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Evaluation of Spot Urine Protein/ Creatinine Ratio As An Index of Quantitative Proteinuria

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Abstract: *This study is to evaluate whether the protein creatinine ratio in a spot urine sample is as reliable as 24 hrs urine protein in quantification of proteinuria, in patients with varying degrees of renal dysfunction and different levels of proteinuria in a tertiary care hospital.This study shows that the protein creatinine ratio by themselves appear to indicate the presence and degree of proteinuria. It can , thus be used as an screening procedure for quantification of proteinuria even in an outpatient clinic as it requires only a spot urine sample.*

I. Introduction

The measurement of proteinuria will help to establish a diagnosis and to predict the outcome of most renal diseases. This also helps to assess the effects of therapy, but requires the measurement of concentration in timed urine collections.24 hrs urine collections are commonly used to mask the wide fluctuation in proteinuria over the day,but are time consuming and often imprecise.An alternative approach,avoiding timed urine collection is measurement of the protein creatinine ratio in single random urine specimen.Protein creatinine ratio measured in spot urine samples prevents the errors related to imprecise urine collections and also may predict the progression of chronic renal disease even more reliably than 24 hrs urine protein analysis.

Aim Of The Study

To evaluate whether the protein creatinine ratio in a spot urine sample is as reliable as 24 hrs urine protein in quantification of proteinuria,in patients with varying degrees of renal dysfunction and different levels of proteinuria.

Materials And Methods

The study population consists of patients over 18 yrs of age who had persistent dipstick positive proteinuria who were either admitted to or visited the outpatient department of Coimbatore Medical College Hospital during the period of one year from May 2015 to May 2016.

The clinical presentation,medical illness and physical examination findings,baseline lab investigations were noted in a profoma.24 hrs urine protein excretion and first morning spot urine sample protein creatinine ratios were estimated and were noted down in the proforma.

Inclusion Criteria

1. Age more than 18 years
2. Persistent dipstick positive proteinuria on two different occasions atleast occasions one week apart

Exclusion Criteria

1. Patients with evidence of urinary tract infections
2. Patients with evidence of overt heart failure
3. Patients with febrile illness
4. Patients with uncontrolled hypertension
5. Patients with gross hematuria

A total of sixty subjects with persistent proteinuria and varying degrees of dysfunction were included in the study.clinical evaluation of these patients and their baseline lab investigations were included in the profoma.

Patients were adviced to give the first morning urine sample for the estimation of urine protein to creatinine ratio.For estimation of 24 hrs urine protein,these patients were provided with a plastic can(5 litres capacity to collect their 24 hrsurine.Toluene was added in to the can to prevent bacterial over growth.The time

was noted and the patients were advised to collect their entire 24 hrs urine in the can provided including the last void urine at the end of 24 hrs)

Coulter Maxm Hematology Flow Cytometry

The collected urine sample was estimated for protein concentration with 24hrs of urine,usingpyrogallol red bio red test in Chiron Express Plus auto analyser.The spot urine sample was estimated for protein concentration by the same technique and for creatinine by modified Jaffes method by urine Chiron Express Plus auto analyser. Spot urine protein creatinine ratio was calculated from the measured values in the first morning urine samples.

Expected 24 hrs urinary protein excretion was calculated from protein creatinine ratio estimated in spot urine sample by the formula.

$$\text{Expected 24 hrs urinary protein} = \frac{[140 - \text{age(yrs)}] \times \text{wt (kg)}}{5000} \times \text{spot urine PCR}^*$$

*spot urine sample protein creatinine ratio

*x0.85 for females

CBC was done on Coulter Maxm J.T 540.serum biochemical analysis was done using Chiron Express Plus auto analyser.urine samples are evaluated by dipstick for albumin,sugar,pH and microscopy for deposits.A correlative study was done by comparing the calculated expected 24 hrs urine protein excretion by linear regression method after segregating these patients in to four groups.

Group 1a

Calculated creatinine clearance≥50ml /min and nephrotic range of proteinuria(>3.5 gm /day)

Group 1b

Calculated creatinine clearance≥ 50ml /min and nephrotic range of proteinuria(<3.5 gm/day)

Group 2a

Calculated creatinine clearance < 50ml /min and nephrotic range of proteinuria(>3.5 gm /day)

Group 2b

Calculated creatinine clearance < 50ml /min and nephrotic range of proteinuria(<3.5 gm /day)

The coefficient of correlation between the estimated and the expected 24 hours urinary protein different groups were calculated and studied.

