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Original Article

Predictive value of IgA combined with IFN-γ/IL-4 ratio for recurrence and renal injury in children with henoch-schönlein purpura after *Helicobacter Pylori* eradication: a propensity score-matched analysis

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Abstract: Objective: To investigate the impact of *Helicobacter pylori* (Hp) eradication therapy on recurrence and renal impairment in children with Henoch-Schönlein purpura (HSP), and to evaluate the predictive value of immunoglobulin A (IgA) combined with the interferon-γ (IFN-γ)/interleukin-4 (IL-4) ratio. Methods: Children with HSP and Hp infection (2021-2024) were retrospectively enrolled and assigned to either a treatment group (conventional + Hp eradication) or a control group (conventional alone). Propensity score matching (1:1) balanced baseline characteristics. Clinical efficacy, recurrence-free survival, and renal impairment-free survival, and safety outcomes were compared. Serum IgA, IFN-γ, and IL-4 were measured pre-treatment and at 6 and 12 months post-treatment. ROC curves assessed predictive values. Results: After PSM, 178 children (89 per group) were included. The treatment group demonstrated a significantly higher overall response rate (91.01% vs. 79.77%, $P<0.05$), as well as better recurrence-free (Log-rank $P<0.001$) and renal impairment-free survival (Log-rank $P=0.004$). Hp eradication was an independent protective factor for recurrence (HR=0.613) and renal impairment (HR=0.550). At 6 and 12 months, the treatment group had lower IgA and higher IFN-γ/IL-4 ratios (all $P<0.001$). The combined marker yielded AUCs of 0.783 (recurrence) and 0.802 (renal impairment), superior to individual indicators. Adverse reactions did not differ significantly between groups. Conclusion: Hp eradication therapy improves efficacy and reduces recurrence and renal impairment risks in children with HSP, likely by modulating IgA levels and restoring the Th1/Th2 balance. The IgA and IFN-γ/IL-4 combination shows good predictive value for prognosis.

Keywords: Henoch-Schönlein purpura, Helicobacter pylori eradication therapy, propensity score matching, immunoglobulin A, Th1/Th2 balance

Introduction

Henoch-Schönlein purpura (HSP) is the most common systemic small-vessel vasculitis that occurs in childhood. Renal involvement, the most serious complication, affects approximately 20%-60% of patients and can progress to Henoch-Schönlein purpura nephritis (HSPN), which significantly impacts long-term quality of life [1]. In recent years, the role of chronic Helicobacter pylori (Hp) infection in the pathogenesis and progression of HSP has drawn increasing attention. Studies have confirmed that the Hp infection rate in children with HSP is significantly higher than that in healthy controls, and Hp infection is associated with more severe gastrointestinal symptoms and an elevated risk of renal impairment [2, 3]. However, whether Hp eradication therapy translates into definitive long-term clinical benefits in children with confirmed Hp infection and HSP remains incompletely understood.

Immune imbalance is central to the pathogenesis of HSP. Immunoglobulin A (IgA), a key immune molecule in HSP, deposits in small vessel walls and represents an important pathological feature [4]. Interferon-γ (IFN-γ) and interleukin-4 (IL-4), as signature cytokines of Th1 and Th2 cells, respectively, reflecting the state of

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immune regulation and are closely associated with disease activity and prognosis in HSP [5]. To date, however, systematic studies on the effects of Hp eradication therapy on IgA levels and IFN-γ/IL-4 balance in children with HSP, as well as the value of these immune markers in predicting disease recurrence and renal impairment, are lacking.

Propensity score matching (PSM), as an effective method for controlling confounding bias in observational studies, can balance baseline characteristics between groups and mimic the effects of randomized controlled trials. PSM has been widely used in clinical efficacy evaluations in recent years [6]. This study used PSM to balance confounders, retrospectively analyzed the impact of Hp eradication therapy on the prognosis of children with HSP, dynamically monitored changes in serum IgA levels and the IFN-γ/IL-4 ratio, and explored their clinical utility in predicting HSP recurrence and renal impairment, aiming to provide new theoretical evidence and clinical references for individualized treatment and prognostic assessment.

Subjects and methods

Study subjects

Children with HSP admitted to the Department of Pediatrics, Affiliated Hospital of Inner Mongolia Minzu University, from January 2021 to December 2024 were retrospectively enrolled. Inclusion criteria: (1) age ≤14 years; (2) diagnosed with HSP according to the *Evidence-Based Recommendations for the Diagnosis and Treatment of Henoch-Schönlein Purpura in Children* [7]; (3) positive Hp infection confirmed by ^{13}C-urea breath test or rapid urease test on gastric mucosal biopsy [8]; (4) first diagnosis and in acute phase; (5) complete clinical data. Exclusion criteria: (1) prior Hp eradication therapy or immunomodulatory treatment before admission; (2) concurrent other autoimmune diseases, chronic infectious diseases, or malignancies; (3) severe hepatic or renal dysfunction; (4) allergy to Hp eradication drugs; (5) loss to follow-up or incomplete follow-up data.

According to whether they received Hp eradication therapy, children were divided into a treatment group (conventional therapy + Hp eradication) and a control group (conventional therapy alone). All procedures follow the principles of the Declaration of Helsinki. This study was approved by the Medical Ethics Committee of Inner Mongolia Minzu University (Approval No.: 20250610). As a retrospective case analysis using existing clinical data without any additional interventions, and with all data de-identified prior to analysis to strictly protect patient privacy, the Ethics Committee approved a waiver of informed consent.

