ORIGINAL ARTICLE

Evaluation of Random Urine Sample Protein-Cretinine Ratio as an Index of Quantitative Proteinuria

Sandeep Garg, Alok Kumar Gupta*, Anurag Rohtgi, SK Sharma

Abstract

The present study was conducted to find out a correlation between protein to creatinine (PC) ratio in random sample and 24 hr. urinary protein (UP) in patients with proteinuria with normal renal functions (serum cretinine<1.5 mg %) -group-I, with impaired renal functions, mild to moderate (s.cretinine 1.5-4.0mg%) group-II and advance renal failure (s.cretinine >4.0mg%) -group-III. 24 hr. and a random urine sample was taken for each patient and was tested for protein and creatinine. PC ratio was found in each random sample. The mean 24 hr.UP (g/24 hr.) estimated by 24 hr. urine collection was 1.15± 0.97, 3.26 ±1.34 and 7.39±2.19 in group I, II and III respectively. However, the mean UP estimated by random sample was 1.35±1.09, 3.94±1.93 and 10.38±3.70 in group-1, group-II and group-III respectively. P value was statistically insignificant in group 1 & II. However, there was significant difference in values in group-III (P=0.012). Coefficient of correlation on univariate analysis was r=0.889 in group-I, 0.788 in group-II and 0.375 in group-III indicating a significant correlation in results in groupI and II and not in group-III. The results in the study have shown that single voided urine method of estimating quantitative proteinuria holds its value in patients with normal, as well as in mild to moderately impaired renal functions. However, this method does not hold good for patients with severely impaired renal functions.

Key Words

Proteinuria, Protein to creatinine ratio

Introduction

Proteinuria is one of the earliest sign of almost all renal diseases (1). Proteinuria occurs due to damage to glomerular apparatus (glomerular proteinuria) or due to failure of reabsorbtion of the filtered protein by tubular cells (tubular proteinuria). Normally most healthy adults excrete between 20-150 mg of protein in urine over 24 hrs and proteinuria >3.5 gm/day is taken to be diagnostic of nephrotic syndrome (2). Estimation of proteinuria helps in differentiating between tubulointerstital and glomerular diseases, to follow the progress of renal disease and to assess the response to therapy (3). Quantitating protein in urine is thus a cornerstone in diagnosis, treatment and prognosis of renal diseases.The most common method relies on estimation of 24hrs UP in a urine specimen collected over 24hrs. However, 24hr UP estmation method has certain pitfalls and thus leads to discarding of nearly 1/3rd of the samples (4). To obviate these difficulities short timed urine collection have been advocated with the hypothesis that protein excretion is nearly constant throughout the day and various studies, have estimated protenuria by taking urine samples at 2 hrs, 3 hrs and 4 hrs (5, 6). These studies however were not validated. Because of problems with timed urine collection, 24 hr. UP excretion using single timed voided sample has been estimated. It has been reported that in the presence of stable GFR (glomerular filtration rate) urinary creatinine excretion is fairly constant in a given individual, the fact serving as principle behind the use of

From Deptt. of Medicine Lady Hardinge Medical College & Smt. Sucheta Kriuplani Hospial & *Appolo Hospital New Delhi.
Correspondece to: Dr. Sandeep Garg, B-403, Street No.4, Majlis Park, Near Adarsh Nagar, Delhi-110033

PC ratio in quantifying 24 hr. proteinuria (7). Many workers have studied the correlation between 24 hr. UP and proteinuria estimated from spot PC ratio in diverse group of patients such as children, diabetes, nondiabetics, SLE group, pregnant females, pre-eclampsia and patients with diverse renal diseases (8-14).

The present study was conducted to establish a use of PC ratio to find out 24 hrs. urinary proteinuria in Indian patients with different renal diseases.

Material and Methods

In this study 80 patients were selected with varying range of proteinuria irrespective of the nature of renal diseases detected by dipstick method . Out of 80 patients 40 subjects were included in group-I (24 hrUP <150mg% with normal renal functions (S. creatinine <1.5 mg%) and 40 patients with proteinurea >150 mg% were further divided into group-II (S. creatinine 1.5-4.0 mg%)and group-III (severely impaired renal functions S.creatinine >4.0 mg%) respectively. Patients with malnutrition, orthostatic proteinuria, malabsorption, hepatic diseases , obstructive uropathy and use of drugs like penicillin, gentamicin, tolbutamide, radiocontrast material and sulfa drugs were excluded from the study.

