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Original Article

Clinical prediction model for progression from henoch-schönlein purpura to nephritis in pediatric patients

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Abstract: Objective: To identify independent risk factors for Henoch-Schönlein purpura nephritis (HSPN) in pediatric patients. Methods: This study enrolled 180 pediatric patients (90 with HSP, 90 with HSPN) hospitalized at the 940th Hospital of the Joint Logistics Support Force of the Chinese People's Liberation Army from December 2022 to October 2023, with a follow-up of at least six months. Clinical data were collected at the time of the first onset of HSP. Logistic regression analysis identified risk factors, which were subsequently evaluated using Receiver Operating Characteristic (ROC) curve analysis, a calibration plot, a nomogram, and decision curve analysis. Results: A predictive model was constructed based on serum cystatin C, serum creatinine, immunoglobulin M, and estimated glomerular filtration rate (eGFR). ROC curve analysis showed high predictive accuracy, with an AUC of 0.9444, sensitivity of 0.82, and specificity of 0.98 at the optimal cutoff point. The calibration curve indicated strong agreement between predicted and actual outcomes. Decision curve analysis suggested that the model provides significant net benefits across different risk thresholds. Conclusion: This model effectively predicts the risk of HSPN, facilitating early intervention and improved patient outcomes.

Keywords: Henoch-schönlein purpura, henoch-schönlein purpura nephritis, pediatric patients, cystatin C, clinical prediction model, ROC curve, nomogram

Introduction

Henoch-Schönlein purpura (HSP), also known as IgA vasculitis (IgAV), is the most common form of vasculitis in children, characterized by IgA immune complex deposits in small blood vessels, leading to systemic vasculitis [1, 2]. HSP primarily affects pediatric patients, though its pathogenesis remains partially understood, with potential links to infections, immune dysregulation, and genetic factors. Clinically, HSP typically manifests with palpable purpura, abdominal pain, arthritis, and nephritis [3]. Kidney involvement is a key prognostic factor, as Henoch-Schönlein purpura nephritis (HSPN) is the most severe complication, affecting approximately 20-60% of HSP patients [4-6]. If untreated, HSPN significantly increases the risk of progression to chronic kidney disease and end-stage renal disease [7].

The pathogenesis of HSPN is complex, involving both immune complex-driven inflammation in the glomeruli and influences from the patient's genetic background, infections, and immune regulation. Persistent hematuria, proteinuria, and hypertension are early clinical and laboratory indicators associated with HSPN progression and a poor prognosis.

Previous studies have highlighted several factors influencing HSP progression to nephritis in children, such as age, seasonality, and living environment. For example, younger children appear at higher risk, and onset in winter correlates with an increase in upper respiratory tract infections, potentially acting as triggers for HSP progression [8]. Additionally, environmental pollutants and allergens may exacerbate disease severity. Obesity, an increasing public health concern, may also worsen HSP and raise the risk of progression to HSPN [9].

The degree of kidney involvement underscores the need for early detection and intervention [10, 11]. Currently, HSPN diagnosis relies on

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clinical symptoms, urinalysis, and sometimes renal biopsy, which are limited in sensitivity and specificity, often delaying diagnosis and treatment. The lack of specific biomarkers impedes effective stratification of HSP patients by renal disease risk, posing a significant clinical challenge in early identification of high-risk patients. Consequently, there is a critical need for reliable biomarkers and predictive models to accurately assess the likelihood of nephritis progression in children with HSP.

This study aims to develop a clinical prediction model for HSPN by utilizing key clinical indicators. By integrating these parameters, we intend to enhance the predictive accuracy for HSPN, thereby supporting earlier diagnosis and intervention. Our research builds on existing findings and seeks to create a reliable tool for clinicians to identify children at high risk for HSPN. For instance, receiver operating characteristic (ROC) models based on clinical parameters have successfully predicted disease progression in diabetic nephropathy, cardiovascular diseases, and chronic liver disease [12-14].

This study focuses on developing a predictive model incorporating serum cystatin C (CysC) and other clinical indicators, which may serve as a valuable tool for managing HSP in clinical practice.

Material and methods

Participant selection criteria and ethics

This retrospective study included patients initially diagnosed with HSP at the 940th Hospital of the Joint Logistics Support Force of the Chinese People's Liberation Army. Inclusion criteria: (1) initial diagnosis of HSP at the 940th Hospital; (2) age under 18 years. Exclusion criteria: (1) presence of cardiovascular disease or diabetes; (2) diagnosis of other systemic vasculitis or autoimmune diseases within six months of follow-up. HSP diagnosis was based on the 2008 Ankara criteria endorsed by EULAR/PRINTO/PReS [15]. HSPN is defined according to the 1990 classification criteria of the American College of Rheumatology, characterized by the presence of hematuria and/or proteinuria in HSP patients [16]. All participants were inpatients at the 940th Hospital from December 2022 to October 2023, with a minimum follow-up period of six months. Ethical approval was granted by the Ethics Review Committee of the 940th Hospital (Approval No. 2022KYLL196).

