Renal Outcomes of Childhood IgA Nephropathy and Henoch Schönlein Purpura Nephritis

Thanaporn Chaiyapak, M.D.*, Anirut Pattaragarn, M.D.*, Suroj Supavekin, M.D.*, Nuntawan Piyaphanee, M.D.*, Kraisoon Lomjansook, M.D.*, Julaporn Pooliam, M.Sc., Achra Sumboonnanonda, M.D.***

**Department of Pediatrics, **Office for Research and Development, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.*

ABSTRACT

Objective: Henoch-Schönlein purpura nephritis (HSPN) is considered the systemic form of IgA nephropathy (IgAN). However, differing clinicopathological features and renal outcomes of children with IgAN and HSPN have been reported in some studies.

Materials and Methods: This study retrospectively reviewed children with IgAN and HSPN younger than 18 years, between January 2004 and December 2015. The clinicopathological characteristics at diagnosis and the renal outcomes after at least 1 year of follow-up were compared between the two groups.

Results: A total of 54 children, comprising 21 with IgAN and 33 with HSPN, were recruited. The children with HSPN were younger than the children with IgAN. Gross hematuria and nephritic syndrome at the initial presentation were more common in children with IgAN. Regarding the pathological findings, IgAN had greater chronicity than HSPN. After a median follow-up period from first presentation to renal outcomes measurement of 4.0 years (1.3-12.2) in children with IgAN and 4.2 years (1.1-11.4) in children with HSPN, the renal outcomes were better in the latter group. The incidence of chronic kidney disease (CKD) was 28.6% in children with IgAN and 6.1% in children with HSPN ($p = 0.02$). Complete recovery was observed more frequently in children with HSPN than in children with IgAN (57.1% in IgAN vs. 87.9% in HSPN, $p = 0.01$).

Conclusion: Childhood IgAN has greater chronicity and worse renal outcomes than childhood HSPN, with a lower rate of complete recovery and a higher frequency of CKD. We recommend long-term follow-up for CKD in children with IgAN.

Keywords: Chronic kidney disease; Chronic renal disease; End-stage renal disease; Henoch-Schönlein purpura nephritis; IgA nephropathy (Siriraj Med J 2021; 73: 687-694)

INTRODUCTION

IgA nephropathy (IgAN) and Henoch-Schönlein purpura (HSP) are common causes of glomerulonephritis in children.[1] IgAN is a type of primary glomerulonephritis.[2,3] HSP is a clinical syndrome that affects many organs, including the kidneys (HSP nephritis, HSPN), and is classified as a type of systemic vasculitis.[1,4] HSP was redesignated IgA vasculitis in the second International Chapel Hill Consensus Conference (CHCC 2012),[5] but this term has not yet come into widespread use. A multivariate analysis showed that age of onset > 4 years, severe abdominal pain, and persistent purpura were significantly associated with the development of HSPN.[6]

HSP is thought to be a systemic form of IgAN because these two conditions share several clinical, histological, and immunological features.[7,8] The renal

Corresponding author: Achra Sumboonnanonda
E-mail: achrasu@gmail.com, thanaporn.cha@mahidol.ac.th
Received 31 March 2021 Revised 11 August 2021 Accepted 26 August 2021
ORCID ID: https://orcid.org/0000-0001-5855-5314
http://dx.doi.org/10.33192/Smj.2021.88

pathological features of HSPN are identical to those in IgAN, which is associated with the deposition of IgA in the mesangium. HSP mainly affects children,[9] whereas IgAN occurs more frequently in adults.[2] Recently, Kamei et al[10] posited that the two disorders were variants of a single disease because 6 children with IgAN developed HSPN 5 months to 14 years later. Few clinical studies have compared IgAN and HSPN in adults.[11,12] A study of adults by Calvo-Rio et al.[11] observed more severe renal outcomes in patients with IgAN than in patients with HSPN (not limited to biopsy-proven HSPN). Another matched cohort in Korea demonstrated that there were no significant differences in renal outcomes between these two conditions.[12] To date, the only one clinical study comparing IgAN and HSPN in children has been published; that study was conducted in 1987[13] and showed that children with HSPN had a higher incidence of chronic kidney disease (CKD) than children with IgAN (16% in HSPN vs. 5% in IgAN), in contrast to comparative studies conducted in adults. However, limited data were available on children receiving immunosuppressive drugs in that study. Additionally, that report included the time period before the routine use of angiotensin-converting enzyme inhibitors (ACEIs) and/or angiotensin receptor blockers (ARBs). The results of previous studies[14,15] revealed an association between treatment with ACEIs and/or ARBs and reduced proteinuria in children with IgAN and HSPN. The reduction of proteinuria over time can slow progression to end-stage renal disease (ESRD) in patients with IgAN and HSPN.[14,16] Therefore, the differences in clinicopathological characteristics and renal outcomes between childhood IgAN and HSPN have not yet been determined.

