



Evaluating the spot urine protein-to-creatinine ratio as a predictor of daily proteinuria in children with nephrotic syndrome; a cross-sectional study

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ABSTRACT

Introduction: Nephrotic syndrome in children is characterized by substantial proteinuria, yet 24-hour urine collection remains difficult to perform reliably in pediatric practice. The spot urine protein-to-creatinine ratio (UP/CrR) offers a more feasible alternative for estimating daily protein loss.

Objectives: This study evaluated the accuracy and predictive performance of this surrogate measure compared with 24-hour urine protein excretion in children with nephrotic syndrome.

Materials and Methods: This cross-sectional study was conducted on 100 children aged 3–14 years who attended two pediatric clinics in Yazd between June and December 2025. Participants with nephrotic syndrome who provided informed written consent and had complete demographic and laboratory data, including spot UP/CrR and 24-hour urine protein excretion, were included. The primary measurement outcome was assessing the correlation between the spot UP/CrR and 24-hour urine protein excretion.

Results: The study included 100 pediatric patients with nephrotic syndrome, with a mean age of 8.82 ± 3.29 years. A significantly strong positive correlation was observed between the UP/CrR and 24-hour urine protein excretion across the whole cohort ($r = 0.772$) and within sex-specific subgroups. Linear regression analyses further confirmed this association in both unadjusted and adjusted models. For all participants, each unit increase in the UP/CrR was associated with a proportional 2.89 mg rise in 24-hour urine protein excretion, an effect that remained stable after adjusting for age, body mass index (BMI), and gender ($B = 2.94$).

Conclusion: These findings demonstrate that the UP/CrR is a strong and reliable predictor of 24-hour urine protein excretion in children with nephrotic syndrome, and the use of the spot UP/CrR as a practical, cost-effective, and accessible surrogate for quantifying daily proteinuria in clinical settings is suggested.

Implication for health policy/practice/research/medical education:

These findings demonstrate that the urine protein-to-creatinine ratio (UP/CrR) is a reliable and strongly predictive marker of 24-hour urine protein excretion in pediatric patients with nephrotic syndrome. The strength and consistency of this association across correlation and regression analyses. The observed increase of approximately 2.9 mg in 24-hour proteinuria for each unit rise in the protein-to-creatinine ratio further supports its clinical utility. Overall, the results reinforce the value of the spot UP/CrR as a practical and accurate surrogate for quantifying daily proteinuria in this population.

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Introduction

Nephrotic syndrome is one of the most common glomerular disorders in childhood and is characterized by nephrotic-range proteinuria, hypoalbuminemia, oedema, and dyslipidaemia (1-3). Persistent heavy proteinuria is central to both the diagnosis and prognosis of nephrotic

syndrome, reflecting disruption of the glomerular filtration barrier and serving as an important predictor of chronic kidney disease progression in children (2,4,5). Nephrotic syndrome has an estimated incidence of about 2 to 7 cases per 100,000 children per year, and it occurs more often in boys than girls (6,7). It typically presents

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between 2 and 6 years of age, and in most children, it is caused by minimal change disease, although the underlying pathology and steroid responsiveness vary across populations (7,8). Accurate quantification of proteinuria is therefore essential for classifying disease severity, monitoring treatment response, and guiding long-term follow-up in pediatric nephrotic syndrome.

The reference standard for assessing protein excretion is a 24-hour urine collection, which allows direct measurement of daily proteinuria but is logistically difficult, time-consuming, and prone to collection errors, particularly in young children (9-11). To overcome these limitations, a random spot urine protein-to-creatinine ratio (UP/CrR) has been proposed as a simpler alternative that corrects protein concentration for urine dilution and can be obtained in routine outpatient settings (10,11). In pediatric cohorts, UP/CrR has shown a strong correlation with 24-hour urinary protein excretion across a wide range of proteinuria, supporting its use to classify physiologic, sub-nephrotic, and nephrotic-range protein loss (9,12). Moreover, UP/CrR appears superior to other semi-quantitative approaches, such as dipstick testing or protein-osmolality ratios, for predicting abnormal proteinuria in children (9).