Data collection

This study included a total of 180 patients, with 90 diagnosed with HSP and 90 with HSPN. The initial 50 HSP and 50 HSPN patients were used as the training set to develop the predictive model, while an additional cohort of 40 HSP and 40 HSPN patients served as the validation set to independently assess the model's performance. This approach ensured robustness in model development and rigorous testing of accuracy and reliability in a separate patient population. Data collected at initial admission included demographic and baseline clinical information. Demographic data included age and gender, while clinical data encompassed purpura, arthritis/arthralgia, abdominal pain, systolic blood pressure (SBP), diastolic blood pressure (DBP), cystatin C (CysC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), hemoglobin (Hb), platelets (Plt), neutrophil percentage (Neut%), D-dimer, blood urea nitrogen (BUN), serum creatinine (Scr), total protein, immunoglobulins G, M, and A (IgG, IgM, IgA), 24-hour urine protein (24hTP), and estimated glomerular filtration rate (eGFR).

Statistical analysis

Normality of continuous variables was assessed using the Shapiro-Wilk test. Normally distributed variables are expressed as mean ± standard deviation (Mean ± SD), whereas non-normally distributed variables are presented as median and interquartile range (Median [IQR]). Baseline comparisons between groups were conducted using an independent sample t-test for normally distributed continuous variables, while the Mann-Whitney U test was used for non-normally distributed continuous variables. Categorical variables were compared using the chi-square test or Fisher's exact test when expected frequencies were low. Univariate logistic regression was performed to identify potential risk factors, with variables showing a P-value < 0.05 considered for multivariate logistic regression. Multivariate logistic regression was conducted with a stepwise selection method to identify independent risk factors, reporting the odds ratio with 95% confidence intervals for each predictor.

Table 1. Baseline characteristic of patients with HSP and HSPN

	HSP	HSPN	Statistic-value	*P*-value
Age (months)	99.50 (69.00-117.00)	96.00 (71.50-118.75)	1281	0.8334
Gender (female/male)	18/32	23/27	0.661	0.3137
Purpura: n (%)	50 (100.0)	50 (100.0)	0	1
Arthritis/arthralgia: n (%)	31 (62.0)	35 (70.0)	0.401	0.4032
Abdominal_pain: n (%)	16 (32.0)	21 (42.0)	0.686	0.3047
SBP (mmHg)	111 ± 13.8	110 ± 12.0	0.471	0.639
DBP (mmHg)	77.1 ± 8.37	80.2 ± 10.7	990.5	0.109
CysC (mg/L)	0.93 (0.76-1.30)	1.52 (1.06-1.83)	461	< 0.0001
ESR (mm/h)	16.54 (12.75-19.75)	17.62 (13.25-21.57)	1140	0.4503
CRP (g/L)	7.62 (5.12-12.98)	9.41 (5.01-12.42)	1151.5	0.4993
Hb (g/L)	131.45 (124.77-134.81)	131.00 (126.00-135.25)	1252	0.9917
Plt (*109/L)	350.55 (312.22-381.26)	368.70 (317.93-405.44)	1065	0.2034
Neut%	50.2 (42.5-61.5)	56.1 (46.5-61.4)	1041	0.15
D-Dimer (mg/L)	0.28 (0.21-0.50)	0.34 (0.21-0.44)	1195.5	0.707
BUN (mmol/L)	4.10 (3.53-4.62)	4.18 (3.70-4.72)	1206.5	0.7669
Scr (μmol/L)	36.45 (33.77-38.41)	40.31 (34.24-44.70)	756	0.0007
TP (g/L)	65.61 (63.11-69.38)	66.06 (63.00-69.02)	1201.5	0.7407
IgG (g/L)	10.36 (9.45-11.56)	10.64 (9.28-11.54)	1226.5	0.874
IgM (g/L)	0.70 (0.66-0.76)	0.85 (0.69-0.97)	635	< 0.0001
IgA (g/L)	1.52 (1.33-1.77)	1.75 (1.45-2.05)	819	0.003
24hTP (g)	0.13 (0.06-0.17)	0.15 (0.09-0.24)	828.5	0.0037
eGFR (mL/min/1.73 m^2)	85.86 (82.66-88.23)	92.65 (85.81-96.17)	603.5	< 0.0001

HSP, Henoch-Schönlein purpura; HSPN, Henoch-Schönlein purpura nephritis; CysC, Cystatin C; SBP, systolic blood pressure; DBP, diastolic blood pressure; Neut%, neutrophil percentage; ESR, Erythrocyte sedimentation rate; CRP, C-reactive protein; Hb, Hemoglobin; Plt, Platelets; BUN, Blood urea nitrogen; Scr, Serum creatinine; TP, Total protein; IgG, Immunoglobulin G; IgM, Immunoglobulin M; IgA, Immunoglobulin A; 24hTP, 24-hour urinary protein; eGFR, Estimated glomerular filtration rate.

The model's discriminative ability was evaluated using ROC curves, calculating the area under the curve (AUC) to assess model performance. Calibration was tested with calibration plots to verify the agreement between predicted probabilities and observed outcomes. A nomogram was constructed from the multivariate logistic regression model, offering a visual tool for predicting individual risk. Decision curve analysis (DCA) was conducted to evaluate the model's clinical utility by quantifying net benefits at different threshold probabilities. All analyses were performed using R software (version 4.3.2), with *P*-values < 0.05 considered statistically significant.