Study methods

Baseline data collection: Baseline data were collected for all children, including (1) demographic characteristics: age, sex, body mass index (BMI), place of residence, season of onset; (2) clinical characteristics: disease duration, purpura distribution, skin rash severity score, joint swelling/pain, abdominal pain, gastrointestinal bleeding, vomiting, and other accompanying symptoms; (3) medications: use of glucocorticoids or immunosuppressants; (4) laboratory parameters: complete blood count [white blood cell count (WBC), platelet count (PLT), hemoglobin (HB)], albumin (ALB), immunoglobulins (IgA, IgG, IgE), complement [complement 3 (C3), complement 4 (C4)], and renal function [blood urea nitrogen (BUN), serum creatinine (SCR), estimated glomerular filtration rate (eGFR)]. All parameters were measured from venous blood samples collected within 24 h of admission using an automated biochemical analyzer.

Treatment regimens: Control group: received conventional therapy, mainly including symptomatic treatments such as antihistamines, hemostatics, antispasmodics and analgesics, combined with antiplatelet agents, anticoagulants, antioxidants, and glucocorticoids.

Treatment group: received Hp eradication therapy in addition to conventional therapy. A pediatric quadruple regimen was used: A proton pump inhibitor (omeprazole, 0.6-0.8 $mg \cdot kg^{-1} \cdot d^{-1}$, orally twice daily) + bismuth (bismuth potassium citrate, 6-8 $mg \cdot kg^{-1} \cdot d^{-1}$, orally twice daily) + two antibiotics (amoxicillin, 50 $mg \cdot kg^{-1} \cdot d^{-1}$, orally twice daily; clarithromycin, 15-20 $mg \cdot kg^{-1} \cdot d^{-1}$, orally twice daily), for 14 days. At least 4 weeks after treatment completion, ^{13}C-urea breath test was repeated, and a negative result was defined as successful eradication.

Efficacy evaluation: After matching, both groups were followed up for 12 months, with outpatient or telephone follow-up at 3, 6, and 12 months after treatment completion. Clinical efficacy was evaluated as: (1) cured: complete resolution of rash and accompanying symptoms (e.g., abdominal pain, gastrointestinal bleeding, joint swelling/pain), with only residual mild pigmentation allowed; (2) improved: a reduction in rash area of ≥30% compared with baseline, accompanying symptoms significantly reduced; (3) ineffective: no change in rash (resolution <30% or worsening), no improvement or worsening of accompanying symptoms. Total effective rate = (cured + improved)/total × 100%.

Prognostic assessment: During follow-up, the following prognostic outcomes were recorded: (1) recurrence-free survival: the time from treatment initiation to the first HSP recurrence, defined as reappearance of rash and accompanying symptoms meeting HSP diagnostic criteria; (2) renal impairment-free survival: time from treatment to first occurrence of renal impairment, defined as proteinuria, hematuria on urinalysis, or abnormal renal function parameters, meeting diagnostic criteria for HSPN [9].

Laboratory indicator measurements: Fasting venous blood samples were collected from all children before treatment and at 6 and 12 months after treatment. Serum IgA was measured by immunoturbidimetry. Serum IFN-γ and IL-4 levels were measured by enzyme-linked immunosorbent assay, and the IFN-γ/IL-4 ratio was calculated to assess Th1/Th2 immune balance.

Adverse reaction observation: Adverse reactions during Hp eradication therapy (e.g., nausea, diarrhea, abdominal discomfort) were recorded in the treatment group. Adverse events during follow-up (e.g., abnormal liver function, gastrointestinal symptoms, anaphylactic shock, severe hepatic/renal impairment) were recorded in both groups to evaluate treatment safety.

Statistical methods

PSM was performed using the "MatchIt" package in R software (version 4.2.1). With "whether Hp eradication was received and successfully achieved" as the dependent variable, baseline variables that might influence treatment decisions and prognosis were included in a multivariate logistic regression model to calculate the propensity score for each patient. Nearest-neighbor 1:1 matching (caliper value 0.02) was then applied. After matching, balance of baseline characteristics between the two groups was tested to ensure comparability (no statistically significant differences).

SPSS 26.0 and R software (version 4.2.1) were used for statistical analysis. Normally distributed continuous data were expressed as mean ± standard deviation ($\bar{x} \pm s$) and compared between two groups using independent-sample t-tests. Non-normally distributed continuous data were expressed as median (Q1, Q3) and compared using Mann-Whitney U tests. Categorical data were expressed as n (%) and compared using χ^2 tests or Fisher's exact test. Kaplan-Meier curves were plotted and compared using the Log-rank test for recurrence-free and renal impairment-free survival. Multivariate Cox proportional hazards regression was used to analyze the independent effect of Hp eradication therapy on recurrence and renal impairment. Repeated-measures ANOVA was used to compare dynamic changes in IgA and IFN-γ/IL-4 over time between groups, examining time effects, group effects, and interaction effects. The predictive value of IgA, IFN-γ/IL-4, and their combination for HSP recurrence and renal impairment was illustrated and evaluated by receiver operating characteristic (ROC) curves, area under the curve (AUC), optimal cut-off values, as well as sensitivity and specificity. Cox regression and interaction tests were also used to perform subgroup analyses stratified by age differences (<6 years/≥6 years), the degree of rash severity (mild-moderate/severe or above), varied HSP types (abdominal/non-abdominal), and the presence of initial renal impairment (yes/no). $P<0.05$ was considered statistically significant.