Several studies in children with nephrotic syndrome have reported significant correlations between spot UP/CrR and 24-hour proteinuria, suggesting that UP/CrR may reliably estimate daily protein excretion and potentially replace cumbersome timed collections in clinical practice (10,12). Abitbol et al demonstrated a highly significant relationship between UP/CrR and total protein excretion in relapsing nephrotic children (12), while Singh et al reported a strong correlation between random UP/CrR and 24-hour proteinuria in pediatric nephrotic syndrome (10). Nevertheless, data remain limited in specific pediatric subgroups, and further cross-sectional evaluations are needed to validate the UP/CrR as a robust predictor of daily proteinuria across the clinical spectrum of childhood nephrotic syndrome. The present cross-sectional study evaluates the spot UP/CrR as a predictor of daily proteinuria in children with nephrotic syndrome, aims to assess the strength of correlation between UP/CrR and 24-hour protein excretion, and to explore its utility as a practical surrogate in this population.

Objectives

This study aimed to evaluate the strength and predictive value of the spot UP/CrR in estimating 24-hour urine protein excretion among pediatric patients with nephrotic syndrome, using correlation and regression analyses to determine its reliability as a practical surrogate for daily proteinuria measurement.

Materials and Methods

Study design and participants

The study was conducted as a cross-sectional investigation

on 100 children aged 3–14 years with dipstick-positive proteinuria who presented to two pediatric clinics in Yazd during the period from June to December 2025. The sampling method used in this study was simple random sampling.

Inclusion and exclusion criteria

The study included pediatric patients diagnosed with nephrotic syndrome aged 3 - 14 years who provided informed written consent and had complete demographic and clinical information available, including age, gender, body mass index (BMI), spot UP/CrR, and 24-hour urine protein excretion. Patients were eligible if they were able to provide both a random urine sample and a complete 24-hour urine collection processed according to standard laboratory procedures. Patients were excluded if they had incomplete or missing laboratory or clinical data or an inability to complete the 24-hour urine collection that could interfere with proteinuria assessment. Those who were unwilling to continue the study under conditions that could compromise the accuracy of urine protein measurements were also excluded.

Data collection

Data were collected using a structured form from pediatric patients diagnosed with nephrotic syndrome who attended the participating clinical centers during the study period. Informed written consent was taken from all participants or their legally authorized representatives. Demographic information, including age, gender, and body mass index BMI was obtained from medical records or by patients' interviews. Clinical data were gathered through routine laboratory assessments, including measurement of the spot UP/CrR and 24-hour urine protein excretion (mg). All laboratory values were recorded using standardized institutional procedures.

Outcome measurement

The outcome includes assessing the spot UP/CrR, assessed from a random urine sample, and evaluating its correlation and predictive accuracy in estimating 24-hour urine protein excretion.

Statistical analysis

Data analysis was conducted using SPSS version 27 (IBM Corp., Armonk, NY, USA). The normality of continuous variables was examined with the Kolmogorov–Smirnov test, and variance equality was assessed using Levene's test. Correlation between the UP/CrR and 24-hour urine protein excretion was examined using Spearman's rank correlation coefficient, given the non-normal distribution of the variables. Linear regression analyses were performed to evaluate the predictive relationship between the UP/CrR and 24-hour urine protein excretion in both unadjusted and adjusted models. For all statistical tests, a *P* value <0.05 was considered statistically significant.

Results

The study population included 100 pediatric patients with nephrotic syndrome, aged 8.82 ± 3.29 years, with more males than females. Overall, the UP/CrR showed wide variability, with males exhibiting slightly higher values than females. A similar pattern was observed for 24-hour urine protein excretion, where the average levels were broadly comparable between sexes, with females showing marginally higher values (Table 1).

The correlation analysis showed a strong positive association between the UP/CrR and 24-hour urine protein excretion across all participants, with similarly strong relationships observed when males and females were analyzed separately. In each group, the confidence intervals indicated a consistently robust correlation, and all statistical tests demonstrated highly significant results (Table 2).

The regression analysis demonstrated a strong positive association between the UP/CrR and 24-hour urine protein excretion in both unadjusted and adjusted models, with this relationship remaining consistent across the overall cohort as well as within male and female subgroups. For all participants, the unadjusted model produced a B coefficient of 2.89, indicating that each unit increase in the UP/CrR corresponded to a proportional rise in 24-hour

urine protein excretion measured in milligrams. This effect persisted after adjustment, with the adjusted model yielding a B coefficient of 2.94, reflecting a nearly identical magnitude of association. In the adjusted analysis, we accounted for age, BMI, and gender for all participants, and for age and BMI when analyzing males and females separately (Table 3).

