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Research Article

A study of random urine protein to creatinine ratio in the diagnosis of nephrotic syndrome in children

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ABSTRACT

Background: The objective of the study was to evaluate the accuracy of urine protein creatinine ratio (UP/UC) in a random sample for quantitative measurement of proteinuria in comparison with 24 hours urinary protein excretion in children of nephrotic syndrome having normal Glomerular Filtration Rate (GFR).
Methods: The present study was a descriptive type of study which was conducted in the department of paediatrics, Jay Kay Lon mother and child hospital, government medical college, Kota. Cases were noted down into the proforma with respect to history, examination and investigation. All the patients were advised regarding 24 hours urine collection. They were asked to give a 24 hours urine sample starting at 9.00 am for total protein excretion rate. A random urine sample was obtained and urine protein/creatinine ratio was calculated. The data was analyzed by linear regression and by calculating the correlation coefficient between urinary protein/creatinine ratio and 24 hour urinary protein. Also chi-square test was applied for non-parametric data.
Results: Urine total protein in a timed 24 hour sample of nephrotic syndrome patients was in the range of 41.98-114.36 mg/m^2/hour with the mean value of 64.76 mg/m^2/hour. While as UP/UC ratio ranged from 2.33-5.2 with the mean value of 3.28. A significant correlation (r = 0.886) was found between timed 24 hour urinary protein and UP/UC ratio.
Conclusions: Thus we conclude that random urine protein-creatinine ratio is highly reliable and rapid test for quantification of proteinuria in children. It reflects the amount of protein in a 24 hour collection. Thus it avoids all the drawbacks which are associated with time collection method.

Keywords: UP/UC ratio, Kidney disease, Renal function tests, Paediatrics, Nephrology

INTRODUCTION

Nephrotic syndrome is a common type of kidney disease seen in children. Historically, Roelans is credited with the first clinical description of nephrotic syndrome in the late fifteenth century, whereas Zuinger later provided a detailed description of the clinical course of the disease and its importance as a cause of chronic renal failure in the presteroid era.[1]

Nephrotic syndrome may be caused by a variety of glomerular and systemic diseases, but by far the most common type in childhood is idiopathic nephrotic syndrome. Before the introduction of antibiotics, corticosteroids, and other immunosuppressive therapies, nephrotic syndrome was associated with mortality as high as 67%, usually following infections. The first significant improvement in mortality was seen in 1939 after the introduction of sulfonamides and then penicillin. The

introduction of adrenocorticotropic hormone and cortisone in the 1950s contributed to an even greater decrease in mortality (to 9%), which was noted to occur in association with dramatic resolution of proteinuria.[2]

Diagnosis of nephrotic syndrome requires the presence of edema, massive proteinuria (>40 mg/m²/hour) or a urine protein/creatinine ratio (>2.0 mg/mg) and hypoalbuminemia (<2.5 gm/dl).[3,4] The annual incidence is 2-3 cases per 100000 children per year and higher in underdeveloped countries resulting predominantly from malaria.[5]

Assessment of urinary protein excretion is not only diagnostic but also has prognostic value in monitoring of nephrotic syndrome.[6] Traditionally urinary protein assessments has been done in 24 hours urine collection specimens but this approach is time consuming, cumbersome, and imprecise.[7] An alternative approach has been advocated by some researchers avoiding 24 hours collection. This is the measurement of protein/creatinine ratio in a random urine sample.[8] This approach is based on the fact that in the presence of a stable glomerular filtration rate, urinary creatinine excretion has been reported to be fairly constant in a given individual.[9]

So this study was done to evaluate the UP/UC ratio as a rapid and reliable test for the estimation of various ranges of proteinuria and thus its usefulness in the diagnosis of nephrotic syndrome in children The objective of the study was to evaluate the accuracy of urine protein creatinine ratio (UP/UC) in a random sample for quantitative measurement of proteinuria in comparison with 24 hours urinary protein excretion in children of nephrotic syndrome having normal Glomerular Filtration Rate (GFR).