Results

Baseline characteristics before and after PSM

Before matching, there were 98 patients in the control group and 152 in the treatment group. Significant differences were found between the two groups in disease duration (P=0.032), PLT

Table 1. Comparison of baseline characteristics between the two groups before PSM

Variable	Control (n=98)	Treatment (n=152)	Statistic	*P* value
Age (years, $\bar{x} \pm s$)	6.82±2.64	7.15±2.78	-0.934	0.351
Sex [n (%)]			0.155	0.693
Male	56 (57.14)	83 (54.61)		
Female	42 (42.86)	69 (45.39)		
BMI (kg/m^2, $\bar{x} \pm s$)	16.42±3.18	17.08±3.46	-1.519	0.130
Disease duration (d, M [Q_1, Q_3])	4.00 [2.00, 6.00]	3.00 [2.00, 5.00]	2.142	0.032
Residence [n (%)]			0.431	0.511
Urban	50 (51.02)	84 (55.26)		
Rural	48 (48.98)	68 (44.74)		
Occurrence Season [n (%)]			0.159	0.691
Spring/autumn	66 (67.35)	106 (69.74)		
Summer/winter	32 (32.65)	46 (30.26)		
Purpura distribution [n (%)]			0.439	0.508
Upper limb/trunk	24 (24.49)	43 (28.29)		
Lower limb	74 (75.51)	109 (71.71)		
Rash severity [n (%)]			0.837	0.841
Mild (<4)	15 (15.31)	18 (11.84)		
Moderate (4-7)	46 (46.94)	70 (46.05)		
Severe (8-11)	31 (31.63)	54 (35.53)		
Very severe (≥12)	6 (6.12)	10 (6.58)		
Joint swelling/pain [n (%)]	44 (44.90)	68 (69.39)	0.011	0.916
Abdominal pain [n (%)]	58 (59.18)	119 (78.29)	10.521	0.001
Gastrointestinal bleeding [n (%)]	23 (23.47)	41 (26.97)	0.384	0.535
Vomiting [n (%)]	18 (18.37)	38 (25.00)	1.508	0.219
Glucocorticoid use [n (%)]	94 (95.92)	137 (90.13)	2.841	0.092
Immunosuppressant use [n (%)]	12 (12.24)	29 (19.08)	2.030	0.154
WBC (×10^9/L, $\bar{x} \pm s$)	9.82±3.42	10.18±3.58	-0.790	0.430
PLT (×10^9/L, $\bar{x} \pm s$)	304.45±86.28	328.16±92.42	-2.032	0.043
HB (g/L, $\bar{x} \pm s$)	118.36±14.25	125.42±15.38	-3.646	0.010
ALB (g/L, $\bar{x} \pm s$)	38.62±5.18	39.38±5.76	-1.059	0.291
IgA (g/L, $\bar{x} \pm s$)	2.46±0.88	2.84±0.92	-3.156	0.002
IgG (g/L, $\bar{x} \pm s$)	9.82±2.42	10.15±2.58	-1.011	0.313
IgE (IU/mL, M [Q_1, Q_3])	285.00 [168.00, 462.00]	298.00 [172.00, 488.00]	0.624	0.533
C3 (g/L, $\bar{x} \pm s$)	1.12±0.28	1.15±0.30	-0.792	0.429
C4 (g/L, $\bar{x} \pm s$)	0.28±0.08	0.29±0.09	-0.895	0.372
BUN (mmol/L, $\bar{x} \pm s$)	4.18±1.22	4.28±1.32	-0.602	0.548
SCR (μmol/L, $\bar{x} \pm s$)	42.58±12.38	44.22±13.82	-0.954	0.155
eGFR (mL/min/1.73 m^2, $\bar{x} \pm s$)	118.25±24.36	116.18±26.42	0.892	0.341

Notes: BMI, body mass index; WBC, white blood cell count; PLT, platelet count; HB, hemoglobin; ALB, albumin; Ig, immunoglobulin; C3, complement component 3; C4, complement component 4; BUN, blood urea nitrogen; SCr, serum creatinine; eGFR, estimated glomerular filtration rate.

(P=0.043), HB (P=0.010), and IgA level (P=0.002), with no significant differences in other baseline characteristics (**Table 1**). After PSM, 89 cases were obtained in each group. After matching, all baseline characteristics including demographics, clinical manifestations, medication use, and laboratory parameters were balanced between the two groups, with no statistically significant differences, indicating comparability (**Table 2**).