Results

Baseline characteristics of patients

No significant differences in age or gender distribution were observed between the HSPN and HSP groups (age: 96.00 months vs. 99.50 months, P = 0.8334; gender: 27/23 vs. 32/18, P = 0.3137). However, biochemical markers showed notable differences: CysC levels were significantly higher in the HSPN group (P < 0.0001), as were serum creatinine (Scr) levels (P = 0.0007). Additionally, IgM and IgA levels were elevated in the HSPN group (IgM: P < 0.0001; IgA: P = 0.003), while 24-hour urine protein (24hTP) increased (P = 0.0037), and eGFR was lower (P < 0.0001) in the HSPN group (**Table 1**; **Figure 1**).

Identification of potential variables for predictive model construction

Univariate logistic regression analysis identified six significant variables as potential predictors of HSP progression to HSPN: CysC (OR = 29.27, 95% CI: 8.25-133.23, P < 0.0001), serum creatinine (OR = 1.20, 95% CI: 1.10-1.34, P < 0.0001), IgM (OR = 40155.39, 95%

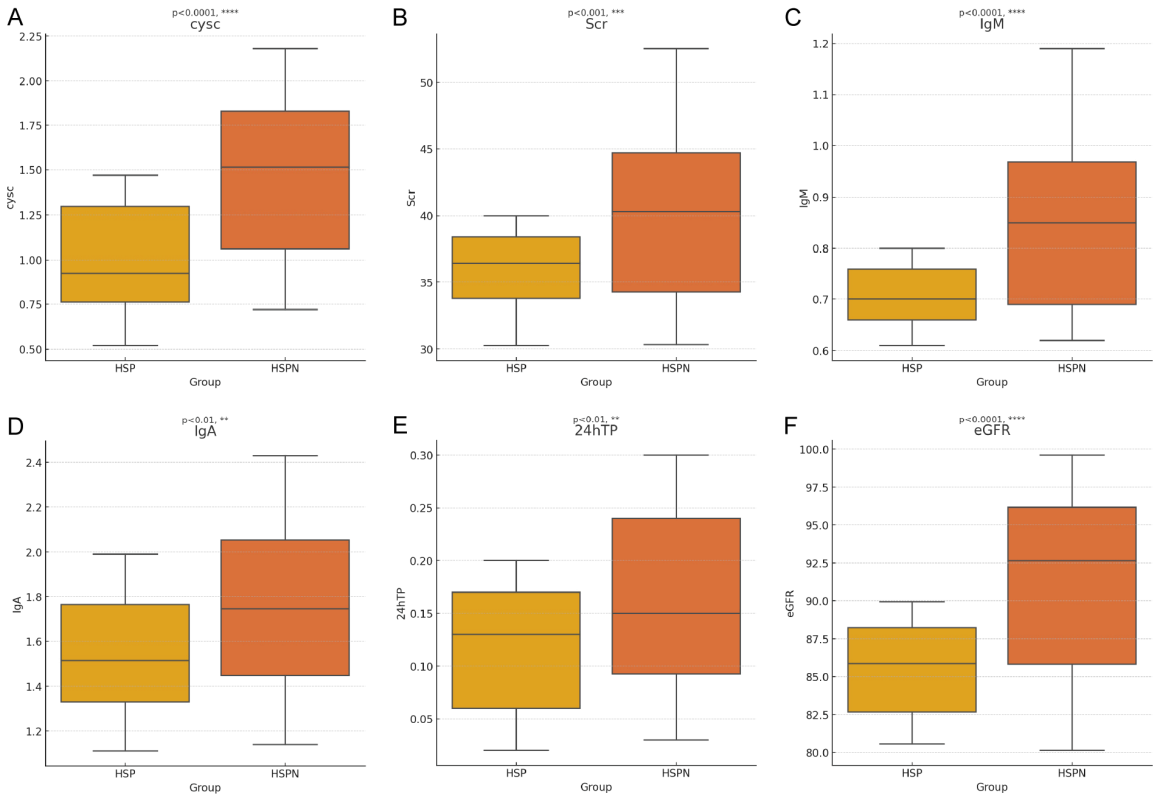

Figure 1. Box plots of baseline clinical indicators showing significant differences between HSP and HSPN groups. Box plots display the distribution of the specified clinical indicators in HSP and HSPN groups. The horizontal line inside each box represents the median, the box represents the interquartile range. A. Serum cystatin C (cysc) levels in HSP and HSPN groups ($P < 0.0001$); B. Serum creatinine (Scr) levels in HSP and HSPN groups ($P < 0.001$); C. Immunoglobulin M (IgM) levels in HSP and HSPN groups ($P < 0.0001$); D. Immunoglobulin A (IgA) levels in HSP and HSPN groups ($P < 0.01$); E. 24-hour urinary protein (24hTP) levels in HSP and HSPN groups ($P < 0.01$); F. Estimated glomerular filtration rate (eGFR) in HSP and HSPN groups ($P < 0.0001$). CysC, Cystatin C; Scr, Serum creatinine; IgM, Immunoglobulin M; IgA, Immunoglobulin A; 24hTP, 24-hour urinary protein; eGFR, Estimated glomerular filtration rate; HSP, Henoch-Schönlein purpura; HSPN, Henoch-Schönlein purpura nephritis (**$P < 0.01$, ***$P < 0.001$, ****$P < 0.0001$).

