

Original Article

Analysis of relevant influencing factors for recurrent urinary tract infections in children: exploring predictive factors and intervention measures

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Abstract: Objective: To analyze the factors influencing recurrent urinary tract infections (UTIs) in children and explore predictive factors and intervention measures. Methods: Data of 158 children with UTIs treated at the Longyan First Affiliated Hospital of Fujian Medical University from January 2020 to June 2023 were analyzed. Among them, 122 children without recurrent UTIs were included in a non-recurrent group, while the remaining 36 were included in a recurrent group. The quality of life prior to treatment and six weeks after treatment, the immunoglobulin A (IgA) and immunoglobulin G (IgG) levels after treatment, the relationship between the quality of life after six weeks of treatment and the levels of IgA and IgG were analyzed. Multivariate logistic regression analysis was conducted to identify factors impacting the recurrence of UTIs, and receiver operating characteristic (ROC) curves were generated to predict recurrent UTIs based on independent risk factors. Results: Before treatment, no notable difference was observed in Short Form 36 Health Survey (SF-36) scores between the non-recurrent group and the recurrent group ($P>0.05$). After treatment, the SF-36 scores notably increased in the non-recurrent group ($P<0.0001$), while there was no notable increase in the recurrent group ($P>0.05$). However, the difference in SF-36 scores after treatment was significant between the two groups ($P<0.0001$). In addition, there was a significantly positive correlation between IgA levels and quality of life after 6 weeks of treatment ($P<0.05$). The recurrent group showed significantly lower IgA and IgG levels than the non-recurrent group ($P<0.05$). Multivariate logistic regression analysis identified anemia, urinary system malformation, constipation, decreased IgA level, and decreased IgG level as independent risk factors for recurrent UTIs in children. ROC curves-based analysis of independent risk factors demonstrated that urinary system malformation had a better performance in predicting recurrent UTIs in children than the other four factors. Conclusion: Urinary system malformation, constipation, anemia, decreased IgA and IgG levels are all identified as independent risk factors for recurrent UTIs in children, and urinary system malformation is a better predictor for recurrent UTIs in children than the other four factors.

Keywords: Recurrent urinary tract infections, urinary system malformation, constipation, anemia, IgA, IgG

Introduction

Urinary tract infections (UTIs) are a general term for diseases such as pyelonephritis, cystitis, and urethritis caused by bacteria. They occur when bacteria invade the urinary tract, multiply in the urine, and cause damage to the urinary tract mucosa or tissues. UTIs are one of the most common bacterial infections in children [1, 2]. UTIs in children are linked to alterations in intestinal flora, anomalies in the anatomical structure and functionality of the urinary system, unique physiological configura-

tions, and variations in immune function [3]. Due to the immaturity of organ functions and weak resistance in children, the incidence of UTIs is increased [4]. In addition to potentially causing severe sepsis in children, UTIs can also trigger chronic kidney diseases such as renal scars, hypertension, and chronic renal insufficiency. The risk of developing these chronic kidney diseases is even higher in individuals who experience recurrent UTIs [5].

Recurrent UTIs are relatively common in children, especially among girls between the ages

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of 2 and 8 years [5]. In children with recurrent UTIs, clinical manifestations may not be readily apparent, often presenting with nonspecific symptoms such as vomiting, fever, abdominal distension, and abdominal pain. Diagnosis typically involves urinalysis and urine culture to confirm the presence of a UTI [6, 7]. Recurrent UTIs are often the result of multiple factors, typically including anatomical abnormalities in the urinary system, urinary stasis, persistent presence of urethral infections, and immune system dysfunction [8, 9]. Due to the nonspecific symptoms associated with recurrent UTIs, there is a relatively high rate of misdiagnosis, which can impact the treatment of the condition [10]. If high-risk children with recurrent UTIs are not identified early and provided with appropriate treatment, it can lead to prolonged illness and even result in permanent renal scarring. This result, in turn, can lead to conditions such as impaired kidney development, chronic pyelonephritis, renal glomerular dysfunction, hypertension, and end-stage renal failure [9]. Therefore, the prevention of recurrent UTIs holds significant clinical importance. Existing literature has identified various influencing factors such as urinary system malformations, and altered immune markers like decreased immunoglobulin A (IgA) and immunoglobulin G (IgG) levels as potential contributors to recurrent UTIs in children [11].

