



MICROALBUMINURIA AS A PREDICTOR OF RENAL DAMAGE IN TYPE-2 DIABETES MELLITUS

Biochemistry

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ABSTRACT

Introduction: Diabetes mellitus is one of the systemic diseases affecting the kidneys which significantly impacts morbidity, mortality and quality of life. The onset of diabetic nephropathy is signaled by microalbuminuria (Albumin/Creatinine ratio, ACR = 30 to \leq 300 mg/g) which progresses to macroalbuminuria and eventually lead to an End Stage Renal Disease (ESRD). **Objectives:** To estimate the concentration of fasting blood glucose, HbA1c & microalbuminuria in detection of renal dysfunction in Type-2 diabetics as compared to healthy controls. **Methodology:** In this study, 50 proven cases of Type-2 Diabetic patients and an equal number of age and sex matched healthy controls were included. **Results:** The serum concentrations of FBG, HbA1C & microalbuminuria were found to be significantly increased in Type-2 Diabetic patients as compared to healthy controls ($p, < 0.001$). **Conclusion:** Estimation of microalbuminuria would allow to detect the degree of renal impairment in diabetic nephropathy. Microalbuminuria has emerged as a very powerful clinical predictor of overt renal disease in diabetes.

KEYWORDS

Type-2 DM; Diabetic Nephropathy; Microalbuminuria.

Introduction

Diabetes mellitus (DM) is a group of aetiologically different metabolic defects characterized by hyperglycemia resulting from defect in insulin secretion as well as insulin action or both.¹ The number of people with diabetes is increasing because of population growth, aging, urbanization and the increasing prevalence of obesity and physical inactivity.²

The development of Diabetic Nephropathy (DN) is characterized by a progressive increase in the excretion of protein, an early and continuing rise in systemic blood pressure and a late decline in glomerular filtration rate, leading eventually to end stage renal failure.³ There are four potential biochemical pathways linking hyperglycemia to the changes within the kidney, which can plausibly be linked to the functional, structural changes characterizing diabetic nephropathy. These include polyol pathway, nonenzymatic glycation, glucose auto-oxidation and de novo synthesis of diglycerol leading to protein kinase C and phospholipase A₂ activation.⁴

Microalbuminuria is well known as a risk factor resulting in macroalbuminuria in Type-1 and Type-2 diabetic patients which progress to end stage renal disease (ESRD).⁵ Type-2 diabetic patients with microalbuminuria shows a rapid decline of glomerular filtration rate (GFR) and also it shows that they had a 1.8 fold increased risk for cardiovascular mortality during 12 years of follow up compared with individuals with normoalbuminuria.⁶

This study is being undertaken to determine the utility of microalbuminuria in predicting the decline of renal function in diabetes. Thus, appropriate & timely interventions can be instituted to delay or arrest the progression of diabetic nephropathy.

Aim And Objectives

Aim:

The aim of this study is to assess microalbuminuria in early detection of impairment in renal function in diabetes.

Objectives

To estimate the concentrations of fasting blood glucose, HbA1c & microalbuminuria in Type-2 diabetics and healthy controls.

Methodology

A case-control study was taken up in group of Type-2 diabetic patients with age and sex matched healthy controls selected from S.S Hospital

attached to SSIMS & RC, DAVANGERE during the study period from November-2013 to August-2015.

The study was approved by the ethical and research committee of SSIMS & RC, Davangere to use human subjects in the research study. Written informed consent was taken from the study subjects.

Patients were selected from the outpatient and inpatient departments of medicine in the hospital. A total of 50 proven cases of Type-2 diabetic patients in the age group of 30-80 years were included. All patients suffering from Type-2 diabetes diagnosed and confirmed by physician with FBG (fasting blood glucose) and PPBS (post prandial blood sugar) according to American Diabetes Association criteria (FBG \geq 126 mg/dL and 2 hour PPBS \geq 200 mg/dL). A total of 50 age and sex matched healthy peoples without any major illness and not on any medications were included.

Fasting blood glucose was analysed by using Erba kit in Semi Auto Analyzer, HbA1c was analysed by using Agappe kit in Nephelometer and Microalbuminuria was analysed by using Turbilyte kit in Semi Auto Analyzer which employs Turbidimetric Immunoassay technique.

Statistical analysis

Continuous variables with normal distribution were compared using students t-test. Categorical variables were compared using chisquare test. Statistical analysis was done using Statistical Package for Social Sciences (SPSS) version 20. A p-value less than 0.05 was considered statistically significant.

RESULTS

The results obtained in this present study were from total number of 100 subjects.