METHODS

The present study was conducted in the department of paediatrics, Jay Kay Lon mother and child hospital, government medical college, Kota

Study design

Descriptive study

Inclusion criteria

Paediatric cases (0-18 years) of nephrotic syndrome (fresh case or case in relapse) (N=30) coming to OPD/IPD department of paediatrics, Jay Kay Lon mother and child hospital, government medical college, Kota.

1. Nephrotic range proteinuria >40 mg/m^2/hour

2. Hypoalbuminemia <2.5 gm/dl

3. Edema

Exclusion criteria

Children in renal failure

Procedure

Cases were noted down into the proforma with respect to history, examination and investigation. All the patients were advised regarding 24 hours urine collection. They were asked to give a 24 hours urine sample starting at 9.00 am for total protein excretion rate.

A random urine sample was obtained and urine protein/creatinine ratio was calculated. Urine protein was estimated by improved Pyrogallol Red-Molybdate method and creatinine is measured by Jaffe's reaction. The random urine, protein-creatinine ratio was calculated mg/mg.

Statistical analysis

Data was analyzed by linear regression and by calculating the correlation coefficient between urinary protein/creatinine ratio and 24 hour urinary protein. Also chi-square test was applied for non-parametric data.

Ethics committee clearance

The study was approved by institutional ethics committee of GMC Kota. Written consent was taken from the parents/guardian of cases included in the study.

RESULTS

During the study 30 patients were included; cases were noted down into the proforma with respect to history, examination and investigation, from whom 60 samples were collected. This included a 24-hour urine sample followed by the next voided random spot sample. The protein/creatinine ratio was calculated on the spot sample. The results analysed were as follows

Out of 30 cases, 14 cases were in the age group of 1-5 years, 13 cases in 6-12 years and 3 cases were above 12 years of age. Among 30 cases, 17 cases were male and remaining 3 were females. So, Male:female ratio found was found to be 1.3:1. Among these cases, 16 patients presented for the first time while remaining 14 cases were of relapse.

Various symptoms with which these patients presented are given in Figure 1. The most common symptom was puffiness of face (96.66%), followed by swelling of the limbs (86.66%), abdominal distension (66.66%) and fever (56.66%). The least common symptom was burning micturition (6.66%).

On examination, the various signs which were obvious are shown in Figure 2. Among these, ascitis was found in

66.66% of cases, pallor in 76.66% of cases, while only 10.00% of cases with hypertension.

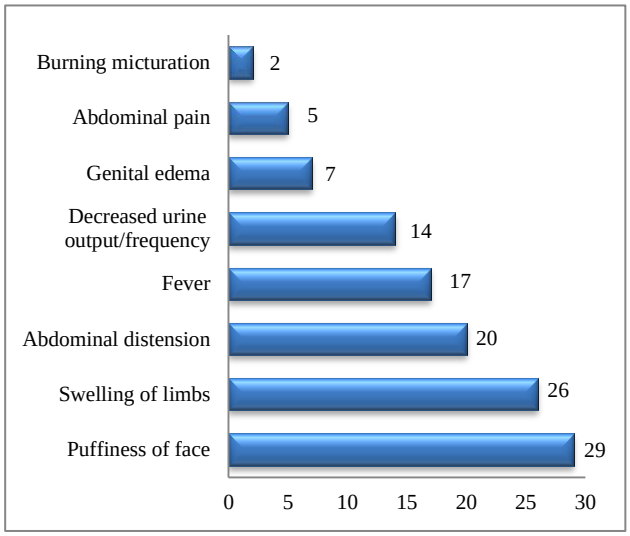

Figure 1: Clinical features of patients with Nephrotic syndrome.

