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Study on correlation of urine specific gravity with other laboratory parameters of urine in children with Nephrotic syndrome

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Abstract

Nephrotic syndrome is a frequent childhood kidney disease in which proteinuria is a significant characteristic. Proteinuria can be a benign condition as well as indicates severe underlying renal or systemic diseases. The variation in the prevalence of proteinuria may occur based on the definition used or the evaluation time of the test. Proteinuria is present in up to 10% of routine urine testing in school-aged children, although this decreases to 0.1% with repeated testing. The study aimed to analyze the correlation of urinary specific gravity with other laboratory parameters of urine in children with nephrotic syndrome.

Methods: This cross-sectional study was conducted in the Department of Pediatric Nephrology (NIKDU), Dhaka from October 2019 to June 2021, and a total of 153 patients with nephrotic syndrome were enrolled after taking written consent. Urine samples were collected for both 24 hours and spot for estimation of urinary protein, urinary creatinine, dipstick protein, and specific gravity by dipstick method. Spot urinary Protein Creatinine Ratio (PCR) and 24 hours urinary protein were also estimated.

Results: Among 153 study subjects maximum (44.4%) were 2-5 years old followed by 58 (37.9%) who were 5-10 years and 27 (17.6%) were >10 years old. Boys (61.4%) were more predominant than girls (38.6%). Mean 24 hours urinary volume was 1097.78±662.63 ml, 24 hours urinary creatinine was 32.17±23.70 mg/dl, 24 hours urinary total protein was 851.42±123.68 mg/dl, 24 hours urinary total protein (UTP) was 7.52±7.65 gm/m²/24 hours urinary specific gravity 1.020±0.02, spot urinary protein 989.49±1136.73 mg/dl, spot urinary creatinine was 46.09±43.73 mg/dl, spot urinary PCR was 21.87±18.24 mg/mg and spot urinary specific gravity was 1.020±0.01. The Scatter diagram showed a significant positive correlation of 24 hours urinary specific gravity with 24 hours urinary protein (r=0.169, p=0.037). There was a significant positive correlation of 24 hours specific gravity with 24 hours urinary creatinine (r=0.380, p<0.001). There was a significant positive correlation of spot urinary protein with spot urinary specific gravity as well (r=0.206, p=0.011). Spot urinary specific gravity showed a significant positive correlation with spot urinary creatinine (r=0.355, p<0.001). There was a significant negative correlation of spot urinary specific gravity with spot urinary PCR (r= -0.305, p<0.001).

Conclusion: It can be concluded that urinary specific gravity had a substantial correlation with other laboratory parameters of urine and can be used as an important diagnostic tool for diagnosing proteinuria in children with nephrotic syndrome

Keywords: Specific Gravity; Albumin; Creatinine; Osmolality

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1. Introduction

Nephrotic syndrome is the commonest glomerular disease affecting children and is also more frequently encountered in pediatrics. The most common subtype is minimal change nephrotic syndrome which usually occurs in preschool children [1]. Nephrotic syndrome is characterized by alterations of selectivity at the glomerular capillary wall, resulting in its inability to restrict the urinary loss of protein. Nephrotic range proteinuria is defined as proteinuria exceeding 1000 mg/m² per day or spot (random) urinary protein creatinine ratio exceeding 2 mg/mg [2]. A measure of urinary concentration (weight of the solution compared with that of an equal volume of distilled water) is called urinary specific gravity which is an important laboratory investigation regarding this disease [3]. The clinical and biochemical features of nephrotic syndrome result from heavy proteinuria followed by hypoalbuminemia, hypercholesterolemia, and edema [4]. Hippocrates described the association between “bubbles on the surface of the urine” and renal disease 2400 years ago [5]. In nephrotic syndrome, quantitative measurement of protein in a 24-hour urine collection is the gold standard. Spot urinary protein creatinine ratio is another reliable method of screening for proteinuria that would be more acceptable as it is less time-consuming [6] [7]. Recent studies have shown that the correlation between spot urinary protein/creatinine ratio (PCR), urinary dipstick, and 24-hours urinary total protein (UTP) estimation is statistically highly significant for all levels of proteinuria. Though 24-hour UTP is the gold standard test for assessment of proteinuria but it is time-consuming, since it is difficult to collect a complete 24-hour urine sample accurately [8] [9]. To obviate some of these difficulties short timed urine collection has been advocated as protein excretion is nearly constant throughout the day. The ratio of urine protein concentration to urine creatinine concentration (PCR) has been adopted as a practical alternative for timed urine collections since it correlates closely with urine albumin excretion rate [10]. Recently, more rapid screening method like dipstick test has been developed for estimating urinary protein concentration. But variation in the rate of diuresis may substantially alter the concentration of protein in the urine without changing the rate of protein excretion which makes dipstick measurement of protein concentration less predictive. It may give a false positive result in the concentrated urine and a false negative result in the dilute urine [11]. The gold standard for estimating urinary concentration is the measurement of its osmolality but this procedure is not readily available to the practicing physician. Therefore, urine concentration is usually determined by measurement of its specific gravity (SG), which provides a fair estimation of urine osmolality. The SG of the urine is the ratio of the density of urine to that of pure water at a constant temperature. In addition to the number of particles, the SG is also affected by the molecular mass of the particles [12]. The study aimed to analyze the correlation of urinary specific gravity with other laboratory parameters in children with nephrotic syndrome.