TABLE 2: Shows the mean serum concentrations of FBG, HbA1c and Microalbuminuria in Healthy Controls and Type-2 diabetic patients.

Parameters	Healthy Controls	Type-2 DM	p -Value, Sig
	Mean \pm SD	Mean \pm SD	
FBG (mg/dl)	92.42 \pm 13.36	221.48 \pm 89.62	<0.001, **
HbA1c	4.49 \pm 0.88	8.91 \pm 2.20	<0.001, **
Microalbuminuria (mg/g)	22.89 \pm 6.47	207.75 \pm 75.23	<0.001, **

Student's unpaired t-test, $p > 0.05$ NS (Not Significant), $p < 0.05$ *S (Significant), $p < 0.001$ **HS (Highly Significant)

Bar Diagram 1: Shows comparison of FBG, HbA1c and Microalbuminuria in Healthy Controls and Type-2DM

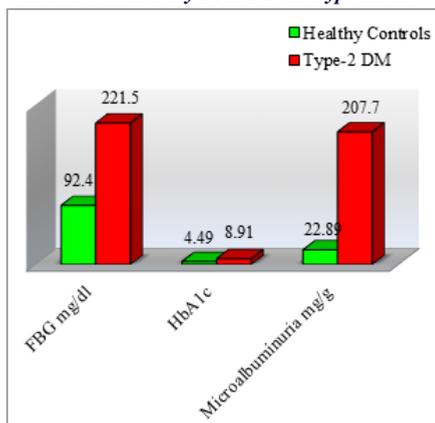


Table 1 and Bar diagram 1: Show comparison of fasting blood glucose, HbA1c and Microalbuminuria between healthy controls and Type-2 diabetic patients.

It is seen from the table that concentrations of fasting blood glucose, HbA1c and Microalbuminuria in healthy controls were in the range of 92.42 ± 13.36 , 4.49 ± 0.88 and 22.89 ± 6.47 , respectively. In Type-2 diabetic patients they were in the range of 221.48 ± 89.62 , 8.91 ± 2.20 and 207.75 ± 75.23 , respectively.

Statistical analysis by student's unpaired t-test showed that the mean concentrations of fasting blood glucose, HbA1c and Microalbuminuria were increased in Type-2 diabetic patients when compared to healthy controls and were statistically highly significant ($p < 0.001$).

DISCUSSION

Diabetic nephropathy is the most common cause of chronic kidney disease which is widely prevalent in developing countries. Diabetic nephropathy develops due to complex interaction between metabolic and haemodynamic pathophysiological factors, which lead to renal damage. It presents with microalbuminuria in the earliest stage. This may progress to macroalbuminuria and later renal insufficiency and ESRD.

In the present study we have included 100 subjects, comprising of 50 Type-2 diabetic patients and 50 healthy controls. In this study, we have evaluated the serum concentrations of FBG, HbA1c and Microalbuminuria in healthy controls and Type-2DM.

Microalbuminuria:

Microalbuminuria is a widely studied renal dysfunction biomarker, since its presence is an established risk factor for mortality, cardiovascular disorders and adverse outcomes, both in the general population and in patients with hypertension and diabetes.

The mean concentrations of microalbuminuria in healthy controls and Type-2 diabetic patients were in the range of 22.89 ± 6.47 mg/g Cr and 207.75 ± 75.23 mg/g Cr, respectively. The mean concentration of microalbuminuria in Type-2 diabetic patients was higher when compared to healthy controls. Microalbuminuria typically occurring after 5 or more years of diabetes. In diabetes, vascular permeability increases and microalbuminuria appears when metabolic regulation is poor, at least in part because of glycosylation and loss of negative charges on the membranes. Compared with normoalbuminuric patients, patients with persistent microalbuminuria have threefold to fourfold greater risk of progression to proteinuria and ESRD. At this microalbuminuric stage, glomerular lesions are generally more severe and blood pressure tends to be increasing, often into hypertensive range. Patients with microalbuminuria showed the fastest GFR decline.

