QUANTITATION OF PROTEINURIA USING PROTEIN-CREATININE RATIO IN RANDOM URINE SAMPLES

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ABSTRACT

Estimation of proteinuria in children is cumbersome when a 24 h urine collection is needed. In the presence of a stable glomerular filtration rate, the ratio of urinary protein and creatinine should reflect the protein excretion. One hundred samples of urine (24 h and random samples) were collected from 50 children with nephrotic syndrome, 25 with nephrotic syndrome in remission and 25 normal children. The 24 h urine total protein and random urine protein-creatinine ratio were assessed on these samples. Linear regression analysis of the results showed excellent correlation between the values ($r=0.81$, $p<0.001$). A random urine protein-creatinine ratio of >3.5 correlated with massive proteinuria, while a ratio <0.2 was suggestive of physiological values. The sensitivity, specificity, positive and negative predictive values of the protein-creatinine ratio in massive proteinuria were very high. We conclude that the random urine protein-creatinine ratio can be used reliably to assess the degree of proteinuria in children.

Key words: *Proteinuria, Nephrotic syndrome.*

A 24-hour collection of urine for estimation of proteinuria in children can be very difficult and inaccurate. A more convenient but accurate method of urinary protein estimation is needed, particularly in the outpatient setting. Dipstick readings are imprecise. Protein-creatinine ratio (Pr/Cr ratio) measured in a random sample of urine has recently been reported to correlate with quantitative protein excretion. Most of the published reports are studies done on adults(1-4). This study was done to determine whether the protein-creatinine ratio on a random sample of urine is reliable for evaluation of proteinuria in children.

Material and Methods

Fifty urine samples were collected from children with nephrotic syndrome and 25 each with nephrotic syndrome in remission and normal children. All children with nephrotic syndrome had varying degrees of edema and had undergone the various biochemical tests for confirming the diagnosis. Renal function was stable in all as documented by normal serum creatinine levels. None of the patients had overt undernutrition. The estimation of total protein (g) in 24 hour urine collections was done by Biuret method after initial precipitation.

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Received for publication August 3, 1990;

Accepted December 10, 1990

A single random urine sample was collected at various times when the child presented at the outpatient between 0800-1300 hours or later in the evening/night in those who were admitted in the ward. The protein content of these samples was estimated by the Biuret method and creatinine by Jaffe method. The random urine protein-creatinine ratio was calculated mg/mg.

The data was analysed by linear regression. A 24 h urine total protein >3.0 g was considered to be massive or in the nephrotic range, 0.1-2.9 g as intermediate range and less than 0.1 g as physiologic. The sensitivity of random urine Pr/Cr ratio was based on the number of 24 h samples with proteinuria of >3 g/day that were correctly indicated by the method. Specificity was based on the number of children with 24 h protein estimation <3 g/day correctly designated by random urine Pr/Cr ratio of <3. The positive predictive value was based on the number of children who truly had nephrotic range of proteinuria and also identified by random urine Pr/Cr ratio. The negative predictive value was based on the number of children, correctly indicated by random urine Pr/Cr ratio, who did not have massive proteinuria even by 24 h estimation.

Results

In children with nephrotic syndrome the total protein excretion in 24 h collection was 4.6±1.8 g and varied between 1.6-8.6 g/day. The random urine Pr/Cr ratio in these children was 5.2±2.17 with a range of 1.7-9.6. *Figure 1* shows the distribution of values of 24 hour urine protein and random urine protein-creatinine ratio in children with nephrotic syndrome at diagnosis. In the linear regression equation $y=0.96x + 0.77$, y is random urine protein-creatinine ratio (mg/mg) and x is total protein (g) in the 24 hour urine collection. The correlation coefficient between these values was 0.81($p<0.001$). When the analysis was performed with log transformation of the data, the correlation coefficient was even better ($r=0.86$). The sensitivity, specificity, positive and negative predictive values were 0.93, 0.75, 0.95 and 0.94, respectively. A Pr/Cr ratio of >3.5 in a random urine sample correlated well with massive proteinuria.

In *Fig. 2*, the values obtained from 25 normal and 25 children with nephrotic syndrome in remission have been plotted. Urine protein in 24 h collection of children in remission ranged from 0.18-0.5 g. In five children it was 1.9-2.7 g/24 hours. The random urine Pr/Cr ratio in these children varied from 0.21-0.53 except in those five children with a higher value where the range was 1.9-2.3. Physiologic proteinuria estimated by 24 h urine collection was 0.09±0.08 g/day and the random urine Pr/Cr ratio was 0.07±0.04. The correlation coefficient in this group was lower ($r=0.50$) than in those children with massive proteinuria but the values were statistically significant ($p<0.05$). The random urine Pr/Cr ratio could be relied upon in the lower range of proteinuria also. A value less than 0.5 suggested physiologic proteinuria and 0.5-2.9 intermediate degree of proteinuria. The protein-creatinine ratio in children with nephrotic syndrome in remission had a poorer correlation but still was never in the nephrotic range.

Discussion

As the level of urinary protein excretion has considerable clinical implications, an accurate assessment is important.