Objective

General Objective

- To correlate urinary specific gravity with other urine laboratory parameters in children with nephrotic syndrome.

Specific Objectives

- To correlate 24 hours urinary specific gravity with 24 hours urinary protein.
- To correlate 24 hours urinary specific gravity with 24 hours urinary creatinine.
- To correlate spot urinary specific gravity with spot urinary protein.
- To correlate spot urinary specific gravity with spot urinary creatinine.

2. Material and methods

2.1. Methods

This cross-sectional study was conducted in the Department of Pediatric Nephrology (NIKDU), Dhaka from October 2019 to June 2021, and a total of 153 patients with nephrotic syndrome were enrolled after taking written consent. After thorough history, physical examination and doing urinary heat coagulation test primarily patients were selected. Urine samples were collected for both 24 hours and spot for estimation of urinary protein, urinary creatinine, dipstick protein, and specific gravity by dipstick method. Spot urinary PCR and 24 hours urinary protein were also estimated. The questionnaire had been developed using the selected variables according to the specific objectives. Data was collected by using a pre-designed data collection sheet. Statistical analysis was done by using SPSS version 22.0 for windows. Spearman rank correlation test was done for correlation. A value of $p < 0.05$ was considered statistically significant for all tests. Laboratory tests were done in the biochemistry lab of Dhaka Shishu Hospital (DSH) after taking written permission from the director of DSH. The research protocol was approved by the Ethical Committee of NIKDU, Dhaka.

2.2. Inclusion Criteria

- Children with nephrotic syndrome.
- Children with both initial and relapse cases.
- The age of the patients was > 2 to ≤18 years.
- Patients who had given consent to participate in the study.

2.3. Exclusion Criteria

- Children having proteinuria other than nephrotic syndrome.

3. Results

Among 153 study subjects maximum (44.4%) were 2-5 years old followed by 58 (37.9%) who were 5-10 years and 27 (17.6%) were >10 years old. Boys (61.4%) were more predominant than girls (38.6%). [Table 1] Mean 24 hours urinary volume was 1097.78±662.63 ml, 24 hours urinary creatinine was 32.17±23.70 mg/dl, 24 hours urinary total protein was 851.42±123.68 mg/dl, 24 hours urinary total protein (UTP) was 7.52±7.65 gm/m²/24 hours urinary specific gravity 1.020±0.02, spot urinary protein 989.49±1136.73 mg/dl, spot urinary creatinine 46.09±43.73 mg/dl, spot urinary PCR 21.87±18.24 and spot urinary specific gravity was 1.020±0.01 [Table 2]. The Scatter diagram showed a significant positive correlation of 24 hours urinary specific gravity with 24 hours urinary protein (r=0.169, p=0.037) [Figure 1]. There was a significant positive correlation of 24 hours specific gravity with 24 hours urinary creatinine (r=0.380, p=<0.001) [Figure 2]. There was a significant positive correlation of spot urinary protein with spot urinary specific gravity as well (r=0.206, p=0.011) [Figure 3] Spot urinary specific gravity showed a significant positive correlation with spot urinary creatinine (r=0.355, p=<0.001) [Figure 4] There was a significant negative correlation of spot urinary specific gravity with spot urinary PCR (r= -305, p=<0.001)[Figure 5]

Table 1 Demographic profile of the study subjects (N=153)

	Features	N	%
Age (years)	2 - 5	68	44.4
	5 - 10	58	37.9
	>10	27	17.6
Gender	Boy	94	61.4
	Girl	59	38.6