Table 2. Comparison of baseline characteristics between the two groups after PSM

Variable	Control (n=89)	Treatment (n=89)	Statistic	*P*
Age (years, $\bar{x} \pm s$)	6.98±2.68	7.05±2.62	-0.176	0.860
Sex [n (%)]			0.091	0.763
Male	51 (57.30)	49 (55.06)		
Female	38 (42.70)	40 (44.94)		
BMI (kg/m^2, $\bar{x} \pm s$)	16.78±3.28	16.92±3.35	-0.282	0.778
Disease duration (d, M [Q_1, Q_3])	3.00 [2.00, 5.00]	3.00 [2.00, 5.00]	0.142	0.887
Residence [n (%)]			0.090	0.764
Urban	49 (55.06)	47 (52.81)		
Rural	40 (44.94)	42 (47.19)		
Occurrence Season [n (%)]			0.026	0.871
Spring/autumn	61 (68.54)	62 (69.66)		
Summer/winter	28 (31.46)	27 (30.34)		
Purpura distribution [n (%)]			0.125	0.724
Upper limb/trunk	22 (24.72)	20 (22.47)		
Lower limb	67 (75.28)	69 (77.53)		
Rash severity [n (%)]			0.060	0.996
Mild (<4)	11 (12.36)	10 (11.24)		
Moderate (4-7)	41 (46.07)	42 (47.19)		
Severe (8-11)	31 (34.83)	31 (34.83)		
Very severe (≥12)	6 (6.74)	6 (6.74)		
Joint swelling/pain [n (%)]	40 (44.94)	42 (47.19)	0.090	0.764
Abdominal pain [n (%)]	60 (67.42)	62 (69.66)	0.104	0.747
Gastrointestinal bleeding [n (%)]	22 (24.72)	21 (23.60)	0.031	0.861
Vomiting [n (%)]	37 (41.57)	39 (43.82)	0.092	0.762
Glucocorticoid use [n (%)]	83 (93.26)	85 (95.51)	0.424	0.515
Immunosuppressant use [n (%)]	17 (19.10)	15 (16.85)	0.152	0.696
WBC (×10^9/L, $\bar{x} \pm s$)	9.98±3.48	10.12±3.42	-0.271	0.787
PLT (×10^9/L, $\bar{x} \pm s$)	320.18±88.25	324.36±90.18	-0.313	0.755
HB (g/L, $\bar{x} \pm s$)	119.82±14.52	119.25±15.18	0.256	0.798
ALB (g/L, $\bar{x} \pm s$)	39.02±5.45	39.22±5.62	-0.241	0.810
IgA (g/L, $\bar{x} \pm s$)	2.79±0.90	2.81±0.91	-0.147	0.883
IgG (g/L, $\bar{x} \pm s$)	10.02±2.48	10.08±2.42	-0.163	0.870
IgE (IU/mL, M [Q_1, Q_3])	292.00 [170.00, 478.00]	288.00 [168.00, 482.00]	0.082	0.935
C3 (g/L, $\bar{x} \pm s$)	1.14±0.29	1.13±0.28	0.234	0.815
C4 (g/L, $\bar{x} \pm s$)	0.29±0.08	0.28±0.10	0.737	0.462
BUN (mmol/L, $\bar{x} \pm s$)	4.25±1.25	4.22±1.28	0.158	0.874
SCR (μmol/L, $\bar{x} \pm s$)	43.38±13.02	43.75±13.25	-0.188	0.851
eGFR (mL/min/1.73 m^2, $\bar{x} \pm s$)	117.25±25.18	117.82±24.65	-0.153	0.879

Notes: BMI, body mass index; WBC, white blood cell count; PLT, platelet count; HB, hemoglobin; ALB, albumin; Ig, immunoglobulin; C3, complement component 3; C4, complement component 4; BUN, blood urea nitrogen; SCr, serum creatinine; eGFR, estimated glomerular filtration rate.

Comparison of clinical efficacy between the two groups

After matching, the overall response rate in the treatment group (91.01%) was significantly higher than that in the control group (79.77%) (*P*<0.05; **Table 3**).

Prognostic analysis between the two groups

Kaplan-Meier survival analysis showed that the treatment group had a significantly higher recurrence-free survival rate than the control group, with a hazard ratio (HR) of 0.487 (95% CI: 0.335-0.709) (Log-rank *P*<0.001) (**Figure**

Table 3. Comparison of clinical efficacy between the two groups

Group	Cured [n (%)]	Improved [n (%)]	Ineffective [n (%)]	Total effective rate [n (%)]
Control (n=89)	39 (43.82)	32 (35.96)	18 (20.22)	71 (79.77)
Treatment (n=89)	52 (58.43)	29 (32.58)	8 (8.99)	81 (91.01)
χ^2				4.504
P				0.034

1A). Similarly, the renal impairment-free survival rate was significantly higher in the treatment group (HR=0.522, 95% CI: 0.330-0.826) (Log-rank P=0.004) (**Figure 1B**).

Multivariate Cox proportional hazards regression analysis of the association between Hp eradication therapy and prognosis

With 1-year recurrence as the dependent variable and Hp eradication therapy as the independent variable, multivariate Cox regression showed that in the unadjusted model (Model 1), Hp eradication therapy had an HR of 0.535 (95% CI: 0.352-0.813) for recurrence. After sequentially adjusting for demographic characteristics (Model 2), clinical symptoms and medication use (Model 3), and laboratory parameters (Model 4), the independent protective effect remained statistically significant (P<0.05), with HRs of 0.550, 0.582, and 0.613, respectively, and all 95% CIs excluded 1, indicating that Hp eradication therapy is an independent protective factor against recurrence (**Table 4**).

Using the occurrence of renal impairment during follow-up as the dependent variable, the unadjusted model showed an HR of 0.400 (95% CI: 0.254-0.629). After sequential adjustments (Models 2-4), HRs were 0.420, 0.450, and 0.550, respectively, all with P<0.05 and 95% CIs excluding 1, indicating that Hp eradication therapy is an independent protective factor against renal impairment (**Table 5**).

