

Clinicopathological Characteristics and Prognosis of Pediatric Immunoglobulin A Nephropathy: A Follow-up Exceeding 10 Years

hua xia

xiahua13752629804@163.com

Children's Hospital Affiliated to Capital Institute Pediatrics <https://orcid.org/0009-0006-7883-1316>

ChaoYing Chen

Children's Hospital Affiliated to Capital Institute Pediatrics

Juan Tu

Children's Hospital Affiliated to Capital Institute Pediatrics

Hua Rong Li

Children's Hospital Affiliated to Capital Institute Pediatrics

Hai Yun Geng

Children's Hospital Affiliated to Capital Institute Pediatrics

Research Article

Keywords: IgA nephropathy, children, long-term prognosis, Oxford classification, proteinuria, risk factor

Posted Date: July 2nd, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10135668/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License. [Read Full License](#)

Abstract

Background

Most studies on pediatric immunoglobulin A nephropathy (IgAN) are limited by relatively short follow-up durations. To address this gap, we aimed to investigate the clinicopathological characteristics, long-term prognosis, and prognostic factors of pediatric IgAN with follow-up exceeding 10 years.

Methods

Clinical data were retrospectively collected from pediatric patients diagnosed with primary IgAN by kidney biopsy at our institution between 2007 and 2015. Patients were divided into endpoint and non-endpoint groups based on a composite endpoint of progression to chronic kidney disease (CKD) stage 5 or a $\geq 30\%$ decline in estimated glomerular filtration rate (eGFR). Baseline clinical characteristics, treatment responses, pathological findings, and immunofluorescence results were compared between groups.

Results

The median follow-up duration was 12.9 years. Three patients (6.0%) progressed to CKD stage 5. The endpoint group showed a higher rate of failure to achieve proteinuria remission at 6 months post-treatment ($P = 0.027$) and prevalence of T1 lesions ($P = 0.002$), and lower rate of immunoglobulin M positivity ($P = 0.016$), compared with the non-endpoint group. No significant differences were observed in sex, age, gross hematuria, hypertension, baseline eGFR, or M/E/S/C lesions. In children with nephrotic-range proteinuria, high-dose methylprednisolone pulse therapy was associated with a higher clinical remission rate, compared with non-high-dose regimens ($P = 0.031$).

Conclusion

Most pediatric patients with IgAN showed favorable long-term prognosis. Failure to achieve proteinuria remission at 6 months post-treatment and the presence of T1 lesions were associated with poor outcomes. Early intensive immunosuppressive therapy may improve clinical outcomes.

1. Introduction

Immunoglobulin A nephropathy (IgAN), the most common primary glomerulonephritis, has an annual global incidence of approximately 2.5 per 100,000 population. It is particularly prevalent in East Asia, and accounts for approximately 30–50% of kidney biopsy cases [1]. IgAN is characterized by deposition of immunoglobulin (Ig) A-containing immune complexes in the glomerular mesangium. Although its prognosis was considered relatively favorable, long-term follow-up studies have shown that approximately 20–40% of patients progress to chronic kidney disease (CKD) stage 5 within 20 years [2]. Major prognostic factors include persistent proteinuria, hypertension, impaired kidney function at diagnosis, and severe pathological lesions reflected in the MEST-C score [3]. Disease onset is often more acute in children than in adults. In China, a multicenter study reported that approximately 90% of pediatric patients present with gross hematuria, with pathological findings predominantly reflecting active lesions. Additionally, glucocorticoids are used more frequently in pediatric populations and appear to confer greater long-term benefit than in adults [4]. Pediatric IgAN has been reported to have a significantly better prognosis than adult IgAN [5]; however, more recent evidence suggests that the prognosis may be less favorable than previously thought. For example, data from the UK National Registry of Rare Kidney Diseases showed that, after 20–30 years of follow-up, kidney survival was approximately 50% in patients with childhood-onset disease compared with 25% in adults. Even in children presenting with initial low levels of proteinuria, normal kidney function, and normal blood pressure, the estimated glomerular filtration rate (eGFR) declines with age, indicating a lifetime risk of progression to CKD stage 5 [2]. However, most studies on pediatric IgAN are limited by relatively short follow-up durations [6]. To address this gap, we aimed to conduct a retrospective study to investigate the clinicopathological characteristics and long-term prognosis of children with IgAN over a follow-up period exceeding 10 years, to inform clinical management and prognostic assessment.

