



RANDOM SPOT URINE PROTEIN / CREATININE RATIO IN THE DIAGNOSIS OF NEPHROTIC SYNDROME IN CHILDREN AGED 2 TO 14 YEARS.

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ABSTRACT **BACKGROUND:** To evaluate the usefulness of urine protein/creatinine ratio (UP/UC) in a random sample of urine as a rapid and reliable test for the quantification of proteinuria. Thus, its accuracy in predicting nephrotic range of proteinuria from other causes of proteinuria in the diagnosis of nephrotic syndrome.

METHODS: It is a prospective case control study was conducted on 78 children aged 2-14 years over a period of April 1st 2016 to October 31st 2018. who are found to have proteinuria are evaluated clinically and investigated further for diagnosis of cause of proteinuria with relevant necessary investigations by making them into 2 groups.

RESULTS: The mean UP/UC in Group 1 is 6.8 that in Group 2 is 0.2 and the difference is significant with a p value of 0.00. The mean 24-hour urine protein in Group 1 is 5327mg/day, that in Group 2 is 177.16mg/day and the difference is significant with a p value of 0.00.

CONCLUSION: There is statistically significant correlation between spot urine protein creatinine ratio and 24 hours urine protein both in lower range and upper range of proteinuria. So, 24-hour protein estimation can be replaced by UP/UC ratio in diagnosis of nephrotic syndrome.

KEYWORDS : Nephrotic syndrome, UP/UC ratio.

INTRODUCTION:

Nephrotic Syndrome (NS) is a common renal disease seen in children. In developed countries the incidence of nephrotic syndrome in childhood is 2-4 per 100000 population, whereas in the Indian subcontinent it is estimated at 9-10 per 100000 population¹.I and at times unreliable due to collection errors. Also, the collection time is too long for the patients patience.²A 24-hour collection of urine for estimation of proteinuria in children can be very difficult or virtually may be impossible in infants and children and usually not possible to collect 24-hour urine in female children.⁴These problems suggest need for a more convenient and accurate method of urine protein estimation particularly in the outpatient setting.⁵A test for quantification of urinary protein excretion in terms of protein: creatinine ratio on a random spot urine can be performed to predict accurately the level of proteinuria.⁶But only a few studies have been conducted in children and most of the published reports are studies done on adults⁷.So, this study is 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. Aims and objectives of the study to evaluate the usefulness of urine protein/urine creatinine ratio (UP/UC) in a random sample of urine as a rapid and reliable test for the quantification of proteinuria. Thus, its accuracy in predicting nephrotic range of proteinuria from other causes of proteinuria in the diagnosis of nephrotic syndrome.

METHODS

This is a prospective case control study was conducted on 78 children aged 2-14 years the OPD who are found to have proteinuria on urine dipstick testing from Trace to 4+ are identified and admitted to paediatric wards of Alluri Sita Ramaraju Academy of Medical Sciences, a tertiary care hospital, Eluru, Andhra Pradesh during the period of April 1st 2016 to October 31st 2018. They are evaluated clinically and investigated to divide them into 2 Groups. children having facial edema with or without edema abdomen and limbs, 24 hour protein >3.5 gms/day, hypoalbuminemia <2.5 gms/dl and serum cholesterol > 200 mg/dl are included in clinical case Group, along with relapse cases of nephrotic syndrome diagnosed by 3+ urine protein on urine dipstick testing on 3 consecutive days as Group 1 Those patients having 24-hour protein <3.5gms/day with or without edema are included in control Group - Group 2. these children are investigated further for diagnosis of cause of proteinuria with relevant necessary investigations. The children are followed for 12 weeks and steroid responsiveness is noted.

INCLUSION CRITERIA

1. Those children diagnosed as first episode or relapse of Nephrotic syndrome by urine protein more than or equal to 3+ on urine dipstick testing for 3 consecutive days are included in the study as group 1.
2. Proteinuria caused by conditions other than NS are included in this study as group

EXCLUSION CRITERIA:

Patients with edema either focal or generalized without proteinuria

STATISTICAL ANALYSIS

The data is recorded in the form of mean and standard deviation for continuous variables and frequency and percentage for categorical variables. The normal distribution of measurement data was by the Kolmogorov - Smirnov test for normality test. Mann Whitney U test was conducted to compare the difference between Groups on the continuous variables. Chi square or Fisher's exact tests were used on those categorical variables. Linear regression was used and the correlation coefficient was calculated between urinary protein/creatinine ratio and 24 hour urinary protein. The statistically significant difference level was set at p<.05. All statistical analyses were conducted using SPSS version 25.0.

RESULTS

In the present study the mean age of children belonging to Group 1 is 4.3 years with SD of 2.4 years. That of Group 2 children the mean age is 5.3 years with SD of 3.4 years. Gender distribution: In Group 1 the Male to Female ratio is 1.8 :1 In Group 2 the male to female ratio is 1.08:1.

