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Screening of Proteinuria by Urinary Specific Gravity in Nephrotic Syndrome

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Abstract

Background: Nephrotic syndrome is the commonest glomerular disease in children and is often characterized by multiple relapses. Twenty-four hours urinary protein estimation is the accepted method used in the quantification of proteinuria, but it's a time-consuming, inconvenient and cumbersome and difficult in very young children. This study emphasized screening of proteinuria by urinary specific gravity in nephrotic syndrome. **Material & Methods:** This cross-sectional study was conducted in the Department of Pediatric Nephrology (NIKDU), Dhaka, Bangladesh from October 2019 to June 2021. A total of 153 patients with nephrotic syndrome were enrolled as the study subjects after taking written consent. Urine samples were collected for both 24 hours and spot for estimation of urinary protein, urinary creatinine (Ucr) and specific gravity by dipstick method. Spot and 24-hour urinary protein creatinine ratio (PCR) were also estimated. From urinary specific gravity, estimated urinary creatinine (estUcr) and estimated urinary protein creatinine ratio (est PCR) were measured. A descriptive method was used and data were processed by using SPSS version 22.0. **Results:** Among 153 study subjects, the maximum (44.4%) were from the 2-5 years age group followed by 58 (37.9%) from 5-10 years and 27 (17.6%) from >10 years age groups. Boys (61.4%) were more predominant than girls (38.6%) in number. Spot and 24-hour urinary specific gravity have a significant positive correlation with urinary creatinine. Urinary creatinine was estimated by using the equation (Ucr = 1.25x1000 Usg – 1.24x1000). Both spot and 24-hour estimated urinary PCR (est PCR) measured by using urinary specific gravity have a significant positive correlation with corresponding urinary PCR. **Conclusion:** This study concluded that spot urinary specific gravity has a significant positive correlation with spot urinary protein and spot urinary creatinine. PCR can be estimated from dipstick urinary specific gravity instead of urinary creatinine in the cumbersome laboratory. Therefore, the study may establish an easy, rapid, inexpensive and alternative method for the detection of proteinuria in nephrotic syndrome so that it will help for early detection of relapse and prevent further complications related to nephrotic syndrome.

Keywords:- Screening, Proteinuria, PCR, Creatinine, Urinary specific gravity.

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INTRODUCTION

Nephrotic syndrome is a frequent childhood kidney disease. The incidence of primary nephrotic syndrome varies worldwide widely between 1.2 and 16.9 cases per 100,000 children and the highest incidence is observed on the Indian subcontinent are 2–3 cases per 100,000 children.[1] Nephrotic syndrome is defined as nephrotic range proteinuria and either hypoalbuminemia (serum albumin level <3gm/dl) or edema when serum albumin level is not available. Nephrotic range proteinuria is first morning or 24 hr urinary PCR ≥2mg/mg (or 200mg/mmol or ≥300mg/dl or 3+ dipsticks).[2] The clinical and biochemical features of nephrotic syndrome result from heavy proteinuria (>40mg/m2/hour; 1gm/m2/24 hours) followed by hypoalbuminemia, hypercholesterolemia, and edema.[3] In nephrotic syndrome, quantitative measurement of protein in a 24-hour urine collection is the gold standard. Spot urinary protein creatinine ratio (PCR) is another reliable method of screening for proteinuria that would be more acceptable as it is less time-consuming.[4,5] It has been widely adopted as a practical alternative for timed urine collections since it correlates closely with urine albumin excretion rate.[6] The spot urinary PCR must be measured in a laboratory and the delay in resulting makes the PCR impractical. Recently, more rapid screening methods like dipstick tests have been developed for estimating urinary protein concentration. But variation in the rate of diuresis may substantially alter the concentration of protein concentration 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 concentrated urine and a false-negative result in dilute urine.[7] 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.[8] 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 (molar mass) of the particles. Therefore, the presence of heavy molecules like radiocontrast agents and abnormal concentrations of glucose and protein in the urine causes a disproportionate increase in SG as compared to its osmolality. Specific gravity, measured by refractometry is influenced by proteinuria, such that for each 10g/l protein the SG increases by 0.003.[9] Urine-specific gravity or relative density, which values changes with urinary protein excretion can be readily measured in the clinic and also at the bedside by dipstick and might be used as sensitive, specific, and rapid screening tests for proteinuria. thereby measurement of specific gravity can be a good guide to assess proteinuria in nephrotic syndrome. Relapse of nephrotic syndrome is usually predicted by bedside urine heat coagulation test or dipstick proteinuria but both of them often give a false negative result. So, an alternative is now time demand. This study aims to establish urine-specific gravity (Usg) as a screening test for the detection of proteinuria. We determined the relation between Usg and urine creatinine (Ucr) so that Ucr can be estimated from Usg therefore urinary specific