2. Materials and Methods

2.1. Participants

This study employed a retrospective cohort design. Pediatric patients hospitalized at our institution between January 2007 and December 2015, diagnosed with primary IgAN by kidney biopsy, were included. All cases met the diagnostic criteria outlined in the Evidence-Based Guidelines for the Diagnosis and Treatment of Primary IgA Nephropathy (2016) issued by the Subspecialty Group of Nephrology, Society of Pediatrics, Chinese Medical Association [7]. IgAN was defined as predominant or isolated IgA deposition in the glomerular mesangium on immunofluorescence, in the absence of secondary causes such as Henoch–Schönlein purpura, systemic lupus erythematosus, or chronic liver disease. The inclusion criteria were: (1) age ≤ 18 years at the time of kidney biopsy and (2) complete clinical data with a follow-up duration ≥ 10 years. The exclusion criteria were: (1) secondary IgAN caused by conditions such as systemic lupus erythematosus and purpura nephritis, and (2) ≥ 10 glomeruli in the biopsy specimen. The study was approved by the Ethics Committee of our institution (approval number: SHERLL2020040).

2.2. Research Methods

Baseline data at the time of kidney biopsy and follow-up data from patients with IgAN were collected. The variables included (1) general characteristics: sex, age at kidney biopsy, time from disease onset to biopsy, gross hematuria, microscopic hematuria, nephrotic-range proteinuria, acute kidney injury (AKI), hypertension, and clinical classification; (2) laboratory parameters: eGFR, serum albumin, hemoglobin, and 24-h urinary protein excretion; (3) pathological data: all kidney biopsy specimens were examined by light microscopy (hematoxylin and eosin, periodic acid-Schiff, periodic acid-silver methenamine, and Masson trichrome staining), immunofluorescence (IgG, IgA, IgM, and C3), and electron microscopy. Patients were graded according to the Lee classification, and kidney histopathology was scored using the Oxford MEST-C classification (2009); and (4) follow-up data: follow-up was conducted through outpatient visits or telephone interviews. Clinical parameters, laboratory findings, and treatment regimens were recorded at each follow-up visit until September 2025.

2.3. Grouping

Patients were divided into the endpoint and non-endpoint groups based on whether the composite endpoint was reached. Patients with nephrotic-range proteinuria were further stratified into the high-dose and non-high-dose groups based on whether they received high-dose methylprednisolone pulse therapy.

2.4. Definitions and Diagnostic Criteria

The following definitions and criteria were used: (1) Nephrotic-range proteinuria [7]: 24-h urinary protein ≥ 50 mg/kg or ≥ 40 mg/m²-h, excluding transient elevations due to factors such as gross hematuria. (2) AKI [8]: defined according to the 2012 Kidney Disease: Improving Global Outcomes (KDIGO) guidelines as any of the following: an increase in serum creatinine (Scr) to ≥ 26.5 μ mol/L within 48 h, an increase in Scr to ≥ 1.5 times baseline within 7 d, or urine output < 0.5 mL·kg⁻¹·h⁻¹ for at least 6 h. (3) Hypertension [9]: systolic or diastolic blood pressure ≥ 95 th percentile (P95) for age- and sex-matched children. (4) Endpoint event [10]: progression to CKD stage 5 or a $\geq 30\%$ decline in GFR from baseline. (5) Clinical remission: 24-h urinary protein ≤ 200 mg/d, blood pressure < 90 th percentile (P90) for age- and sex-matched children [11], and normal eGFR ≥ 90 mL/min/1.73 m².

2.5. Statistical Analysis

Data analysis was performed using SPSS version 30.0 (IBM Corp., Armonk, NY, USA) and MedCalc 22.0.x. For continuous variables, normally distributed data were expressed as the mean $\pm$ standard deviation, and group comparisons were conducted using the independent-samples *t*-test. Non-normally distributed data were presented as the median (interquartile range), and comparisons were performed using the Wilcoxon rank-sum test. Cumulative kidney survival was estimated using the Kaplan–Meier method. To compare cumulative kidney survival between the high-dose and non-high-dose groups among patients with nephrotic-range proteinuria, the log-rank test was used. All tests were two-sided, and $P < 0.05$ was considered statistically significant.

3. Results

3.1. General Characteristics

Between 2006 and 2015, 81 patients with primary IgAN were diagnosed in our department, accounting for 24.5% of all kidney biopsy cases. Among these, 50 patients met the inclusion criteria and underwent regular follow-up. The median follow-up duration was 12.9 (11.5, 14.9) years. Table 1 presents the clinical characteristics, pathological findings, and treatment regimens of these 50 pediatric patients. Regarding combination therapy, 12 patients (24.0%) received glucocorticoids plus cyclophosphamide, 19 patients (38.0%) received glucocorticoids plus mycophenolate mofetil, and five patients (10.0%) received two or more immunosuppressive agents (Table 1).

