Original Article

Albumin: Creatinine Ratio during long term Diabetes Mellitus in the Assessment of early Nephropathy in Sudanese Population

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ABSTRACT

Background: Diabetic nephropathy is one of the major causes of chronic renal failure. Microalbuminuria (MAU) has been recognized as an independent and reliable predictor for future development of overt proteinuria in diabetic patients.

Objectives: This descriptive cross-sectional study was carried during the period of January-April 2012, in Omdurman Teaching Hospital, to determine Microalbuminuria creatinine ratio, in long term Diabetic patients.

Materials and Methods: Immunoturbidmetric method was used to asses' microalbuminuria in 50 cases (50%) and 50 controls (50%). Ordinary chemical method (Jaffe reaction) was used for the determination of creatinine for both the groups.

Results: Microalbuminuria in Diabetic patients showed an increase when compared with the control group with P value 0.000. Similarly creatinine also showed an increase in diabetic patients.

Conclusion: It was concluded and is in further affirmation of the previous studies that microalbuminuria should be used as an early indicator for Diabetic Nephropathy. Further studies with 24 hour urine sample are recommended for assessment of Microalbuminuria in long term Diabetic patients, provided that the patients are on a normal diet with regular treatment for diabetes.

Key words: Microalbuminuria, Creatinine, Diabetes mellitus, Nephropathy.

Diabetes mellitus is a metabolic disorder characterized by chronic hyperglycemia due to derangement in carbohydrate, fat and protein metabolism that are associated with absolute or relative deficiencies in insulin secretion, insulin action or both[1,2]. Over 170 million people worldwide and about 2.6% of the Sudanese population are affected[3].

Different statistics have led to diabetes being described as one of the main threat to human health in the 21st century[4]. DM is the major cause of renal morbidity and mortality, and diabetic nephropathy is one of the reasons for chronic kidney failure[5]. Non-nephritic protienuria, nephrotic syndrome and chronic renal failure are the most common lesions involving the glomeruli[6]. Diabetes nephropathy is the kidney disease that occurs as a result of diabetes. After many years of diabetes the delicate filtering system in the kidney becomes destroyed, initially becoming leaky to larger blood proteins such as albumin which are then lost in urine. This is more likely to occur if the blood sugar is poorly controlled[7]. The recommended albumin (µg)/creatinine (mg) ratio (ACR) (30 µg/mg) to detect microalbuminuria does not account for sex or racial differences in creatinine excretion. In a nationally representative sample of subjects, the distribution of urine albumin and creatinine concentrations was examined by using one ACR value (≥30 µg/mg) and sex-specific cutpoints (≥17 µg/mg in men and ≥25 µg/mg in women) measured in spot urine

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specimens. Microalbuminuria (MAU) has been recognized as an independent and reliable predictor for future development of overt proteinuria in diabetic patients. It represents the condition in which minute quantities of albumin not detectable by simple urine dipstick are excreted into the urine. MAU is associated with a form of diabetic nephropathy that has a high morbidity and mortality as well as with coronary artery diseases. Furthermore, there have been many reports on the correlation of MAU with an increasing incidence of diabetic retinopathy. Therefore, MAU is an important biomarker for predicting complications of diabetic patients. In cases where high blood sugar control was successful, MAU also decreased.

Microalbuminuria is an independent predictor of cardiovascular disease and all-cause mortality in both diabetic[8] and nondiabetic men and women[9], and may be a stronger indicator for future cardiovascular events than systolic BP (SBP) or serum cholesterol[10]. Detecting microalbuminuria is an important screening tool to identify people who are at high risk for cardiovascular events and the progression of kidney disease and who need more intensive therapy compared with subjects with normal albumin excretion rates[11]. According to the American Diabetes Association (ADA), the gold standard for measuring urine albumin excretion is a 24-h urine collection[10]. However, a more convenient method to detect microalbuminuria is the albumin (μg)/creatinine (mg) ratio (ACR) measured in a random urine specimen[12]. Currently, the National Kidney Foundation recommends the use of spot urine ACR obtained under standardized conditions (first voided, morning, midstream specimen) to detect microalbuminuria. The ACR is a more convenient test for patients and may be less prone to errors due to improper collection methods and variations in 24-h protein excretion compared with a random urine specimen[13].

The ADA and the National Kidney Foundation define microalbuminuria as an ACR between 30 to 300 μg/mg in both men and women[10,11]. These guidelines do not take into account sex differences in creatinine excretion, and several researchers have advocated sex-specific cutpoints of the ACR to define microalbuminuria[12,13]. However, no published studies have demonstrated how the use of a single ACR cut point *versus* sex-specific ACR cut points measured in random urine samples affects the estimated prevalence of microalbuminuria in a nationally representative sample of United States subjects[14].

This descriptive cross-sectional study was carried to determine Microalbuminuria creatinine ratio, in long term Diabetic patients.

MATERIAL AND METHODS:

This study was descriptive analytical case control hospital based study. The study was carried out with fifty patients aged 35-55 years who attended the Outpatient department of Omdurman teaching hospital, Medical Centre and Khartoum teaching hospital, Sudan from November 2011 to April 2012. All had type 2 diabetes mellitus diagnosed based on World Health Organization criteria. None had any apparent proteinuria with the dipstick test (Albustix, Boeringher Manheim, Manheim, Germany). All subjects were asked to supply their informed consent before the study. Subjects with long standing diabetes mellitus were regarded as test group and non-diabetes persons were considered as control group.

Sample size:

Fifty urine samples from diabetic patients were collected randomly, for more than 10 years and 50 samples from apparently healthy individuals as control.