CI: 508.41-9017124.00, $P < 0.0001$), IgA (OR = 8.04, 95% CI: 2.27-32.27, $P = 0.0019$), and eGFR (OR = 1.25, 95% CI: 1.14-1.40, $P < 0.0001$) (**Table 2**). Multivariate logistic regression confirmed that cystatin C (OR = 70.40, 95% CI: 5.06-980.25, $P = 0.0015$) and serum creatinine (OR = 1.29, 95% CI: 1.05-1.57, $P = 0.0136$) were independent predictors, along with IgM (OR = 26417.17, 95% CI: 2.58-270137500.00, $P = 0.0307$) and eGFR (OR = 1.25, 95% CI: 1.05-1.49, $P = 0.0135$) (**Table 3**).

Model construction and calibration

The predictive model, based on CysC Scr, IgM, and eGFR, was evaluated using ROC curve analysis, showing high accuracy with an AUC of 0.9444 (**Figure 2**). The optimal cutoff of 0.63 provided a sensitivity of 0.82 and specificity of 0.98, indicating strong diagnostic performance. Calibration curves showed that the bias-corrected calibration curve closely matched the ideal line, suggesting good concordance between predicted probabilities and observed outcomes. The mean absolute error of 0.03 further demonstrated the model's excellent calibration and low prediction error (**Figure 3**).

Construction of nomogram

A nomogram was developed based on four identified risk indicators to visually represent the scoring system for predicting HSPN progression risk (**Figure 4**). This nomogram converts each patient's indicator values into scores, which are then summed to estimate the

Table 2. Univariate logistic regression analysis results

Variable	OR	Lower_CI	Upper_CI	*P*_Value
Age (months)	1.00	0.98	1.01	0.88
SBP (mmHg)	0.99	0.96	1.02	0.63
DBP (mmHg)	1.03	0.99	1.08	0.11
CysC (mg/L)	29.27	8.25	133.23	0.00
ESR (mm/h)	1.04	0.95	1.14	0.41
CRP (g/L)	1.03	0.94	1.13	0.50
Hb (g/L)	1.00	0.94	1.07	0.96
Plt (*109/L)	1.00	1.00	1.01	0.25
Neut%	1.02	0.99	1.06	0.19
D-Dimer (mg/L)	1.37	0.12	15.60	0.80
BUN (mmol/L)	1.11	0.56	2.23	0.76
Scr (μmol/L)	1.20	1.10	1.34	0.00
TP (g/L)	1.02	0.92	1.12	0.72
IgG (g/L)	1.03	0.75	1.42	0.85
IgM (g/L)	40155.39	508.41	9017124.08	0.00
IgA (g/L)	8.04	2.27	32.27	0.00
24hTP (g)	18190.63	60.60	10324764.99	0.00
eGFR (mL/min/1.73 m^2)	1.25	1.14	1.40	0.00

SBP, systolic blood pressure; DBP, diastolic blood pressure; CysC, Cystatin C; ESR, Erythrocyte sedimentation rate; CRP, C-reactive protein; Hb, Hemoglobin; Plt, Platelets; BUN, Blood urea nitrogen; Scr, Serum creatinine; TP, Total protein; IgG, Immunoglobulin G; IgM, Immunoglobulin M; IgA, Immunoglobulin A; 24hTP, 24-hour urinary protein; eGFR, Estimated glomerular filtration rate.

Table 3. Multivariate logistic regression analysis results

Variable	OR	Lower_CI	Upper_CI	*P*_Value
CysC (mg/L)	70.40	5.06	980.25	0.00
Scr (μmol/L)	1.29	1.05	1.57	0.01
IgM (g/L)	26417.17	2.58	270137543.11	0.03
IgA (g/L)	15.21	0.67	345.59	0.09
24hTP (g)	11244.70	0.27	465735962.53	0.09
eGFR (mL/min/1.73 m^2)	1.25	1.05	1.49	0.01

CysC, Cystatin C; Scr, Serum creatinine; IgM, Immunoglobulin M; IgA, Immunoglobulin A; 24hTP, 24-hour urinary protein; eGFR, Estimated glomerular filtration rate.

probability of HSPN, supporting clinical risk assessment and decision-making.

Clinical utility evaluation

The clinical utility of the predictive model was assessed through DCA. The DCA curve (**Figure 5**) demonstrated that the model provided greater net benefits across various risk thresholds.

Model validation

Model validation was conducted using an independent cohort of 40 HSP and 40 HSPN patients. No statistically significant differences in baseline data were observed between the training and validation cohorts (**Table 4**). The ROC curve for the validation set showed an AUC of 0.879, confirming the model's robustness and reliability in a separate patient population (**Figure 6**).