Table 1
Baseline characteristics of pediatric patients with IgAN^a

Variable	Total (n = 50)
Sex (male), n (%)	32 (64.0)
Age at onset (y)	9.2 ± 3.6
Age at kidney biopsy (y)	9.7 ± 3.6
Time from onset to biopsy (mo)	7.8 ± 18.6
Gross hematuria at onset, n (%)	35 (70.0)
Microscopic hematuria, n (%)	10 (20.0)
Nephrotic-range proteinuria, n (%)	32 (64.0)
Concomitant AKI, n (%)	15 (30.0)
Hypertension at onset, n (%)	11 (22.0)
Clinical classification, n (%)	
Isolated hematuria	2 (4.0)
Hematuria with proteinuria	16 (32.0)
Nephrotic syndrome	12 (24.0)
Acute nephritic syndrome	20 (40.0)
Kidney biopsy	
Immunofluorescence intensity	
M 0–1 (n)	23–27
E 0–1 (n)	22–28
S 0–1 (n)	31–19
T 0–1–2 (n)	46–4–0
C 0–1–2 (n)	33–13–4
Lee classification	
Grade II, n (%)	24 (48.0)
Grade III, n (%)	24 (48.0)
Grade IV, n (%)	1 (2.0)
Grade V, n (%)	1 (2.0)
Immunofluorescence intensity	
IgA 0–1–2–3–4 (n)	0–6–13–24–7
IgG 0–1–2–3 (n)	30–16–4–0
IgM 0–1–2–3 (n)	23–14–9–4
C3 0–1–2–3 (n)	15–23–8–4
C1q 0–1–2–3 (n)	0–3–0–0
Treatment regimen	
Glucocorticoids, n (%) (excluding pulse therapy)	31 (62.0)
Methylprednisolone pulse therapy, n (%)	11 (22.0)
Cyclophosphamide, n (%)	17 (34.0)
Mycophenolate mofetil, n (%)	22 (44.0)
Cyclosporine A, n (%)	3 (6.0)
<i>Tripterygium wilfordii</i> , n (%)	2 (4.0)
ACEI/ARB, n (%)	39 (78.0)

^aM, mesangial hypercellularity (M1, ≥ 50% of glomeruli affected); E, endocapillary hypercellularity (E1, present); S, segmental glomerulosclerosis or adhesion (S1, present); T, tubular atrophy/interstitial fibrosis (T1, 26–50%; T2, > 50%); C, cellular or fibrocellular crescents (C1, < 25%; C2 as ≥ 25%).

3.2. Comparison of Clinical and Pathological Data between Endpoint and Non-endpoint Groups

Patients in the endpoint group exhibited a significantly higher rate of failure to achieve proteinuria remission at 6 months post-treatment and a higher prevalence of T1 lesions on kidney biopsy, compared with those in the non-endpoint group. In contrast, the rate of IgM positivity on immunofluorescence was significantly lower in the endpoint group versus non-endpoint group ($P < 0.05$). Compared with the endpoint group, a higher proportion of patients in the non-endpoint group received glucocorticoids or immunosuppressive therapy prior to biopsy; however, the difference was not significant ($P > 0.05$) (Table 2).

Table 2
Comparison of baseline clinical and pathological data between the two groups of pediatric patients with IgAN

Variable	Total (n = 50)	Nonendpoint group (n = 45)	Endpoint group (n = 5)	Test statistic	P-value
Age (y)	9.7 ± 3.6	9.8 ± 3.4	8.9 ± 4.9	-0.437	0.662
Sex (male), n (%)	32 (64.0)	28 (62.2)	4 (80.0)	0.087	0.768
Systolic blood pressure (mmHg)	105.5 (90.0, 120.0)	106.0 (92.0, 120.0)	100.0 (89.0, 136.0)	-0.179	0.858
Diastolic blood pressure (mmHg)	66.0 (60.0, 80.0)	67.0 (60.0, 79.0)	65.0 (60.0, 96.0)	-0.608	0.543
Gross hematuria, n (%)	35 (70.0)	33 (73.3)	2 (40.0)	1.058	0.304
Nephrotic-range proteinuria, n (%)	32 (64.0)	28 (62.2)	4 (80.0)	0.087	0.768
Concomitant AKI at onset, n (%)	15 (30.0)	14 (31.1)	1 (20.0)	0.000	1.000
Time from onset to biopsy (mo)	2.0 (1.5, 5.0)	2.0 (1.0, 4.5)	3.0 (1.0, 10.5)	-0.873	0.383
Use of glucocorticoids or immunosuppressants within 2 weeks before diagnosis, n (%)	18 (36.0)	18 (40.0)	0 (0)		0.145
Failure to achieve proteinuria remission at 6 mo, n (%)	14 (28.0)	10 (22.2)	4 (80.0)	4.861	0.027
eGFR (mL/min.1.73 m ²)	102.4 ± 36.0	101.5 ± 35.6	110.6 ± 42.8	-0.485	0.627
Serum albumin (g/L)	29.2 (21.6, 40.5)	28.4 (21.3, 40.5)	31.9 (23.9, 38.2)	-0.356	0.722
Hemoglobin (g/L)	127.2 ± 16.5	128.8 ± 15.1	113.2 ± 23.6	-1.667	0.096
Lee classification ≥ grade III, n (%)	24 (48.0)	21 (46.7)	3 (60.0)	0.009	0.925
M1, n (%)	27 (54.0)	25 (55.6)	2 (40.0)	0.036	0.850
E1, n (%)	28 (56.0)	26 (57.8)	2 (40.0)	0.081	0.776
S1, n (%)	19 (38.0)	16 (35.6)	3 (60.0)	0.340	0.560
T1, n (%)	5 (10.0)	2 (4.4)	3 (60.0)	9.877	0.002
C1 + C2, n (%)	17 (34.0)	14 (31.1)	3 (60.0)	0.634	0.426
IgM positivity, n (%)	27 (54.0)	27 (60.0)	0 (0)		0.016
IgG positivity, n (%)	20 (40.0)	19 (42.2)	1 (20.0)	0.231	0.630
C1q positivity, n (%)	3 (6.0)	2 (4.4)	1 (20.0)	0.158	0.691
C3 positivity, n (%)	35 (70.0)	33 (73.3)	2 (40.0)	1.058	0.304
Risk prediction score: ≥30% decline in GFR or ESRD progression*	13.6 (8.3, 22.6)	12.4 (8.1, 22.4)	19.2 (12.4, 58.4)	-1.116	0.265
* According to the international pediatric IgAN prognostic prediction tool, www.qxcalc.app.link/igarisk .					