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gravity can be used to calculate urinary PCR at bedside.

Objectives

General Objective

- To evaluate the usefulness of specific gravity for the detection of proteinuria in nephrotic syndrome.

Specific Objectives

- To assess the relationship between both spot and 24 hours urinary creatinine (mg/dl) and urinary specific gravity and estimate urinary creatinine from urinary specific gravity.
- To see the relationship between estimated urinary PCR and urinary PCR.

MATERIAL AND METHODS

This was a cross-sectional study, conducted in the Departments of Paediatric Nephrology, National Institute of Kidney Diseases & Urology (NIKDU), Dhaka, Bangladesh from October 2019 to June 2021. A total of 153 patients with nephrotic syndrome were enrolled as the study subjects after taking written consent. Laboratory investigations were done in the Biochemistry lab of Dhaka Shishu Hospital (DSH), Dhaka, Bangladesh. Before the commencement of this study, the research protocol was approved by the "Ethical Committee" of NIKDU, Dhaka, Bangladesh. Suspected patients with nephrotic syndrome were at first diagnosed clinically then based on urinary heat coagulation Test and also confirmed by other investigators. Urine samples were collected over 24 hours in a clean container after discarding 1st-morning urine up to the next morning's 1st urine. The total volume was estimated and recorded. An aliquot of 20 ml urine was collected in a 20 ml plastic pot after mixing well. On the next morning 2nd void urine sample was collected in a 20ml plastic pot as spot urine. Both samples were used for the estimation of urinary protein, urinary creatinine, and specific gravity. Urine protein was measured by the UCFP method using the pyrogallol red molybdate complex. Urine creatinine was measured by the CRE2 method which uses a modified kinetic Jaffe method. SIEMENS, Dimension EXL with LM instrument was used to measure urinary protein and urinary creatinine. Urinary specific gravity was measured on both spot urine and 24-hour urine specimen with an H Series urinalysis strip (H10) and was read visually. A value of $p<0.05$ was considered statistically significant. Statistical analysis was done by using SPSS version 22.0. Spearman ranks correlation test was done between Usg and Ucr and the equation was determined as (UCr = 1.25x1000 Usg – 1.24x1000). Urinary specific gravity was measured as 1.0005-1.030 and urinary creatinine was determined in mg/dl.

Inclusion Criteria

- Patients with nephrotic syndrome.
- Patients with both initial episodes and relapse.
- Both male and female patients.
- Patients between the age of >2 and ≤18 years.

Exclusion Criteria

- Patients having proteinuria other than nephrotic syndrome.

