nephrotic syndrome with glomerulonephritis hematuria is common in membranous glomerulopathy, membranous proliferative glomerulonephritis, IgA nephropathy… [15]. Therefore, gross hematuria is a valuable symptom to help identify the etiology of glomerular diseases.

The majority of patients did not have oliguria, or anuria (table 3). The results of our study were lower than that of Nguyen Thi Hong Duc with 21.9% of patients with oliguria [6].

Extrarenal manifestations were the majority in the secondary pathology group, while the primary glomerular disease group had no extrarenal manifestations. Notably, 7 of 11 patients with Lupus nephritis had no extrarenal manifestations, which easily led to the omission of diagnosis in centers that were not able to do advance medical tests.

Assessing the rate of diagnostic change before and after the kidney biopsy, we found in Table 4 that the diagnosis of pure nephrotic syndrome was changed

the most after kidney biopsy, and IgA nephropathy had a 100% concordance rate between clinical diagnosis and post - biopsy diagnosis. The overall rate of change in diagnosis post - biopsy was 38%.

According to research by Huynh Thoai Loan and Tran Thi Kim Anh, the diagnosis of nephrotic syndrome and Lupus nephritis were the two pre-biopsy diagnosis that changed the most [8, 16]. The rate of Tran Thi Kim Anh's study was 10% [16]. According to the study of Pilania, the diagnosis after biopsy was changed at 47% [17]. This ratio varied between the diagnostic orientation, the laboratory centers, and the experience of doctors. However, renal biopsy and histopathology have shown an important role in the definitive diagnosis of glomerular diseases, thereby providing the basis for selecting the best treatment methods for the patient.

V. CONCLUSIONS

In children with glomerular diseases, minimal change disease was most common in the primary group, Lupus nephritis was seen mainly in the secondary group. Hematuria and extrarenal manifestations were clinically significant differences among glomerular diseases. The rate of change in diagnosis after renal biopsy was 38%, in which IgA nephropathy had the lowest ratio, Lupus nephritis and nephrotic syndrome had the highest ratio.

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