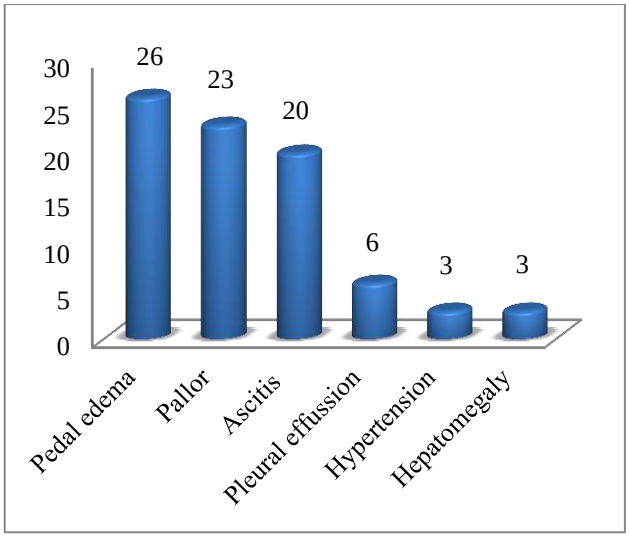

Figure 2: Signs at presentation/hospital stay.

Analysis of investigative parameters

The observed values are shown in Table 1.

Table 1: The investigation parameters of all the 30 cases.

Parameter	Hemoglobin	Serum albumin	Blood urea	Serum creatinine	Serum cholesterol
Mean	9.32 gm%	2.07 gm/dl	35.043 mg/dl	0.8 mg/dl	320 mg/dl
Range	6.7-12.7 gm%	1.5-2.4 gm/dl	13-98 mg/dl	0.4-0.9 mg/dl	161-530 mg/dl

Hemoglobin: Hb (gm/dl) was evaluated in all cases. Hb less than 11 g/dl in children between six months to six years and less than 12 g/dl in children aged 6-14 years was taken as the cut-off point for defining anaemia (according to WHO). Range is 6.7-12.7 gm%, mean Hb is 9.32 gm%, SD is 1.42 and SE is 0.26. In the present study, 90% of cases showed presence of anaemia. And 43.33% of cases had their Hb in range of 10-11.99 gm%.

Serum albumin: In present study, all patients had their serum albumin level below 2.5 gm/dl. Range is 1.5-2.4 gm/dl, Mean serum level of 2.07 gm/dl, SD is 0.27 and SE is 0.053.

Blood urea: Range is 13-98 gm/dl, Mean serum level of 35.043 gm/dl, SD is 16.21 and SE is 2.96

Serum creatinine: Range is 0.4-0.9 gm/dl, Mean serum level of 0.8 gm/dl, SD is 0.2 and SE is 0.038.

Serum cholesterol: Among these patients, 86.66% of cases showed serum cholesterol level more than 250 mg/dl. Range is 161-530 gm/dl, mean serum level of 320 gm/dl, SD is 92.88 and SE is 16.95.

Urine analysis

Hematuria: In urine microscopy, presence of more than 5 RBC/ml was considered as hematuria and more than 50 RBC/ml as significant hematuria. Haematuria was absent in 24 (80%) cases of cases and 6 cases (20%) showed hematuria on microscopy, and the data obtained is statistically significant. ($\chi 2 = 10.8$, $p = 0.001$).

Urine protein by sulphosalicylic acid method (random sample): All cases showed urine protein to be >3+. In present study, the range of timed 24 hours urine total protein was found to be 41-114.36 mg/m^2/hour, mean is 64.76 mg/m^2/hour, SD is 18.49 and SE is 3.37.

Urine protein/creatinine ratio (UP/UC) (mg/mg): In present study, the range of urine protein/creatinine ratio (UP/UC) was found to be 2.33-5.2 mg/mg with a mean of 3.28 mg/mg, showing that all values were above 2 mg/mg. DS is 0.8 and SE is 0.146.

Linear regression of random urine protein creatinine ratio against 24 hour urine protein is shown in Figure 3.

Correlation coefficient: $r = 0.886$ $P < 0.01$

The Figure 3 shows the distribution of values of 24 hour urine protein and random urine protein creatinine ratio in children with nephrotic syndrome. In the linear regression equation (Y = 1.27 X + 0.95, Y) is the random urine protein creatinine ratio and X is total protein (mg/m^2/hour) and it revealed that as X increased Y also increased linearly. The correlation coefficient between these values was 0.886 and this was highly significant (P <0.01), that means as the 24 hours urinary protein excretion value increased, the spot UP/UC value also increased linearly.