3.3. Comparison of Clinical Indicators and Remission between High-dose and Non-high-dose Groups among Patients with Nephrotic-range Proteinuria

Among patients with nephrotic-range proteinuria, the proportions with Lee classification grade III or higher and S1 lesions in the Oxford classification were greater in the high-dose methylprednisolone pulse therapy group than in the non-high-dose group. The clinical remission rate was also higher at 6 months in the high-dose group versus non-high-dose group; however, the difference did not reach statistical significance. Kaplan–Meier survival analysis revealed a significantly higher cumulative remission rate in the high-dose group versus non-high-dose group at the end of follow-up (log-rank test, $\chi^2 = 4.634$, $P = 0.031$) (Table 3, Fig. 1).

Table 3
Comparison of clinical indicators between high-dose and non-high-dose methylprednisolone pulse therapy groups

Variable	Total (n = 32)	High-dose group (n = 9)	Non-high dose group (n = 23)	Test statistic	P-value
Sex (male), n (%)	32 (64.0)	5 (55.6)	16 (69.6)	0.113	0.737
Age at onset (y)	8.3 ± 3.5	8.1 ± 4.5	8.4 ± 3.2	-0.198	0.845
Time from onset to treatment (mo)	1.3 (1.0, 4.0)	1.5 (0.7, 4.5)	1.0 (1.0, 4.0)	0.300	0.764
eGFR (mL/min.1.73 m ²)	98.4 ± 40.8	89.9 ± 36.1	105.6 ± 36.8	-1.087	0.286
Baseline 24-h urinary protein per kg (mg/kg)	105.3 (80.1, 159.9)	99.0 (70.8, 192.0)	110.0 (80.0, 145.0)	-0.168	0.867
Hypertension, n (%)	7 (21.9)	3 (33.3)	4 (17.4)		0.642
Gross hematuria, n (%)	19 (59.4)	7 (77.8)	12 (52.2)		0.249
ESRD, n (%)	4 (12.5)	1 (11.1)	3 (13.0)		1.000
Lee classification ≥ grade III, n (%)	18 (56.3)	9 (100.0)	9 (39.1)		0.002
M1, n (%)	23 (71.9)	6 (66.7)	17 (73.9)		0.685
E1, n (%)	20 (62.5)	5 (55.6)	15 (65.2)		0.696
S1, n (%)	15 (46.9)	8 (88.9)	7 (30.4)		0.005
T1, n (%)	4 (12.5)	2 (22.2)	2 (8.7)		0.557
C1 + C2, n (%)	13 (40.6)	6 (66.7)	7 (30.4)		0.109
Clinical remission at 6 mo, n (%)	12 (37.5)	6 (66.7)	6 (26.1)	2.978	0.084

3.4. Clinical, Pathological, and Treatment Characteristics of Patients Reaching the Endpoint and Outcomes at the End of Follow-up

Overall, 50 pediatric patients with IgAN were followed up until the end of the study period, of whom 38 were followed up into adulthood. Three patients (6.0%) progressed to CKD stage 5 at 3, 10, and 14 years after kidney biopsy, respectively. Forty-one patients (82.0%) achieved sustained clinical remission. Six patients exhibited persistent mild-to-moderate proteinuria; among these, four maintained normal blood pressure and kidney function, whereas the other two experienced a ≥ 30% decline in eGFR. One patient (2.0%) had persistent microscopic hematuria, and another (2.0%) experienced recurrent gross hematuria. Table 4 summarizes their kidney outcomes.

