



Original Research Article

Random Urine Microalbumin: Creatinine Ratio as a Better Diagnostic Marker of Progression of Chronic Kidney Disease in the High Risk Population - A Pilot Study

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Received: 01/02/2015

Revised: 19/02/2015

Accepted: 21/02/2015

ABSTRACT

Introduction: Chronic kidney disease (CKD) is a world health concern as its prevalence is increasing especially in the high risk population, i.e., patients suffering from type 2 diabetes mellitus (DM) or/and hypertension (HT). Microalbuminuria is considered as the best tool for early detection of renal damage. Although, different sample types and estimation techniques are used for quantification of urine microalbumin, the results are dependent on the accuracy of sample collection since 24 hours urine sample is needed. This study aims at comparing the efficacy of a random sample with the conventional 24 hours sample of urine.

Materials and Methods: Parameters such as urinary microalbumin, microalbumin : creatinine ratio in the random sample and microalbumin in the 24 hours sample were estimated and correlated with the various glycemic and hypertension markers in the 60 study subjects.

Results and Discussion: The results show that although all the three parameters had positive correlation with the markers of glycemia and hypertension, the urine microalbumin creatinine ratio of the random sample has better positive correlation. Hb_{A1c}, FBS and SBP ($r = 0.525, 0.458$ and 0.324 respectively) have better correlation with the microalbumin creatinine ratio. In conclusion, this preliminary investigation suggests that screening for MAU in a random sample of urine is better than 24 hours urine sample, even when the adequacy of 24 hours urine collection is validated, to identify the high risk population at a very early stage. In addition the data also suggests that, controlled FBS and SBP play a major role in the prevention and progression of CKD.

Key words: Chronic Kidney Disease (CKD), Microalbumin, Microalbuminuria, Microalbumin creatinine ratio (MAU)

INTRODUCTION

Chronic kidney disease is a common disorder among type 2 diabetics and hypertensives and its prevalence is increasing worldwide. [1,2] Early diagnosis on the basis of microalbuminuria (MAU) or decreased estimated glomerular filtration rate (eGFR) can lead to early intervention to reduce the

risks of End Stage Renal Disease (ESRD) and cardiovascular disease (CVD). [3,4] In developed countries, screening for the disorder in the high-risk groups including elderly people and those with concomitant illness such as diabetes, hypertension, or CVD or a family history of chronic kidney

disease is most efficient. [5,6] Effective strategies are available to slow the progression of CKD to ESRD and thus reduce the cost. [7-9] However, in developing countries like India, such screening protocols are not followed.

Microalbumin test measures albumin concentration in urine, which is not detectable by the conventional dipstick test or proteinuria test, and is used to identify the early renal damage in the high risk population for CKD, i.e., either Type 2 diabetes mellitus or hypertension or patients suffering from both. Since proteinuria, by the time it is detected, causes significant damage to kidney, there is a need for early detection using urine microalbumin so as to prevent further progression to kidney disease. [2,10-13]

There are different sample types and reporting methods practiced for urinary albumin excretion for the assessment of renal involvement. [12,14,15] This study aims to identify the diagnostic accuracy of microalbumin levels reported using two different sample types, i.e., random sample and 24 hours sample, and their correlation with the glycation status and the blood pressure to identify the better sample type.

MATERIALS AND METHODS

60 subjects were selected for the study. Anthropometric measurements taken and are recorded. Samples were collected after getting informed consent. Blood (4 mL) was drawn from all the subjects after 10 - 12 hours fasting, 2 mL was transferred in to fluoride tube for fasting blood glucose (FBG), and remaining 2 mL was transferred to EDTA tube. Random urine sample was also collected. 24 hours urine samples were collected from all the participants. A sample of blood (2 mL) was collected 2 hours after food for measurement of Post prandial blood glucose (PPBS). Hb_{A1c} was estimated using HPLC method in EDTA blood on Bio-Rad D-10 analyser (Bio-Rad, USA) and is reported as percent. Random urine is

analysed for microalbumin and urine creatinine on Beckman AU 480 analyser (Beckman, Germany) and the microalbumin creatinine ratio (MAU) is calculated as mg of microalbumin per gram of creatinine (Equation 1). 24 Hr urine was analysed for microalbumin and is calculated as mg of microalbumin per day (Equation.2.). FBG and PPBS were analysed using the hexokinase method on Beckman AU 480 analyser. The random urine microalbumin, microalbumin creatinine ratio and the 24 hr urine microalbumin is compared against the Hb_{A1c} levels, average blood glucose level calculated from Hb_{A1c}. (Equation.4.), FBG, PPBS, Diastolic Blood Pressure and the Systolic Blood Pressure using the pearson correlation coefficient.