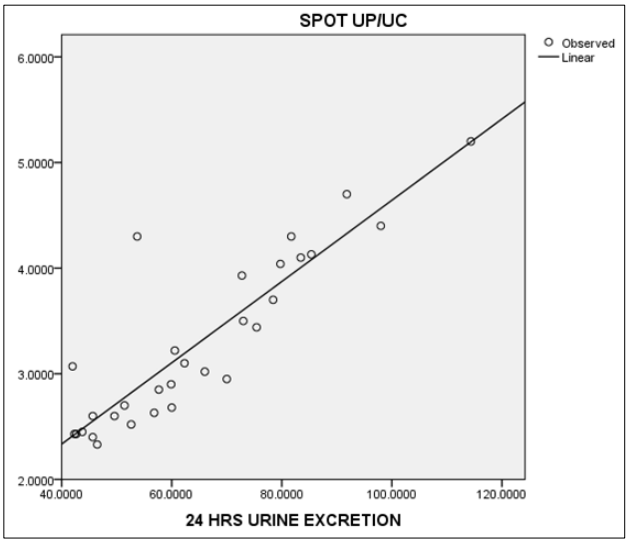

Figure 3: Linear regression of random urine protein creatinine ratio against 24 hour urine protein.

DISCUSSION

This study on evaluating the utility of random urine protein/creatinine ratio in the diagnosis of nephrotic syndrome in children was conducted in the department of paediatrics, Jay Kay Lon mother and child hospital, government medical college, Kota. Taking into study both inpatients and outpatients of nephrotic syndrome.

Age distribution

In the present study the age distribution of cases ranged from 1 year to 15 years. The mean age in the present study was 6.18 years. Similar observations were made by Chahar OP et al.[10] and Shastri NG et al.[11]

Table 2: Age distribution.

Study	N	Range	Mean
Present study	30	1-15 years	6.17 years
Chahar OP et al.[10]	30	2.5-14 years	6.7 years
N. J. Shastri et al.[11]	79	1.5-12 years	7.3 years
Abitbol et al.	64	1.5016 years	*

*Not specified

Even though commonly nephrotic syndrome is seen in pre-school children, in our study the mean age was 6.18 years as 46.66% of cases were relapses.

Sex distribution

In the present study (n = 30) male:female ratio was noted to be 1.3:1.

Table 3: Sex distribution.

Source	N	M:F ratio
Present study	30	1.3 :1
Nelson 19th edition[5]	-	2:1
Siegel NJ et al. [12]	61	3.35:1

As compared to Nelson 19th edition[5] and Seigel NJ et al.[12] the male female ratio was found less in present study. The disparity may be due to smaller sample size.

Hypertension

In present study hypertension was found in 10% of cases.

Table 4: Hypertension.

Source	% of hypertension
Present study	10%
Nelson[13]	10%
Struss J et al. (ISKDC)[14]	20.7%

According to Nelson[5,7] hypertension can be present in about 10% of MCNS while as in nephrotic syndrome due to significant glomerular lesion, the incidence of HTN varies from 20-35%. In a review of ISKDS study by Struss J et al.[14] hypertension was found to be present in 20.7% of cases with MCNS and in 25.7% of cases with other histological types.

Serum albumin

In the present study, serum albumin ranged from 1.5 gm to 2.4 gm/dl. The mean serum albumin level observed was 2.07 gm/dl. Similar observations were made by Hiraoka et al.[15] None of patient showed their serum albumin level <1.5 gm/dl (severe hypoalbuminemia).

Table 5: Serum albumin.

Study	Serum albumin
Present study	2.07 gm/dl
Hiraoka et al.[15]	1.8 gm/dl

Serum cholesterol

The range of serum cholesterol in the present study was 161-530 mg/dl and the mean serum cholesterol was noted to be 320 mg/dl. Similar observations were made by Appeal GB et al.[16]

In our study, 86.66% of patient had serum cholesterol level >250 mg/dl.

