COMPARISON OF FIRST MORNING VOID URINE SPECIMEN FOR ALBUMIN TO CREATININE RATIO COMPARING WITH 24-HOUR URINARY ALBUMIN EXCRETION IN DETECTING MICROALBUMINURIA IN TYPE 2 DIABETICS

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ABSTRACT

Objectives: To determine the accuracy of first morning void urine specimen for Albumin to Creatinine Ratio (ACR) comparing with 24-hour urinary albumin excretion in detecting microalbuminuria in type 2 diabetics.

Study Design: Cross Sectional study

Place and Duration of Study: Military Hospital Rawalpindi, from Apr 2013 to Oct 2013.

Patients and Methods: One hundred & twenty patients with type 2 Diabetes Mellitus (DM) fulfilling the inclusion criteria were included in study using consecutive non-probability sampling. A standard protocol was followed for specimen collection. Urine collection was started from the next day of admission.

Results: Mean random plasma glucose level was 174.54 ± 33.06 mg/dL, mean HbA1c was 8.5 ± 1.32 %, mean urinary albumin 130.26 ± 47.25 mg/24 hour and mean ACR was 104.30 ± 51.56 mg/g. Area under ROC curve was 0.964 for microalbuminuria by ACR. Spearman's rank-order coefficient (rs) was 0.696 for ACR and 24 hour albumin excretion.

Conclusion: ACR in first morning void urine accurately detected early microalbuminuria in type 2 diabetics.

Keywords: Albumin to Creatinine Ratio, Diabetes Mellitus, Microalbuminuria, 24 Hour Urinary Albumin.

INTRODUCTION

Globally, DM has emerged as one of the important public health problems in recent past. According to International Diabetic Foundation, an estimated 366 million people had DM in 2011; by the year 2030 this figure will rise to 552 million[1]. DM constitutes a major health problem in Pakistan with a prevalence of 12% in Punjab province[2]. Diabetic nephropathy remains the leading cause of End Stage Renal Disease (ESRD) and accounts for about 40% of all cases of Chronic Kidney Disease (CKD)[3,4].

An increased albuminuria is associated with an increased risk of progressive renal failure, cardiovascular diseases and death[4]. The conventional 24-hour urine collection is a cumbersome procedure and is subject to collection errors. Many professional organizations are now advocating for random urine sample collection and reporting the Urinary Albumin Concentration (UAC) or ACR based on various studies[5,6].

There are certain problems related to creatinine estimation in a muscular person with high creatinine excretion rates, albumin excretion will be underestimated and in a cachectic patient it will be overestimated[7]. A validation study has shown 83% sensitivity of ACR in patients with type 2 DM at the cut off value of >30mg/24-hour for urinary albumin excretion[5].

Limited local data is available to assess the accuracy of ACR in detecting microalbuminuria as compared to 24-hour urinary albumin excretion in diabetics. This study is planned to explore the accuracy of first morning void urine specimen for ACR for detecting microalbuminuria, in type 2 diabetics and this can later on be recommended for early diagnosis of microalbuminuria.

MATERIAL AND METHODS

This cross sectional study was carried out at MH Rawalpindi from April 2013 to Oct 2013. Permission from hospital ethical review committee was taken. Sample size was

calculated using WHO calculator for sample size determination in health studies keeping Confidence level = 95%, Absolute precision = 7%, Anticipated population proportion = 83%. A total number of one hundred and twenty patients with type 2 DM were selected after taking informed written consent.

Inclusion criteria: Adult (36-60 years) patients with type 2 DM on oral hypoglycemic agents and/or insulin who were admitted or

conditions, Connective tissue disorders like SLE, Obstructive uropathy, Hypertension, Pregnant women, Past history of hospitalization for hemodialysis and the renal transplant.

A brief history was taken from each patient including onset and duration of DM, medication history and various macro vascular complications. A brief clinical exam was carried out to find out complications of DM. A standard protocol was followed for urinary

Table 1:Age distribution of patients among cases.

Age Distribution		
Age (Years)	No of Cases	Percentage
36-40	28	23.3
41-45	30	25.0
46-50	44	36.7
51-55	13	10.8
56-60	5	4.2
Total	120	100.0
Mean + SD	45.14 + 5.59	

Table 2: Gender distribution of patients among cases.

Gender	No of Cases	Percentage
Male	74	61.8
Female	46	38.2
Total	120	100.0

Table-3: Variables of the patients.

Variables	Unit	Mean + SD (n=120)
Random plasma glucose level	mg/dL	174.54 + 33.059
HbA1c	%	8.5 + 1.32
24-hour Urinary Albumin	mg/24 hour	130.26 + 47.25
Albumin- Creatinine Ratio	mg/g	102.16 + 54.29

Table-4: The association between the ACR and 24 hours albumin excretion.

Correlations				ACR	24h AER
Spearman's rho	ACR	Correlation Coefficient		1.000	.696**
		Sig. (2-tailed)			.000
		N		120	120
	24 hour AER	Correlation Coefficient		.696**	1.000
		Sig. (2-tailed)		.000	
		N		120	120

**Correlation is significant at the 0.01 level (2-tailed).

willing for hospitalization for 24 hours for collection of urinary samples.