Impact of Hp eradication therapy on prognosis in different subgroups

Subgroup analyses showed that the protective effect of Hp eradication therapy against recurrence and renal impairment was consistent across most subgroups. For recurrence, more pronounced protection was observed in children aged ≥6 years (HR=0.418, 95% CI: 0.248-0.705), those with severe rash (HR=0.382, 95% CI: 0.212-0.688), those with abdominal HSP (HR=0.442, 95% CI: 0.261-0.748), and those without initial renal impairment (HR=0.512, 95% CI: 0.322-0.814) (all *P*<0.05). Similar trends were observed for renal impairment. All interaction *P* values were >0.05, suggesting consistent protective effects across different clinical characteristics without significant heterogeneity (**Table 6**).

Comparison of IgA and IFN-γ/IL-4 levels before and after treatment between the two groups

Repeated-measures ANOVA showed significant time effects, group effects, and interaction effects for both IgA levels and IFN-γ/IL-4 ratio (all P<0.001). Before treatment, IgA and IFN-γ/IL-4 levels were comparable between the two groups. At 6 and 12 months post-treatment, the treatment group had significantly lower IgA levels and significantly higher IFN-γ/IL-4 ratios than the control group (*P*<0.05) (**Table 7**).

Predictive value of IgA, IFN-γ/IL-4, and their combination for HSP prognosis

ROC curve analysis showed that IgA, IFN-γ/IL-4, and their combination all had predictive value for HSP recurrence. For recurrence, IgA yielded an AUC of 0.683 (95% CI: 0.543-0.823), with an optimal cut-off of 2.65 g/L, a sensitivity of 50.00%, and a specificity of 78.57%. IFN-γ/IL-4 yielded an AUC of 0.721 (95% CI: 0.582-0.860), cut-off 1.72, sensitivity 78.57%, and specificity 64.29%. The combination gave an AUC of 0.783 (95% CI: 0.648-0.917), with sensitivity 82.14% and specificity 85.71%, outperforming individual indicators (**Table 8**; **Figure 2A**).

For renal impairment, IgA gave an AUC of 0.723 (95% CI: 0.559-0.887), cut-off 2.85 g/L, sensitivity 80.00%, and specificity 62.50%. IFN-γ/IL-4 gave an AUC of 0.741 (95% CI: 0.574-0.908), cut-off 1.65, sensitivity 95.00%, and specificity 56.25%. The combination

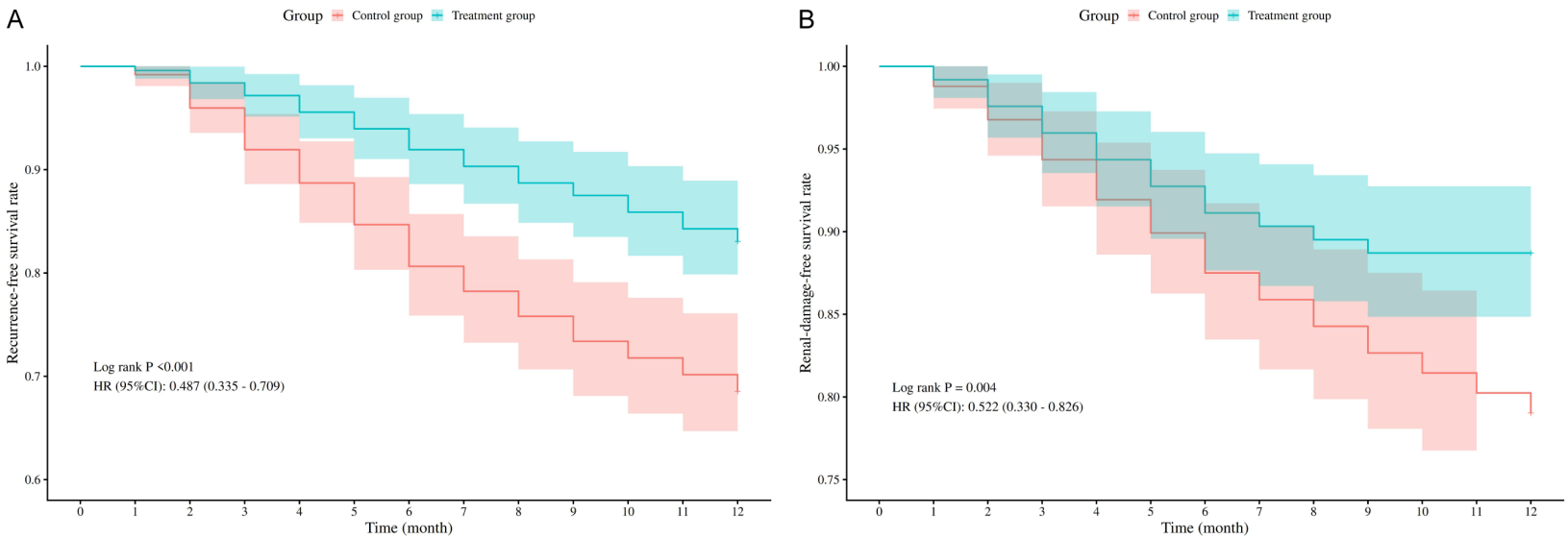


Figure 1. Kaplan-Meier survival curves. A. Recurrence-free survival; B. Renal impairment-free survival.

