ORIGINAL RESEARCH PAPER

Medical Science

STUDY OF SPOT URINARY PROTEIN CREATININE RATIO AS AN INDEX OF QUANTITATIVE PROTEINURIA

KEY WORDS:
Microalbuminuria, urine albumin measurement, albumin:creatinine ratio,

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ABSTRACT

INTRODUCTION Proteinuria is a condition in which urine contains an excess amount of proteins . Examination of urine is one of the most rewarding tests in clinical biochemistry ,as not only does it uncovers renal diseases but also frequently points to a specific diagnosis . Normal daily protein excretion in an adult does not exceed 150 mgs . Persistent proteinurea or microalbuminuria in any adult suggests not only the existence of renal disease but also an increased risk of MI and stroke .

AIMS AND OBJECTIVES To compare spot urine protein creatinine ratio with 24 hours urine protein as an index of quantitative proteinuria .

CONCLUSIONS

1) Protein creatinine in the first morning urine sample is found to be a useful index for quantification of proteinuria in pts with varying degree of proteinuria and renal dysfunction
2) There was a goood positive correlation between spot urine protein creatinine ratio and 24 hours estimated protein .
3) The correlation was best in pts with normal or mildly impaired renal function with no nephrotic range proteinuria .
4) The positive correlation was least in patients with moderate to severe renal dysfunction .
5) Urine protein creatinine ratio is easy to perform , inexpensive and less time consuming . it can be used in outpatient setting for screening and quantification of proteinuria .

Introduction

Proteinuria is a condition in which urine contains an excess amount of proteins . examination of urine is one of the most rewarding tests in clinical biochemistry ,as not only does it uncovers renal diseases but also frequently points to a specific diagnosis . Normal daily protein excretion in an adult does not exceed 150 mgs . Persistent proteinuria or microalbuminuria in any adult suggests not only the existence of renal disease but also an increased risk of MI and stroke .

Persistent proteinuria of >1gm/day, usually indicates renal disease. proteinuria may be minimal(,1gm/day), moderate(1-3 gm/day) and heavy (>3gm/day). current methods for measuring proteinuria vary significantly. commonly used methods are dipstick urine analysis , 24 hrs urine protein estimation and spot urine protein creatinine ratio. very few indian studies have compared the efficacy of 24 hrs urinary protein with spot urine protein creatinine ratio , which this study attempts to do .

Aims and objectives

To compare spot urine protein creatinine ratio with 24 hours urine protein as an index of quantitative proteinuria .

Pathophysiological classification of proteinuria

Benign	Pathological
Postural	Glomerular
Functional	tubular
Transient	overflow
Intermittent	secretory

Pathological proteinuria – this is persistent proteinuria that is detected on multiple ambulatory clinical visits . this is seen in both recumbent and upright positions

1) glomerular proteinuria – ranges from few hundred mgs to 100gm per 24 hours. Excretion of more than 2 gm per 24 hours is usually a result of glomerular disease . It is of 2 types - selective &non selective
2) Tubular proteinuria – causes are

Hypertensive nephrosclerosis
Tubulointerstitial diseases d/t-fanconi syndrome , heavy metals , uric acid nephropathy , acute hypersensitivity , interstitial nephritis , sickle cell disease , drugs(nsaids , antibiotics)

3) Overflow proteinuria- causes are ---multiple myeloma , myoglobinuria , rhabdomyolysis , lymphoproliferative disorders

Microalbuminuria – is defined as daily albumin excretion of 30-300 mg/mg creatinine in a spot collection . diseases such as diabetes and hypertension can manifest as microalbuminuria . it is thought to be the earliest sign of nephropathy in diabetes mellitus .

Whom to screen ?

1) Type 1 annually from 5 yrs after diagnosis
2) Type 2 annually from the time of diagnosis

Semiquantitative analysis by dipstick

Grade	Protein level
Negative	<10mg/dl
Trace	10-20 mg/dl
1+	30mg/dl
2+	100 mg/dl
3+	300 mg/dl
4+	>2000mg/dl

Urinary creatinine estimation was done by Folin's method on the photoelectric colorimeter.

Reagents used are :-

1. Creatinine Standard Solution .
2. Saturated Solution Of Picric Acid.
3. 10%(W/V) Sodium Hydroxide Solution.

Three Test tubes marked as unknown (U) , standard(S),& Blank (B) were taken. Their optical densities were measured on a photoelectric colorimeter and creatinine in 100 ml urine was calculated as

$$\text{Albumin (mg/dl)} \quad \textbf{ACR} \text{ (mg/g)} = \frac{\text{U-B/S-B} \times \text{creatinine standard (100 mg)}}{\text{Creatinine (mg/dl)}} \times 1000.$$

ACR (mg/g) can be calculated by albumin (mg/dl) divided by creatinine (g/dl).