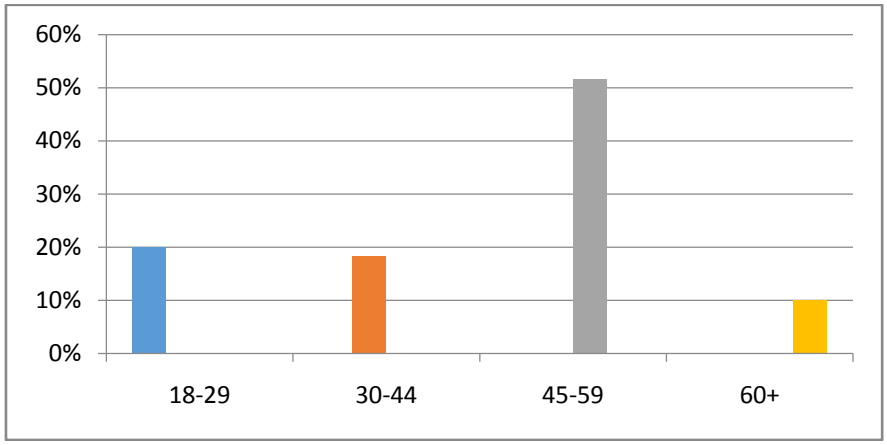
II. Results And Discussion

This study is done on patients with persistent proteinuria having varying degree of renal dysfunction.Patients with evidence of urinary tract infection,congestive heart failure,fever,hypertension and gross hematuria were excluded for the study.The total of sixty patients with persistent dipstick positive proteinuria were included in this study.The clinical evaluation and lab investigation were included in the profoma.Patients were segregated in to groups based on varying degrees of renal dysfunction and proteinuria.

The aim of the study was to evaluate whether the protein creatinine ratio in a spot urine sample is as reliable as 24 hours urine protein in quantification of proteinuria in patients with varying degrees of renal dysfunction and different levels of proteinuria.Results are tabulated and analysed for the following.

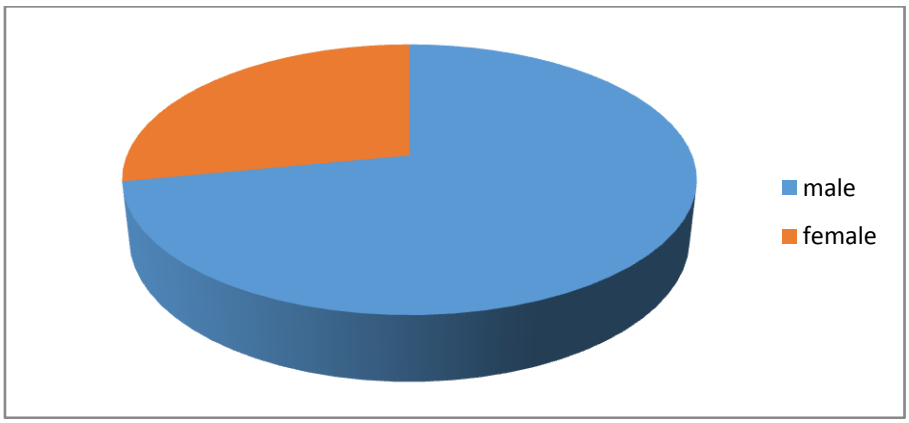
Persistent Proteinuria In Various Age Groups

Age in years	No. of Patients	Percentage
18-29	12	20
30-44	11	18.3
45-59	31	51.7
60+	6	10



In this study the incidence of proteinuria is maximum in the age group of 45-50 years(52%).Since the incidence of diabetes and hypertension increase with age and the consequence of microvascular disease due to these systemic disorders,also increases the persistent proteinuria is common as age advances.

SEX	NO OF PATIENTS	PERCENTAGE
Male	41	68
Female	19	32



The majority of primary glomerular diseases that are associated with proteinuria such as membranous nephropathy and secondary renal diseases such as diabetic nephropathy are more common in males than in females.

Hence,the prevalence of persistent proteinuria is atleast twice as common in males than in females. In our study,the ratio of males to the females with persistent proteinuria is 2.15:1.