The aim of this study was to compare the clinical characteristics, renal pathology, and renal outcomes of children with IgAN and HSPN during the period when ACEIs and/or ARBs were routinely used at a single tertiary care hospital.

MATERIALS AND METHODS

Study population

The study population included all children aged less than 18 years who were diagnosed with IgAN or HSPN at Siriraj Hospital between January 2004 and December 2015. The exclusion criteria were (i) a renal biopsy performed at another institution, (ii) less than 1 year of follow-up, and (iii) missing data. All children with IgAN underwent renal biopsy and were diagnosed according to the Oxford classification[17] which is based on the presence of dominant or codominant IgA staining in glomeruli without systemic disease.

HSP was diagnosed according to the European League Against Rheumatism (EULAR)/Paediatric Rheumatology European Society (PreS)-endorsed consensus criteria for the classification of childhood vasculitides.[18] The diagnostic criteria included palpable purpura in the presence of at least one of the following four features: (i) diffuse abdominal pain, (ii) any biopsy showing predominant IgA deposition, (iii) arthritis or arthralgia, and (iv) renal involvement. HSPN was defined as HSP accompanied by renal involvement including at least one of the following: (i) proteinuria, (ii) hematuria, (iii) acute kidney injury or rapidly progressive glomerulonephritis (RPGN), or (iv) renal biopsy showing predominant IgA deposition. Renal biopsy was performed in patients with nephrotic syndrome, decreased renal function, or substantial proteinuria that persisted for more than 1 month.

Clinical definitions

Proteinuria was defined as a urine protein-to-creatinine ratio (UPCR) greater than 0.2 mg/mg and categorized as absent, mild or severe proteinuria. Mild and severe proteinuria were defined as UPCR 0.2-1 and > 1 mg/mg, respectively. The estimated glomerular filtration rate (eGFR) was calculated using the Schwartz formula with an enzymatic method.[19] Nephritic syndrome was defined as hematuria with either hypertension or eGFR < 90 ml/min/1.73 m^2 at presentation. Nephrotic syndrome was diagnosed if nephrotic-range proteinuria (UPCR > 2 mg/mg) and hypoalbuminemia (serum albumin < 2.5 g/dL) were present. Hypertension was diagnosed if blood pressure was greater than the 95th percentile for age, gender, and height or greater than 130/90 mmHg in adolescent participants. RPGN was a clinical syndrome diagnosed if children manifested features of nephritis syndrome and had progressive loss of renal function over a short period of time.

Renal outcomes were classified into 3 categories according to renal manifestations observed at the last follow-up visit: (i) remission, (ii) isolated microscopic hematuria, or (iii) CKD. Remission was defined as normal renal function with no proteinuria or microscopic hematuria. Hematuria was defined as > 5 red blood cells per high-power field in a centrifuged urine specimen. Isolated microscopic hematuria was diagnosed if children had microscopic hematuria with normal renal function and no proteinuria. We defined CKD as a persistent eGFR < 60 ml/min/1.73 m^2 for at least 3 months or persistent proteinuria > 3 months. ESRD was defined as eGFR < 15 ml/min/1.73 m^2.

Treatment

All patients received supportive treatment according to their individual needs, including fluid and electrolyte control, blood pressure control, correction of acidosis, and renal replacement therapy. Furthermore, the children received immunosuppressive drugs, such as pulse methylprednisolone, glucocorticoids, cyclophosphamide, or azathioprine, depending on the disease severity. Some children with HSPN received glucocorticoids due to extrarenal symptoms such as severe abdominal pain. The children received ACEIs and/or ARBs to reduce proteinuria and treat hypertension.

Statistical analysis

Descriptive statistics were calculated for the baseline demographic and clinical characteristics. Continuous data were presented as the mean (± standard deviation) for variables with a normal distribution or as the median and range for variables that were not normally distributed. Categorical data were expressed as absolute numbers and percentages. Statistical significance was determined using Pearson's chi-square test or Fisher's exact test for categorical variables and Student's *t*-test or the Mann-Whitney *U* test for continuous variables, as appropriate. A *P* value < 0.05 was considered statistically significant. All statistical calculations were performed using PASW Statistics (SPSS) 18.0 (SPSS Inc., Chicago, IL, USA).