Discussion

We developed an early prediction model to assess HSP progression to HSPN, utilizing clinical data from 90 HSP and 90 HSPN patients. Univariate and multivariate logistic regression analyses identified four key indicators - CysC, Scr, eGFR, and IgM, to construct the predictive model. The primary objective was to enable early identification of HSP patients at high risk of progressing to HSPN, thus facilitating early intervention and closer monitoring. Early and targeted interventions may reduce kidney damage severity and improve long-term outcomes for pediatric patients. Early prediction and intervention are essential in mitigating the risk of chronic kidney disease and end-stage renal disease, which are severe complications of untreated HSPN.

Diagnostic performance was evaluated using ROC curve analysis, achieving an AUC of 0.9444, indicating high discriminative ability. This AUC value suggests that the model effectively distinguishes between high- and low-risk patients for HSPN progression. With an optimal cutoff of 0.63, the model reached a sensitivity of 0.82 and specificity of 0.98.

Identifying high-risk HSP patients early is crucial for timely treatment, as HSPN is the most serious complication of HSP [17]. Prior research has linked biochemical markers such as Scr, urinary protein, and eGFR with HSPN develop-

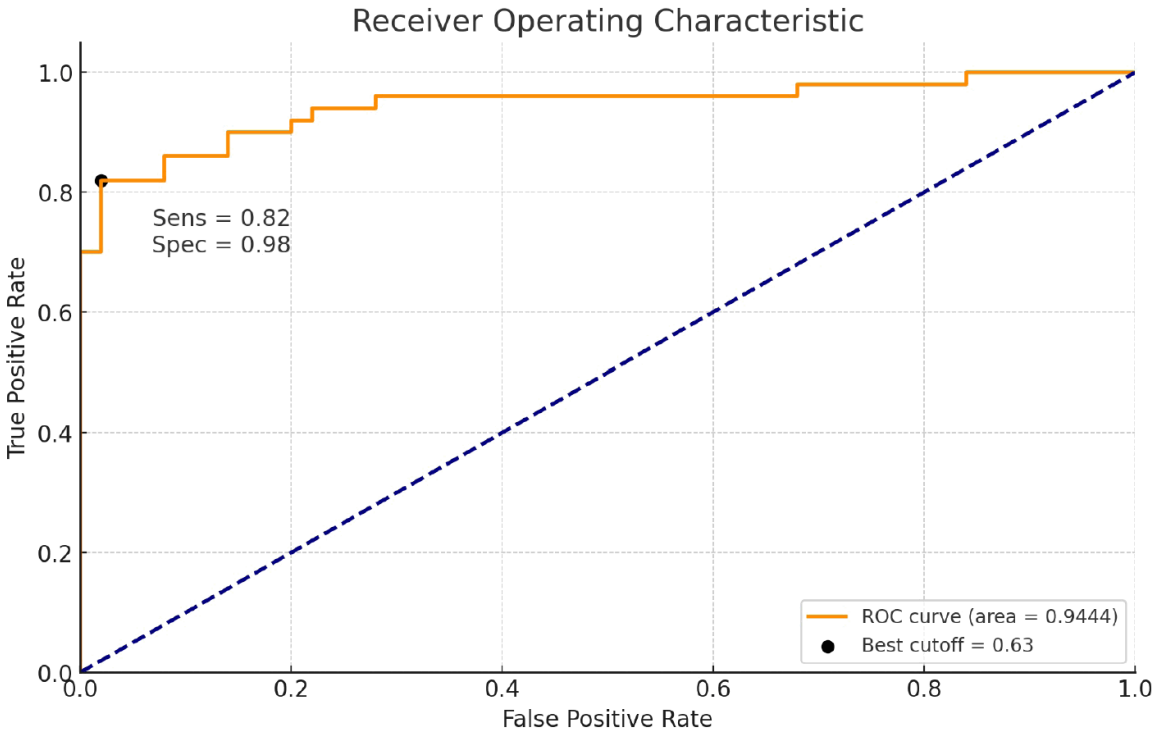

Figure 2. ROC curve for predicting the progression of HSP to HSPN using the multivariate logistic regression model. This figure illustrates the ROC curve for predicting the progression from HSP to HSPN. The AUC is 0.9444, indicating high discriminative ability. The optimal cutoff value is 0.63, with a sensitivity of 0.82 and a specificity of 0.98. ROC Curve, Receiver Operating Characteristic Curve; Sens, Sensitivity; Spec, Specificity; ROC, receiver operating characteristic; HSP, Henoch-Schönlein purpura; HSPN, Henoch-Schönlein purpura nephritis.