Table 2 Laboratory urine findings of the study subjects (N=153)

Laboratory parameters	Mean SD	Min-Max
24hrs urinary volume (ml)	1097.78 ± 662.63	200.00 - 3400.00
24hrs urinary creatinine(mg/dl)	32.17 ± 23.70	3.24 - 155.69
24hrs urinary total protein (mg/dl)	851.42 ± 123.68	8.00 - 11046.00
24hrs UTP (gm/m ² /24hrs)	7.52 ± 7.65	0.10 - 67.00
24hrs urinary specific gravity	1.02 ± 0.02	1.00 - 1.025
Spot urinary protein (mg/dl)	989.49 ± 1136.73	0.70 - 6147.30
Spot urinary creatinine (mg/dl)	46.09±43.73	0.87-306.79
Spot urinary PCR (mg/mg)	21.87 ± 18.24	0.14 - 148.06
Spot urinary specific gravity	1.020 ± 0.01	1.000 - 1.030

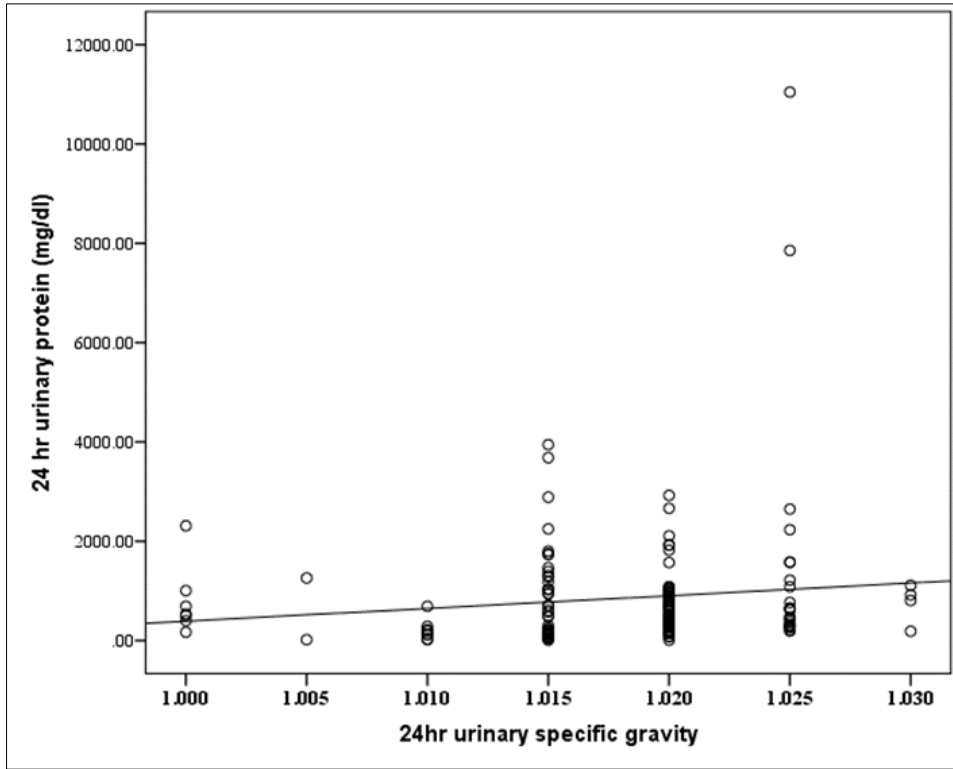


Figure 1 Correlation of 24hrs urine specific gravity with 24hrs urinary protein

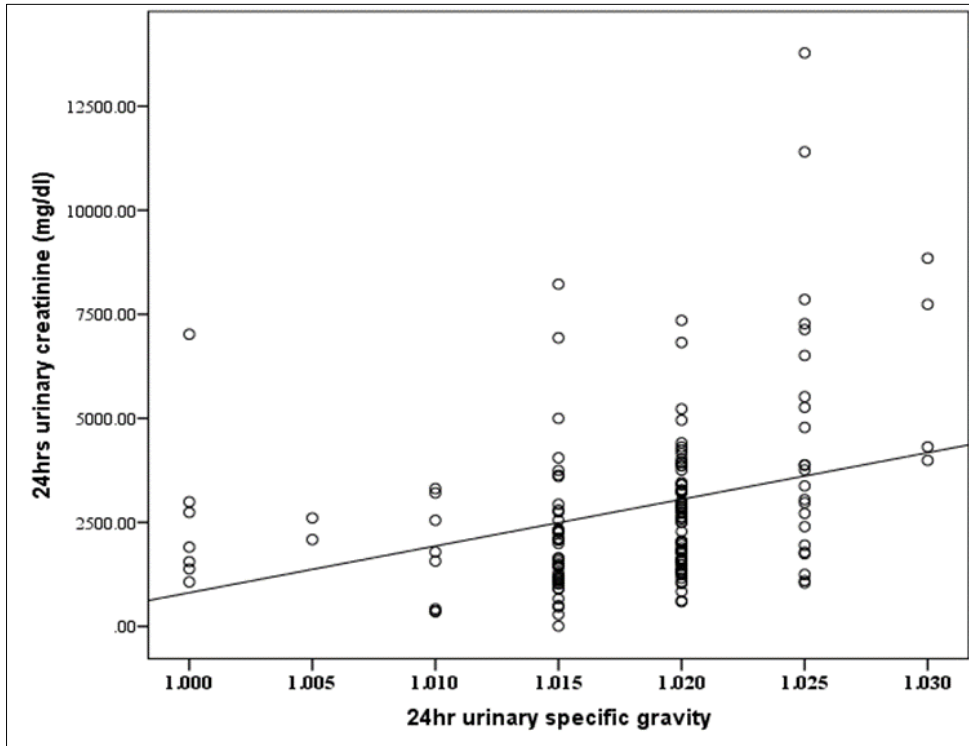


Figure 2 Correlation of 24hrs urine specific gravity with 24hrs urinary creatinine