Table 6: Serum cholesterol.

Study	N	Serum cholesterol
Present study	30	320 mg/dl
Appeal GB et al.[16]	20	302 mg/dl

Hematuria

In the present study 20% of cases showed presence of hematuria. Similar observations were made by Siegal NJ et al.[12]

Table 7: Hematuria.

Study	N	Percentage of cases with haematuria at the onset of disease
Present study	30	20%
Siegal NJ et al.[12]	61	11.4%

Among 6 of these cases with microscopic haematuria, 5 cases had UTI (>5 white cells/ hpf in a centrifuged urine) responded to antibiotics, remaining 1 case responded to steroids and haematuria subsided. Siegal NJ et al.[12] have discussed the cause of haematuria and have observed that microscopic haematuria may be either asymptomatic or accompany UTI. Whereas macroscopic haematuria in patients of nephrotic syndrome should be expected only in cases with UTI, renal vein thrombosis and other secondary causes of nephrotic syndrome associated with significant glomerular lesions.

Urine protein/creatinine ratio in a random sample of cases

In the present study (n=30) the range of values observed was 2.33-5.2 mg/mg with a mean of UP/UC 3.28 mg/mg. The observed value for range and the mean of UP/UC in various studies are given below.

Table 7: Urine protein/creatinine ratio in a random sample of cases.

Study	N	Range (mg/mg)	Mean (mg/mg)
Present study	30	2.33-5.2	3.28
Chahar OP et al.[10]	30	1.25-6.22	2.52
Iyer RS et al.[17]	50	1.7-9.6	5.55 ± 2

Correlation coefficient (r) between values of 24 hour urine protein and random UP/UC ratio

In the present study, correlation coefficient obtained was 0.886 and value obtained was statistically significant (P <0.01). The correlation coefficient obtained in the other studies is mentioned below and in their studies also values obtained were highly significant.

Table 8: Correlation coefficient (r) between values of 24 hour urine protein and random UP/UC ratio.

Study	Correlation coefficient (r)
Iyer RS et al.[17]	r = 0.81
Wahbeh AM et al.[18]	r = 0.83
Siwach SB et al.[19]	r = 0.88
Lane C et al.[20]	r = 0.92
Shastri NJ et al.[11]	r = 0.95
Morales JV et.al.[21]	r = 0.91
Guy M et al.[22]	r = 0.87
Parag KB et al.[23]	r = 0.90

CONCLUSION

Urine total protein in a timed 24 hour sample of nephrotic syndrome patients was in the range of 41.98-114.36 mg/m^2/hour with the mean value of 64.76 mg/m^2/hour. While as UP/UC ratio ranged from 2.33-5.2 with the mean value of 3.28. A significant correlation (r = 0.886) was found between timed 24 hour urinary protein and UP/UC ratio.

Thus we conclude that random urine protein-creatinine ratio is highly reliable and rapid test for quantification of proteinuria in children. It reflects the amount of protein in a 24 hour collection. Thus it avoids all the drawbacks which are associated with time collection method.

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Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee of GMC Kota

REFERENCES

1. Arneil GC. The nephrotic syndrome. Pediatr Clin North Am. 1971;18(2):547-59.
2. Arneil GC, Lam CN. Long-term assessment of steroid therapy in childhood nephrosis. Lancet. 1966;2(7468):819-21.
3. ISKDC. The primary nephrotic syndrome in children. Identification of patients with minimal change nephrotic syndrome from initial response to prednisone. J Pediatr. 1981;98(4):561-4.
4. Niaudet P. Steroid-resistant idiopathic nephrotic syndrome in children. In: Avner ED, Harmon WE, Niaudet P, eds. Pediatric Nephrology. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2004.
5. Priya Pais, Ellis D. Avner. Nephrotic syndrome. In: Kleigman, Stanton, St. Geme, Schor, Behrman, eds. Nelson Textbook of Paediatrics. 19th ed. USA: Elsevier Saunders; 2011: 1801.
6. Kassirer JP, Harrington JT. Laboratory evaluation of renal function. In: Sclurier RW, Gottschalk CW,