Inclusion criteria:

Patients with long standing diabetes mellitus for more than 10 years were included in this study, while diabetic patients having blood glucose of less than 200 mg/dl at time of study were excluded**.**

Microalbuminuria analysis:

All urine samples were analyzed for micro-albumin level by the immunoturbidimetric method using the Microalb kit. The

coefficient of variation (CV) is 7.0% at an albumin concentration of 21.4 mg/l and 5.5% at a concentration of 124 mg/l (normal value 0-15 µg/minute; 0-20 mg/l). 2 ml of urine was used for the immunoturbidimetry test. The urine albumin concentrations were determined blindly by one of the authors. The reproducibility of the test was assessed by another author on 10 occasions for precision analysis.

Estimation of creatinine by kinetic Jaffe method:

Principle: The procedure is based upon the modification of the original picrate reaction (Jaffe). Creatinine under alkaline conditions reacts with picrate ions forming a yellowish complex.

The formation rate of the complex is measured through the increase of absorbance in a prefixed interval of time which is proportional to the concentration of creatinine in the sample.

$$Creatinine + alkaline\ picrate \rightarrow Yellowish\ complex$$

Calculation of Creatinine: Albumin ratio (CrAlbR)

$$\frac{Urine\ creatinine\ (g/dl)}{Urine\ albumin\ (mg/dl)} = CrAlbR$$

Ethical consideration:

Permission to carry out this study was obtained from the ethical committee of the University of Medical Sciences and Technology, Khartoum, Sudan.

The objectives of the study were explained to all individuals participating in this study.

An informed consent was taken from both patients and control groups

Data analysis:

Statistical analysis was performed using statistical package for social science (SPSS) software version 12. Mean values of normally distributed continuous data were compared using student's t test. P value of 0.00 was considered significant at 95% confidence limit.

RESULTS:

The results of this study are presented in table (1) and figure (1). Microalbuminuria in Diabetic patients showed an increase when compared with the control group with P value 0.000. Similarly creatinine also showed an increase in diabetic patients.

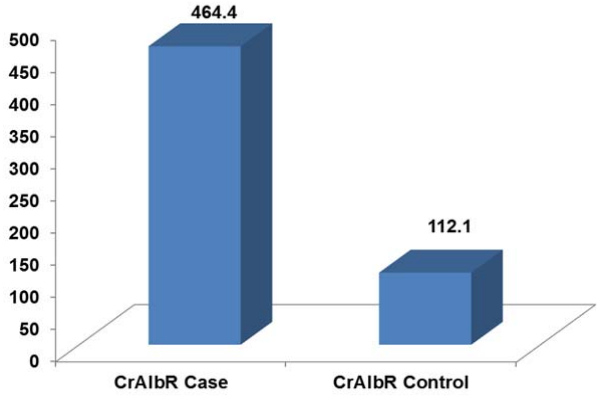

Figure (1): Showing comparison between the mean of creatinine: albumin ratio in both healthy individuals and patients.

DISCUSSION:

The rates of albuminuria were very high in this large primary care population with type 2 diabetes. One limitation of the study is that a single ACR result was used in this analysis, and the coefficient of variation of measures of albuminuria can be up to 20% [15]. Although serial measures would increase precision, it is unlikely that they would move many individuals across categories of albuminuria or substantively change the findings. It has been suggested that ACR reference ranges should be adjusted by sex, age and race[16-18], perhaps in relation to differences in muscle mass[17,19]. We are not aware of any validation studies of a single ACR compared to timed collections across our ethnic groups. We did not have a direct measure of renal function, such as serum creatinine, consistently available. It is likely that factors not measured in this study contribute to the association of albuminuria with ethnicity. A genetic predisposition to renal disease is possible, such as that found in African-Americans with non-diabetic renal disease[20], but has yet to be demonstrated among other ethnic groups and for those with diabetes. Fetal programming with subtle dietary deficiencies, stress and high rates of smoking during pregnancy is considered to affect renal development in utero and may be associated with

hypertension, proteinuria and decreased renal function later in life[21]. Differential access to health care, delayed diagnosis of diabetes and differential rates of medication prescription and adherence are all potential contributors to ethnic variations in albuminuria. Low medication adherence among people with a long-term condition is a widespread problem[22]. Poverty, itself recognized as having multiple relationships to renal disease and race or ethnicity[23], is also associated with many of the factors we have described above. We determined the risk of nephropathy due to diabetes mellitus in Sudanese population. Our results indicated that the genetics of Sudanese race are more prone to microalbuminuria and thus to renal diseases. Therefore we observed a high ratio of albumin:creatinine ratio (112.1 g/mg) even in non-diabetes individuals and hence there is a very high albumin:creatinine ratio (464.4 g/mg) in type 2 diabetes patients.

Table (1): Showing comparison between the mean of creatinine / albumin ratio in both healthy individuals and patients.

Samples	N	Mean (g/mg)	Std. Deviation	Std. Error Mean	P. value
CrAlbR Case	50	464.4	94.43	13.49	0.000**
CrAlbR Control	50	112.1	7822	11.06	

Table (2): Showing the correlation between the duration of diabetes mellitus and creatinine: albumin ratio in long term diabetic patients

		Duration	CrAlbR
Duration	Pearson Correlation	1	-0.092
	Sig. (2-tailed)		0.527
	N	50	50
CrAlbR	Pearson Correlation	-0.092	1
	Sig. (2-tailed)	0.527	
	N	50	50

CONCLUSION:

It is obvious from these results that, long standing diabetes mellitus decline the renal function, which was reflected as raised microalbuminuria:creatinine ratio. This in-turn may lead to increased risk of developing renal failure.

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