This study analyzed the influencing factors of recurrent UTIs in children to reduce the recurrence rate of UTIs in pediatric patients, and explored predictive factors and intervention measures to enable targeted prevention. The innovative aspect of this study, compared to others, lies in its comprehensive approach to explore a wider range of potential influencing factors for predicting UTIs in children. By analyzing data from 158 children with UTIs, the study delves deeper into the roles of factors such as anemia, urinary system malformations, constipation, and immune marker levels.

Methods and data

Sample source and processing

With approval from the Medical Ethics Committee of the Longyan First Affiliated Hospital of Fujian Medical University, this retrospective analysis collected the clinical data of 200 chil-

dren with UTIs treated at the Longyan First Affiliated Hospital of Fujian Medical University between January 2020 and June 2023. After the initial screening of the 200 children, 158 children who met the inclusion and exclusion criteria were included. Inclusion criteria: (1) Children with symptoms of UTI with more than 5 white blood cells/high power field in centrifugal urinary sediment; (2) Children who were diagnosed with UTI by laboratory examinations, and met the diagnostic criteria of “Chinese expert consensus on diagnosis and treatment of urinary tract infection (2015 version)” [12]; (3) Children who were younger than 12 years old; (4) Children with required follow-up and clinical data. Exclusion criteria: (1) Children with other systemic infections; (2) Children with immunodeficiency; (3) Children with underlying diseases such as diabetes.

Grouping

Based on the follow-up results, 122 patients who did not experience recurrent UTIs were assigned to the non-recurrent group, while 36 patients who experienced recurrent UTIs were assigned to the recurrent group. Recurrence of UTI refers to the reappearance of symptoms in the child within 6 weeks, with a urine bacterial colony count $\geq 10^5$ /mL, and the presence of the same or different bacterial species compared to the previous infection [5]. The non-recurrent group consisted of 79 females and 43 males, ranging in age from 2 months to 12 years. The recurrent group was comprised of 27 females and 9 males, with ages ranging from 3 months to 11 years. No significant difference was found in the baseline characteristics between the two groups, indicating comparability between the two groups ($P > 0.05$).

Data collection

Relevant data of the children were collected from the electronic medical record system in the Longyan First Affiliated Hospital of Fujian Medical University, including age, sex, anemia status, allergic constitution, constipation status, urinary system malformation, IgA levels, IgG levels, and distribution of pathogens.

Outcome measures

Primary outcome measures: (1) IgA and IgG levels after treatment were compared between

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Table 1. Baseline data of patients

	Non-recurrent group (n=122)	Recurrent group (n=36)	χ^2	P value
Age			0.493	0.483
≥ 6 years old	79	21		
< 6 years old	43	15		
Sex			3.035	0.082
Male	50	9		
Female	72	27		
BMI			3.382	0.068
≥ 20 kg/m ²	72	15		
< 20 kg/m ²	50	21		
Course of disease			0.250	0.617
1-20 days	62	20		
20-40 days	60	16		
Place of incidence			0.047	0.829
Urban areas	35	11		
Rural areas	87	25		

the two groups. (2) The relationship between the quality of life after six weeks of treatment and the levels of IgA and IgG in the two groups was analyzed. (3) Based on the recurrence status of UTIs, the clinical data of the children were included in a univariate analysis. Factors showing significant differences were then subjected to a multivariate logistic regression analysis.

Secondary outcome measures: (1) The clinical data of patients were compared. (2) The quality of life was compared between the two groups prior to treatment and six weeks after treatment using Short Form 36 Health Survey (SF-36) scores. A higher SF-36 score indicates higher quality of life. (3) Based on the independent risk factors, we plotted ROC curves to predict the recurrence of UTIs in children, and the predictive efficacy of the independent risk factors was explored.