Our findings of the study is in accordance with several other studies^{7,8,9,10}

Yun Kyung Jeon, et al., showed that cystatin-C levels of serum and urine increased with increasing degree of albuminuria, reaching higher levels in macroalbuminuric patients and could be a useful marker for

renal dysfunction in type-2 diabetic patients with normoalbuminuria.⁷ **Mukherjee Brijesh and Patra Saurav** pointed out that both Microalbuminuria and Cystatin-C are equally effective in detecting early diabetic nephropathy. But Cystatin-C has added advantage in being able to estimate eGFR to stage the diabetic nephropathy over Microalbuminuria. So Cystatin-C can be suitable marker in early DN.⁸

El-Shafey E M, et al., showed that serum cystatin C and creatinine were significantly higher in macroalbuminuric Type-2 diabetic patients with renal dysfunction than macroalbuminuric Type-2 diabetic patients with normal renal function, the microalbuminuric group as well as normoalbuminuric group.⁹

Byung-Wan Lee, et al., showed that serum cystatin-C seems to be more accurate serum marker than serum creatinine in evaluating a prognostic stage of Type-2 diabetic nephropathy. This study suggests that, in Korean Type-2 diabetic patients, cystatin-C based GFR might be more valuable than creatinine based GFR in the prediction of the microalbuminuric stage.¹⁰

Strength and further scope of the study:

The concentrations of fasting blood glucose, HbA1c and Microalbuminuria were significantly increased in Type-2 diabetic patients as compared to healthy controls.

The diagnosis of diabetic nephropathy can be improved by measuring several new biochemical markers that have the potential to detect early renal impairment in Type-2 DM than the traditional markers. These new markers include cystatin-C, Kidney Injury Molecule-1 (KIM-1), N-acetyl- β -glucosaminidase (NAG), human neutrophil gelatinase-associated lipocalin (NGAL), β 2-microglobulin, α 1-microglobulin, transferrin, type-IV collagen, interleukin-18 (IL-18), clusterin and ceruloplasmin.

CONCLUSION

Microalbuminuria has emerged as a very powerful clinical predictor of overt renal and cardiovascular disease. Presence of microalbuminuria at baseline was associated with higher risk of macroalbuminuria which then progress to end stage renal disease. Microalbuminuria should be considered as a risk factor of renal prognosis in type 2 diabetic patients. Our results show that microalbuminuria is superior for renal function assessment in a well-defined patient group and its measurement may be recommended in the routine management of diabetic patients. So serial measurement of microalbuminuria would allow to detect and stage the degree of renal impairment in diabetic nephropathy and would indicate how the disease evolves in these patients, allowing us to adopt early measures to control the disease.

Thus, microalbuminuria can be recommended as routine biomarker to screen and to monitor the progress of diabetic nephropathy.

REFERENCES

- (1) Bharat, Hijam D, Gangte D, Lalnupui, Premchand and Devi I, et al., Thyroid Status in Diabetes Mellitus. *J GlycomicsLipidomics* 2013; 3: 106.
- (2) Ueckermann V, Van Zyl DG. The prevalence of subclinical hypothyroidism among patients with diabetes mellitus at the Kalafong Hospital Diabetes Clinic: a cross-sectional study. *J EndocrinolMetab Diabetes S Afr* 2013; 18(2): 106-110.
- (3) Alberti KGMM, Zimmet P, DeFronzo RA, Keen H. International textbook of diabetes mellitus. 2nd ed. Chichester: Wiley; 1997. p.1379.
- (4) Schmitz A, Gunderson HJ, Osterby G. Glomerular nephropathy in NIDDM. *Diabetes* 1988;37:1499-1504.
- (5) Moriya T, Tanaka S, Kawasaki R, Ohashi Y, Akanuma Y, Yamada N, et al. Diabetic Retinopathy and Microalbuminuria Can Predict Macroalbuminuria and Renal Function Decline in Japanese Type 2 Diabetic Patients. *Diabetes Care* 2013; 36: 2803-809.
- (6) Heerspink HJL, Holtkamp FA, Zeeuw DD, Ravid M. Monitoring Kidney Function and Albuminuria in Patients With Diabetes. *Diabetes care* 2011; 34:S325-S329.
- (7) Yoo JS, Lee YM, Lee EH, Kim JW, Lee SY, Jeong KC, et al. Serum Cystatin C Reflects the Progress of Albuminuria. *Diabetes Metab J* 2011; 35: 602-609.
- (8) Brijesh M and Saurav P. Comparative study of significance of serum cystatin-C, serum creatinine and microalbuminuria estimation in patients of early diabetic nephropathy. *J Diabetes Metab* 2015; 6(2): 1-6.
- (9) El-Shafey EM, El-Nagar GF, Selim MF, El-Sorogy HA, Sabry AA. Is serum cystatin-C an accurate endogenous marker of glomerular filtration rate for detection of early renal impairment in patients with type-2 diabetes mellitus? *Ren Fail* 2009; 31: 355-359.
- (10) Lee BW, Ihm SH, Choi MG, Yoo HJ. The comparison of cystatin-C and creatinine as an accurate serum marker in the prediction of type-2 diabetic nephropathy. *Diab Res* 2007; 6: 15.