Table 4. Multivariate Cox regression analysis of factors affecting HSP recurrence

Model	β	SE	Wald χ^2 value	*P* value	HR value	95% CI
Model 1	-0.625	0.213	8.610	0.003	0.535	0.352-0.813
Model 2	-0.598	0.208	8.266	0.004	0.550	0.366-0.827
Model 3	-0.542	0.201	7.271	0.007	0.582	0.392-0.863
Model 4	-0.489	0.195	6.289	0.012	0.613	0.418-0.899

Note: Model 1: unadjusted; Model 2: adjusted for demographic characteristics (age, sex, BMI, disease duration, residence, season); Model 3: further adjusted for purpura distribution, rash severity, joint swelling/pain, abdominal pain, gastrointestinal bleeding, vomiting, glucocorticoid use, immunosuppressant use; Model 4: further adjusted for WBC, PLT, HB, ALB, IgA, IgG, IgE, C3, C4, BUN, SCR, eGFR. Same below.

Table 5. Multivariate Cox regression analysis of factors affecting renal impairment in HSP

	β	SE	Wald χ^2 value	*P* value	HR value	95% CI
Model 1	-0.916	0.231	15.724	<0.001	0.400	0.254-0.629
Model 2	-0.868	0.228	14.493	<0.001	0.420	0.269-0.656
Model 3	-0.798	0.224	12.691	<0.001	0.450	0.290-0.698
Model 4	-0.598	0.218	7.525	0.006	0.550	0.359-0.843

Table 6. Impact of Hp eradication therapy on prognosis in different subgroups

	HR (95% CI)	*P* value	Interaction *P* value	HR (95% CI)	*P* value	Interaction *P* value
Age			0.184			0.206
<6 years	0.682 (0.418-1.112)	0.112		0.712 (0.428-1.185)	0.184	
≥6 years	0.418 (0.248-0.705)	0.001		0.452 (0.260-0.785)	0.004	
Rash severity			0.142			0.158
Mild-moderate	0.712 (0.438-1.158)	0.165		0.682 (0.402-1.156)	0.150	
Severe or above	0.382 (0.212-0.688)	0.002		0.412 (0.222-0.765)	0.005	
HSP type			0.156			0.172
Abdominal	0.442 (0.261-0.748)	0.003		0.472 (0.271-0.822)	0.008	
Non-abdominal	0.662 (0.402-1.092)	0.105		0.702 (0.412-1.196)	0.197	
Initial renal impairment			0.092			0.108
Yes	0.732 (0.382-1.402)	0.345		0.762 (0.392-1.482)	0.425	
No	0.512 (0.322-0.814)	0.004		0.482 (0.290-0.801)	0.004	

Table 7. Comparison of IgA and IFN-γ/IL-4 levels before and after treatment between the two groups

	IgA (g/L)			IFN-γ/IL-4 ratio		
	Pre-treatment	6 months post-treatment	12 months post-treatment	Pre-treatment	6 months post-treatment	12 months post-treatment
Control (n=89)	2.79±0.91	2.14±0.72	1.89±0.68	1.82±0.65	1.96±0.67	2.07±0.71
Treatment (n=89)	2.81±0.90	1.62±0.68*	1.45±0.62*	1.78±0.62	2.84±0.92*	2.91±0.95*
F_{time}, P_{time}		139.1, <0.001			50.81, <0.001	
F_{group}, P_{group}		28.38, <0.001			84.88, <0.001	
$F_{interaction}$, $P_{interaction}$		8.185, <0.001			24.46, <0.001	

Notes: IgA, immunoglobulin A; IFN-γ, interferon gamma; IL-4, interleukin 4. *P<0.05, compared with control group.

gave an AUC of 0.802 (95% CI: 0.671-0.932), sensitivity 87.50%, and specificity 62.50%, superior to single indicators (**Table 8**; **Figure 2B**).

Table 8. ROC curve analysis

Prediction target	Predictor	AUC	95% CI	Optimal cutoff	Sensitivity	Specificity
HSP recurrence	IgA	0.683	0.543-0.823	2.65 g/L	50%	78.57%
	IFN-γ/IL-4 ratio	0.721	0.582-0.860	1.72	78.57%	64.29%
	Combination	0.783	0.648-0.917	-	82.14%	85.71%
Renal impairment	IgA	0.723	0.559-0.887	2.85 g/L	80.0%	62.5%
	IFN-γ/IL-4 ratio	0.741	0.574-0.908	1.65	95%	56.25%
	Combination	0.802	0.671-0.932	-	87.5%	62.5%

Notes: IgA, immunoglobulin A; IFN-γ, interferon gamma; IL-4, interleukin 4.