Systemic Illness With Proteinuria

MEDICAL ILLNESS	NO. OF PATIENTS	PERCENTAGE
Diabetes	27	45
Hypertension	29	48.5
IHD	14	23.3
CVD	5	8.3
CRF	14	23.3
Vasculitis	2	3.3
Diabetes+Hypertension	23	38.3
Diabetes+Hypertension+IHD	10	16.7

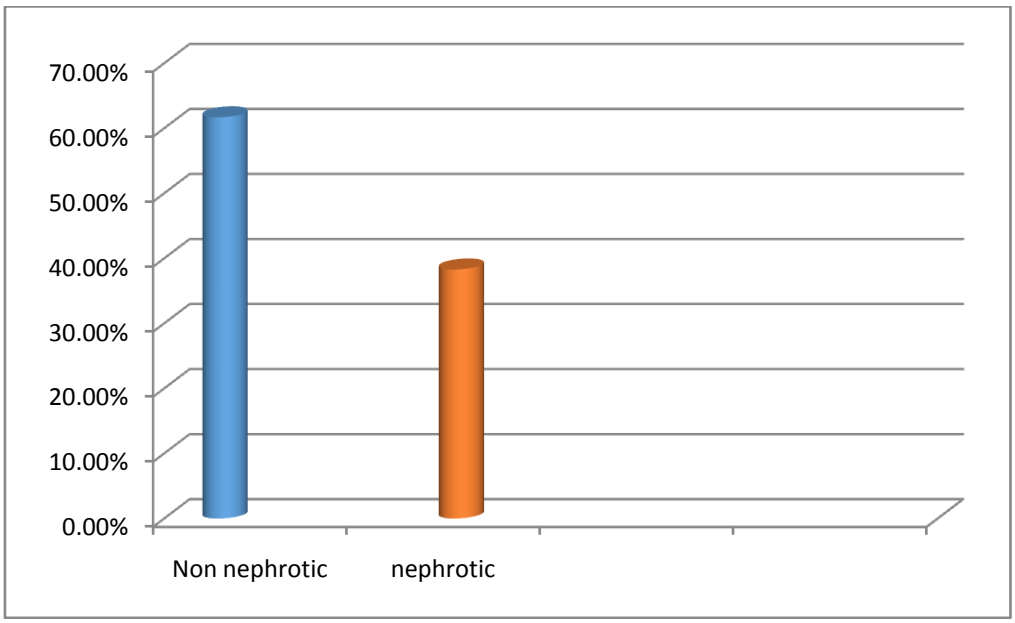
In our study,the systemic disorders hypertension and diabetes were present separately in 30 out of 60 patients(50%)with persistent proteinuria.Diabetes and Hypertension were present together in 23 patients(38%).IHD,CVD,CRF were present in 23%,8%,23% of patients respectively.

Mohan et al., and Vijay et al., showed in their study that the prevalence of diabetes related proteinuria was 9.4% and 18.7% respectively in patients with type 2 diabetes mellitus.Mersent et al.,showed in study that the presence of microalbuminuria in patients with type 1 diabetes mellitus is a useful marker for those patients at greater risk for the development of microvascular and macrovasculardiseases.The Framingham study concluded that when persistent proteinuria appears,the patient is likely to have or will soon develop hypertension,insulinresistance,cardiovascular disease or overt renal disease.Proteinuria with excess risk of death ,seems to be a marker for cardiovascular damage and adds to the end organ vulnerability effects of hypertension and diabetes.

Miettinen et al., evaluated the incidence of stoke in patients with proteinuria and showed that incidence of ischemic stroke in nondiabetic were 1.6% without proteinuria,3.2% with borderline proteinuria and 8.5% with clinical proteinuria.In another study on diabetes,the incidence were 7.2%,11.1%and 23% respectively.

Classification Of Patients Based On Degree Of Proteinuria

Proteinuria	No. Of Patients	Percentage
Non Nephrotic	37	61.7
Nephrotic	23	38.3



In this study,37 patients (61.7%) had proteinuria less than 3.5 gm/day.23 patients (38.3%) had proteinuria more than 3.5 gm/day.

The patients included in this study were segregated in to four group based on varying degrees of proteinuria and renal dysfunction.

GROUP 1A

Normal or mildly impaired renal function.Calculated creatinine clearance ≥50 ml/min and nephrotic proteinuria (>3.5 gm/day).