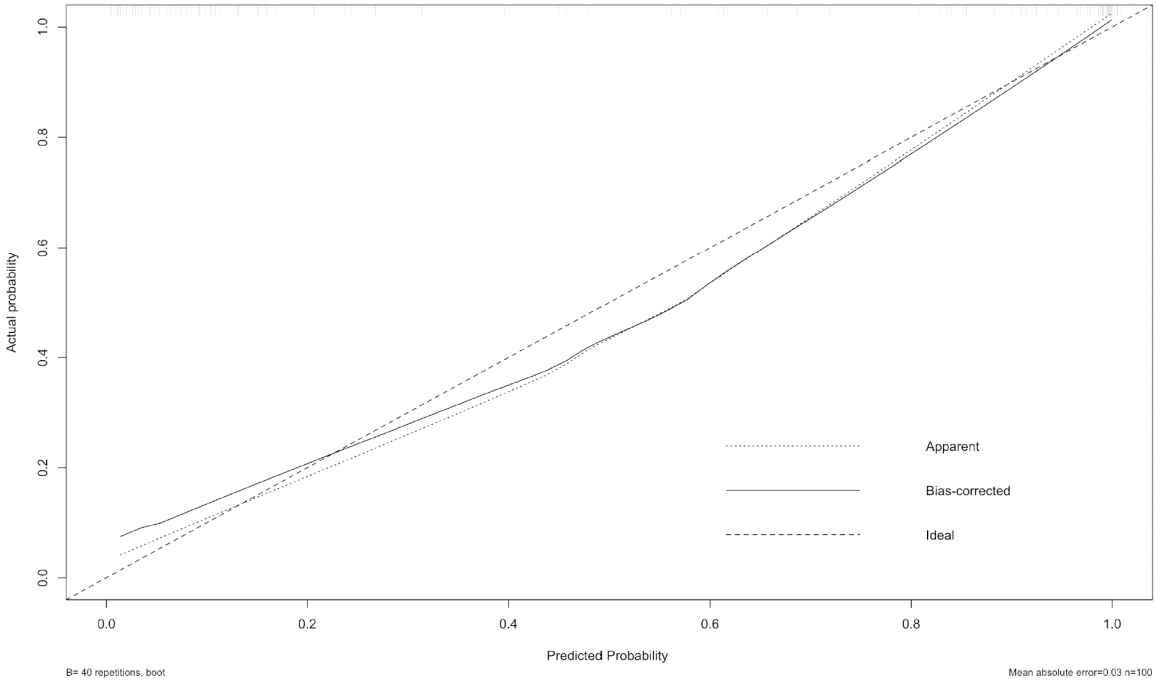

Figure 3. Calibration curve for the predictive model of HSP progression to HSPN. This figure shows the calibration curve for the predictive model, comparing predicted probabilities against actual probabilities. The bias-corrected curve closely matches the ideal curve, indicating good agreement and demonstrating the model's accuracy in predicting the progression from HSP to HSPN. The mean absolute error of the model is 0.03. Apparent: The calibration curve for the apparent probabilities; Bias-corrected: The calibration curve corrected for bias using bootstrapping;

Ideal: The ideal calibration curve where predicted probabilities perfectly match actual probabilities. HSP, Henoch-Schönlein purpura; HSPN, Henoch-Schönlein purpura nephritis.

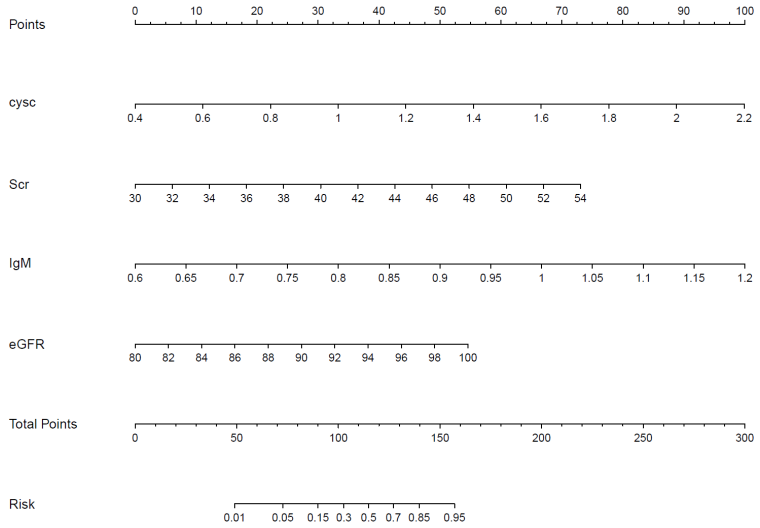

Figure 4. Nomogram for predicting the risk of progression from HSP to HSPN. This figure presents a nomogram constructed from the predictive model, which visually represents the risk scoring system for predicting the progression from HSP to HSPN. The nomogram allows for the conversion of clinical indicator values into total points, which can then be used to estimate the patient's risk of progression to HSPN. CysC, Cystatin C; Scr, Serum creatinine; IgM, Immunoglobulin M; eGFR, Estimated glomerular filtration rate; HSP, Henoch-Schönlein purpura; HSPN, Henoch-Schönlein purpura nephritis.