All patients were subjected to a detailed history and clinical examination. Routine haematological tests,serum urea, creatinine, electrolytes-Na+, K+ , Ca_2+,$PO_4$3-, uric acid, cholesterol,urine for albumins, sugar, ketones, x-ray for kidney, ureter and bladder, USG-abdomen and special investigations like protein and creatinine content in 24 hr urine sample and random sample were done in each subject. There was no change in the treatment and diet of patients during the course of the study. On the test day, in the morning at the commencement of collection period (6.00 a.m.) patients were asked to void urine and discard this sample (as it contains the overnight urine present in the bladder). Subsequently urine was collected for next 24 hrs. The last sample was to be collected on next day at 6.00 a.m. A random sample was also collected at around 11.0 a.m. on the day of deposition of 24 hr sample (the test day). A blood sample was also taken on the test day (after random urine sample) for estimation of serum creatinine. Protein and creatinine contents were found in both 24 hr urine sample and in random urine sample (by using Beckman- Synchron CX-5 autoanalyzer). Also volume of 24 hr urine sample was noted on the test-day. Detection of quantitative proteinuria in the autoanalyzer was based on the calorimetric optical density method as described by Teitz (15) .

Testing for urinary and serum creatinine was done by using random kit in CX-5 synchron autoanalyzer based on calorimetric method utilizing Jaffes reaction (16). For serum sample no dilution was done but for urine sample (spot sample and 24 hr sample) a dilution of 1:5 was done with normal saline.

Finally PC ratio was calculated for each voided random urine sample. Expected creatinine excretion(gm per 24 hr) was found by using Cockcroft Gault Formula (8, 17-20).

$$\text{For Men} = \frac{(140\text{-Age in Years})\ (\text{wt.in Kg})}{5000}$$

$$\text{For Women} = \frac{(140\text{-Age in Years})\ (\text{wt.in Kg}) \times 0.85}{5000}$$

- 24 hour urinary protein in gm/24 hr was estimated by formula = (Protein/creatinine ratio) x (expected creatinine excretion)

-24 hr. Urinary volume was multiplied by the estimated protein (g/l) which gave total amount of protein in g/24 hrs.

Finally predicted and observed 24 hr urinary protein values were compared to find a correlation between the two.The arithmetic mean (x) and standard deviation (S.D.) were calculated by standard statistical methods. For comparison student paired 't' test was used and p-value<0.05 was considered statistically significanct. Also coefficient of correlation (r value) was found by Pearson and Spearman Correlation formula between single voided and 24 hr collection method.

Results

Out of total 80 patients studied (control and subjects) 28 (35%) were male and 52 (65%) were female. Their age ranged between 14-70, years the mean age being 46.3 years.The age and sex distribution of both control and subjects are shown in the table-1 and etiological breakup is given in table-2.The mean 24 hr urine volume was 1426.66±556.27 ml, 1780.0±768.99 ml and 1363.33±656.95 ml in group-I, group-II and group-III respectively. The mean 24 hr urinary protein estimated by 24 hr collection method and by single vioded method

were 1.157±0.975 gm/24 hr & 1.354±1.093 gm./24 hr in group I (P>0.10), 3.26±1.34 gm/24 hr and 3.94±1.93 gm/24hr(P>0.10) in group-II respectively. However, in group-III the mean 24 proteinuria by 24 hr collection method was 7.39±2.19 gm/24 hr and by single voided method was 10.38±3.7 gm/24 hr (P < 0.05). Thus, a significant high correlation was found in group I patients in between two methods with coefficient of correlation i.e. the r value being 0.889. Similar results were obtained in group-2 with r value = 0.788. However, in group III the correlation between two methods was not found to be significant r value being 0.375 .

Table 1. Age and Sex distribution of the patients under study

Age group (in years)	Control			Subjects		
	Male	Female	Total	Male	Female	Total
11-20	0	1	1	0	2	2
21-30	1	2	3	1	2	3
31-40	3	7	10	3	8	11
41-50	3	7	10	4	5	9
51-60	3	6	9	4	6	10
61-70	3	4	7	3	2	5
>70 and Above	-	-	-	-	-	-
Total	13	27	40	15	25	40

Table 2:Etiological Breakup of patients.

S.NO	Diagonosis	No.of cases	Percentage(%)
1	Type-2 with nephropathy	28	50%
2	Type-2 with hyperetension wiht CRF	12	
3	Idiopathic Nephrtic Syndrome	7	24%
4	Hypertension with Nephrotic syndrome	3	
5	Chronic Glomerulopathies	3	
6	Rheumatoid Arthritis with Nephrotic Syndrome	6	
7	Urinary Track Infection	5	6%
8	Connective Tissue disorders	5	6%
9	Others	11	14%
	Total	80	

Table 3. Clinical and biochemical data in all 3 groups.