Statistical analyse

Statistical analyses in this study were performed using SPSS 20.0 (IBM Corp, Armonk, NY, USA). Categorical data were described as [n (%)] and compared between the two groups using the chi-square test. Mean \pm standard deviation (SD) was used to describe the continuous variables, and the t-test was used to compare the continuous variables between the

two groups. Pearson correlation coefficient was adopted for correlation analysis. The predictive performance of independent risk factors for UTI recurrence in children was assessed using ROC curve analysis, and a corresponding Nomogram was generated on the website <https://shiny.medsta.cn/coxpre1/> to visualize the risk factor predictive model. Graphs were generated using GraphPad Prism 7 (GraphPad Software, San Diego, USA). $P < 0.05$ suggests a significant difference.

Results

Baseline data of patients

According to comparison of baseline data of the non-recurrent group and the recurrent group, the two groups did not differ notably in terms of age, sex, BMI, course of disease, etc. (**Table 1**).

Comparison of IgA and IgG levels between the two groups

As shown in **Figure 1**, the IgA and IgG levels were markedly lower in the recurrent group when compared to those in the non-recurrent group ($P < 0.05$).

Comparison of quality of life between the two groups

Prior to treatment, the two groups did not differ significantly in SF-36 scores ($P > 0.05$). After treatment, the SF-36 scores significantly increased in the non-recurrent group ($P < 0.0001$), while there was no notable increase in the recurrent group ($P > 0.05$). However, a significant difference was observed in SF-36 scores between the two groups after treatment ($P < 0.0001$, **Table 2**).

Relationship between IgA and IgG levels and the quality of life in patients with UTIs

The study found a strong positive correlation between IgA levels and the quality of life after 6 weeks of treatment ($P < 0.05$). However, no significant relationship was observed between

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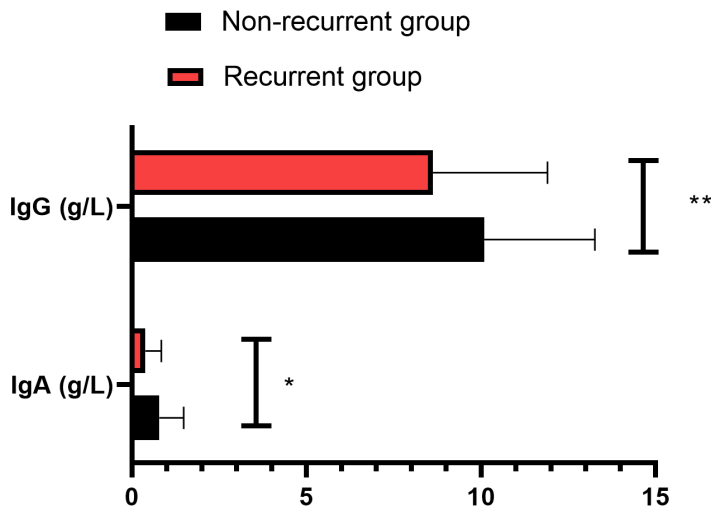


Figure 1. Comparison of IgA and IgG levels between the two groups. Notes: * $P < 0.05$; ** $P < 0.01$. IgA: immunoglobulin A; IgG: immunoglobulin G.

Table 2. Comparison of quality of life between the two groups

Group	SF-36 score	
	Before treatment	After treatment
Non-recurrent group (n=122)	97.20±10.36	111.26±8.29 ^a
Recurrent group (n=36)	96.73±9.25	99.37±9.62 ^b

^aindicates $P < 0.0001$ vs. Before treatment. ^bindicates $P < 0.0001$ vs. non-recurrent group. Note: SF-36: Short Form 36 Health Survey.

IgG levels and the quality of life after 6 weeks of treatment ($P > 0.05$, **Figure 2**).