Data were obtained from electronic patient records. This study was approved by the Siriraj Hospital Ethics Board.

RESULTS

Clinical and pathological features

Seventy children were diagnosed with either IgAN or HSPN from January 2004 to December 2015 at Siriraj Hospital. Of these children, 16 were followed up for less than 1 year, thus meeting the exclusion criteria. Fifty-four children were included in the final study population, with 21 (38.9%) in the IgAN group and 33 (61.1%) in the HSPN group. The median follow-up durations in the IgAN and HSPN groups were 4.0 years (1.3-12.2) and 4.2 years (1.1-11.4), respectively, and there was no statistically significant difference between them (p = 0.97). Baseline demographic and clinical characteristics are summarized in Table 1. Children with IgAN were significantly older. The mean age of onset was 11.2±3.0 years and 9.0±3.3 years (p = 0.02) for children with IgAN and HSPN, respectively. The two groups were similar in sex distribution and severity of renal involvement (proteinuria, initial eGFR, and nephrotic syndrome) at presentation. However, children with IgAN were more likely than those with HSPN to present with gross hematuria (61.9% in IgAN vs. 30.3% in HSPN, p = 0.03) and nephritic syndrome (81.0% in IgAN vs. 39.4% in HSPN, p = 0.01). Baseline eGFR was comparable between the two groups (87.5 (9.2-253.2) ml/min/1.73 m^2 in IgAN vs. 104.5 (9.5-261.4) ml/min/1.73 m^2 in HSPN, p= 0.13).

Renal biopsy was performed in all children with IgAN and 20 (60.6%) children with HSPN. The median (min-max) time from first presentation to renal biopsy were similar between groups: 10 days (0-359) in the IgAN group and 7 days (0-271) in HSPN group (p = 0.71). Table 2 shows the frequency of renal pathological features at the time of diagnosis. The most common pathological finding was mesangial proliferation in both groups (76.2% in IgAN vs. 70.0% in HSPN, p = 0.73). Crescents (57.1% in IgAN vs. 55.0% in HSPN, p = 1.00) and endocapillary proliferation (23.8% in IgAN vs. 40.0% in HSPN, p = 0.33) were similar in both groups. Children with IgAN were more likely than those with HSPN to show chronicity on renal biopsy, including tubular atrophy and interstitial fibrosis (76.2% in IgAN vs. 25.0% in HSPN, p = 0.002). Additionally, children with IgAN had a higher percentage of global sclerosis than those with HSPN, but the difference was not statistically significant (42.9% in IgAN vs. 15.0% in HSPN, p = 0.09).

Treatment

The immunosuppressive medications used within the 1st year after diagnosis are summarized in Table 3. Due to the retrospective nature of the study, treatment showed some variation among physicians. Pulse methylprednisolone 30 mg/kg (maximum 1 g) for 3-5 consecutive days was initially prescribed to 19.0% of children with IgAN and 12.1% of children with HSPN due to RPGN (p=0.70). Most children with HSPN received prednisolone (90.9%), whereas only 57.1% of children with IgAN received prednisolone (p = 0.006). One possible reason is that prednisolone was generally prescribed in many children with HSP because of extrarenal symptoms such as severe abdominal pain. In contrast, all children with IgAN received prednisolone due to renal indications. However, the prescription frequency of other immunosuppressive drugs, such as cyclophosphamide and azathioprine, did not differ between the groups. These drugs were used in a small number of children who did not respond to corticosteroids. None of the children in this study received mycophenolate mofetil. ACEIs were prescribed to 42.9% (9/21) and 36.4% (12/33) of children with IgAN and HSPN (p = 0.64), respectively.

TABLE 1. Baseline demographic and clinical characteristics of children with HSPN and IgAN.