The adequacy of 24 Hour urine collection was evaluated using the measurement of creatinine of 24 hour urine collection of all the subjects and the excretion of creatinine in urine per kg per day is calculated using the Equation 5. Levels less than 14mg/kg/day in men and less than 11mg/kg/day in women indicated inadequate collection. [16,17]

Equation 1.

$$\text{Microalbumin creatinine ratio} = \frac{\text{Microalbumin in mg/L}}{\text{Creatinine in mg/dL}} \times 100$$

in mg/g of creatinine

Equation 2.

$$24 \text{ Hr microalbumin} = \frac{\text{Microalbumin in mg/L} \times 24 \text{ Hr Urine Volume in mL}}{1000}$$

in mg per day

Equation 3.

$$\text{UAER} = \frac{\text{Microalbumin in mg/L} \times 24 \text{ Hr Urine Volume in L} \times 1000}{24 \text{ hrs in minutes (ie } 24 \times 60 = 1440)}$$

in ug/min

Equation 4.

$$\text{Estimated Average Glucose (eAG)} = (28.7 \times \text{Hb}_{A1c}) - 46.7$$

in mg/dL

Equation 5.

$$\text{Excretion of Cr} = \frac{\text{Creatinine in 24 Hr Urine in mg} \times 24 \text{ Hr Urine volume in Deciliters}}{\text{Weight in kg}}$$

in mg/Kg/Day

RESULTS

The adequacy of the 24 hour urine collection was verified in all subjects and since right information for collection was given to all participants in the study. All the 24 Hours Urine collections done were adequate (Figure 1.). Glycemic markers and blood pressure were compared using Pearson correlation and are shown in the Table 1. It was found that the microalbuminuria is better correlating with the Hb_{A1c} levels ($r=0.525$ & $p<0.0001$) compared to 24 Hr urine microalbumin ($r=0.504$ & $p<0.0001$) and random microalbumin ($r=0.507$ & $p<0.0001$). It was also noted that the Fasting Blood Glucose ($r=0.458$ & $p=0.0002$) in glycemic

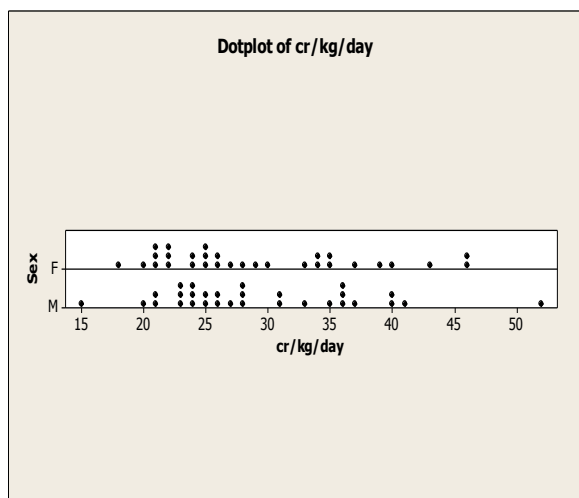


Figure 1. Verification of adequacy of 24 Hr Urine sample collection
Cr: Creatinine, M: Male, F: Female.

status and the systolic blood pressure ($r=0.324$ & $p=0.0133$) among blood pressure were better correlating with the microalbumin creatinine ratio (Figure 2 - 7.). The study concludes that the microalbumin creatinine ratio in random urine is a good tool for evaluation of progression of CKD in patients with type 2 diabetes and hypertension (Figure 8). The strict control of the routine measurements, fasting blood glucose and the Systolic blood pressure, has a profound effect in controlling the microalbumin and thus limiting the progression of CKD in high risk population as they have a better correlation with microalbumin creatinine ratio.

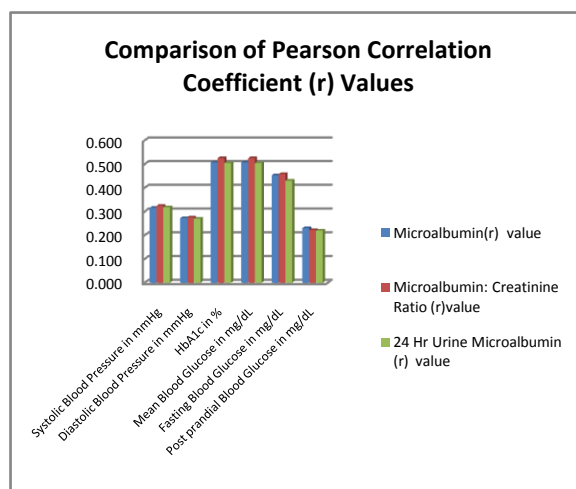


Figure 2. Comparison of Pearson Correlation Coefficient (r) value

The results show that the Hb_{A1c} is the most correlating measurement with all the three Microalbumin Measurements. In Glycemic Markers Fasting Blood Sugar and in Blood Pressure Systolic Blood Pressure has better correlation to the Urine Microalbumin Measurements. In all the three microalbumin measurements microalbumin creatinine ratio has better correlation than the microalbumin in random and 24 Hour urine sample.

