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RESEARCH ARTICLE

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RUMA and RUPCR in children with Henoch–Schonlein purpura

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Abstract

Objective: The aim of this study was to compare the qualitative and quantitative targets in the detection of proteinuria in children with HSP.

Methods: Three hundred and forty children were taken as the research subjects. Qualitative and a series of quantitative indicators of urine protein were tested.

Results: The qualitative and quantitative of protein in 340 children were analyzed retrospectively. Correlation analysis found that 24hUTP had a strong correlation with age, RUMA, RUPCR, and qualitative urine occult blood ($p < 0.01$, for all). After regression analysis, RUMA and RUPCR were still significantly correlated with 24hUTP ($p < 0.01$). At the same time, RUMA and RUPCR had good diagnostic accuracy for proteinuria. When the RUPCR ratio was set as 0.415, the diagnostic sensitivity was 83%, and the specificity was 98.7%. When RUMA was set as 68.215, the sensitivity was 94.3% and the specificity was 96.2%.

Conclusion: Compared with 24hUTP, RUMA and RUPCR had high sensitivity and specificity for monitoring proteinuria in children with HSP.

KEYWORDS
24hUTP, ROC curve, RUMA, RUPCR

1 | INTRODUCTION

Henoch–Schonleinpurpura (Henoch–Schonleinpurpura, HSP) is a more common type of systemic vasculitis mediated by autoimmune response in childhood, and its incidence has been increasing in recent years.[1] It takes extensive small blood vessel necrosis and inflammation as the main symptoms,[2] and clinically, it usually manifests as tetralogy of digestive tract injury, skin purpura, arthritis, and kidney injury. HSP in children is caused by many factors, most of which are related to infections, drugs, and special foods. HSP in children is also divided into many types. The renal type of HSP involves the kidneys and causes a large amount of proteinuria, tubular urine, and so on. The daily detection of urine protein is an indicator of the severity of the disease in children with HSP.

Routine urine examination is one of the most commonly used inspection items in hospitals. It is not only one of the basic indicators reflecting the health of the body, but also has important value for the screening of urinary system diseases.[3,4] The detection of urine protein is of great significance for early diagnosis of kidney damage caused by kidney and related diseases, and is an important part of laboratory examination of urinary system diseases.[5,6] Twenty-four-hour urine total protein quantity (24hUTP) is the gold standard to detect urine protein, but there are many limiting factors in urine retention and collection, and it is more difficult for children to retain and collect 24-h urine.[7] In order to explore the difference and correlation between the results of the two detection methods, the urine dry chemical method in this study often leads to incorrect judgments due to the influence of many factors. We want to know whether there are corresponding indicators that can be used to replace children with HSP when it is inconvenient to keep urine for 24 h. Random urine microalbumin (RUMA) and the determination of random urine protein/creatinine ratio (RUPCR) are simple, fast,

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TABLE 1 Comparison of random urine protein qualitative with 24hUTP quantitative results

Types	24hUTP > 150 mg and qualitatively negative urine protein	24hUTP < 150 mg and qualitatively positive urine protein	Occult blood positive	24hUTP < 150 mg and qualitatively positive urine protein with positive occult blood
Cases	12 (168)	146 (366)	161 (534)	50 (146)
Proportion (%)	7.1	12.6	30.2	34.2

Note: The content of this table was a comparison of the results of 534 routine urine tests and quantitative tests done on 340 patients. Take 150 mg/24 h as the criterion.

and sensitive and which is closely related to kidney damage and can judge the degree of kidney damage. These two indicators are also frequently done during the detection period of children with HSP. Therefore, in this study, we want to explore whether the correlation between RUMA and RUPCR and 24hUTP in children with HSP is expected to become a satisfactory surrogate index.

2 | MATERIALS AND METHODS

2.1 | Patients

Data were selected from 340 children with HSP diagnosed in the Children's Hospital of Zhejiang University School of Medicine from November 2019 to June 2020. All patients met the criteria for diagnosis of HSP, which as follows:

There may be a history of upper respiratory tract infection or taking certain foods and drugs before the onset of the disease. The onset is more acute, purpura is more common in the distal end of the lower limbs and buttocks, symmetrical distribution, different shapes, higher than the skin surface, pressure does not fade. It may be accompanied by urticaria, vascular nerve edema, swollen and painful joints, abdominal pain, blood in the stool and hematuria, protein, and so on.

Platelet counts are mostly normal or elevated, and bleeding, clotting time, and clot contraction time are normal. Regular examination of urine routine may show signs of kidney damage such as microscopic hematuria and proteinuria. Kidney biopsy can determine the nature of kidney lesions.