Characteristics	HSPN (n=33)	IgAN (n=21)	*P*
Sex, n (%)			
Male	18 (54.5)	16 (76.2)	0.15
Age, years (mean±SD)	9.0±3.3	11.2±3.0	0.02
Gross hematuria, n (%)	10 (30.3)	13 (61.9)	0.03
Proteinuria[a], n (%)			
No proteinuria	5 (15.2)	8 (38.1)	0.15
Mild proteinuria	14 (42.4)	5 (23.8)	
Heavy proteinuria	14 (42.4)	8 (38.1)	
eGFR, ml/min/ 1.73m^2 (median, max-min)	104.5 (9.5-261.4)	87.5 (9.2-253.2)	0.13
Nephritic syndrome[b], n (%)	13 (39.4)	17 (81.0)	0.01
Nephrotic syndrome[c], n (%)	2 (14.3)	3 (23.1)	0.65

HSPN, Henoch Schönlein Purpura Nephritis; IgAN, IgA nephropathy; UPCR, urine protein to creatinine ratio; eGFR, estimated glomerular filtration rate

[a] No, UPCR < 0.2; mild, UPCR 0.2-1; heavy proteinuria, UPCR > 1 mg/mg

[b] Nephritic syndrome includes hematuria with either hypertension or eGFR < 90 ml/min/ 1.73m^2

[c] Nephrotic syndrome includes hypoalbuminemia (serum albumin < 2.5 g/dL) and nephrotic range proteinuria (UPCR > 2 mg/mg)

TABLE 2. Frequency of renal pathologic features at time of diagnosis.

Renal pathology	HSPN (n=20)	IgAN (n=21)	*P*
Mesangial proloferation, n (%)	14 (70.0)	16 (76.2)	0.73
Endocapillary proliferation, n (%)	8 (40.0)	5 (23.8)	0.33
Crescents[a], n (%)	11 (55.0)	12 (57.1)	1.00
Global sclerosis, n (%)	3 (15.0)	9 (42.9)	0.09
Tubular atrophy and interstitial fibrosis, n (%)	5 (25.0)	16 (76.2)	0.002

[a]Any crescents

TABLE 3. Immunosuppressive medications within the 1st year after diagnosis.

Medication	HSPN (n=33)	IgAN (n=21)	*P*
Pulse methylprednisolone, n (%)	4 (12.1)	4 (19.0)	0.70
Prednisolone, n (%)	30 (90.9)	12 (57.1)	0.006
Cyclophosphamide, n (%)	9 (27.3)	4 (19.0)	0.54
Azathioprine, n (%)	2 (6.1)	2 (9.5)	0.64

Renal outcomes

The renal outcomes at the last follow-up visit in 21 children with IgAN and 33 children with HSPN are summarized in Table 4. The median (min-max) length of follow-up from first presentation to renal outcomes measurement was similar between groups: 4.0 years (1.3-12.2) in the IgAN group and 4.2 years (1.1-11.4) in the HSPN group (p = 0.97). The renal outcomes were better in children with HSPN than with IgAN. Complete recovery was more frequent in children with HSPN than with IgAN (87.9% in HSPN vs. 57.1% in IgAN, p = 0.01). Persistent isolated microscopic hematuria was observed more frequently in children with IgAN than with HSPN (14.3% in IgAN vs. 6.1% in HSPN, p = 0.32).

The incidence of CKD was 28.6% in children with IgAN and 6.1% in those with HSPN (p = 0.02). There was no significant difference in ESRD in either group (14.3% in IgAN vs 6.1% in HSPN, p = 0.37). Three children with IgAN (14.3%) required renal replacement therapy. Two children with HSPN (6.1%) progressed to ESRD and required renal replacement therapy. All children with ESRD exhibited significant crescentic involvement greater than 50% and tubular atrophy and interstitial fibrosis greater than 25% on their first renal biopsy. They received immunosuppressive drugs, including pulse methylprednisolone, prednisolone, and pulse cyclophosphamide, but did not respond.

None of the children in this study died.

DISCUSSION

IgAN and HSPN are common glomerular disorders in pediatric patients with the potential to progress to CKD.[1,2,7] The pathogenesis of these two conditions is similar, being associated with galactose-deficient IgA1 and increased formation of IgA1 immune complexes in circulation; these complexes are ultimately deposited in glomeruli.[20,21] This study demonstrated that childhood IgAN has greater chronicity and worse renal outcomes than childhood HSPN. The incidence of CKD was 28.6% in children with IgAN and 6.1% in children with HSPN (p= 0.02). Complete recovery was observed more frequently in children with HSPN than in children with IgAN.