Figure 1: Data regarding frequencies of 1st episode and relapses among cases of Nephrotic syndrome

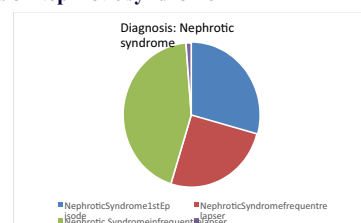


Table 1: Data regarding frequencies of other causes of proteinuria:

Diagnosis	n(%)
Acute glomerulonephritis / post infectious glomerulonephritis	9(18.0%)
Urinary tract infection	22(44.0%)
Drug induced acute kidney injury	3(6.0%)
Complicated malaria with acute kidney injury	4(8.0%)
Insulin dependent diabetes mellitus with UTI	6(12.0%)
Hemolytic uremic syndrome	2(4.0%)
SLE nephritis	2(4.0%)
Pyelonephritis	1(2.0%)
Henoch schonlein purpuric nephritis	1(2.0%)

Table 2: Comparison of blood tests in Group 1 and Group 2

	Diagnosis				P value
	Nephrotic syndrome(n=28)		Other causes of proteinuria(n=50)		
	Mean	Standard Deviation	Mean	Standard Deviation	
Haemoglobin (g/dl)	9.8	.5	8.83	0.711	0.03(S)
WBC (cells/mm ³)	12574	5149	13705	3763	0.118 (NS)
Blood urea(mg/dl)	25.7	9.1	95	12.1	0.093 (NS)
Serum creatinine(mg/dl)	.26	.16	.7	1.0	0.149 (NS)
Serum albumin (g/dl)	1.7	.5	3.1	.3	0.000 (S)
Serum cholesterol(mg/dl)	357	74	154	24	0.034 (S)
Triglycerides (mg/dl)	349	101	122	15	0.041 (S)

Serum albumin level decreased in group 1 and serum cholesterol and triglyceride levels are elevated but in both groups leucocyte count elevated.

Table 3: Comparison of spot UP/UC ratio with 24hours urine protein in Group 1 and Group 2.

	Nephrotic syndrome		Other causes of Proteinuria		P value
	Mean	Standard Deviation	Mean	Standard Deviation	
Spot UP/UC	6.8	2.2	0.2	.044	0.00 (S)
24hrs urine protein (mg/day)	5327	1203	177.16	52.574	0.00 (S)

The mean UP/UC in Group 1 is 6.8 that in Group 2 is 0.2 and the difference is significant with a p value of 0.00. The mean 24-hour urine protein in Group 1 is 5327mg/day, that in Group 2 is 177.16mg/day and the difference is significant with a p value of 0.00.

Table 4: Comparison of UP/UC and Urine dipstick protein.

UP/UC	Trace n (%)	+1 n (%)	+2 n (%)	+3 n (%)	+4 n (%)
<0.2 (n=50)	1(2%)	44(88%)	5(10%)	0(0%)	0(0%)
0.2 to 3.5 (n= 2)	0	0	0	1(50%)	1(50%)
>3.5 (n=26)	0	0	0	18(69.3%)	8(30.7%)

On comparing the levels of spot UP/UC ratio with dipstick protein it is found to be significant with Chi – square of 26.96 (<0.001).

Table 5: Data regarding linear regression of spot UP/UC ratio against 24hrs urinary protein in Group 1 and Group 2

Linear Regression	R	R Square	Equation X=24hrs urinary protein; Y= spot UP/UC ratio	P value
Nephrotic Syndrome	.911	.829	Y = 0.001664X - 2.054	0.00 (S)
Other causes of Proteinuria	.923	.853	Y = 0.0007783X + 0.03612	0.00 (S)

In linear regression equations(Y = 0.001664X - 2.054 & Y = 0.0007783X + 0.03612) Y is the random urine protein creatinine ratio and X is total protein (gms in 24 hours) and it revealed as X increased Y also increased linearly. There is statistically significant association between spot UP/UC ratio and 24 hours urine protein (p < 0.00).

Table 6: Data regarding linear regression of spot UP/UC ratio against serum albumin in Group 1 and Group 2

Linear Regression	R	R Square	Equation X=Serumalbumin; Y= spot UP/UC ratio	P value
Nephrotic Syndrome	0.174	0.030	Y = -0.7631X + 8.119	(NS)0.377
Other causes of Proteinuria	0.187	0.035	Y = 0.032X + 0.076	(NS)0.193

There is no significant correlation between spot UP/UC ratio and serumalbumin in both Groups -Group 1 (p value 0.377), Group (p value 0.193).

DISCUSSION

In present study a total of 78 cases are enrolled in the study the age distribution in group 1 ranged from 2 to 14 years and the mean age is 4.2 years and male female ratio of Group 1 is noted to be 1.8:1. That is 64% of children are males and 36% of children are females which is similar to a study done by A Madani et al⁸.