Table 4
Clinicopathological and treatment characteristics of pediatric patients with IgAN who reached the endpoint^a

Case	Sex	Age (y)	Age at kidney biopsy (y)	Family history	Hematuria	Blood pressure (mmHg)	24UTP (mg)	Hemoglobin (g/L)	eGFR (mL/min.1.73 m ²)	Serum albumin (g/L)	Lee classification
1	Male	4.5	5.5	None	Microscopic	88/60	1480	114	160	41.8	3
2	Male	6.3	6.3	Mother had IgAN, who progressed to CKD and underwent transplantation	Microscopic	90/60	1900	121	110	31.9	3
3	Male	15	15	None	Microscopic	150/110	4182	148	123	29.2	2
4	Male	3.5	4.3	None	Gross	100/65	215	93	107	34.6	2
5	Female	13.5	13.5	None	Gross	122/82	10524	90	52.2	18.6	3

Continued Table 4. Clinical and treatment characteristics of pediatric patients with IgAN who reached the endpoint

Case	Immunofluorescence IgA	Immunofluorescence IgM	Immunofluorescence IgG	Immunofluorescence C1q	Immunofluorescence C3	ACEI/ARB	Glucocorticoids/immunosuppressants
1	3+	-	-	-	±~+	Captopril	GCs + MMF
2	+~2+	-	-	-	-	Captopril, Ramipril	GCs + MMF
3	3+	-	+	+	3+	None	GCs + C
4	+	-	-	-	-	Captopril	None
5	2+ ~ 3+	-	-	-	-	None	GCs + methylprednisolone pulse + C

^aElectron microscopy showed mesangial cell proliferation with increased mesangial matrix, small amounts of electron-dense deposits in the mesangial area, diffusely thinned glomerular basement membrane (approximately one-half to one-third of the normal thickness), with no significant tubulointerstitial abnormality, proliferative glomerulonephritis and thin basement membrane disease.

4. Discussion

IgAN is one of the most common forms of primary glomerulonephritis worldwide, with highly heterogeneous clinical manifestations. Approximately 30% of adults with IgAN progress to CKD stage 5 within 10–20 years [12], whereas approximately 20% of children develop CKD stage 5 within 20 years of diagnosis [13]. Using data from the United Kingdom registry, Pitcher et al. [2], reported a kidney survival rate of approximately 50% after 20–30 years of follow-up among children with IgAN. In this context, a retrospective analysis was performed to characterize the long-term clinicopathological trajectories of pediatric IgAN in China, focusing on patients with disease duration exceeding 10 years who received standardized and proactive treatment.

Most patients (82.0%) achieved sustained clinical remission during long-term follow-up, consistent with findings from another single-center study in China [14]. This finding suggests that, with standardized treatment, most children with IgAN can achieve long-term disease stability. However, a small proportion of patients (6.0%) progressed to CKD stage 5, highlighting the need for long-term monitoring and risk stratification in pediatric IgAN.

Regarding prognostic factors, results suggest that failure to achieve proteinuria remission at 6 months post-treatment and presence of T1 lesions (defined as tubular atrophy/interstitial fibrosis involving ≥ 26% of the cortical area) on kidney biopsy are significant risk factors for progression to endpoint events. These findings are consistent with those of the international Validation of the Oxford Classification for IgAN (VALIGA) study [15] and a recent pediatric cohort study [16]. The VALIGA study [15], which included a median long-term follow-up of 7 years in 1130 patients with IgAN (including 174 children), demonstrated that T lesions in the Oxford classification are strong pathological predictors of adverse kidney outcomes. In the pediatric subgroup, T1–T2 lesions were significantly associated with a rapid decline in eGFR. Furthermore, regardless of baseline proteinuria, time-averaged proteinuria during follow-up was strongly associated with prognosis, highlighting the importance of sustained proteinuria control and assessment of chronic pathological changes.

Mesangial IgM deposition has traditionally been considered nonspecific or incidental [17]; however, a study demonstrated that high-intensity IgM deposition is closely associated with tubulointerstitial injury and segmental sclerosis. Furthermore, that study reported that strong IgM deposition (≥ 2+) may serve as an independent risk factor for poor kidney prognosis, whereas the clinical significance of simple IgM positivity remains uncertain and may reflect distinct immunopathogenic mechanisms or specific histopathological subtypes [18]. In this study, the absence of IgM positivity was associated with poor prognosis. Only 13 patients (26.0%) exhibited IgM intensity ≥ 2+. These findings may suggest that disease progression in this cohort was driven primarily by IgA immune-complex deposition, rather than by injury mechanisms involving multiple immunoglobulins. However, this hypothesis requires validation in larger cohorts with analyses that incorporate the intensity and distribution of IgM deposition and its relationship with complement activation.