Demographic data demonstrated a predominance of males in both diseases (76.2% in IgAN vs. 54.5% in HSPN), and children with HSPN were significantly younger than children with IgAN (11.2±3.0 years in IgAN vs. 9.0±3.3 years in HSPN, p = 0.02), as in previous pediatric studies.[8,9,13,22-25] Both groups included in this study exhibited similar characteristics of initial renal involvement, including proteinuria, nephrotic syndrome and initial eGFR, except that children with IgAN were more likely to present with gross hematuria (61.9% in IgAN vs. 30.3% in HSPN, p =0.03) and nephritic syndrome (81.0% in IgAN vs. 39.4% in HSPN, p = 0.01). In this regard, no major differences were observed when our results were compared with those from other pediatric series.[9,14,23,24,26]

Although IgAN is the most common glomerular disease during the second and third decades of life, the mean age of children with IgAN in previous studies was approximately 10-15 years old.[8,15,23,25] In support of this notion, the mean age of children with IgAN in this study was 11.2±3.0 years. Gross hematuria is commonly present in children with IgAN (71.0%).[23] As expected, our results showed that 13 of 21 (61.9%) children with IgAN had gross hematuria at initial presentation. The presence of nephrotic syndrome in previous pediatric series was 1.1-14%,[8,26] which was lower than the rate observed in this study (23.1%).

The mean age of HSP in children is approximately 6-8 years old.[1,8,14] However, the mean age of children with HSPN in pediatric series is higher, at approximately 8-14 years old.[8,9,14,24,27,2] Likewise, the mean age at presentation in children with HSPN in this study was 9.0 ± 3.3 years. Gross hematuria is uncommon in children with HSPN, occurring in approximately 10-14% of cases.[24,27] In this

TABLE 4. Renal outcome at last follow up.

Renal outcome	HSPN (n=33)	IgAN (n=21)	*P*
Complete recovery, n (%)	29 (87.9)	12 (57.1)	0.01
Isolated microscopic hematuria, n (%)	2 (6.1)	3 (14.3)	0.32
Chronic kidney disease, n (%)	2 (6.1)	6 (28.6)	0.02

study, however, a larger proportion of children with HSPN (30.3%) had gross hematuria at presentation. Previous series demonstrated that the rate of nephrotic syndrome in childhood HSPN was 5-45%.[8,9,14,24,27,28] This range was supported by this study, in which 14.3% of children with HSPN had nephrotic syndrome at the initial presentation.

Pathological findings in children with IgAN and HSPN have been shown to depend on the timing of renal biopsy.[9,29] Children in the early stages of both disorders generally have mesangial and endocapillary proliferation, while those with late-stage disease generally have segmental or global sclerosis and tubular atrophy interstitial fibrosis.[9,22] Consistent with a previous study,[8] considerable mesangial proliferation was the most common renal pathological feature observed in patients with both disorders in this study (76.2% in patients with IgAN vs 70.0% in patients with HSPN). Tubular atrophy and interstitial fibrosis are pathological features that are independently associated with unfavorable renal outcomes.[9,23,30] Our results would appear to confirm a higher rate of tubular atrophy and interstitial fibrosis in children with IgAN than in children with HSPN (76.2% in IgAN vs 25% in HSPN, p=0.002), which led us to hypothesize that renal biopsy in children with HSPN was performed earlier.

Corticosteroids decrease the intensity and duration of abdominal pain and the severity of arthritis in children with HSP.[4,31] However, the use of corticosteroids in children with HSP does not effectively prevent the development of nephritis.[31,32] The use of corticosteroids was more common in children with HSPN than with IgAN in this study (57.1% in IgAN vs 90.9% in HSPN, p=0.006), probably due to the frequent extrarenal manifestations presented in children with HSPN. In contrast, corticosteroids were generally given to children with IgAN only if there were renal indications. To date, there is little evidence to support the additional use of adjunctive therapy with immunosuppression, such as mycophenolate mofetil or azathioprine, as a standard regimen in either children with IgAN or children with HSPN.[33,34]

Data on renal outcomes in children with IgAN and HSPN varied from complete recovery to ESRD. In a series of pediatric patients, 5-43% of children with IgAN[13,23] and 4-13% of children with HSPN[13,14,24,35] developed CKD, including ESRD. However, these results should be interpreted with caution because discrepancies could be related to several factors, such as differences in patient selection, treatment strategies, duration of follow-up, and outcome measurement. Patient selection bias existed, particularly for HSPN, can make renal outcomes highly variable. In this regard, some centers included only biopsy-proven HSPN,[9,14,27,28] while others analyzed data regardless of whether a biopsy was performed.[13,24,36] Additionally, some countries have active urine screening programs, which increase the likelihood that children with IgAN will be diagnosed and treated in the early stages of disease; this may affect renal outcomes. Moreover, immunosuppressive medications differed depending on the preferences of individual centers, and different treatment strategies may also affect renal outcomes. Furthermore, the discrepancy between renal outcome measurements among centers made these variables difficult to compare.