Table 1. Correlation of microalbumin using different sample type against glycemic markers and blood pressure

Parameters (n=60)	Microalbumin (r) / p value	Microalbumin: Creatinine Ratio (r) / p value	24 Hr Urine Microalbumin (r) / p value
Systolic Blood Pressure in mmHg	0.316/0.0139†	0.324/0.0133†	0.318/0.0115†
Diastolic Blood Pressure in mmHg	0.272/0.0356†	0.275/0.0335†	0.270/0.0367†
Hb _{A1c} in %	0.507/<0.0001*	0.525/<0.0001*	0.504/<0.0001*
Mean Blood Glucose in mg/dL	0.507/<0.0001*	0.525/<0.0001*	0.504/<0.0001*
Fasting Blood Glucose in mg/dL	0.453/0.0003*	0.458/0.0002*	0.430/0.0006†
Post prandial Blood Glucose in mg/dL	0.230/0.0775†	0.222/0.088†	0.220/0.0908

* Very high correlation, † Moderate Correlation, r=Pearson correlation coefficient.
Systolic Blood pressure among blood pressure and Fasting blood sugar among Blood glucose is better correlation with all microalbumin measurements (low p value). Among the microalbumin sample types all parameters better correlates with the microalbumin creatinine ratio.

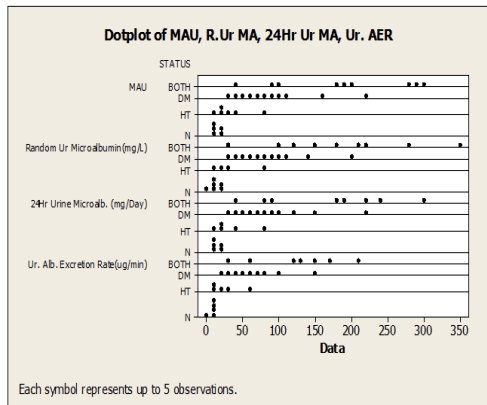


Figure 3. Dot plot of Urine random microalbumin, microalbumin creatinine ratio, 24 hr urine microalbumin and Urine albumin excretion rate in the four study groups

N: Control Population, HT: Hypertensive group, DM: Type 2 Diabetic group & Both: Subjects with both Hypertension and type 2 Diabetes Mellitus. R. Ur MA: Urine Random Micro albumin in mg/L, MAU: Microalbumin Creatinine Ratio in mg/g of creatinine, 24 Hr Ur MA: 24 Hr Microalbumin in mg/Day, Ur AER : Urine albumin excretion rate in ug/min.

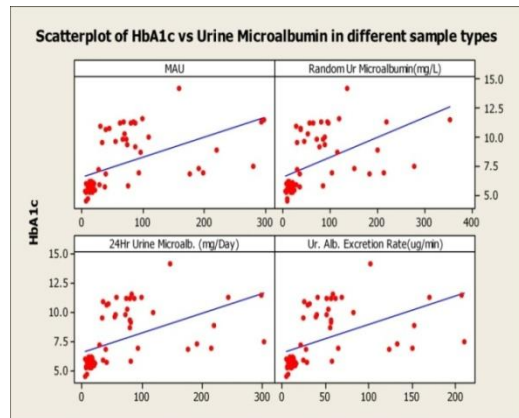


Figure 4. Scatter plot of Urine random microalbumin, microalbumin creatinine ratio, 24 hr urine microalbumin and Urine albumin excretion rate against HbA_{1c}

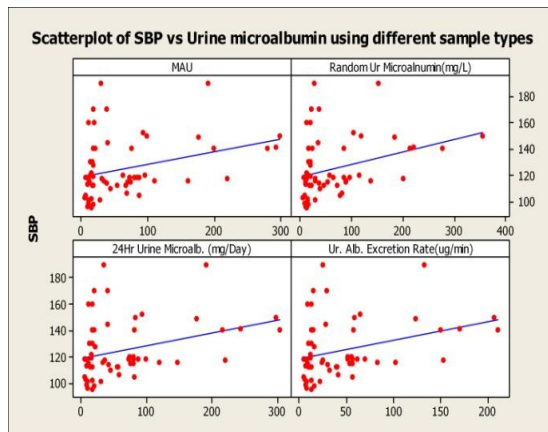


Figure 7. Scatter plot of Urine random microalbumin, microalbumin creatinine ratio, 24 hr urine microalbumin and Urine albumin excretion rate against Systolic Blood pressure
 MAU: Microalbumin Creatinine Ratio in mg/g of creatinine, SBP : Systolic blood pressure in mmHg.