Among pediatric patients with IgAN and nephrotic-range proteinuria, the proportions with Lee classification grade III or higher and S1 lesions in the Oxford classification were significantly higher in the high-dose methylprednisolone pulse therapy group than in the non-high-dose group. In addition, the high-dose group achieved a higher clinical remission rate, compared with the non-high-dose group. These findings suggest that patients in the high-dose group had more severe baseline pathological injury and that clinicians preferentially selected pulse therapy for those with more severe disease. For pediatric patients exhibiting pronounced pathological activity and substantial proteinuria, early intensive immunosuppressive therapy may improve long-term kidney outcomes. Moreover, 40.0% of patients in the non-endpoint group received glucocorticoids or immunosuppressive therapy within 2 weeks of disease onset, whereas none in the endpoint group did; this suggests that early immunosuppressive intervention may be associated with improved long-term prognosis. According to the updated 2021 KDIGO guidelines [11], glucocorticoids may be considered in patients with IgAN with persistent proteinuria > 1 g/d and an eGFR > 50 mL/min/1.73 m² despite optimized supportive care, while intensified immunosuppressive regimens, including methylprednisolone pulse therapy, are recommended for rapidly progressive disease. A study involving a large Japanese pediatric cohort of 500 patients with IgAN demonstrated that adoption of aggressive glucocorticoid-based treatment protocols in the early 1990s significantly improved long-term kidney survival, particularly in patients with moderate-to-severe pathological changes such as diffuse mesangial proliferation [5].

Among the five patients who reached the endpoint, two exhibited poor treatment adherence or irregular follow-up (cases 3 and 4), and one achieved only partial proteinuria remission after 3 months of treatment (case 5). These findings highlight the importance of treatment adherence and early achievement of complete remission for long-term outcomes. Notably, the patient with a 50% decline in eGFR had a family history of IgAN, with progression of the disease to CKD stage 5 in the mother. A genome-wide association study has shown that IgAN is a complex polygenic disease, with the susceptibility genes primarily involving the mucosal immune (e.g., HLA-DQB1/DRB1 and *ITGAM-ITGAX*) and complement pathways (e.g., *CFH/CFHRs*) [19, 20]. Polygenic risk scores derived from these findings are associated not only with disease susceptibility but also with disease progression rate [21]. Therefore, clinicians should carefully assess family history in children with IgAN. The incorporation of genetic information into risk stratification may represent an important future direction for personalized management. In the present cohort, kidney biopsy of patients with disease progression consistently showed coexisting active and chronic lesions, including T1 lesions; most patients presented with nephrotic-range proteinuria at disease onset. These findings further support the importance of early proteinuria control and assessment of chronic pathological changes in prognostic evaluation.

Regarding the application of the international pediatric IgAN prognostic prediction tool (<http://www.qxcalc.app.link/igarisk>), the median predicted risk score was higher in the endpoint group than in the non-endpoint group, although the difference was not significant ($P = 0.265$). Several factors may explain this finding. First, the sample size of the endpoint group was small ($n = 5$), which may have limited statistical power. Second, as the tool was developed using large multicenter datasets, its performance may be affected in small single-center cohorts by selection bias. Third, the high prevalence of T1 lesions (60.0%) in the endpoint group suggests that existing models may not fully capture the prognostic impact of T lesions, particularly given the potentially nonlinear pathological evolution in pediatric disease [22]. Although not significant, the observed trend suggests potential clinical utility. Future studies should incorporate larger pediatric cohorts and dynamic variables, such as treatment response and genetic background, to improve the precision of individualized risk prediction.

In summary, beyond identifying baseline risk factors, clinicians should emphasize treatment adherence and achievement of early complete remission to improve long-term outcomes in children with IgAN.

Declarations

Competing interests

The authors have no relevant financial or non-financial interests to disclose.

Ethics approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Children's Hospital Capital Institute of Pediatrics (date, no. SHERLL2020040).

Consent to participate

Due to the retrospective nature of this study and the anonymization of patient data, the requirement for written informed consent was waived by the Ethics Committee. As this study is retrospective and utilized anonymized clinical data from pediatric patients, written informed consent was not applicable. The Ethics Committee approved the waiver of consent in compliance with national legislation and institutional regulations. No personally identifiable information was used or disclosed in the analyses.

Consent to publish

Not applicable

Author contributions

The manuscript was drafted by Hua Xia; the study was conceived by ChaoYing Chen and Juan Tu; and Hua Xia, Huarong LI, and Haiyun Geng contributed to data interpretation and data analysis. All authors read and approved the final manuscript.