Variables	Group I		Group II		Group III	
	Mean±S.D	Range	Mean± S.D	Range	Mean± S.D	Range
Age	48.40±14.15	15-70Yrs	45.06±15.06	14-68Yrs	`43.33±14.00	16-65Yrs
Weight	58.73±12.19	35-96Kg	63.33±18.45	30-96Kg	62.46±17.86	29-96Kg
Duration of Symptoms	11.5±7.54	1-30 mths	10.0±5.23	4-20months	16.0±6060	6-36months
Heart rate	82.53±11.88	70-110bmp	88.0±9.53	76-106bmp	86.08.57	76-100bmp
Systolic BP	119.1±11.7	90-150mmHg	137.20±30.80	100-210mmHg	153.73±23.12	`110-180mmHg
Diastolic BP	79.44±7.51	66-96mmHg	87.46±15.88	70-130mmHg	91.86±1054	70-106mmHg
Serum Cretinine	0.68±0.44	0.1-1.4mg/dl	2.36±0.64	1.0-3.2mg/dl	5.50±1.94	3.2-8.9mg/dl
Blood Urea	40.0±19.79	20-140mg/dl	56.66±24.16	32.0-46.0mg/dl	135.33±39.84	76.0-210.0mg/dl
Serum Uric acid	4.51±1.69	2.5-9.4mg/dl	6.03±1.95	3.5-8.5mg/dl	9.58±1.69	7.0-13.6mg/dl
Sodium	138.53±3.10	130-146mmol/L	135.20±5.22	128.0-144.0mmol/L	130.40±3.29	126.0-140.0mmol/L
Potassium	4.11±0.64	2.9-5.8mmol/L	4.98±0.96	3.8-7.0mmol/L	6.43±0.50	5.7-7.5mmol/L
Serum Calcium	9.81±0.66	8.4-11.0mg/dl	9.10±0.80	7.6-10.3mg/dl	7.76±0.85	6.8-10.4mg/dl
S.Cholesterol	207.20±54.97	140.0-333.0mg/dl	321.33±103.46	160.0-456.0mg/dl	199.26±43.29	127-280.0mg/dl

Table 4. Various parameters compared in all three groups.

Group (mg/dl)	Protein (mg /dl)	Cretinine	P/C ratio	Expected cretinine(gm/24hr)	Single voided method 24 hrUP(g./24hrs)	24 hr method 24 hr. UP (g/24hrs)	P value	r value Pearson Coefficient
	Mean±S.D	Mean±S.D	Mean±S.D	Mean±sS.D	Mean±S.D	Mean±S.D		
I	48.33±69.97	38.32±35.93	1.40±1.2	0.943±0.23	1.35±1.09	1.15±0.97	0.408	0.889
II	235±248.41	83.16±89.87	3.84±2.3	1.157±0.31	3.94±1.93	3.267±1.34	0.227	0.778
III	567.33±331.71	62.90±44.98	16.76±23.74	1.070±0.319	10.38±3.70	7.39±2.19	0.012	0.375

Discussion

Quantitative assessment of proteinuria from 24 hr urine collection still remains a gold standard for urinary protein estimation. But 24 hr collection are often inaccurate, time consuming, cumbersome, inconvenient and unreliable. Short timed urine collection is not suitable for patients with severe oliguria and in patients who are not able to pass urine over a short span of time and for pediatric age group patients. One has to be very careful during sample collection because slight error in duration of collecting period or missing a sample of urine will exaggerate the results. To overcome the above shortcomings, efforts have been made to estimate 24 hr UP excretion by single voided urine sample.

In the present study on comparison of quantitative proteinuria estimated from conventional 24 hr method and single voided method it was observed that there was no significant difference between the results obtained by the two methods in group-1 and group-2. Moreover, a significant correlation was observed between the two values both in group-1 and group-2. However, in patients with advanced renal functions i.e. group III the results by two methods did not correlate.

Thus it is evident from these results that quantitative proteinuria estimated from single voided urine method accurately reflects the 24 hr proteinuria in patients without renal impairment and in patients with mild to moderate renal function impairment. However, the possible reason for the poor correlation in patients with advanced renal failure is the decreased GFR. Thus, the results of our study are in agreement with previous studies that suggested that correlation between two methods of estimation depends upon the GFR and is independent of sex, age and weight of patient and degree of proteinuria (10, 13, 14, 18). Various studies by different workers have been published where a ratio of < 0.2 indicated proteinuria with in normal limits and a ratio of >3.5 indicated nephrotic range proteinuria (20). Therefore, P/C ratio provided a very useful, simple and convenient method for quantitative assessment of protein and can replace 24 hr urine collection method in indoor, outpatients and in follow up clinics as it gives quick and reliable results and avoids the inconvenience and shortcomings associated with 24 hr urine collection.

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