The mean hemoglobin observed in the study is 9.8 with standard deviation of 0.5. The mean leucocyte count was 12574 cells/mm³ TLC is elevated in cases, the mean blood urea observed in the present study is 25.7mg/dl when compared to its level in Navale RA et al it is 35.04mg/dl serum albumin level below 2.5g/dl in all children and ranged from 1 gm to 2.5 gm/dl. The mean serum albumin level observed is 1.7 gm/dl. Similar observations are made by Hiraoka et al¹⁰ the mean serum cholesterol observed in the study is 357mg/dl. Similar observations are made by Navale RA et al⁹. The Total leucocyte count is elevated in Group 2 also which is due to infectious causes of proteinuria. Blood urea and serum creatinine are elevated in some patients of Group 2 where children presented with drug induced acute kidney injury and malaria with acute kidney injury. Serum albumin is normal in Group 2 children with a mean serum albumin of 3.1g/dl. Serum cholesterol and triglycerides are normal in Group 2 with a mean serum cholesterol value of 154mg/dl and mean serum triglycerides value of 122mg/dl.

In this present study in Group 1, the range of values observed for spot UP/UC is 2.6 to 10.6 with the mean value of 6.8. In Iyer et al⁸ study, the range of observed value of UP/UC 1.7-9.6 with the mean value of 5.5±2. Group 2, the range of values observed for spot UP/UC ratio is 0.1 to 0.2 with mean of 0.2.

When spot PCR is compared with 24-HUP, the result is statistically significant (P ≤ 0.001) in all ranges. This is similar to Ananthakumar et al³, Navale RA et al⁹, Shastri et al⁵, Chahar et al⁴, Indira Agarwal et al¹¹, Biswas et al¹², and Ginsberg et al¹³ studies where spot PCR correlates well with 24-HUP irrespective of the degree of proteinuria. A similar study done by Navale RA et al⁷ showed urine protein to be >3+ in all cases and the range of timed 24 hours protein was found to be 41- 114.36mg/m²/hour.

The range of UP/UC ratio was found to be 2.33-5.2 with a mean of 3.28 showing all values were above 2 and SD was 0.8.

In the present study in Group 1, the range of 24-hour urine protein observed is 1.5 to 8g/day with mean observed is 5.327g/day with standard deviation of 1.203. Iyer RS et al⁷ found the range of timed 24 hours urine protein to be 0.8-7 gm/24 hour and a mean value of 4.6/24 hour was observed and Group 2, the range of 24-hour urine protein observed is 0.37-0.227g/day with mean of 177.16g/day.

In present study there is statistically significant correlation between 24-hour urinary protein and UP/UC ratio in both groups, r value is 0.911 in Group 1 (p value 0.00) and r value is 0.923 in Group 2 (p value 0.00)

The excellent correlation between UP/C ratio and 24-hour urinary protein is corroborated by other studies. Chitalia et al¹⁵ studying patients with glomerular diseases found correlation between UP/UC ratio and 24-hour urine protein was good at p < 0.05 and correlation

coefficient of 0.97. High correlation coefficients ($r=0.91, 0.95$ and 0.98) were observed in patients with normal, reduced and severely reduced renal function in a study done by Antunes et al¹⁴. A study done by Rajkumar et al⁶ 2017, where r was highly significant and showed that on performing logistic regression analysis, spot PCR was found to be significant predictors of relapse. In a study done by Navale RA et al, the random UPC ratio in the diagnosis of nephrotic syndrome in children where the mean 24-hour urine protein was $64.76\text{mg/m}^2/\text{hr}$ which is nephrotic range of proteinuria. The mean UPC ratio was 3.28. In that study the linear regression equation was $Y=1.27X+0.95$.

In the present study the mean 24-hr urine protein is 5.347 g/day and the mean UPC ratio is 6.8. The linear regression equation is $Y = 0.001664X - 2.054$.

With substitution of mean 24 Hr urine (X) of our study in the equation by Navale et al $Y=1.27X+0.95$ the UPC ratio derived is 7.7. The mean UPC ratio in the present study is 6.8. This disparity may be due to a smaller number of children in group 1.

In a study done by Pallavi patil et al, the mean 24-hour urine protein was 0.820g/day which is non nephrotic range of proteinuria. The mean UP/UC ratio was 0.715. In that study the linear regression equation was $Y=1.005X+0.078$. In the present study the mean 24-hr urine protein is 0.177 g/day and the mean UPC ratio is 0.2. The linear regression equation is $Y=0.0007783X + 0.03612$ with substitution of mean 24 Hr urine (X) of our study in the equation by Pallavi patil et al $Y=1.005 X + 0.078$ the UPC ratio derived is 0.2 which is similar to the mean UPC ratio in the present study (0.2). Navale RA et al⁷ also performed linear regression of random urine protein creatinine ratio against 24-hour urine protein which showed $r=0.886$, $p<0.01$

CONCLUSION

There is statistically significant correlation between spot urine protein creatinine ratio and 24 hours urine protein both in lower range and upper range of proteinuria. From linear regression formula spot UP/UC ratio can be used for quantification of 24-hour protein estimation.

The UP/UC ratio more than 2 is considered as nephrotic range of proteinuria and can be used as a criteria in diagnosis of 1st episode and relapse of nephrotic syndrome. So, 24-hour protein estimation can be replaced by UP/UC ratio in diagnosis of nephritic syndrome.

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