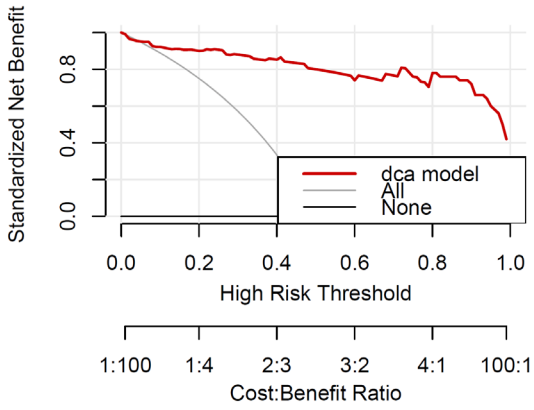

Figure 5. DCA for the predictive model of HSP progression to HSPN. The DCA curve shows the net benefits of the model across different high-risk thresholds compared to the "all patients are high-risk" and "no patients are high-risk" scenarios. DCA model: Decision curve analysis for the predictive model; All: Assumes all patients are at high risk; None: Assumes no patients are at high risk. HSP, Henoch-Schönlein purpura; HSPN, Henoch-Schönlein purpura nephritis.

ment [18, 19]. However, these indicators often become significantly altered only in advanced nephritis stages, limiting their utility for early detection. For instance, Scr tends to rise only after substantial renal function loss, making it less sensitive for detecting early kidney injury. Routine urine tests also show low sensitivity and specificity for assessing HSPN, as some early-stage HSPN patients may present with normal results [20]. This underscores the need for more sensitive and specific biomarkers capable of detecting early kidney involvement before significant damage occurs.

In this study, we confirmed that both Scr and eGFR are effective predictors of HSPN, consistent with existing literature. These markers are valuable in evaluating renal function, and their combined use provides a more comprehensive assessment of a patient's risk of nephritis. Although Scr is commonly used, it is influenced by factors such as age, muscle mass, and hydration status, which can limit its accuracy in specific patient populations. eGFR, calculated from Scr levels, offers a more standardized measure of kidney function, yet still shares the inherent limitations associated with Scr. Our findings emphasize these limitations, especially in the early stages of HSPN, and highlight the need for supplementary biomarkers to enhance early detection.

This study improved the model's performance by incorporating multiple clinical indicators, including novel biomarkers CysC and IgM. CysC, a small protein primarily filtered by the glomeruli and subsequently reabsorbed and broken down in the proximal tubules, is commonly used to assess kidney function. Due to its stable production rate and independence from factors such as age, gender, muscle mass, and diet, CysC is considered a more accurate marker of glomerular filtration rate than creatinine [21]. CysC levels rise earlier and more sensi-

Table 4. Baseline characteristics of training and validation cohorts

	Training cohort N = 100	Validation cohort N = 80	*P*_Value
Age (months)	98.5 [69.0; 119]	90.0 [70.8; 114]	0.347
Gender (female/male)	41/59	31/49	0.878
Arthritis/arthralgia: n (%)	66 (66.0%)	55 (68.8%)	0.817
Abdominal_pain: n (%)	37 (37.0%)	31 (38.8%)	0.932
CysC (mg/L)	1.16 [0.84; 1.51]	1.14 [0.95; 1.29]	0.523
ESR (mm/h)	17.0 [12.9; 21.0]	15.7 [13.0; 20.7]	0.671
CRP (g/L)	8.83 [5.01; 12.6]	8.75 [4.67; 12.1]	0.354
Hb (g/L)	131 [126; 135]	129 [125; 134]	0.177
Plt (*109/L)	357 [312; 395]	349 [312; 388]	0.686
BUN (mmol/L)	4.14 [3.68; 4.63]	4.31 [3.79; 4.62]	0.245
Scr (μmol/L)	37.8 [33.9; 40.2]	38.1 [33.0; 42.2]	0.76
TP (g/L)	65.8 [63.0; 69.2]	66.7 [62.9; 69.0]	0.604
IgG (g/L)	10.5 [9.38; 11.6]	10.2 [9.23; 11.0]	0.355
IgM (g/L)	0.74 [0.67; 0.84]	0.73 [0.65; 0.79]	0.079
IgA (g/L)	1.62 [1.35; 1.90]	1.75 [1.26; 1.98]	0.551
24hTP (g)	0.14 [0.08; 0.19]	0.14 [0.07; 0.22]	0.545
eGFR (mL/min/1.73 m^2)	87.4 [83.4; 92.6]	87.5 [83.9; 89.7]	0.327
SBP (mmHg)	110 (12.9)	108 (19.0)	0.337
DBP (mmHg)	78.0 [73.0; 85.0]	76.0 [66.2; 87.2]	0.172
D-Dimer (mg/L)	0.32 [0.21; 0.46]	0.29 [0.17; 0.44]	0.264
Neut%	53.5 [43.8; 61.5]	57.2 [45.9; 68.3]	0.285

SBP, systolic blood pressure; DBP, diastolic blood pressure; CysC, Cystatin C; ESR, Erythrocyte sedimentation rate; CRP, C-reactive protein; Hb, Hemoglobin; Plt, Platelets; BUN, Blood urea nitrogen; Scr, Serum creatinine; TP, Total protein; IgG, Immunoglobulin G; IgM, Immunoglobulin M; IgA, Immunoglobulin A; 24hTP, 24-hour urinary protein; eGFR, Estimated glomerular filtration rate.

tively than creatinine in cases of both acute kidney injury and chronic kidney disease [22-25], making it a valuable marker for early detection. Although studies on CysC in HSP and HSPN are limited, some findings suggest that CysC levels increase when kidney involvement occurs in HSP patients [26]. Our results support that elevated CysC levels indicate early kidney involvement in HSP, reinforcing its value as a key predictive marker in our model. This finding contributes to the growing evidence for CysC's utility in predicting kidney dysfunction, especially in pediatric patients, where early intervention is crucial for long-term kidney health.