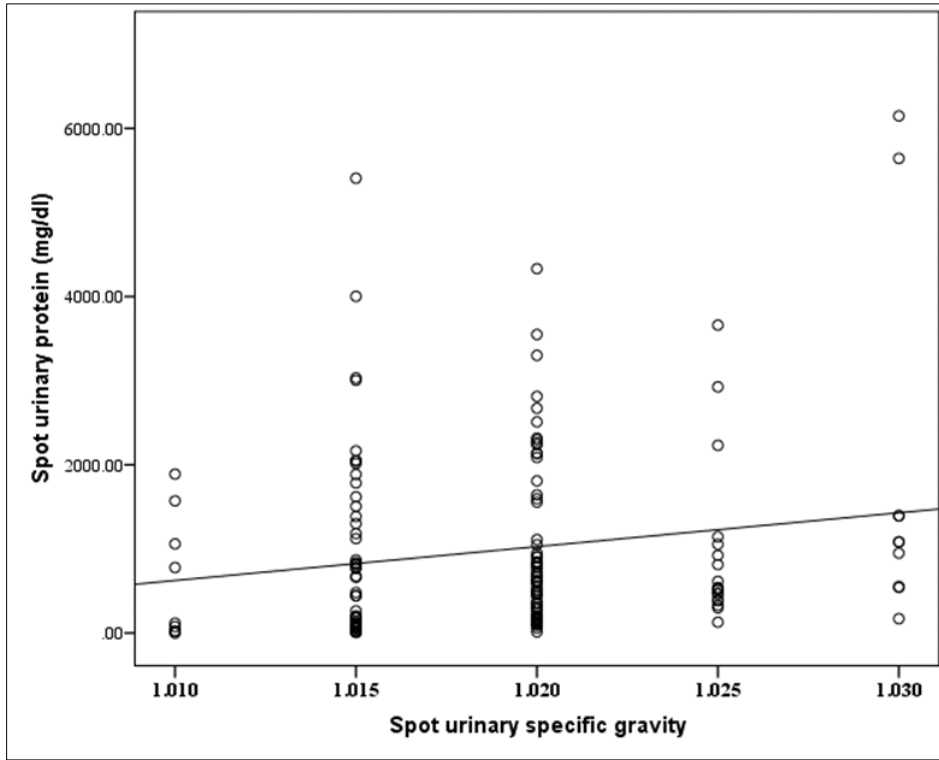


Figure 3 Correlation of spot urinary specific gravity with spot urinary protein

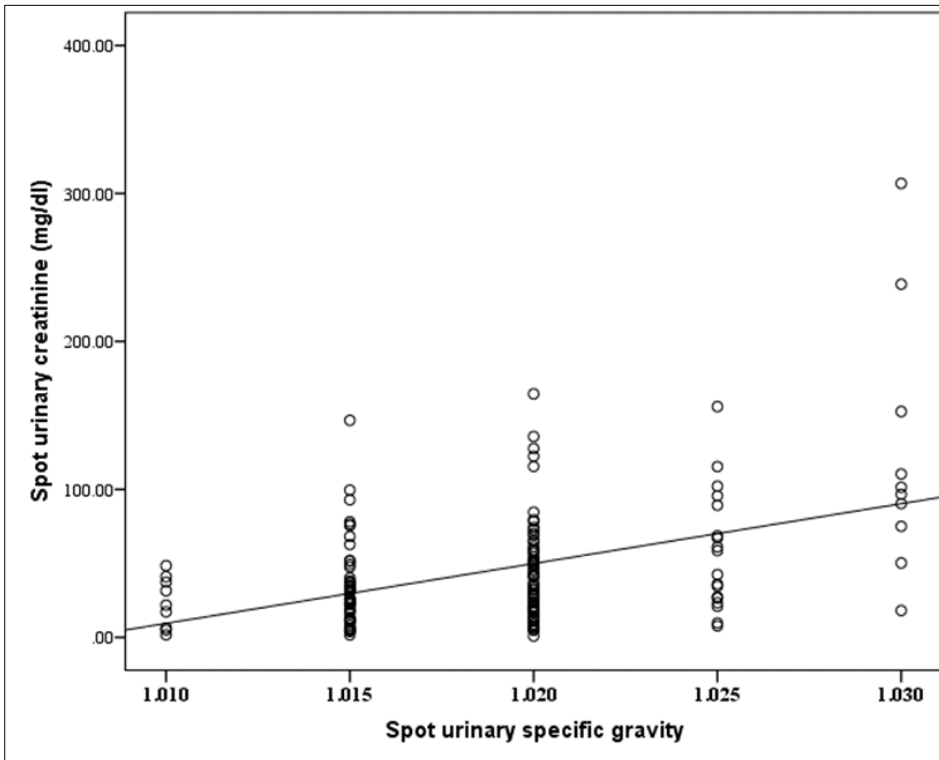


Figure 4 Correlation of spot urine specific gravity with spot urinary creatinine

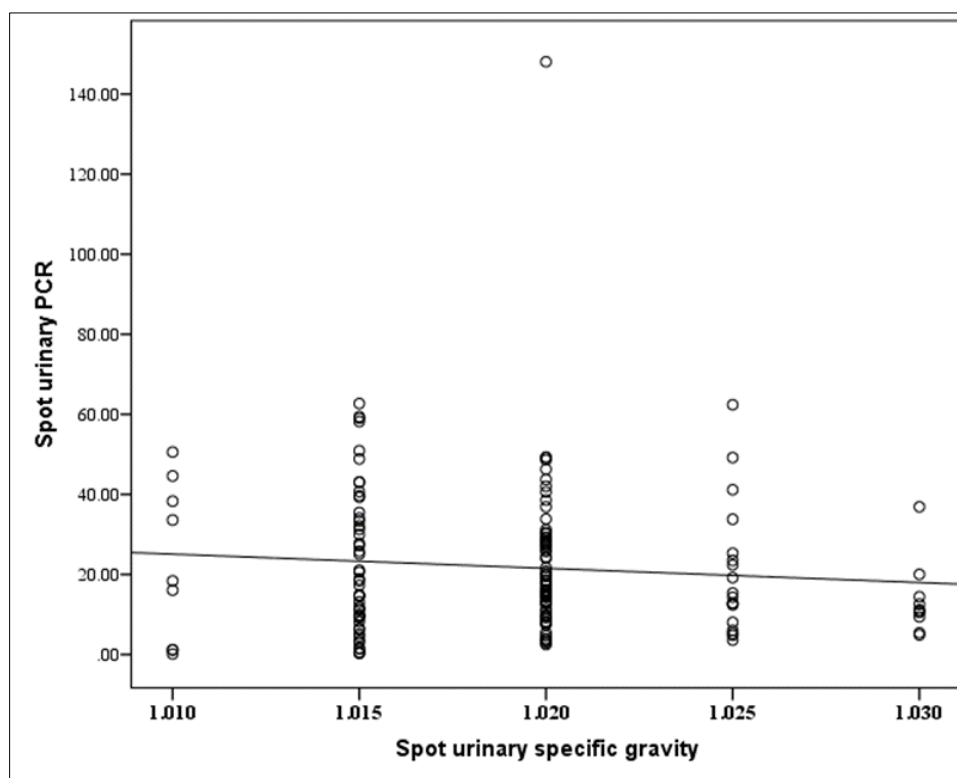


Figure 5 Correlation of spot urinary specific gravity with spot urinary PCR

4. Discussion

In this study, the maximum study population (44.4%) were 2 – 5 years old and 58 (37.9%) were 5-10 years and 27 (17.6%) were >10 years old. In a study, the mainstream of the patients belonged to the 1-5 years age group i.e. 45% between 0-5 years and 42.5% between 6-10 years, and only 12.5% of cases belonged to >10 years of age which was similar to this study [13]. Male prevalence was observed in a study, where males were 62.0% and females were 38.0%.