GROUP 1B

Normal to moderate impaired renal function.calculated creatinine clearance ≥ 50ml/min and nephrotic proteinuria (<3.5 gm/day).

GROUP 2A

Moderate to severe impaired renal function.calculated creatinine clearance <50 ml/min and nephrotic proteinuria (>3.5 gm/day).

GROUP 2B

Moderate to severe impaired renal function.calculated creatinine clearance <50 ml/min and nephrotic proteinuria (<3.5 gm/day).

Calculated Creatinine Clearance	Nephrotic Proteinuria	Non Nephrotic Proteinuria
≥ 50 Ml/Min	N=10(Group 1a)	N=18(Group 1b)
<50 Ml/Min	N=13(Group 2a)	N=19(Group 2b)

n=No. of patients in each group

Correlation between expected 24 hours urine protein with estimated 24 hours urine protein in patients with persistent proteinuria showing regression equation and the linear correlation is as follows

Group	Correlation Coefficient(r)
1A	0.8282
1B	0.9645
2A	0.8727
2B	0.9030

The results of this correlative study between the expected 24 hours urine protein obtained from the spot urine protein creatinine ratio and the estimated 24 hours urine protein showed that these values positively correlated well in patients with non nephrotic range of proteinuria with the best positive correlation in those patients with non nephrotic proteinuria and normal or mildly impaired renal function(Group 1B r=0.96,Group 2B r=0.90) the positive correlation was less in patients with nephrotic range of proteinuria with the least in those with nephrotic range of proteinuria and normal or mildly impaired renal function(Group 1A r=0.83,Group 2A=0.87).

Mohan et al., studied the correlation between the expected 24 hours urine protein calculated from spot urine protein creatinine ratio and the estimated 24 hours urine protein in type 2 diabetes.The positive correlation was good,but was less with increasing degrees of proteinuria.Correlation Coefficient (r) values were 0.96,0.86,0.74 in groups of patients with proteinuria <200 mg/day,201-999 mg/day and more than 1gm/day respectively.

Sharma et al., studied the correlation between the protein creatinine ratio in spot urine sample with 24 hours urine protein in patients with varying degrees of renal dysfunction and concluded a good positive correlation in patients with advanced renal failure.Correlation coefficient (r) values were 0.889,0.788,0.375 in patients with serum creatinine <1.5 mg/dl,1.5-4 mg/dl and >4mg/dl respectively.

Swach et al., showed that the product of protein creatinine ratio (in a random urine specimen) to estimated daily urinary creatinine excretion positively correlated well with the estimated 24 hours urine protein in patients with normal or mild to moderately impaired renal function (r=0.88 and 0.99) but poorly correlated in patients with advanced renal failure(r=0.56).

In our study the correlation between the expected 24 hours urine protein calculated from the spot urine protein creatinine ratio and the estimated 24 hours urine protein showed good positive correlation in patients with non nephrotic range proteinuria.The positive correlation was less than patients with moderate to severe renal dysfunction and non nephrotic range of proteinuria in compared more with normal or mildly impaired renal function with non nephrotic proteinuria(r=0.90 vs 0.96).The positive correlation better in patients with moderate to severe renal dysfunction and nephrotic range proteinuria when compared with those normal or mildly impaired renal function (r=0.87 vs 0.82).

Rodby et al., and Ruggenentietal., in their study have concluded that the 24 hours urine protein can be directly predicted from a random urine specimen by estimating protein creatinine ratio.

Viswanathan et al., in his study showed that estimated proteinuria calculated using the protein creatinine ratio in a random urine sample is useful in serial evaluation of kidney function on a follow up basis.

III. Conclusion

Estimation of 24 hours urine protein by using the protein creatinine ratio in the first morning urine sample is found to be an useful index for quantification of protein creatinine excretion in patients with varying degree of proteinuria and renal dysfunction. There was a good positive correlation between spot urine protein creatinine ratio and 24 hours urine protein in patients with non nephrotic range proteinuria with varying degree of renal dysfunction. In patients with nephrotic range of proteinuria,the positive correlation was less between the expected and the estimated 24 hours urine protein

This study shows that the protein creatinine ratio by themselves appear to indicate the presence and degree of proteinuria. It can , thus be used as an screening procedure for quantification of proteinuria even in an outpatient clinic as it requires only a spot urine sample.

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