A study comparing childhood IgAN and HSPN in a single center[13] found that HSPN could be more aggressive than IgAN, since higher incidence of CKD was observed in children with HSPN (5.0% in IgAN vs. 16.0% in HSPN). In contrast, this study reported better renal outcomes in children with HSPN than with IgAN, since children with HSPN achieved a higher rate of complete recovery (57.1% in IgAN vs 87.9% in HSPN, p=0.01) and a lower incidence of CKD than children with IgAN (28.6% in IgAN vs. 6.1% in HSPN, p=0.02). The median time from first presentation to renal outcomes measurement was similar between groups in this study. One possible explanation is that children with IgAN had a longer course of disease before being diagnosed and this was supported by the findings that IFTA was more common in children with IgAN than in children with HSPN in this study. Although the median time from first presentation to renal biopsy were similar between groups in this study, the diagnosis of IgAN depended on a renal biopsy, and thus children with early-stage IgAN and subtle clinical symptoms might be missed initially and present later with full-blown disease and had chronicity on the renal pathology. In addition, our country has no routine screening urinalysis in children; therefore, mild cases of IgAN are probably missed. In contrast, the diagnosis of HSP was based on clinical symptoms; almost all children with HSP presented with obvious, palpable purpura that led them to seek medical attention. Routine urinalysis was required in all children with HSP; therefore, renal involvement may be identified and treated in the early stages of disease. This finding might explain why children with IgAN had worse renal outcomes than children with HSPN in this study.

Long-term follow-up studies revealed that the urinalysis of 29-43% of pediatric patients with IgAN returned to normal.[13,23,34] This was supported by this study, in which more than half of children with IgAN (57.1%) completely recovered. The incidence of CKD in this study was 28.6% which was close to the overall

incidence of childhood IgAN in previous pediatric studies (5-43%).[13,23] Three (14.3%) of the 21 children with IgAN in our study developed ESRD, similar to the long-term ESRD rate (11%) reported by a Finnish study.[23] All patients with ESRD in this study experienced significant tubular atrophy and interstitial fibrosis.

The course of HSPN is usually favorable. Most children with HSPN (87.9%) achieved complete recovery after a median follow-up period of 3.5 years (1.1-11.4) in this study. These results are consistent with previously reported rates (66-85%).[24,28,35] However, approximately 4-13% of children with HSPN develop CKD.[14,24,35] Similar to the previous study, the incidence of CKD in this study was 6.1%. Two (6.1%) of the 33 children with HSPN in this study developed ESRD, which was similar to the rates reported in other pediatric studies (0-7%).[24,27,34,36]

This study has several strengths. First, this report is the first to compare renal outcomes between children with HSPN and IgAN in the era of ACEIs and/or ARBs, revealing superior renal outcomes in childhood IgAN. Second, this study is homogenous in terms of the analysis of renal outcomes because the same diagnostic criteria were used for both IgAN and HSPN. Third, the children received similar immunosuppressive treatment according to disease severity, despite the absence of standardized management for both diseases. Our study also has several limitations. First, this study employed a retrospective design. Second, the renal outcome data for childhood IgAN and HSPN in this study were obtained from a tertiary center in Thailand; therefore, these data may be difficult to generalize to the whole population. For example, many children with HSPN were referred when they had severe renal involvement at onset. Patients with mild cases of HSPN, might not be referred and might instead be followed at primary and secondary hospitals. Third, our country does not perform school urinalysis screening programs; therefore, children with early-stage IgAN are not detected and were not included. Overall, children with IgAN in this study are not representative of the whole childhood IgA population, especially mild cases. Fourth, relatively fewer patients were analyzed in this study. Further prospective cohort multicenter studies and studies comparing the renal outcomes between 2 groups with similar renal pathologies are required to clarify these limitations.

CONCLUSION

In conclusion, differences were observed between childhood IgAN and HSPN. Children with HSPN were younger than children with IgAN. Gross hematuria and nephritis syndrome occurred more frequently in children with IgAN than in those with HSPN, and the chronicity of renal pathology was also higher in children with IgAN. Additionally, the renal outcomes of children with IgAN were worse than children with HSPN. We recommend long-term follow-up for CKD in children with IgAN.

ACKNOWLEDGEMENTS

The authors are grateful to all of the participants and attending physicians for their contributions.