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RESULTS

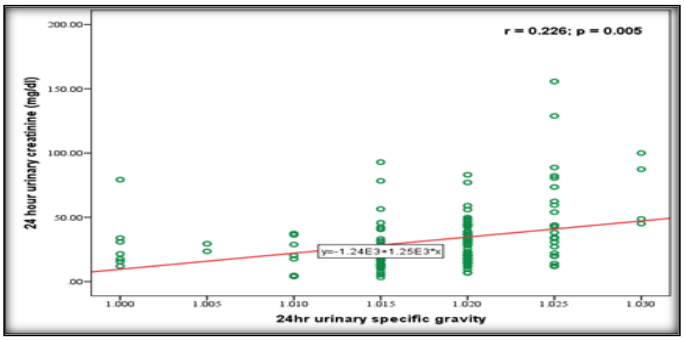

Figure 1: Correlation of 24-hour urinary creatinine with 24-hour urinary specific gravity (N=153)

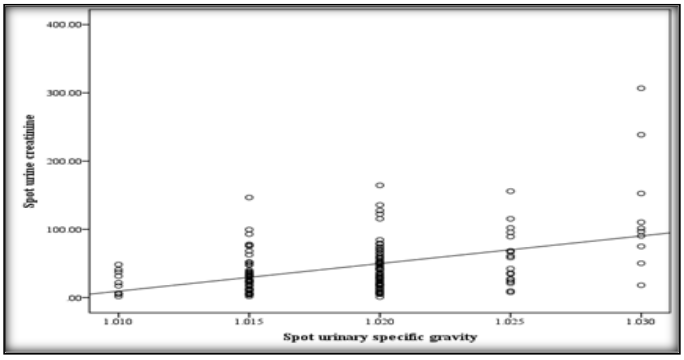

Figure 2: Correlation of spot urinary creatinine with spot urinary specific gravity (N=153)

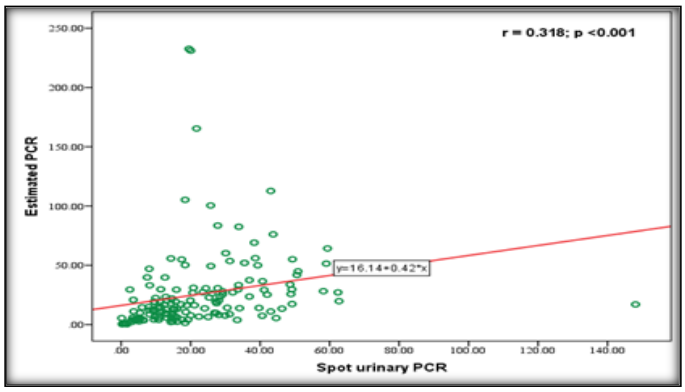

Figure 3: Correlation of spot urinary PCR with spot estimated urinary PCR (N=153)

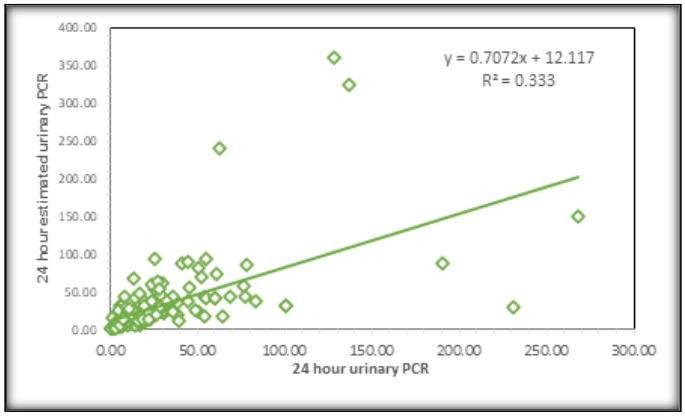

Figure 4: Correlation of 24-hour urinary PCR with 24-hour estimated urinary PCR (N=153)

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)

Characteristics	Mean SD	Min-max
24 hrs urinary creatinine (mg/dl)	32.17 ± 23.70	3.24 – 155.69
24 hrs urinary specific gravity	1.020 ± 0.02	1.00 - 1.025

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Spot urinary protein (mg/dl) Spot urinary creatinine (mg/dl)	989.49 ± 1136.73 46.09 ± 43.73	0.70 - 6147.30 0.87-306.79
Spot urinary specific gravity	1.020 ± 0.01	1.000 - 1.030