Univariate analysis of recurrent UTIs in children

A comparative analysis was conducted on several factors including age, sex, anemia, allergic constitution, constipation, urinary system malformation, as well as IgA and IgG levels, in the two groups. The results revealed that anemia, allergic constitution, constipation, urinary system malformation, and decreased levels of IgA and IgG were significant risk factors influencing recurrent UTIs ($P < 0.05$, **Table 3**).

Assignment

Logistic regression analysis was carried out on the indicators with significant differences in **Table 3**, with the occurrence of recurrent UTIs as the dependent variable, and anemia, allergic constitution, urinary system malformation, constipation, IgA level, and IgG level as independent variables (**Table 4**).

Multivariate logistic regression analysis of recurrent UTIs in children

Multivariate logistic regression analysis identified anemia, urinary system malformation, constipation, and decreased levels of IgA and IgG as independent risk factors influencing recurrent UTIs (**Table 5**).

Predictive efficacy of independent risk factors for recurrent UTIs in children

ROC curve-based analysis results in **Figure 3** revealed the prediction of recurrent UTIs based on anemia, urinary system malformation, constipation, IgA, and IgG levels. It was found that urinary system malformation has a better performance in predicting recurrent UTIs in children than the other four factors (**Figure 3** and **Table 6**). Based on the logistic regression analysis results, we also constructed a Nomogram prediction model incorporating five independent factors

to predict the risks of recurrent UTIs in children (**Figure 4**).

Discussion

This study explored the relevant influencing factors and intervention measures for recurrent UTIs in children and found that urinary system malformation, constipation, anemia, and decreased IgA and IgG levels are independent risk factors for recurrent UTIs in children, and the prediction using these risk factors demonstrates good efficacy.

UTI refers to a common inflammatory condition caused by the invasion of pathogens into the urinary tract mucosa or tissues, which occurs in individuals of all ages and both genders [13-15]. Children are predisposed to recurrent UTIs because of their relatively shorter urethra, the proximity of the urethral opening to the anus, and the incomplete maturation of their immune system [16]. Recurrent UTIs can trigger abdominal pain, frequent urination, urgency of urina-

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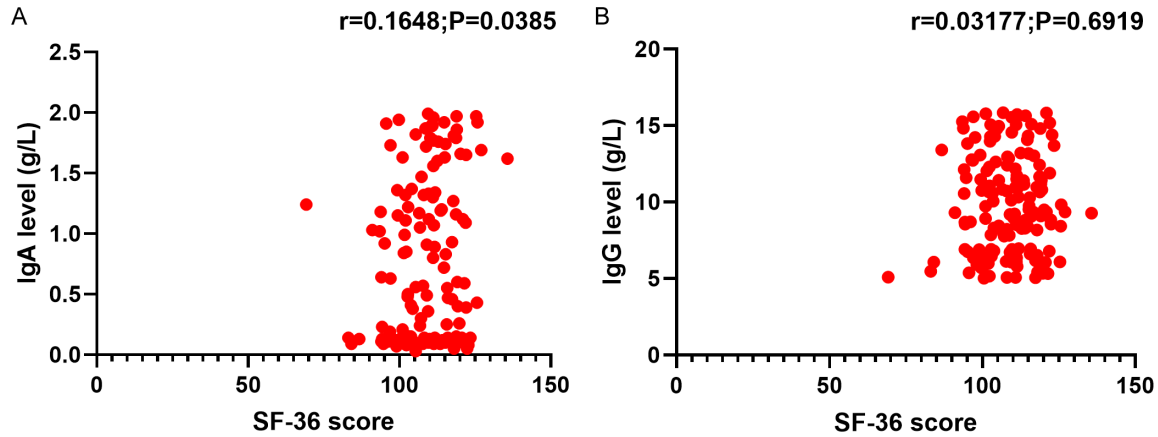


Figure 2. Relationship between IgA (A) and IgG (B) levels and the quality of life in patients with urinary tract infections. Notes: IgA: immunoglobulin A; IgG: immunoglobulin G; SF-36: Short Form 36 Health Survey.