Discussion

Our cross-sectional study of 100 children with nephrotic syndrome demonstrated that the spot UP/CrR is a strong and reliable predictor of 24-hour urine protein excretion, supporting its use as a practical surrogate for daily proteinuria in routine pediatric care. Previous pediatric studies have consistently reported that spot UP/CrR correlates strongly with 24-hour urinary protein excretion in children with nephrotic syndrome and other proteinuric kidney diseases, and have suggested that it can substitute for timed urine collections in most clinical situations (9,10,12,13). Morgenstern et al evaluated the validity of protein-osmolality and protein-creatinine ratios for estimating quantitative proteinuria in children. Their findings demonstrated that the protein-creatinine ratio provided a more accurate and reliable estimate of true protein excretion than the protein-osmolality ratio. Based on this superiority, the authors concluded that screening pediatric urine samples for proteinuria should preferentially rely on the protein-creatinine ratio rather than the protein-osmolality ratio, as it offers better diagnostic performance and clinical utility (9). Abitbol et al demonstrated that the UP/CrR provides strong reliability for classifying the severity of proteinuria in children with nephrosis. Their results showed that this ratio accurately distinguishes nephrotic-range from physiologic proteinuria and performs better than random dipstick testing. The authors concluded that the UP/CrR is the most sensitive and practical method for assessing proteinuria in pediatric patients, offering advantages in speed and convenience over traditional 24-hour urine collection (12). Singh et al reported a statistically significant correlation between the spot UP/

Table 1. Demographic characteristics and clinical data of participants

Demographic and clinical data	Frequency	Percent
Gender		
Male	69	69
Female	31	31
	Mean	SD
Age (year)	8.82	3.29
Spot UP/CrR		
All patients	276.74	228.24
Male	289.10	238.17
Female	249.23	205.42
Urine protein 24 hours (mg)		
All patients	1252.92	957.43
Male	1250.03	935.18
Female	1259.35	1027.288

UP/CrR: Urine protein-to-creatinine ratio, SD: Standard deviation.

Table 2. The correlation between the urine random UP/CrR and urine protein 24 hours in the participating patients

Spot UP/CrR	Urine protein 24 hours (mg)		
	r	95% CI	P value
All patients	0.772	0.675-0.843	<0.001*
Female	0.767	0.559-884	<0.001*
Male	0.760	0.634-847	<0.001*

UP/CrR: Urine protein-to-creatinine ratio, CI: Confidence interval. *Spearman coefficient.

Table 3. The association between the UP/CrR and urine protein 24 hours in the participating patients using univariate and multivariate linear regression

Spot UP/CrR		Urine protein 24 hours (mg)		
		B	95% CI	P value
Unadjusted	All patients	2.89	2.29-3.50	<0.001
	Female	3.78	2.55-5.02	<0.001
	Male	2.63	1.92-3.41	<0.001
Adjusted	All patients	2.94	2.34-3.55	<0.001
	Female	4.09	2.83-5.35	<0.001
	Male	2.68	1.98-3.38	<0.001

UP/CrR: Urine protein-to-creatinine ratio, CI: Confidence interval, B: Unstandardized coefficient.

CrR and 24-hour urine protein excretion in children with nephrotic syndrome. Their findings support the use of the spot protein-creatinine ratio as a reliable and practical test for detecting and quantifying proteinuria in the pediatric population, offering an effective alternative to the more burdensome 24-hour urine collection (10). Akhter et al conducted a study to evaluate the spot UP/CrR as an alternative to 24-hour urinary protein measurement in children with a first episode of nephrotic syndrome. Fifty-one children aged 2–12 years provided both a complete 24-hour urine collection and a subsequent spot urine sample. The investigators observed that the spot protein-creatinine ratio increased proportionally with rising 24-hour urinary protein levels, demonstrating a strong positive correlation (13). Kamińska et al conducted a comprehensive literature review examining the diagnostic performance of the spot UP/CrR across routine clinical practice. Their analysis demonstrated a strong correlation between protein to creatinine ratio values and 24-hour urine protein measurements, supporting its validity as an alternative to full-day urine collection (14).