Funding

No funds, grants, or other support was received.

Acknowledgements

We thank the patients and their families.

Data availability

The datasets generated during and/or analyzed during the current study are not publicly available due to participant privacy considerations.

References

1. Ghaddar M, Canney M, Barbour SJ (2024) IgA nephropathy: epidemiology and disease risk across the world. *Semin Nephrol* 44:151564. <https://doi.org/10.1016/j.semnephrol.2025.151564>
2. Pitcher D, Braddon F, Hendry B et al (2023) Long-term outcomes in IgA nephropathy. *Clin J Am Soc Nephrol* 18:727–738. <https://doi.org/10.2215/CJN.000000000000135>
3. Aseem S, Zheng S (2024) Immunoglobulin A nephropathy: a review. *Perm J* 28:87–94. <https://doi.org/10.7812/TPP/24.089>
4. Su B, Jiang Y, Li Z et al (2024) Are children with IgA nephropathy different from adult patients? *Pediatr Nephrol* 39:2403–2412. <https://doi.org/10.1007/s00467-024-06361-1>
5. Yata N, Nakanishi K, Shima Y et al (2008) Improved renal survival in Japanese children with IgA nephropathy. *Pediatr Nephrol* 23:905–912. <https://doi.org/10.1007/s00467-007-0726-5>
6. Cattran DC, Floege J, Coppo R (2023) Evaluating progression risk in patients with immunoglobulin A nephropathy. *Kidney Int Rep* 8:2515–2528. <https://doi.org/10.1016/j.ekir.2023.09.020>
7. Subspecialty Group of Nephrology, Society of Pediatrics, Chinese Medical Association (2017) Evidence-based guidelines for the diagnosis and treatment of primary IgA nephropathy. *Chin J Pediatr* 55:643–646
8. Khwaja A (2012) KDIGO clinical practice guidelines for acute kidney injury. *Nephron Clin Pract* 120:c179–c184. <https://doi.org/10.1159/000339789>
9. (2011) Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents: summary report. *Pediatrics* 128 (Supplement 5):S213–S256. <https://doi.org/10.1542/peds.2009-2107C>
10. Rauen T, Wied S, Fitzner C et al (2020) After ten years of follow-up, no difference between supportive care plus immunosuppression and supportive care alone in IgA nephropathy. *Kidney Int* 98:1044–1052. <https://doi.org/10.1016/j.kint.2020.04.046>
11. Rovin BH, Adler SG, Barratt J et al (2021) KDIGO 2021 clinical practice guideline for the management of glomerular diseases. *Kidney Int* 100:S1–S276. <https://doi.org/10.1016/j.kint.2021.05.021>
12. Barbour SJ, Espino-Hernandez G, Reich HN et al (2016) The MEST score provides earlier risk prediction in IgA nephropathy. *Kidney Int* 89:167–175. <https://doi.org/10.1038/ki.2015.322>
13. Kamei K, Harada R, Hamada R et al (2016) Proteinuria during follow-up period and long-term renal survival of childhood IgA nephropathy. *PLoS ONE* 11:e0150885. <https://doi.org/10.1371/journal.pone.0150885>
14. Mao Y, Zhou W, Zhou Z, Zhang C, Shen J, Yin L (2023) Treatment and outcome of IgA nephropathy in children from one single center experience. *BMC Pediatr* 23:377. <https://doi.org/10.1186/s12887-023-04195-8>
15. Coppo R, D'Arrigo G, Tripepi G et al (2020) Is there long-term value of pathology scoring in immunoglobulin A nephropathy? A validation study of the Oxford Classification for IgA Nephropathy (VALIGA) update. *Nephrol Dial Transpl* 35:1002–1009. <https://doi.org/10.1093/ndt/gfy302>
16. Shima Y, Nakanishi K, Hama T et al (2012) Validity of the Oxford classification of IgA nephropathy in children. *Pediatr Nephrol* 27:783–792. <https://doi.org/10.1007/s00467-011-2061-0>
17. Mubarak M, Kazi JI (2012) IgM nephropathy revisited. *Nephrourol Mon* 4:603–608. <https://doi.org/10.5812/numonthly.2805>
18. Tan L, Tang Y, Pei GQ et al (2021) Mesangial IgM deposition predicts renal outcome in patients with IgA nephropathy: a multicenter, observational study. *Clin Exp Med* 21:599–610. <https://doi.org/10.1007/s10238-021-00703-1>
19. Gharavi AG, Kiryluk K, Choi M et al (2011) Genome-wide association study identifies susceptibility loci for IgA nephropathy. *Nat Genet* 43:321–327. <https://doi.org/10.1038/ng.787>
20. Kiryluk K, Li Y, Scolari F et al (2014) Discovery of new risk loci for IgA nephropathy implicates genes involved in immunity against intestinal pathogens. *Nat Genet* 46:1187–1196. <https://doi.org/10.1038/ng.3118>
21. Shi M, Ouyang Y, Yang M et al (2018) IgA nephropathy susceptibility loci and disease progression. *Clin J Am Soc Nephrol* 13:1330–1338. <https://doi.org/10.2215/CJN.13701217>
22. Barbour SJ, Coppo R, Er L et al (2021) Updating the international IgA nephropathy prediction tool for use in children. *Kidney Int* 99:1439–1450. <https://doi.org/10.1016/j.kint.2020.10.033>