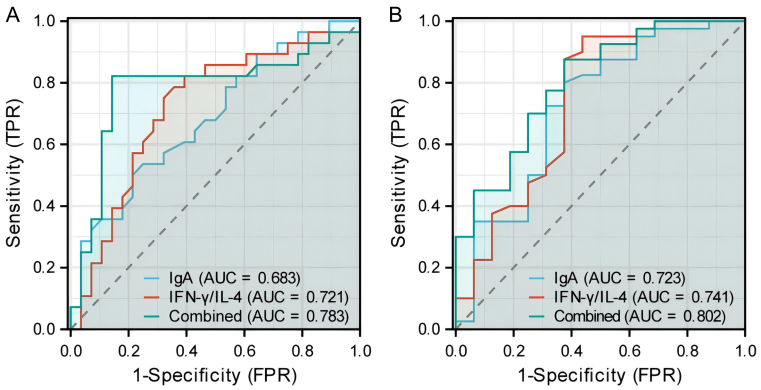


Figure 2. ROC curve analysis of factors for predicting HSP recurrence and renal impairment in HSP. A. ROC curves of IgA, IFN-γ/IL-4 ratio, and their combination for predicting HSP recurrence; B. ROC curves of IgA, IFN-γ/IL-4 ratio, and their combination for predicting renal impairment in HSP. Notes: ROC, receiver operating characteristic; IgA, immunoglobulin A; IFN-γ, interferon gamma; IL-4, interleukin 4.

Adverse reactions and adverse events during follow-up

During eradication therapy, 19 patients (21.35%) experienced mild adverse reactions, including nausea (n=8), diarrhea (n=6), and abdominal discomfort (n=5), all of which resolved spontaneously without treatment interruption. During follow-up, abnormal liver function occurred in 3 cases (3.37%) in the control group and 2 cases (2.25%) in the treatment group; gastrointestinal symptoms occurred in 11 cases (12.35%) and 13 cases (14.61%), respectively. No significant differences were found between the two groups (liver function: χ^2=0.206, P=0.650; gastrointestinal symptoms: χ^2=0.193, *P*=0.661). No severe adverse events such as anaphylactic shock, severe hepatic injury, or severe renal insufficiency were observed in either group.

Discussion

This study used PSM to balance confounders and retrospectively analyzed the impact of Hp eradication therapy on the prognosis of children with HSP. Additionally, the value of IgA combined with IFN-γ/IL-4 in predicting recurrence and renal impairment was explored. The results showed that Hp eradication therapy significantly improved clinical efficacy, reduced recurrence and renal impairment risks, possibly through modulating IgA levels and restoring Th1/Th2 immune balance. Moreover, the combination of IgA and IFN-γ/IL-4 demonstrated good predictive performance for both recurrence and renal impairment. These findings provide new evidence-based medical support for clinical intervention and prognostic assessment in HSP.

Hp infection, as an important trigger for HSP, has been extensively studied for its association with HSP. Through molecular mimicry, Hp antigens and toxins can trigger cross-immune responses, stimulate the production of aberrant IgA antibodies, and activate inflammatory signaling pathways in vascular endothelial cells, inducing small-vessel vasculitis and exacerbating HSP symptoms [10]. In our study, the total effective rate in the treatment group was significantly higher than that in the control group after matching. Kaplan-Meier curves showed significantly improved recurrence-free and renal impairment-free survival in the treatment group. Multivariate Cox regression, after sequential adjustment for demographic, clinical, and laboratory factors, confirmed Hp eradication as an independent protective factor against both recurrence and renal impairment. A meta-analysis reported that Hp eradication reduced HSP recurrence risk by 62%, which is

consistent with our findings [11]. This indicates the combination of Hp eradication and conventional therapy can effectively improve clinical patients' outcomes and reduce their long-term complication risks through eliminating chronic infectious source and interrupting infection-mediated immune inflammation, so as to provide an important therapeutic direction for future searches. Findings from subgroup analyses further identified that some populations may benefit most from Hp eradication and pronounced protective effects were observed, including children aged ≥6 years, those with severe rash, those with abdominal HSP, and those without initial renal impairment. This may be explained by more evident immunomodulatory effects after eradication via stronger immune responses to Hp antigens released by more mature immune systems in older children [12]. Severe rash and abdominal HSP often indicate stronger systemic inflammation, and Hp infection, as a modifiable aggravating factor, yields greater relative benefits from eradication [12]. Children without initial renal impairment are at an early disease stage, and timely Hp eradication may effectively block progression to HSPN. Moreover, all interaction *P* values were >0.05, indicating consistent protective effects across different clinical subgroups without significant heterogeneity, supporting broad clinical application.