Funding Sources: This study was supported by the Research Department, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand.

Conflicts of interest: The authors declare that there are no conflicts of interest in this study.

Statement of Ethics: This study was approved by the Siriraj Hospital Ethics Board (Si 380/2016).

REFERENCES

1. Delos Santos NM, Wyatt RJ. Pediatric IgA nephropathies: clinical aspects and therapeutic approaches. Semin Nephrol. 2004;24(3):269-86.
2. Wyatt RJ, Julian BA. IgA nephropathy. N Engl J Med. 2013;368(25):2402-14.
3. Calviño MC, Llorca J, García-Porrúa C, Fernández-Iglesias JL, Rodriguez-Ledo P, González-Gay MA. Henoch-Schönlein purpura in children from northwestern Spain: a 20-year epidemiologic and clinical study. Medicine (Baltimore). 2001;80(5):279-90.
4. Saulsbury FT. Clinical update: Henoch-Schönlein purpura. Lancet. 2007;369(9566):976-8.
5. Jennette JC, Falk RJ, Bacon PA, Basu N, Cid MC, Ferrario F, et al. 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. Arthritis Rheum. 2013;65(1):1-11.
6. Sano H, Izumida M, Shimizu H, Ogawa Y. Risk factors of renal involvement and significant proteinuria in Henoch-Schönlein purpura. Eur J Pediatr. 2002;161(4):196-201.
7. Sanders JT, Wyatt RJ. IgA nephropathy and Henoch-Schönlein purpura nephritis. Curr Opin Pediatr. 2008;20(2):163-70.
8. Komatsu H, Fujimoto S, Yoshikawa N, Kitamura H, Sugiyama H, Yokoyama H. Clinical manifestations of Henoch-Schönlein purpura nephritis and IgA nephropathy: comparative analysis of data from the Japan Renal Biopsy Registry (J-RBR). Clin Exp Nephrol. 2016;20(4):552-60.
9. Lu S, Liu D, Xiao J, Yuan W, Wang X, Zhang X, et al. Comparison between adults and children with Henoch-Schönlein purpura nephritis. Pediatr Nephrol. 2015;30(5):791-6.
10. Kamei K, Ogura M, Sato M, Ito S, Ishikura K. Evolution of IgA nephropathy into anaphylactoid purpura in six cases--further evidence that IgA nephropathy and Henoch-Schonlein purpura nephritis share common pathogenesis. Pediatr Nephrol. 2016;31(5):779-85.
11. Calvo-Río V, Loricera J, Martín L, Ortiz-Sanjuán F, Alvarez L, González-Vela MC, et al. Henoch-Schönlein purpura nephritis