Interconversion of units:

ACR (1 mg/g = 1 µg/mg = 0.113 mg/mmol). Dividing the ACR by 8.84 converts the units (from µg/mg or mg/g to mg/mmol. There is conversion factor for creatinine in various units . Another easy way

of conversion of creatinine is to convert mg/dl to g/L.

Urinary protein creatinine ratio-

The ratio is about the same numerical as the number of grams of protein excreted in urine per day . thus a ratio less than 0.2 is equivalent to 0.2 gms of protein/day and is considered normal and a ratio of 3.5 is equivalent to 3.5 gm of protein/day .

Interpretation of findings of microscopic examination of urine

Fatty casts , free fat or oval fat bodies	Nephritic proteinuria
Leukocytes , leukocyte cats with bacteria	UTI
Leucocytes , leucocyte casts without bacteria	Renal interstitial disease
Normal shaped erythrocytes	s/o lower UT lesions
Dysmorphic erythrocytes	s/o upper UT lesions
Erythrocyte casts	Glomerular disease
Eosinophiluria	Drug induced acute interstitial nephritis
Waxy granular casts	Adv CRF
Hyaline casts	Dehydration , diuretics

Methodology :-

The study was done from opd & ipd Patients reporting to Dept. of Biochemistry for Biochemical Analysis at Darbhanga Medical College & Hospital during the period of March 2017 to October 2018.

Inclusion criteria

1) Patient of either sex
2) Patient above 14 yrs
3) Patient with persistent dipstick positive proteinuria

Exclusion criteria

1) patients of age less than 14 yrs
2) gross hematuria
3) patients with a febrile illness
4) dehydration
5) head injury and cardiac failure

Observations

In this study the age ranged from 15-90 , the incidence of proteinuria was maximum in the age group 31-60 since the incidence of diabetes and hypertension increases with age , and as a consequence of micro vascular disease due to these systemic disorders persistent proteinuria is common as the age advances .

In this study , renal biopsy was performed as and when indicated .

Renal morphology	No of patients
Chronic GMN	10
Acute interstitial nephritis	6
MPGN	6
Membranous GMN	4
Diabetic nephropathy	4
Chronic interstitial nephritis	4
Crescentic GMN	2
Diffuse proliferative GMN	2
FSGS	2
IgA nephropathy	2

Classification of patients on basis of proteinuria

Proteinuria	No of pateints	percentage
Nephrotic	40	40
Non nephrotic	60	60

Calculated Crcl in patients with proteinuria

Calculated Crcl	No of pts	percentage
>50 ml/min	28	28
<50 ml/min	72	72

In this study 32 pateints had moderate to severe renal dysfunction with nephritic range proteinuria . There were 40 patients with moderate to severe renal dysfunction and non nephritic range proteinuria . 20 patients had normal to mild renal dysfunction with non nephritic range proteinuria and 8 pts had a normal to mild renal dysfunction with nephritic range proteinuria .

There was a good correlation between spot urine protein creatinine and 24 hrs urine protein . the correlation was best in patients with creatinine clearance >50 and non nephrotic range proteinuria . the correlation was least in patients with crcl<50 and non nephrotic range proteinuria .

SUMMARY & CONCLUSIONS

(1) Protein creatinine in the first morning urine sample is found to be a useful index for quantification of proteinuria in patients with varying degree of proteinuria and renal dysfunction.
(2) There was a positive correlation between spot urine protein creatinine ratio and 24 hours estimated protein .
(3) The correlation was best in patients with normal or mildly impaired renal function with no Nephrotic range proteinuria .
(4) The positive correlation was least in patients with moderate to severe renal dysfunction .
(5) Urine protein creatinine ratio is easy to perform , inexpensive and less time consuming . it can be used in outpatient setting for screening and quantification of proteinuria .
(6) In this study 100 pts with a varying degree of proteinuria and creatinine clearance were investigated. An excellent correlation was found between 24 hours urine protein and protein creatinine ratio . This study supports the use of single voided protein creatinine ratio to predict 24 hours urinary protein . it avoids collection errors , less time consuming and is suitable for OPD PATIENTS .