In this study, we found a good correlation between 24-hour urinary specific gravity and 24-hour urinary creatinine (r=0.226, p=0.005) [Figure 1]. There was also a good correlation between spot urinary specific gravity and spot urinary creatinine (r=0.355; p <0.001). We could estimate urinary creatinine (Ucr)from urinary specific gravity by the equation (UCr = 1.25x1000 Usg – 1.24x1000) which was derived from regression analysis (r=0.226, p=0.005). By using estimated urinary creatinine estimated urinary PCR was determined. Spot urinary estimated PCR was significantly correlated with spot urinary PCR (r= 0.318, P<0.001) in [Figure 3]. Twenty-four-hour urinary estimated PCR was also correlated with 24-hour urinary PCR [Figure 4].

DISCUSSION

The major objective of this study was to evaluate the usefulness of specific gravity for the detection of proteinuria in nephrotic syndrome. Among the total 153 study subjects, the maximum (44.4%) was from the 2-5 years age group followed by 58 (37.9%) from 5-10 years and 27 (17.6%) from >10 years age groups. In the study of Singh et al. (2019), the majority 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, only 12.5% of cases belonged to >10 years of age which was similar to this study.[10] In this current study, the scattered diagram showed that spot urinary specific gravity has a significant positive correlation with spot urinary creatinine [Figure 2] and 24-hour urinary specific gravity has a significant positive correlation with 24-hour urinary creatinine [Figure 1]. In the study by Kim et al. urine SG also accurately estimated urine creatinine concentration (r=0.407, P<0.001, Cr=SG x 4485.82-4482.87).[11] There was a strong correlation between spot urine creatinine concentration and spot urine specific gravity [r =0.79,95% CI (0.73 to 0.84), P < 0.001] in the study by Moore et al.[12] Parikh et al. (2002) also found a very good correlation between Usg and Ucr (r = 0.83, P< 0.001). They derived a simplified formula where Ucr can be predicted from Usg. These revealed that Usg can be used instead of Ucr to normalize the varied urine concentration while screening for microalbuminuria.[13] In this study, we also derived a formula to predict urinary creatinine from urinary specific gravity (UCr = 1.25x1000 Usg-1.24x1000) which was derived from regression analysis (r=0.226, p=0.005). By using Ug, both spot and 24-hour estimated urinary PCR were determined which had a very good correlation with corresponding urinary PCR [Figure 3,4]. Kim et al. (2000) showed that urinary PCR correlated with 24-hour urinary total protein (UTP) (r=0.771, P<0.001) and estimated urinary protein creatinine ratio correlated with a 24-hour collected urine protein (r=0.723, P<0.001). These results suggest that estimated urinary PCR with urine SG could be a useful method for screening proteinuria in children.[11] Moore et al. (1997) also showed in their study that the albumin estimated-creatinine ratio (ACestR) in a random spot urine sample correlated with urine albumin excretion measured in a 24-hour urine collection (r = 0.98,

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P <0.001), as did the ACR (r = 0.95, P < 0.001).[12] So estimated urinary PCR derived from urinary specific gravity may be a useful screening method for proteinuria in the case of nephrotic syndrome.

Limitations of the study

During the sample collection hydration statusof the nephrotic children could not be estimated properly. It was not possible to overcome this confounding factor.

CONCLUSIONS

As per the findings of this study, we can conclude that spot urinary specific gravity has a significant positive correlation with spot urinary protein and spot urinary creatinine. PCR can be estimated from dipstick urinary specific gravity without estimating urinary creatinine in the cumbersome laboratory. Therefore, the study may establish an easy, rapid and inexpensive method for the detection of proteinuria in nephrotic syndrome so that it will help for early detection of relapse and prevent further complications related to nephrotic syndrome.

Recommendations

Urinary specific gravity can be used in the estimation of spot urinary PCR for the detection of proteinuria in children with nephrotic syndrome so that it can guide us in the early detection of relapse of nephrotic syndrome.

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