eds. Diseases of the Kidney. 4th ed. Boston: Little, Brown; 1988: 393.
7. Ruggenentic P, Gaspari F, Perna A, Remuzzi G. Cross sectional longitudinal study of spot morning urine proteins: creatinine ratio 24 hours urine proteins excretion rate, glomerular filtration rate and end stage renal failure in chronic renal disease in patients without diabetes. BMJ. 1998;316:504-9.
8. Ginsberg JM, Chang BS, Matarese RA, Garella S. Use of single voided urine samples to estimate quantitative proteinuria. N Engl J Med. 1983;309:1543-6.
9. Vestergaard P, Leverett R. Constancy of urinary creatinine excretion. J Lab Clin Med. 1958;51:211-8.
10. Chahar OP, Bundella B, Chahar CK, Purohit M. Quantitation of proteinuria by use of single random spot urine collection. J Indian Med Assoc. 1993;91(4):86-7.
11. Shastri NJ, Shendurnikar N, Nayak U, Kotecha PV. Quantitation of proteinuria by urine protein/creatinine ratio. Indian Pediatrics. 1994;31:334-7.
12. Siegal NJ, Golberg B, Krassner CS. Long term follow-up of children with steroid responsive nephrotic syndrome. J Pediatr. 1972;81:251-8.
13. Behrman RE, Kleigman RM, Jenson HB. The nephrotic syndrome. In: Behrman RE, Kleigman RM, Jenson HB, eds. Nelson Textbook of Pediatrics. 17th ed. New Delhi: Elsevier India Private Limited; 2004: 1753-1757.
14. Strauss J, Zillreeulo G, Freundlich M. Less commonly recognised features of childhood nephrotic syndrome. Pediatr Clin North Am. 1987;34:591-607.
15. Hiraoka M, Takeda N, Tsukahara H, Kimura K, Takagi K, Havashi S, et al. Favourable course of steroid responsive nephrotic children with mild initial attack. Kidney Int. 1995;47(5):1392-3.
16. Appel GB, Blum CB, Chien S. The hyperlipedemia of the nephrotic syndrome - relation to plasma albumin concentration, oncotic pressure, viscosity. N Eng J Med. 1985;312:1544-8.
17. Iyer RS, Shailaja SN, Bhaskaranand N, Baliga M, Venkatesh A. Quantitation of proteinuria using protein-creatinine ratio in random urine samples. Indian Pediatr. 1991;28(5):463-7.
18. Wahbeh AM, Ewais MH, Elsharif ME. Comparison of 24-hour urinary protein and protein-to-creatinine ratio in the assessment of proteinuria. Saudi J Kidney Dis Transpl. 2009;20(3):443-7.
19. Siwach SB, Kalra OP, Sharma R, Singh V, Chopra JS. Estimation of 24 hour protein excretion from single random urine specimen. Indian J Med Res. 1990;92:105-8.
20. Lane C, Brown M, Dunsmuir W, Kelly J, Mangos G. Can spot urine protein/creatinine ratio replace 24 h urine protein in usual clinical nephrology? Nephrology. 2006;11(3):245-9.
21. Morales JV, Weber R, Wagner MB, Barros EJ. Is morning urinary protein/creatinine ratio a reliable estimator of 24-hour proteinuria in patients with glomerulonephritis and different levels of renal function? J Nephrol. 2004;17(5):666-72.
22. Guy M, Borzomato JK, Newall RG, Kalra PA, Price CP. Protein and albumin-to-creatinine ratios in random urines accurately predict 24 h protein and albumin loss in patients with kidney disease. Ann Clin Biochem. 2009;46(6):468-76.
23. Parag KB, Seedat YK. The protein/creatinine index. A semiquantitative assessment of 24-hour protein excretion. S Afr Med J. 1986;69(1):42-3.

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