REFERENCES

1) Cameron JS The pateint with proteinuria and/or hematuria
2) Oxford textbook of clinical nephrology
3) Denker & Brenner - azotemia and urinary abnormalities .
4) Harrisons Principles of Internal Medicine
5) Alder sg- The pateint with hematuria , proteinuria or both and abnormal urinary finding on microscopy .
6) Keane wf -Proteinuria ; its clinical imporatnce and role in progressive renal disease
7) Carrol mf proeinuria in adults : a diagnostic approach
8) Bectham r , catell wr . proteinuria :pathophysiology , significance and recommendation for measurement in clinical practice . Khosla N, Sarafidis PA, Bakris GL. Microalbuminuria. Clin Lab Med 2006;26(3):635-53.
9) David B, Sacks MB. Carbohydrates. In: BurtisCA, Ashwood ER, Bruns DE (ed). Tietz textbook of clinical chemistry and molecular diagnostics, 4 th edition, (Indian reprint). New Delhi, Saunders an imprint of Elsevier, 2006;837-901.
10). Sarafidis PA, Khosla N, Bakris GL. Antihypertensive therapy in the presence of proteinuria. Am J Kidney Dis 2007;49(1):12-26.
11). Molitch ME, DeFronzo RA, Franz MJ, Keane WF, Mogensen CE, Parving HH, Steffes MW. American Diabetes Association: Nephropathy in diabetes. Diabetes Care 2004;27(suppl 1):S79-83.
12). Kessler MA, Meinitzer A, Petek W, Wolfbeis OS. Microalbuminuria and borderline-increased albumin excretion determined with a centrifugal analyzer and the Albumin Blue 580 fluorescence assay. Clin Chem 1997;43(6):996-1002.
13. Olivarius ND, Mogensen CE. Danish general practitioners' estimation of urinary albumin concentration in the detection of proteinuria and microalbuminuria. Br J Gen Pract 1995;45(391):71-3.
14). Waugh J, Bell SC, Kilby MD, Lambert PC, Blackwell CN, Shennan A, et al. Urinary microalbumin/creatinine ratios: reference range in uncomplicated pregnancy. Clin Sci (Lond) 2003;104(2):103-7.
15). Sarafidis PA, Riehle J, Bogojevic Z, Basta E, Chugh A, Bakris GL. A comparative evaluation of various methods for microalbuminuria screening. Am J Nephrol 2008;28(2): 324-9.
16). Dyer AR, Greenland P, Elliott P, Daviglus ML, Claeys G, Kesteloot H, et al; INTERMAP Research Group. Evaluation of measures of urinary albumin excretion in epidemiological studies. Am J Epidemiol 2004;160(11):1122-31.
17). Lambers Heerspink HJ, Brantsma AH, de Zeeuw D, Bakker SJL, de Jong PE, Gansevoort RT; PREVEND Study Group. Albuminuria assessed from first-morning-void urine samples versus 24-hour urine collections as a predictor of cardiovascular morbidity and mortality. Am J Epidemol 2008;168(8):897-905.
18). Keane WF, Eknoyan G. Proteinuria, albuminuria, risk, assessment, detection, elimination (PARADE): a position paper of the National Kidney Foundation. Am J Kidney Dis 1999;33(5):1004-10.
19). American Diabetic Association: Standards of medical care in diabetes-2009. DiabetesCare 2009;32(suppl 1):S13-S61.
20). Levey AS, Coresh J, Balk E, Kausz AT, Levin A, Steffes MW, et al; National Kidney Foundation. National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Ann Intern Med 2003;139(2):137-47.
21. Halimi JM , Hadjadj S, Aboyans V, Allaert FA, Artigou JY, Beaufils M, et al. Microalbuminuria and urinary albumin excretion: French clinical practice guidelines. Diabetes Metabo 2007;33(4):303-9.
22). WeekersL, Scheen AJ, LefebvrePJ. How I evaluate...diabetic nephropathy. First part: micro-and macroalbuminuria. Rev Med Liege 1998;53(8):494-8.
23). Yusuf S, Reddy S, Ounpuu S, Anand S. Global burden of cardiovascular diseases: Part I: general considerations, the epidemiologic transition, risk factors, and impact of urbanization. Circulation 2001;104(22):2746-53.

24). McQueen MJ, Don-Wauchope AC. Requesting and interpreting urine albumin measurements in the primary health care setting. Clin Chem 2008;54(10):1595-7.
25) Robert WL, McMillin GA, Burtis CA, Bruns DE. Reference information for the clinical laboratory. In: Burtis CA, Ashwood ER, Bruns DE (ed). Tietz textbook of clinical chemistry and molecular diagnostics, 4thedition, (Indian reprint). New Delhi, Saunders an imprint of Elsevier, 2006;2251-2318