IgA is a key immune molecule in HSP, and its aberrant glycosylation and immune complex deposition are central to disease pathogenesis [13]. Its aberrant glycosylation-particularly galactose deficiency in the O-glycans of the hinge region-alters the conformation of IgA molecules, leading to the formation of pathogenic immune complexes that deposit in the walls of small vessels, activate complement and inflammatory cascades, and represent the core pathological mechanism underlying renal injury in HSP [14]. Recent studies suggest that H. pylori infection may affect the expression of glycosyltransferases (such as C1GALT1) and its molecular chaperone Cosmc in B cells through the activation of specific immune signaling pathways, resulting in galactose-deficient IgA1 in the hinge region and increasing the production of aberrant IgA and the risk of immune complex formation [15, 16]. According to our findings, before treatment, no significant difference was observed in IgA levels between groups, but significantly lower IgA levels in the treatment group at 6 and 12 months post-treatment indicates that Hp eradication helps reduce HSP patients' IgA levels. The action mechanism may be that gastric mucosa-associated lymphoid tissue was activated by Hp infection to produce large amounts of IgA antibodies; and eradicating Hp interrupts this mechanism and reduces IgA production [17]. Moreover, beyond reducing total IgA, eradication may also improve the quality of IgA molecules by restoring normal expression of glycosylation-related enzymes, thereby decreasing the formation of pathogenic immune complexes [18, 19]. The imbalanced ratio of Th1/Th2 in HSP has also attracted people's attention. Specifically, IFN-γ and IL-4, as a signature Th1 cytokine and a signature Th2 cytokine respectively, reflects immune regulatory status by their ratio. Previous studies have demonstrated that children with acute HSP exhibit elevated IL-4 and decreased IFN-γ levels, representing reduced IFN-γ/IL-4 ratio and Th2-dominant immune profile [20]. Our results showed that at 6 and 12 months post-treatment, the treatment group had significantly higher IFN-γ/IL-4 ratios compared to control group, and this indicates that Hp eradication helps restore Th1/Th2 balance. This finding is consistent with the experimental result of Du Sanjun, who reported that Hp eradication maintains Th1/Th2 dynamic balance by down-regulating Th2 responses and up-regulating Th1 responses [21]. However, we acknowledge that the immunopathology of HSP involves a complex network of interconnected pathways beyond the Th1/Th2 axis. Emerging evidence highlights the critical role of Th17/Treg imbalance in HSP pathogenesis, characterized by elevated Th17 cells and IL-17 production alongside reduced Treg numbers and suppressive function, which together promote vascular inflammation and tissue injury [22]. Moreover, abnormal B-cell differentiation into IgA-producing plasmablasts and altered dendritic cell function in presenting antigens and polarizing T-cell responses also contribute substantially to the immunopathological cascade [23]. Regarding the mechanistic link between Hp infection and Th2-dominant differentiation, several potential upstream pathways have been proposed: Hp virulence factors such as CagA and VacA may directly modulate T-cell polarization through interactions with antigen-presenting

cells; Hp-induced chronic gastric inflammation can alter the gut microbiome composition, which in turn influences systemic immune homeostasis via the gut-vascular axis; and Hp infection may impair regulatory T-cell function, relieving the suppression on Th2 differentiation [24-26]. Therefore, while the IFN-γ/IL-4 ratio serves as a practically useful marker for monitoring Th1/Th2 dynamics, it should not be equated with complete restoration of the overall immune balance. The favorable prognosis associated with Hp eradication likely reflects multifaceted immunomodulatory effects across multiple immune compartments, rather than a single-axis correction. Through repeated-measures ANOVA, significant interaction effects for both IgA and IFN-γ/IL-4 were observed in time and group, and further confirm the time-cumulative benefit of immunomodulatory effects of Hp eradication. Therefore, longer follow-up periods will have better prognosis.

To individualize treatment and improve long-term prognosis, it is crucial to quickly identify high-risk children and accurately predict whether recurrence and renal impairment occur. Based on ROC analyses, the AUC of IgA alone, IFN-γ/IL-4 and their combination for predicting recurrence was 0.683, 0.721, and 0.783 (sensitivity 82.14% and specificity 85.71%). The combination also yielded an AUC of 0.802 (sensitivity 87.50%) for predicting renal impairment. This proves the superior prediction capability of combined markers compared to a single indicator. Elevated IgA levels reflect increased immune complex burden which is closely linked to disease activity and recurrence risk [5]. A decreased IFN-γ/IL-4 ratio reflects Th2 dominance, the possible predisposition of immune complex deposition and vascular inflammation, as well as higher risks for renal impairment [27]. The combination of these markers captures different dimensions of the patient's immunopathological state, improves predictive accuracy and complements current clinical protocols.

In clinical practice, safety is a crucial factor that must be considered. Our study found that the rate of adverse incidents during eradication was 21.35%, mainly mild gastrointestinal symptoms which were resolved spontaneously, without interrupting treatment. During the follow-up period, no significant differences were observed between groups in the presence of abnormal liver function or gastrointestinal symptoms, and no severe adverse events occurred. This indicates that the children with HSP have a good tolerance to pediatric quadruple regimen, consistent with previous studies on the safety of Hp eradication in children [28]. It is still recommended to have individualized dosing protocols and closely monitor adverse reactions in clinical application.

In conclusion, for children with HSP, Hp eradication therapy significantly improves clinical efficacy and reduces risks for recurrence and renal impairment. The mechanism mainly involves the modulation of IgA levels and restored balance of Th1/Th2. Moreover, the combination of IgA and the IFN-γ/IL-4 ratio may serve as a reference for clinical prognostic assessment given it shows good predictive value for recurrence and renal impairment. Active Hp eradication is also recommended for children with HSP with Hp infection, especially those aged ≥6 years, have severe rash, abdominal type, and have no initial renal impairment.

Nevertheless, there are also limitations in the study. Firstly, it may have selection bias due to its single-center retrospective nature and relatively limited sample size. Secondly, the follow-up duration of 12 months is not enough to demonstrate and clarify the long-term effects of Hp eradication on prognosis. To further validate our findings and provide more evidence-based support for comprehensive HSP management, multicenter and prospective studies with large-sample and longer follow-up period are required in the future. Beyond these limitations, we acknowledge that the observed changes in IgA and the IFN-γ/IL-4 ratio are phenotypic readouts rather than direct evidence of causal molecular events. Future mechanistic studies integrating transcriptomic, proteomic, and phospho-signaling profiling of immune cells, combined with in vitro co-culture systems and animal models, are warranted to elucidate the molecular networks through which Hp eradication exerts its immunomodulatory and renoprotective effects in HSP.

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Disclosure of conflict of interest

None.

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