Exclusion Criteria: Patients with following conditions were excluded from study:- Urinary tract infection, Chronic renal failure, Glomerulonephritis due to other systemic

sample collection. Urine collection was started from next day of admission. First urine voided in the morning was collected in container-1 for ACR and the urine passed subsequently on the same day till next morning first void/till completion of 24 hour was collected in container-2 for 24 hour urinary albumin. No

specific recommendations were made to the patients about fluid intake or diet. Samples for random plasma glucose were taken irrespective of meal timings (cut off value =11.1 mg/dl).

All the parameters were carried out in clinical laboratories affiliated with the hospital and reports were verified by a qualified pathologist.

Laboratory Analysis

Various parameters included in study were urine albumin and creatinine. Urine albumin was analyzed using Albumin Tina-quant Roche/Hitachi reagent kit, based on immunoturbidimeteric technology. Urine creatinine was measured by the Jaffé assay using Beckman UniCel® DxC 600 Synchron® Clinical System(Lot numbers of kit not aviable). ACR was calculated by dividing the UAC with urinary creatinine concentration. All the data was entered in a specially designed proforma attached as Annexure A. Data analysis was done by using SPSS 20 statistical software. Descriptive statistics for qualitative variables like gender were calculated as frequency and percentages. Descriptive statistics for quantitative variables like age, random plasma glucose level, HbA1C, 24-hour urinary albumin and ACR were shown as mean and SD. Receiver Operating Characteristic (ROC) curves was calculated to compare the discriminative power of the ACR to 24-hour urinary albumin. The correlation of ACR with 24-hour urinary albumin was tested with Spearman's coefficient.
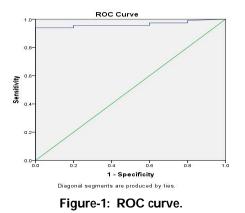
RESULTS

A total of 120 patients fulfilling the inclusion/exclusion criteria were included in study. Subjects showed a mean age 45.14 + 5.59 years (Table - 1). About 36.7% (n=44) of patients were between 46-50 years. In our study, there were 61.8% (n=74) males and 38.2% (n=46) females (table-2). Mean random plasma glucose level was 174.54 + 33.059 mg/dL, mean HbA1c was 8.5 + 1.32 %, mean urinary albumin 130.26 + 47.25 mg/24 hour and mean ACR was 102.16 + 54.29 mg/g (Table - 3). ROC curve for ACR and microalbuminuria showed 0.964% area under the curve with 95% confidence interval

(fig-1). The best discriminator was 28.15 mg/g creatinine with sensitivity of 95.7% and specificity of 80.0%. Spearman's rank-order coefficient was 0.696 which showed significant association between ACR and 24 hour albumin excretion (table-4).

DISCUSSION

DM has now become the top most common cause of ESRD in the USA and Europe[8]. Microalbuminuria is the initial biochemical marker of diabetic nephropathy when it is incipient. Progression to overt nephropathy from microalbuminuria occurs in around 20-40% diabetics over a period of 10-years. Out of these approx. 20% of the patients ultimately progress to ESRD requiring renal replacement therapy[9].

Figure-1: ROC curve.

In all patients with newly diagnosed type 2 DM, a test for the presence of microalbuminuria must be carried out at the time of diagnosis because of the difficulty in predicting the exact time of the onset of type 2 DM. On the other hand in patients with type 1 DM, microalbuminuria occurs rarely with shorter duration of disease; therefore, in such patients screening should start after at least 5 years of disease duration. However, there is some evidence suggesting the importance of prepubertal duration of DM in the development of microvascular complications; therefore, clinicians should apply their judgment to individualize these recommendations. After the initial screening as well as in the absence of previously documented microalbuminuria, testing for microalbuminuria should be carried out annually in all diabetics. 24-hour urine

collection is considered the gold standard test for estimating urinary albumin excretion[10]. since urinary albumin excretion follows a circadian rhythm. Various mechanisms like orthostasis, variations in GFR, blood pressure and serum albumin concentration explain the diurnal variations in albuminuria[11]

The test which has been found to be the easiest to perform is urinary ACR. It can be performed in a clinic setting as outdoor patient and generally considered to provide accurate information and hence is the preferred choice.

Based upon the results of our study, diabetic patients may be offered ACR on first morning void urine specimen for timely diagnosis hence prevention of diabetic nephropathy. This will significantly reduce the incidence of diabetic nephropathy, progression to ESRD and improve the quality of life in patients with DM.

The findings of our study are in agreement with a study carried out by Sampaio et al. This study shows the sensitivity of ACR is 83% in type 2 diabetics using cut off value of >30mg/24-h for urinary albumin excretion[5].

Incerti J et al in the assessment of different tests for microalbuminuria screening in diabetic patients concluded 100% sensitivity and 73.0% specificity at cut off value of 15.7 mg/g for urine ACR[12].

However, there is a limitation of ACR. Variation in muscle mass can affect ACR, because urinary creatinine concentration is a reflection of muscular mass. Thus in a person with lower body muscle mass, urinary creatinine will be low accordingly leading to an over estimation of ACR[13].

CONCLUSION

ACR in first morning urine specimens had similar accuracy in screening microalbuminuria in type 2 diabetic patients when compared to 24-hour urinary albumin excretion and all patients with DM should be offered urinary ACR on first morning urine specimens for timely diagnosis of diabetic nephropathy. ACR can be carried out in OPD settings obviating the need to admit the patient as in case of 24-hour urinary excretion thus reducing burden on health care system and at the same time convenient to the patient as well.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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