Figures

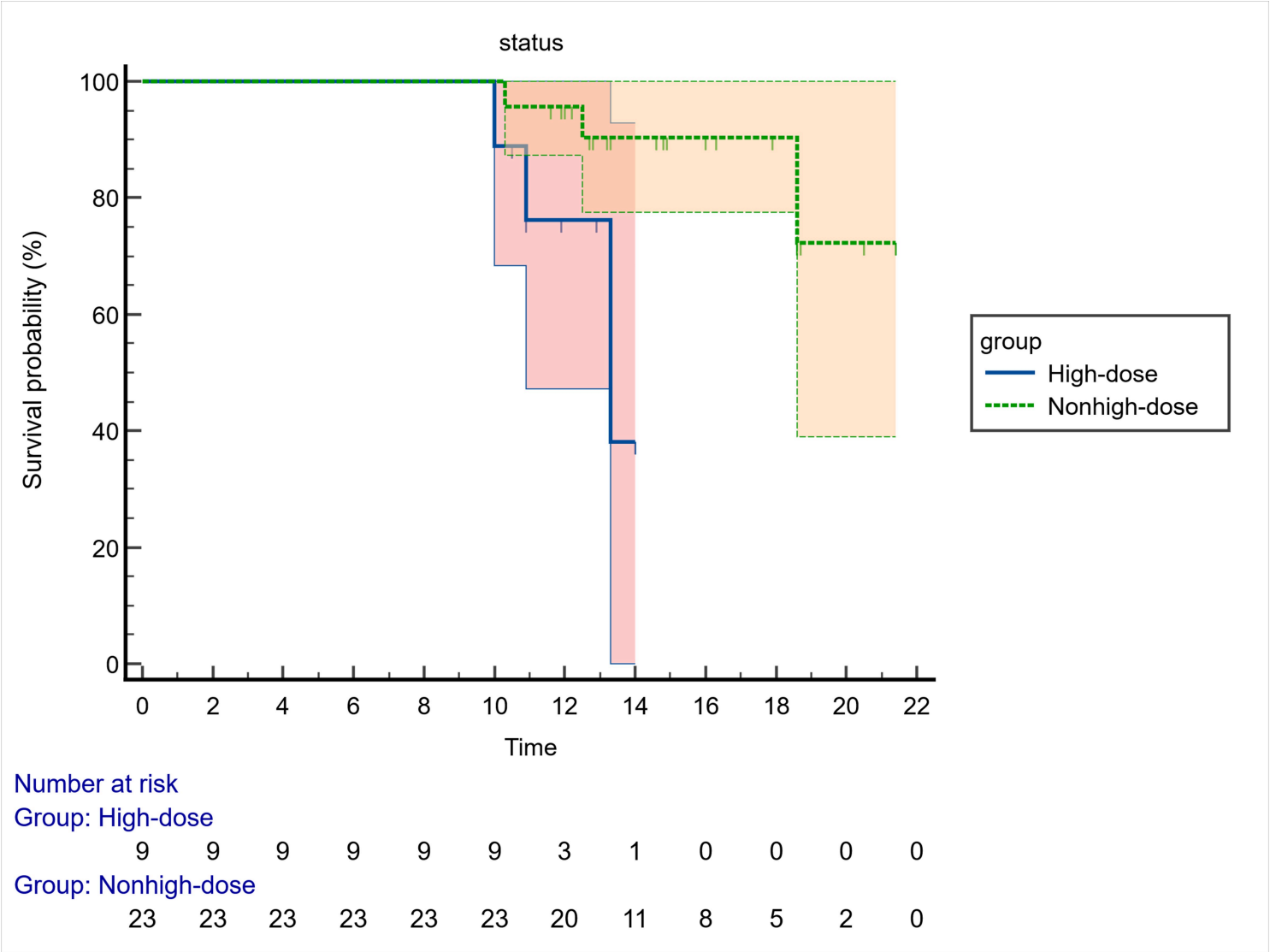


Figure 1

Kidney survival curves (Kaplan–Meier survival analysis) for the high-dose and non-high-dose groups