Research on biomarkers related to HSP and HSPN remains limited [27-29]. Recent studies have indicated that increased e-GST activity may predict renal impairment in children with HSP [30, 31]. Other research has suggested that serum Gd-IgA1 may be elevated in individuals with HSP, potentially serving as a diagnostic biomarker [32, 33]. Urinary IgA and IgM have also been proposed as possible diagnostic aids for HSPN [34]. Our study aligns with these findings, as we observed that HSP patients with elevated serum IgM levels are at greater risk of progressing to HSPN.

Previous studies have primarily focused on IgA, particularly the deposition of the IgA1 subtype in glomeruli, as a key pathogenic mechanism in HSPN [15]. In contrast, the role of IgM in HSPN has been less explored. Some evidence suggests that IgM, along with IgA, may deposit in blood vessels and glomeruli, causing tissue damage, and that in some cases, IgM deposition may even exceed that of IgA [35, 36]. Our study identified serum IgM as a significant predictor of HSPN progression, a novel finding within HSP research. While IgA has been the focus due to its role in glomerular deposition [37], our data revealed that IgM levels were significantly higher in HSPN patients. Specifically, 50% of HSPN patients had IgM levels above 0.842 g/L, compared to none in the HSP group. This distinct difference underscores the potential role of IgM in HSPN pathogenesis, though further studies are needed to clarify the mechanisms involved.

The wide confidence interval associated with IgM in our model may be due to the limited data on IgM levels, especially the pronounced difference between the HSP and HSPN groups. This variability introduces some uncertainty into the statistical model; however, IgM remains a strong predictor of HSPN progression. These findings suggest that IgM may play a critical role in the immune response contributing to HSPN development, warranting further investigation. The role of IgM in glomerular injury is particularly noteworthy, as research has largely focused on IgA deposition. IgM deposition may suggest a different or complementary patho-

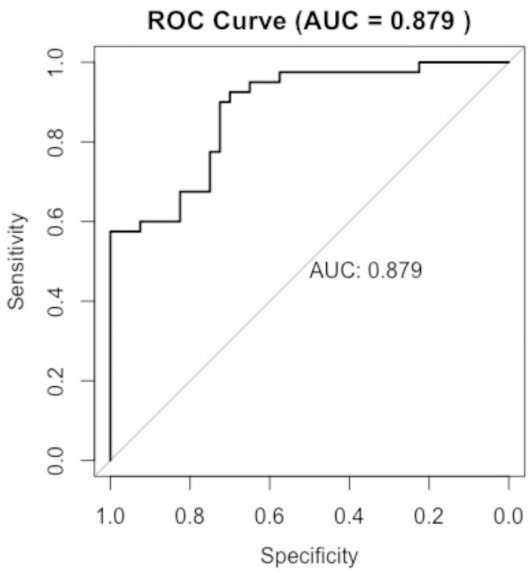

Figure 6. ROC curve for predicting the progression of HSP to HSPN in the validation cohort using the multivariate logistic regression model. This figure illustrates the ROC curve for predicting the progression from HSP to HSPN in the independent validation cohort. The AUC is 0.879, confirming good discriminative ability. ROC, receiver operating characteristic; AUC, area under the curve.

genic mechanism, possibly involving immune complex formation that exacerbates renal inflammation and tissue damage.

This study offers clinicians a non-invasive model for early prediction of HSPN risk, facilitating timely intervention and management of high-risk patients. Built on routine clinical examinations and biochemical markers, the model is straightforward to implement in practice. However, the study has limitations: the sample size is relatively small, and the six-month follow-up may limit the generalizability of the results. Additionally, as a single-center study, external validation with a larger, more diverse patient population is necessary to confirm the model's robustness. Future research should aim to validate this model through multicenter studies and investigate additional biomarkers to further enhance predictive accuracy.

While this model incorporates several key biomarkers, other factors, such as genetic and environmental influences, may also play roles in HSPN progression. For instance, genetic polymorphisms associated with immune regulation and inflammation have been implicated in other forms of glomerulonephritis, and similar mechanisms may contribute to HSPN. Continued research into HSPN pathogenesis, particularly immune dysregulation and inflammatory pathways, could uncover new biomarkers that might further strengthen the model's predictive power.

In conclusion, this study identifies independent risk factors for HSPN in pediatric patients and presents a predictive model based on CysC, Scr, IgM, and eGFR. With an AUC of 0.9444, the model shows high predictive accuracy, aiding early identification and intervention. These findings highlight the potential for improved HSP management, ultimately enhancing patient outcomes.

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Disclosure of conflict of interest

None.

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