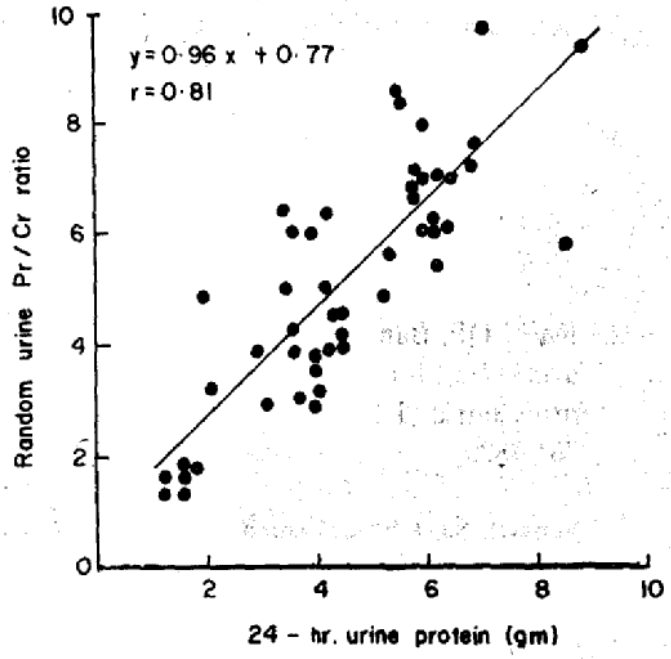

Fig. 1. Linear regression of random urine protein/creatinine ratio against 24 hour urine protein value in children with nephrotic syndrome.

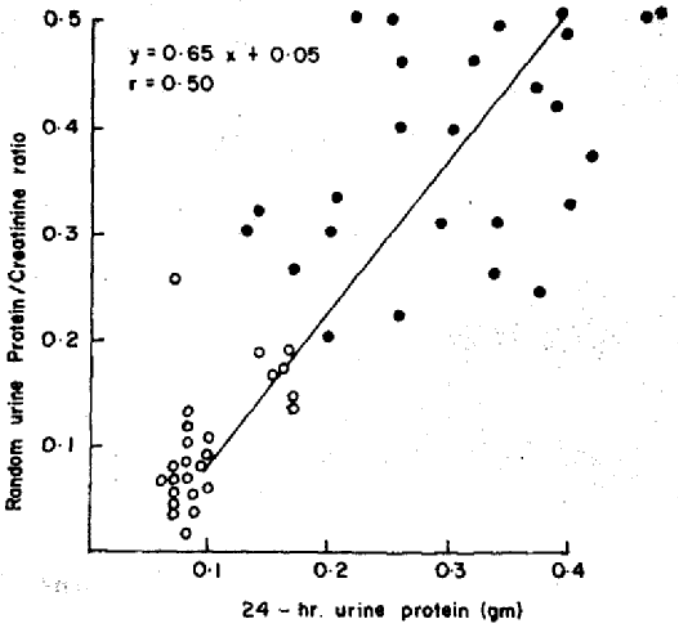

Fig. 2. Linear regression of random urine protein-creatinine ratio against 24 hour urine total protein in normal (open circles) and children with acute glomerulonephritis (closed circles).
**Five patients with acute glomerulonephritis had a Pr/Cr ratio between 1.9-2.3 and 24 h urine protein between 1.8 to 2.7 g.*

Quantitation of 24 h urinary protein excretion has so far been the only reliable method for establishing proteinuria. Collection of urine over 24 hours is especially cumbersome and inaccurate in pediatric patients. Random dipstick assessment of proteinuria is not reliable and is also susceptible to interobserver variation between technicians in interpretation of results(5). False positive results may be obtained when urine pH is high or with Gram-negative bacterial contamination of urine; the values may be misleading at the extremes of urine flow rate(6).

The urine protein-creatinine ratio on a random sample has been reported to be as accurate as the 24 h urine total protein estimation(1-4). In fact, some authors contend that it is more reliable, as the ratio is corrected for creatinine excretion(1). There is also an attempt to reclassify proteinuria based on urine protein-creatinine ratio(7). Even though a number of authors have reported on the reliability of this ratio, very few studies are available on children(8-10). Despite these excellent reports many institutions still go through the tedious process of collecting a 24 hour urine to quantify proteinuria in children.

It has been suggested that the sample collected between 0800 and 1200 hours has a higher correlation with 24 h protein excretion than samples obtained at 1600 hours(11). This correlation was not dependent on the degree of proteinuria or on the sex of the patients, but was slightly dependent on the glomerular filtration rate. The protein-creatinine ratio was virtually identical with the 24 hour protein excretion. Thus, the normal range of proteinuria was represented by a ratio of less than 0.2, while nephrotic patients had a ratio above 3.5. However, Koopman has reported a cir-

cadian rhythm in patients with proteinuria and suggests that the best estimate was obtained with the 0600 to 0900 hours urine samples(12). In this study an attempt was made not to standardize the time of collection of a random sample of urine.

Studies comparing dipstick, 24 hour urine protein and protein-creatinine ratio in random urine samples show a high sensitivity and specificity (97%) for protein-creatinine ratio in diagnosis of heavy proteinuria(13). In our study an excellent correlation was found between the 24 hour urine protein and random urine protein-creatinine ratio. In most instances the two results were numerically close. In children with nephrotic range of proteinuria the ratio was more than 3.5 (sensitivity=0.93). However, there were a few children with nephrotic syndrome in whom the ratio was very high. The positive predictive value (0.95) was high. The ratio was also very useful in assessing proteinuria at lower levels in normal children and those with nephrotic syndrome in remission (negative predictive value=0.93).

The ratio can be used reliably in following up children with nephrotic syndrome to monitor their proteinuria. These children had intermediate range of proteinuria and the random Pr/Cr ratio was 0.5-2.3. In normal children with physiologic range of proteinuria the random urine Pr/Cr ratio was <0.2.

We conclude that the random urine protein-creatinine ratio is a highly reliable test for quantification of proteinuria in children. A wider application of this technique is indicated in view of the obvious advantages in terms of cost, time and patient convenience.

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