Table 3. Univariate analysis of factors affecting recurrent urinary tract infections in the two groups

	Non-recurrent group (n=122)	Recurrent group (n=36)	χ^2	P value
Age			0.493	0.483
≥ 6 years old	79	21		
< 6 years old	43	15		
Sex			3.035	0.082
Male	50	9		
Female	72	27		
Anemia			19.601	< 0.0001
Yes	35	25		
No	87	11		
Allergic constitution			10.021	0.002
Yes	36	21		
No	86	15		
Urinary system malformation			17.371	< 0.0001
Yes	37	23		
No	85	13		
Constipation			26.411	< 0.0001
Yes	31	26		
No	91	10		
IgA level			13.961	0.001
Normal	80	11		
Decreased	42	25		
IgG level			12.321	0.001
Normal	92	16		
Decreased	30	20		
Pathogenic bacteria			2.392	0.122
Escherichia coli	50	20		
Non-Escherichia coli	72	16		

Notes: IgA: immunoglobulin A; IgG: immunoglobulin G.

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Table 4. Assignment

Covariates	Assignment	
	0	1
Anemia	No	Yes
Allergic constitution	No	Yes
Urinary system malformation	No	Yes
Constipation	No	Yes
IgA level	Normal	Decreased
IgG level	Normal	Decreased
Dependent variable		
Recurrent urinary tract infection	No	Yes

Notes: IgA: immunoglobulin A; IgG: immunoglobulin G.

tion, and dysuria in children, affecting their appetite, sleep, and daily activities, and can even trigger complications such as pyelonephritis and renal scarring in severe cases [17].

In this study, it was observed that after treatment, the SF-36 scores significantly increased in the non-recurrent group ($P < 0.0001$), while there was no significant increase in the recurrent group. However, there was a significant difference in SF-36 scores between the two groups. This indicates that recurrent UTIs have a significant impact on the quality of life of patients.

Furthermore, this study found a positive correlation between IgA levels in patients and the quality of life after 6 weeks of treatment. This may be attributed to the fact that IgA is primarily present on mucosal surfaces and takes part in protecting mucosal membranes from infection [18]. In patients with UTIs, the presence of inflammation during the treatment process can result in a decline in immune function, including a decrease in mucosal IgA levels. However, as the treatment progresses and inflammation subsides, immune function is restored, and mucosal IgA levels increase, thereby reducing the occurrence of infections and improving the quality of life. Additionally, this study found no significant relationship between IgG levels and the quality of life after 6 weeks of treatment, which may be due to the limited sample size. We did find significantly lower levels of IgA and IgG in children with recurrent UTIs compared to those in children without recurrent UTIs. This finding suggests a potential association between IgA and IgG levels and the occurrence of recurrent UTIs in children.

The influencing factors for initial and recurrent UTIs differ significantly. Initial UTIs may be influenced by anatomical factors, sexual activity, hygiene practices, voiding habits, and hormonal changes like those in menopause. In contrast, recurrent UTIs can be linked to structural abnormalities in the urinary tract, incomplete treatment of previous infections, and urinary tract obstructions such as kidney stones [16, 17]. In this study, through logistic multivariable analysis, we identified anemia, urinary system malformation, constipation, decreased IgA levels, and decreased IgG levels as independent risk factors for recurrent UTIs in children. Anemia may increase susceptibility to infections by weakening the immune system, particularly in the context of UTIs, where decreased immune function due to anemia may heighten the risk of recurrent infections [19]. Additionally, tissue hypoxia caused by anemia, including in the urinary tract tissues, can impact the body's ability to fight infections and maintain urinary system health [20, 21]. The identification of anemia as an independent risk factor for recurrent UTIs in children is a significant finding, indicating a substantial association between anemia and recurrent UTIs in children. Anemia may raise the risk of recurrent infections in children through mechanisms such as compromised immune function and reduced tissue oxygen supply. Therefore, addressing anemia could be a key strategy in reducing the recurrence of UTIs in children. This research finding, highlighting the impact of anemia on UTIs in children, is innovative and provides important insights for further clinical practice. Lee et al. [22] found that compared to non-anemic individuals, anemic patients showed elevated levels of plasma neutrophil gelatinase-associated lipocalin (NGAL), and the increased levels of plasma NGAL may be associated with febrile UTIs in anemic children and the presence of renal scars, which supports the conclusions of this study.