A similar reflection was also made by another study which was quite similar to this study [14][15]. In a study, mean urinary protein was found to be 1.85 ± 0.94 (gm/L) or 185 ± 94 mg/dl which was lower than this study, creatinine 38.08 ± 14.34 (mg/dl) was near to this study, and the ratio was 5.32 ± 3.08 mg/mg when spot urine investigations were done at the first week that was lower compared to this study [13] In the present study, spot urinary protein creatinine ratio was 21.87 ± 18.24 mg/mg. According to the study of an author, the ratio was found to be 5.55 mg/mg, other studies also showed a lower ratio of 3.28 mg/mg and 2.52 mg/mg correspondingly. Before taking a sample of 2nd-morning urine for spot urinary protein creatinine ratio most of the study patients were given I/V diuretics routinely for treatment purposes as a result creatinine concentration became little in the sample, which may be the reason for getting a higher value of spot PCR in this study than in others [16][17][18]. In the current study, 24 hours urine specific gravity had significant positive correlation with 24 hours urinary protein ($r=0.169$, $p=0.037$) and 24 hours urinary creatinine ($r=0.380$, $p<0.001$). This study also showed that spot urinary specific gravity had a significant positive correlation with spot urinary protein ($r=0.206$, $p=0.011$), spot urinary creatinine ($r=0.355$, $p<0.001$), and a significant negative correlation with spot urinary protein creatinine ratio. Other studies also showed a significant positive correlation between urine specific gravity and urine creatinine [11] [19]. A study was done to see whether urine specific gravity could be used in place of urine creatinine to correct albumin concentration for different urine volumes. Urine specific gravity accurately estimated urine creatinine concentration ($r=0.79$, $p<0.001$). The albumin estimated creatinine ratio (ACestR) in a random spot urine sample correlated with urine albumin excretion measured in a 24 hours urine collection ($r=0.98$, $p<0.001$), as did the ACR ($r=0.95$, $p<0.001$). To determine microalbuminuria, the sensitivity (0.88) and specificity (0.93) of the ACestR were similar to those of ACR (0.89 and 0.93 respectively) [20].

Another study randomly selected 42 consecutive patients from the primary clinical and 34 patients from the diabetic clinic. They found a very good correlation between urine specific gravity and urinary creatinine. Patients from the

diabetic clinic who had well-controlled blood sugar showed a similar trend. They derived a simplified formula where urinary creatinine can be predicted from urinary specific gravity. These revealed that urinary specific gravity can be used instead of urinary creatinine to normalize the varied urine concentration while screening for proteinuria [11].

Limitations of the Study

Urinary specific gravity is influenced by several factors and hydration status is most important of them. Children with nephrotic syndrome usually have low effective blood volume. Moreover the patients of my study got diuretics daily 12 hourly that aggravate dehydration status more. During sample collection hydration status could not be estimated properly. It was not possible to overcome this confounding factor.

5. Conclusion

The study showed a significant positive correlation of 24 hours urinary specific gravity with 24 hours urinary protein. There was a significant positive correlation of 24 hours specific gravity with 24 hours urinary creatinine. There was a significant positive correlation of spot urinary protein with spot urinary specific gravity as well. Spot urinary specific gravity showed a significant positive correlation with spot urinary creatinine and this study also showed a significant negative correlation of spot urinary specific gravity with spot urinary PCR. So, it can be concluded that urinary specific gravity had a substantial correlation with other laboratory parameters of urine and can be used as an important diagnostic tool for screening of proteinuria in children with nephrotic syndrome.

Recommendation

Urinary specific gravity is positively correlated with both 24 hours urinary protein and spot urinary protein. Further study should be done to establish urinary specific gravity as a screen tool of proteinuria in children with nephrotic syndrome.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

No conflict of interest

Statement of ethical approval

The study was approved by the Institutional Ethics Committee.

Statement of informed consent

Informed consent was obtained from all individual participants parents included in the study.

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