In adult patients, Olayinka et al examined the diagnostic performance of the random UP/CrR in women with suspected pre-eclampsia and found a strong correlation between this ratio and 24-hour urine protein excretion. Their results indicated that the protein-creatinine ratio is an effective and more easily compliant screening tool for detecting proteinuria in preeclamptic patients, offering a practical alternative to the traditional 24-hour urine collection (11). A prospective study on patients with multiple myeloma demonstrated a strong correlation between the spot UP/CrR and 24-hour urine protein excretion. The study findings indicated that the spot protein-creatinine ratio provides a reliable estimate of total proteinuria and serves as a simpler, more convenient alternative to the traditional 24-hour urine collection (15). A study in Japan comparing spot UP/CrRs with 24-hour proteinuria in glomerular diseases found that the spot UP/CrR reliably estimated 24-hour protein excretion in patients with immunoglobulin A nephropathy; however, this relationship did not hold for patients with membranous nephropathy, indicating that the diagnostic accuracy of the spot UP/CrR may vary depending on the underlying renal pathology (16).

Overall, our results show that spot UP/CrR is a strong and reliable predictor of 24-hour urine protein excretion in children with nephrotic syndrome, and they support the use of spot UP/CrR as a practical, cost-effective, and accessible surrogate for quantifying daily proteinuria in pediatric clinical practice. While 24-hour urine collection remains the reference method, the evidence from this and previous pediatric studies suggests that spot UP/CrR can safely replace timed collections in most routine settings, provided that its limitations are recognized and that clinicians remain alert to clinical scenarios in which confirmatory 24-hour measurements may still be warranted

Conclusion

These results indicate that the UP/CrR serves as a robust and dependable indicator of 24-hour urine protein excretion in pediatric nephrotic syndrome. The strength and consistency of this association across all analytical models support its clinical value, suggesting that a spot urine protein-to-creatinine measurement can function as a practical, accessible, and cost-efficient alternative to full 24-hour urine collection. This reinforces its usefulness as a surrogate marker for estimating daily proteinuria in routine pediatric nephrology practice.

Limitations of the study

The cross-sectional design of this study prevents assessment of temporal or causal relationships between the spot UP/CrR and 24-hour proteinuria. The sample was drawn from two pediatric clinics in Yazd, which may limit generalizability to broader or more diverse pediatric populations. Although standardized procedures were used, the accuracy of 24-hour urine collection in children may be affected by incomplete collection or reporting errors. Additionally, potential confounders such as hydration status and dietary protein intake were not controlled, which may influence proteinuria measurements. Further multicenter studies with larger samples and longitudinal follow-up are needed to validate these findings.

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Authors' contribution

Conceptualization: Zahra Aflatonian and Ahmad Shajari.

Data curation: Zahra Aflatonian and Somayeh Talaeipour.

Formal analysis: Somayeh Talaeipour.

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Methodology: Ahmad Shajari and Somayeh Talaeipour.

Project Management: Ahmad Shajari.

Resources: All authors.

Supervision: All authors.

Validation: Zahra Aflatonian.

Writing—original draft: All authors.

Writing—review and editing: All authors.

Conflicts of interest

The authors declare no conflict of interest.

Declaration of generative artificial intelligence (AI) and AI-assisted technologies in the writing process

While preparing this work, the authors utilized AI

(Grammarly, Perplexity, and Copilot) to refine grammar points and language style. Subsequently, they thoroughly reviewed and edited the content as necessary, assuming full responsibility for the publication's content.

Data availability statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethical issues

The research was conducted in accordance with the principles outlined in the Declaration of Helsinki. Informed written consent was taken from all participants or their legally authorized representatives. This study was conducted at Baghai-Pour and Shah-Vali pediatric clinics in Yazd and was derived from the thesis work of Zahra Aflatoonian (Thesis #162887243), approved by the ethics committee of the Islamic Azad University - Isfahan, Iran, under the ethical code (IR.IAU.KHUISF.REC.1404.085; <https://ethics.research.ac.ir/form/xl1vgusw12xfikny.pdf>) registered on May 6, 2025. Besides, the authors have ultimately observed ethical issues (including plagiarism, data fabrication, and double publication).

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