MAU: Microalbumin Creatinine Ratio in mg/g of creatinine

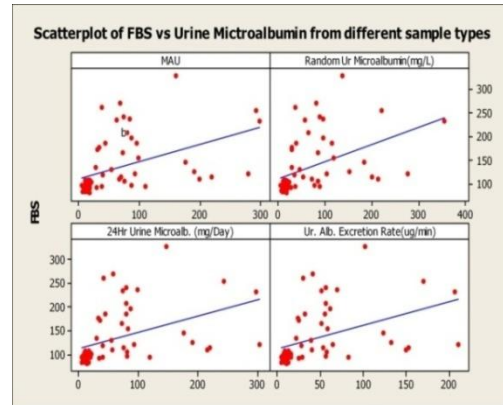


Figure 5. Scatter plot of Urine random microalbumin, microalbumin creatinine ratio, 24 hr urine microalbumin and Urine albumin excretion rate against Fasting Blood Glucose

MAU: Microalbumin Creatinine Ratio in mg/g of creatinine, FBS: Fasting Blood Glucose

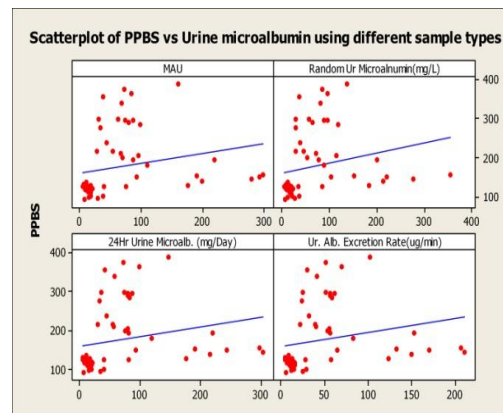


Figure 6. Scatter plot of Urine random microalbumin, microalbumin creatinine ratio, 24 hr urine microalbumin and Urine albumin excretion rate against Postprandial Blood Glucose
 MAU: Microalbumin Creatinine Ratio in mg/g of creatinine, PPBS: post prandial blood glucose in mg/dl

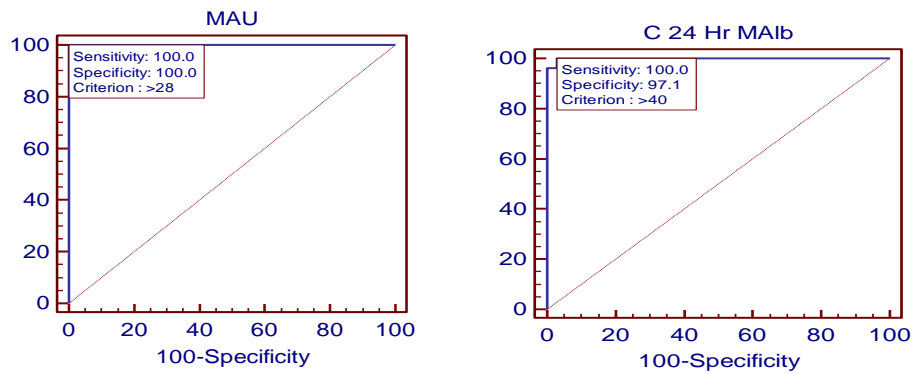


Figure 8. ROC curve of Microalbumin creatinine ratio and 24 Hour Urine Creatinine
 MAU: Microalbumin Creatinine Ratio, C 24 Hr MAIb: 24 Hur Urine Microalbumin

DISCUSSION

There have been contradictory reports regarding sampling types used for the estimation of microalbuminuria. 24 hr urine microalbumin and urine microalbumin excretion rate has been used as reference procedures for the microalbumin measurements. Timed sample collection is always inadequate and most often incomplete which leads to non reproducible results which intern affects the clinical decision making. Random urine microalbumin reported in mg/dL is always affected the hydration status. Random urine microalbumin creatinine is a better choice as it is gives reproducible results which are well correlating with the glycemic status and hypertension. A higher positive correlation of fasting blood glucose to microalbuminuria is seen in the present study ($r=0.458/p=0.0002$) than reported by A. Schmitz et al reported in their 10 year follow up study in 503 Denmark type 2 Diabetic subjects($r=0.12/ p<0.01$). [18] It is also recommended that the high risk population for CKD need to screened for microalbuminuria for preventing the progression of CKD to ESRD and CVD.

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How to cite this article: Mathew R, Pai VR, Vijayakumar T. Random urine microalbumin: creatinine ratio as a better diagnostic marker of progression of chronic kidney disease in the high risk population - a pilot study. *Int J Health Sci Res*. 2015; 5(3):183-188.