and IgA nephropathy: a comparative clinical study. Clin Exp Rheumatol. 2013;31(1 Suppl 75):S45-51.
12. Oh HJ, Ahn SV, Yoo DE, Kim SJ, Shin DH, Lee MJ, et al. Clinical outcomes, when matched at presentation, do not vary between adult-onset Henöch-Schönlein purpura nephritis and IgA nephropathy. Kidney Int. 2012;82(12):1304-12.
13. Yoshikawa N, Ito H, Yoshiya K, Nakahara C, Yoshiara S, Hasegawa O, et al. Henoch-Schoenlein nephritis and IgA nephropathy in children: a comparison of clinical course. Clin Nephrol. 1987; 27(5):233-7.
14. Tudorache E, Azema C, Hogan J, Wannous H, Aoun B, Decramer S, et al. Even mild cases of paediatric Henoch-Schönlein purpura nephritis show significant long-term proteinuria. Acta Paediatr. 2015;104(8):843-8.
15. Yata N, Nakanishi K, Shima Y, Togawa H, Obana M, Sako M, et al. Improved renal survival in Japanese children with IgA nephropathy. Pediatr Nephrol. 2008;23(6):905-12.
16. Coppo R, Peruzzi L, Amore A, Piccoli A, Cochat P, Stone R, et al. IgACE: a placebo-controlled, randomized trial of angiotensin-converting enzyme inhibitors in children and young people with IgA nephropathy and moderate proteinuria. J Am Soc Nephrol. 2007;18(6):1880-8.
17. Roberts IS, Cook HT, Troyanov S, Alpers CE, Amore A, Barratt J, et al. The Oxford classification of IgA nephropathy: pathology definitions, correlations, and reproducibility. Kidney Int. 2009;76(5):546-56.
18. Ozen S, Ruperto N, Dillon MJ, Bagga A, Barron K, Davin JC, et al. EULAR/PReS endorsed consensus criteria for the classification of childhood vasculitides. Ann Rheum Dis. 2006;65(7):936-41.
19. Schwartz GJ, Muñoz A, Schneider MF, Mak RH, Kaskel F, Warady BA, et al. New equations to estimate GFR in children with CKD. J Am Soc Nephrol. 2009;20(3):629-37.
20. Moldoveanu Z, Wyatt RJ, Lee JY, Tomana M, Julian BA, Mestecky J, et al. Patients with IgA nephropathy have increased serum galactose-deficient IgA1 levels. Kidney Int. 2007;71(11):1148-54.
21. Kauffmann RH, Herrmann WA, Meÿer CJ, Daha MR, Van Es LA. Circulating IgA-immune complexes in Henoch-Schönlein purpura. A longitudinal study of their relationship to disease activity and vascular deposition of IgA. Am J Med. 1980;69(6):859-66.
22. Mao S, Xuan X, Sha Y, Zhao S, Zhu C, Zhang A, et al. Clinico-pathological association of Henoch-Schoenlein purpura nephritis and IgA nephropathy in children. Int J Clin Exp Pathol. 2015; 8(3):2334-42.
23. Ronkainen J, Ala-Houhala M, Autio-Harmainen H, Jahnukainen T, Koskimies O, Merenmies J, et al. Long-term outcome 19 years after childhood IgA nephritis: a retrospective cohort study. Pediatr Nephrol. 2006;21(9):1266-73.
24. Soylemezoglu O, Ozkaya O, Ozen S, Bakkaloglu A, Dusunsel R, Peru H, et al. Henoch-Schönlein nephritis: a nationwide study. Nephron Clin Pract. 2009;112(3):c199-204.
25. Shibano T, Takagi N, Maekawa K, Mae H, Hattori M, Takeshima Y, et al. Epidemiological survey and clinical investigation of pediatric IgA nephropathy. Clin Exp Nephrol. 2016;20(1):111-7.
26. Villatoro-Villar M, Crowson CS, Warrington KJ, Makol A, Ytterberg SR, Koster MJ. Clinical Characteristics of Biopsy-Proven IgA Vasculitis in Children and Adults: A Retrospective Cohort Study. Mayo Clin Proc. 2019;94(9):1769-80.
27. Edström Halling S, Söderberg MP, Berg UB. Predictors of outcome in Henoch-Schönlein nephritis. Pediatr Nephrol. 2010;25(6): 1101-8.
28. Delbet JD, Hogan J, Aoun B, Stoica I, Salomon R, Decramer S, et al. Clinical outcomes in children with Henoch-Schönlein purpura nephritis without crescents. Pediatr Nephrol. 2017; 32(7):1193-9.
29. Shima Y, Nakanishi K, Hama T, Sato M, Mukaiyama H, Togawa H, et al. Biopsy timing and Oxford classification variables in childhood/adolescent IgA nephropathy. Pediatr Nephrol. 2015; 30(2):293-9.
30. Coppo R. Clinical and histological risk factors for progression of IgA nephropathy: an update in children, young and adult patients. J Nephrol. 2017;30(3):339-46.
31. Ronkainen J, Koskimies O, Ala-Houhala M, Antikainen M, Merenmies J, Rajantie J, et al. Early prednisone therapy in Henoch-Schönlein purpura: a randomized, double-blind, placebo-controlled trial. J Pediatr. 2006;149(2):241-7.
32. Floege J, Feehally J. Treatment of IgA nephropathy and Henoch-Schönlein nephritis. Nat Rev Nephrol. 2013;9(6):320-7.
33. Barratt J, Feehally J. Treatment of IgA nephropathy. Kidney Int. 2006;69(11):1934-8.
34. Shima Y, Nakanishi K, Hama T, Mukaiyama H, Togawa H, Sako M, et al. Spontaneous remission in children with IgA nephropathy. Pediatr Nephrol. 2013;28(1):71-6.
35. Narchi H. Risk of long term renal impairment and duration of follow up recommended for Henoch-Schonlein purpura with normal or minimal urinary findings: a systematic review. Arch Dis Child. 2005;90(9):916-20.
36. Ronkainen J, Nuutinen M, Koskimies O. The adult kidney 24 years after childhood Henoch-Schönlein purpura: a retrospective cohort study. Lancet. 2002;360(9334):666-70.