It has typical symptoms of skin purpura, arthralgia or arthritis, abdominal pain, gastrointestinal bleeding, and kidney damage, and can also involve the reproductive system, nervous system, and respiratory system, manifesting as genital pain, pneumonia, etc. Nephritis is a feature of HSP that can have chronic consequences, and long-term prognosis depends largely on the severity of nephritis.[8] Children with more severe clinical symptoms can cause hypertension, and 14.1% (48) of the children developed hypertension in this article, which was basically consistent with the reports in the literature.[9]

2.2 | Determination of indicators of urine

Urine protein was qualitatively tested on ARKRAY AX4030 automatic urine analyzer. 24hUTP, UTP of random urine, RUMA, Creatinine of random urine, and RUPCR were completed on the Roche automatic biochemical analyzer (770). The urine total protein detection reagent came from Ningbo Ruiyuan Biotechnology Company, and the other reagents were the original reagents of the instrument.

2.3 | Statistical analysis

The results were expressed as *n* (%), mean ± SD, or median (interquartile range). The data obtained were non-normal distribution,

and Spearman's analysis was used for correlation analysis. Logistic regression analysis was used for the odds ratio (95% CI) of the parameters. In order to study the association of 24hUTP with RUMA and RUPCR in children with HSP, we performed conditional logistic regression analysis. We used ROC curve to evaluate the diagnostic value of RUMA and RUPCR. A two-tailed test should be indicated for the p value. $p < 0.05$ was considered to be statistically significant.

3 | RESULTS

3.1 | Comparison of random urine protein qualitative with 24hUTP quantitative results

Taking 24hUTP quantitative <150 mg/24 h as the reference standard, 534 times of urine protein qualitative for these 340 children were compared and found that among 168 children with 24hUTP > 150 mg, there were 12 cases of random urine protein qualitative as negative; among the 366 samples with 24hUTP < 150 mg, 146 cases of urine protein were qualitatively positive. Among the 146 cases of urine protein positive, 50 cases were accompanied by occult blood qualitatively positive (Table 1).

3.2 | Basic information of quantitative results

Among the 340 children studied, there were 197 males, accounting for 57.9% of the total, with an average age of 7.86 ± 3.18 years. All children were quantified by 24hUTP, UTP of random urine, RUMA, Creatinine of random urine, and RUPCR ratio was calculated. The specific results were shown in Table 2.

3.3 | Correlation analysis between 24hUTP and other indicators

Due to the limitations of the qualitative urine protein and the difficulty of 24 h urine retention in children, we made a correlation analysis of the 24hUTP results of 340 children with age, gender, UTP of random urine, RUMA, Creatinine of random urine, RUPCR, and qualitative urinary occult blood. We found that 24hUTP had a strong correlation with age, RUMA, RUPCR, UTP of random urine, and qualitative urine occult blood ($p < 0.01$, all) (Table 3).

3.4 | Regression analysis of 24hUTP and other indicators

In order to clarify the definite relationship between 24hUTP quantification and other indicators, we did a stepwise linear regression analysis. When factors such as age, sex, and urinary occult blood were gradually added to the regression analysis, we found that RUMA and RUPCR were still significantly correlated with 24hUTP ($p < 0.01$) (Table 4).

3.5 | Diagnostic accuracy of RUMA and RUPCR in children with HSP

We made the corresponding ROC curve to verify the accuracy of RUMA and RUPCR in diagnosing proteinuria in children with HSP. We found that the area under the ROC curve of RUPCR was 0.947, while the area under the ROC curve of RUMA was 0.973. When the RUPCR ratio was set as 0.415, the diagnostic sensitivity was 83% and the specificity was 98.7%. When RUMA was set as 68.215, the sensitivity was 94.3% and the specificity was 96.2% (Figure 1).

4 | DISCUSSION

Urine protein testing is recognized as a diagnostic method for people at risk of kidney diseases and is promoted as a part of regular check-ups for such patients.[10,11] Proteinuria is a manageable adverse event, and if it is properly monitored and managed, it usually does not lead to clinically significant adverse results.[12] The effective detection of proteinuria is crucial, but the detection of urine dry chemistry cannot be performed alone for proteinuria detection due to many factors, such as diet, bacteria, and so on.

RUPCR can reflect the excretion of urine protein. Many research results suggest that RUPCR can be used to monitor urinary protein excretion. The United States NKF-K/D0QI also recommended the use of random urine and morning urine PCR to replace 24hUTP[13] and many documents have successively reported the feasibility of using urine protein/creatinine ratio to monitor pregnancy and chronic kidney disease.[14–16] Our study found that there was also a good correlation between 24hUTP and RUPCR in children with HSP ($r = 0.759$, $p = 0.000$), and after correction for age, gender, other quantitative indicators, and qualitative urinary occult blood, there is still a good correlation ($p = 0.006$). At the same time, we found that

TABLE 2 Basic information of quantitative results

Sex male (%)	Age (year)	24hUTP (mg/24 h)	RUMA (mg/L)	UTP in random urine (mg/L)	Creatinine in random urine (μmol/L)	RUPCR (mg/mgCr)
197 (57.9)	7.86 ± 3.18	67.1 (29.1–239.1)	13.3 (4.9–124.6)	749.3 (286.9–2457.6)	5156 (2724–9342)	0.13 (0.06–0.48)

Note: The results were expressed as *n* (%), mean ± SD, or median (interquartile range).