Furthermore, constipation was also found to be a factor that increased the risk of recurrent UTIs. Constipation can decrease the normal vaginal bacterial population, raising the risk of bacterial infections. Bacterial infections in the vagina can spread to the urinary tract via the urethra, triggering UTIs [23]. Furthermore, constipation can result in incomplete emptying of

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Table 5. Multivariate logistics regression analysis

Factors	B	S.E.	Wald	df	Sig.	Exp (B)	95% C.I. for EXP (B).	
							Lower limit	Upper limit
Anemia	2.157	0.546	15.598	1	<0.001	8.648	2.965	25.229
Allergic constitution	0.832	0.507	2.697	1	0.101	2.299	0.851	6.207
Urinary system malformation	1.909	0.519	13.505	1	0.000	6.746	2.437	18.673
Constipation	1.670	0.545	9.406	1	0.002	5.314	1.827	15.455
IgA level	1.487	0.520	8.188	1	0.004	4.424	1.598	12.249
IgG level	1.464	0.517	8.019	1	0.005	4.322	1.569	11.901

Notes: IgA: immunoglobulin A; IgG: immunoglobulin G.

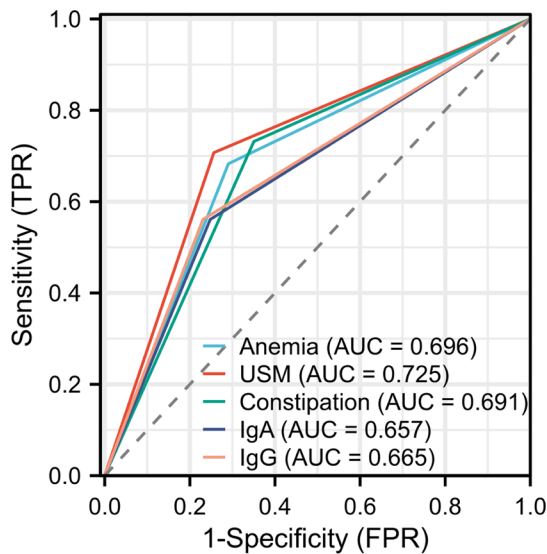


Figure 3. ROC curves illustrating the predictive efficacy of independent risk factors for recurrent UTIs. Notes: USM: Urinary system malformation; UTIs: urinary tract infections; IgA: immunoglobulin A; IgG: immunoglobulin G; ROC: receiver operating characteristic.

Table 6. Related parameters of ROC curves illustrating the predictive efficacy of independent risk factors for recurrent UTIs

	Sensitivity	Specify	Accuracy	AUC
Anemia	68.29%	70.94%	70.25%	0.696
USM	70.73%	74.340	73.42%	0.725
Constipation	73.17%	64.96	67.09%	0.691
IgA	56.10%	75.21%	70.25%	0.657
IgG	56.10%	76.92%	71.52%	0.665

Notes: ROC: receiver operating characteristic; USM: Urinary system malformation; UTIs: urinary tract infections; IgA: immunoglobulin A; IgG: immunoglobulin G.

the bladder during urination, allowing bacteria to reside and multiply in the residual urine,

increasing the risk of infection [24]. For children with UTIs, it is important to focus on dietary adjustments to ensure an adequate intake of dietary fiber and foods rich in iron, vitamin B12, and folic acid. It is also imperative to encourage children to drink plenty of water to maintain adequate hydration. Additionally, children should engage in regular physical activity to promote bowel movements. If necessary, iron supplements can be prescribed to improve constipation and anemia, thereby preventing recurrent UTIs.

Urinary system malformation in children refers to the structural or functional abnormalities of the urinary system present at birth or during the developmental process. These abnormalities can result in obstructed or refluxed urine flow, making it easier for bacteria to enter the urinary tract and cause infection [25]. Furthermore, urinary system malformation can lead to urine retention during the voiding process, preventing complete emptying of the bladder. The stagnant urine provides a favorable environment for bacterial growth and reproduction, increasing the likelihood of infection [26, 27]. Visuri et al. [28] have found that children with ureterocele or double ureter collection system related to giant ureter without reflux face a high risk of UTI, which is consistent with the results in this study. Therefore, for children who experience UTIs, it is important to promptly conduct imaging examinations to determine if there is any urinary system malformation. If malformation is detected, timely treatment is necessary to prevent recurrent UTIs.

Decreased levels of IgA and IgG increase the likelihood of recurrent UTIs in children. IgA is an immunoglobulin that is primarily found on the surface of mucous membranes, including the

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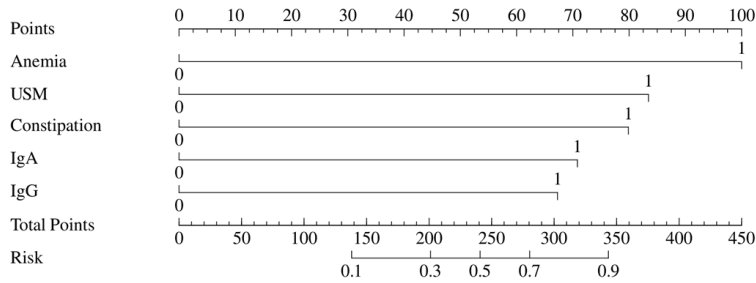


Figure 4. Nomogram for predicting recurrent UTIs. Notes: USM: Urinary system malformation; UTIs: urinary tract infections; IgA: immunoglobulin A; IgG: immunoglobulin G.

mucosa of the urinary tract. It plays a vital role in defending against infections by preventing the invasion and attachment of pathogens, thus protecting the mucosal surfaces from infection. In the cause of decreased IgA levels, the immune defense capacity of the mucosa weakens, making the urinary tract more susceptible to infection [29]. IgG is another important immunoglobulin that primarily functions in the humoral immune response. It is involved in neutralizing pathogens and promoting inflammatory reactions within the body. In the case of decreased IgG levels, the body's ability to fight infections is weakened, making it easier for pathogens to proliferate and cause infections in the urinary tract [11]. When both IgA and IgG levels are reduced, the immune defense of the urinary tract is weakened, making it more susceptible to bacterial and other pathogenic infections. This can lead to the recurrence of UTIs. For patients with decreased levels of IgA and IgG, further immunological evaluation and treatment are necessary to enhance immune defense to reduce the recurrence of UTIs.

The study explored the predictive efficacy of anemia, urinary system malformation, constipation, IgA, and IgG levels in predicting the recurrence of UTIs, and it was found that urinary system malformation has a better performance in predicting recurrent UTIs in children than the other four factors.

This study has several limitations. Firstly, the sample size was relatively small, which may introduce potential bias into the results. Future research should aim to include a larger sample size to enhance the generalizability of the findings and minimize bias. Secondly, as this study employed a retrospective design, there may be

limitations in terms of incomplete or biased information retrieval. Moreover, the absence of a validation set to verify the model's performance and the lack of evaluation of the model, including discrimination and calibration analyses, limit reliability and generalizability of the predictive model developed in this study. Future research with larger sample sizes, prospective designs, and comprehensive assess-

ments of potential influencing factors, along with validation procedures and thorough model evaluation, are warranted to enhance the validity and utility of the study findings.

Conclusion

In summary, urinary system malformation, constipation, anemia, and decreased IgA and IgG levels are independent risk factors for recurrent UTIs in children, and urinary system malformation has a better performance in predicting recurrent UTIs than the other four factors. Therefore, it is important to systematically evaluate and address the presence of malformations, anemia, constipation, and decreased IgA and IgG levels in children with UTIs to prevent recurrence.

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Disclosure of conflict of interest

None.

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