TABLE 3 Correlation analysis of 24hUTP and other indicators

	r	*p*
Sex	−0.077	0.154
Age (year)	0.253	0.000
RUMA (mg/L)	0.713	0.000
UTP in random urine (mg/L)	0.751	0.000
Creatinine in random urine (μmol/L)	0.002	0.968
RUPCR (mg/mgCr)	0.759	0.000
Qualitative of occult blood in random urine	0.696	0.000

Note: Spearman's analysis was used for correlation analysis.

that there was a good correlation between 24hUTP and RUMA in children with HSP ($r = 0.713$, $p = 0.000$), and there was still a good correlation ($p = 0.009$) after adjusting for age, gender, other quantitative indicators, and qualitative urinary occult blood. At the same time, we found that RUMA had a good sensitivity and specificity for the diagnosis of proteinuria (when the RUMA ratio was 68.125, the diagnostic sensitivity was 94.3% and the specificity was 96.2%).

In summary, 24hUTP was a highly accurate method for detecting urine protein,[18] but children and children with urinary incontinence and other diseases had the disadvantage of inaccurate urine output records. At the same time, there were problems of poor patient compliance and complicated sampling process. Also, the children's diet and weight would affect the accuracy of the test results.[19] Our study found that compared with 24hUTP, the detection of RUMA and RUPCR also had high sensitivity and specificity for monitoring proteinuria in children with HSP, but this did not completely abandon 24hUTP.

TABLE 4 Regression analysis of 24hUTP and other factors

	Model 1		Model 2		Model 3	
Variables	**OR**	***p***	**OR**	***p***	**OR**	***p***
RUPCR (mg/mgCr)	741.522 (4.416–124,525.875)	0.011	1345.907 (4.884–370,898.388)	0.012	2878.848 (10.204–812,181.976)	0.006
RUMA (mg/L)	1.026 (1.013–1.038)	0.000	1.023 (1.009–1.037)	0.001	1.019 (1.005–1.034)	0.009

Note: Model 1 was not adjusted; Model 2 was adjusted for age and gender; Model 3 was adjusted for Model 2 + qualitative urine occult blood.

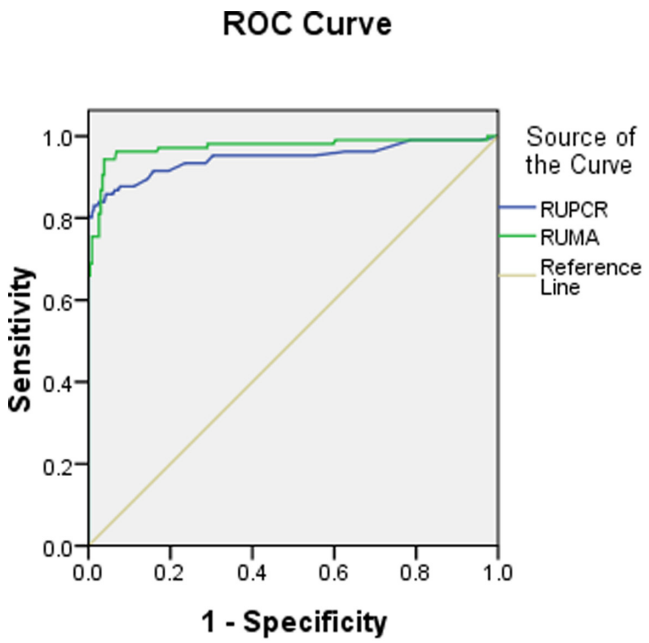

FIGURE 1 ROC curve of RUMA and RUPCR in the diagnosis of proteinuria in children with HSP

RUPCR had a good sensitivity and specificity for the diagnosis of proteinuria (when the RUPCR ratio was 0.415, the diagnostic sensitivity was 83% and the specificity was 98.7%).

UMA is a globular urine protein synthesized by the liver, which cannot directly pass through the glomerular filtration membrane and has a high reabsorption rate. The concentration of urinary microalbumin in healthy people is low; when the glomerular filtration membrane of the child is damaged, it will lead to an increase in the level of urinary microalbumin in the urine.[17] Our study had found

This study had certain limitations. First of all, this study was a retrospective research analysis. The ratio of male to female patients in this period of study could not be controlled, and the selected children could not achieve strict staging of HSP. It might be necessary to consider and study the inclusion of patients and the severity of the disease.

In short, for children who have difficulty in keeping urine for 24 h, this study could also be applied and clinically. The monitoring of proteinuria by RUMA and RUPCR in this study was only applicable to children with HSP, and other nephropathy needs further study.

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Not applicable.

CONFLICT OF INTEREST

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article.

AUTHOR CONTRIBUTIONS

Xiucui Han was responsible for the collection and analysis of data. Pengfei Xu performed the statistics of the data and wrote the article. Both the authors read and approved the final manuscript.

DATA AVAILABILITY STATEMENT

All data generated or analyzed during this study are included in this published article.

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