Journal of Pharmaceutical and Scientific Innovation
www.jpsionline.com
Research Article

STUDY OF LEVELS OF MICROALBUMINURIA IN CORONARY ARTERY DISEASE AND DIABETES MELLITUS

Suvarna Tryambak Jadhav*[1], Ajit V Sontakke[2], Bipin M Tiwale[3], Nilima Patil[1], Smita Patil[1]
[1]Bharati Vidyapeeth University Dental College and Hospital, Sangli, Maharashtra, India
[2]Krishna Institute of Medical Sciences, Karad, Maharashtra, India
[3]Dr. D. Y. Patil Medical College, Kolhapur, Maharashtra, India
*Corresponding Author Email: suvarnat.jadhav@gmail.com

DOI: 10.7897/2277-4572.04340

Received on: 15/04/15 Revised on: 25/05/15 Accepted on: 19/06/15

ABSTRACT

Coronary Artery Disease (CAD) leads to Angina and Myocardial Infarction (MI). Premature mortality on Coronary Heart Disease (CHD) is more common in diabetic atherosclerosis. In the present study serum level was Microalbuminuria estimated in patients of CAD with DM, CAD without DM, DM without CAD and CAD with DM and other risk factors compared to healthy normal subjects. The level of Microalbuminuria was significantly increased in all four groups of patients as compared to control group. On the basis of our results we conclude that microalbuminuria is a marker of vascular damage and thus is an early finding in atherosclerosis. Microalbuminuria is associated with wide spread abnormalities in the vasculature that may manifest as altered vascular reactivity and endothelial dysfunction.

Keywords: Coronary Artery Disease, Diabetes Mellitus, Microalbuminuria

INTRODUCTION

Microalbuminuria is known to be an independent risk factor for cardiovascular death in type 2 diabetic patients but the mechanisms underlying this association have not been clarified. It could be that other cardiovascular risk factors that are frequently associated with microalbuminuria, such as hyperglycemia, hypertension and endothelial dysfunction, might also contribute to the increased cardiovascular mortality observed in these patients. In addition, dyslipidemia has also been described in type 2 diabetic patients with microalbuminuria. Although those studies did not specifically assess the effect of nutrient intake, the effect of dietary habits on the development of dyslipidemia in these microaluminuric patients cannot be ruled out.

Microalbuminuria is a well – known risk factor for coronary artery disease in diabetics and nondiabetics. However there are few data linking angiograghic severity of CAD to microalbuminuria [1].

Early studies in patients with renal insufficiency clearly document that lower levels of blood pressure results in slower rates of decline in renal function. Proteinuria is the hallmark of renal disease in diabetes and is now recognized as an independent risk factor for cardiovascular disease. Microalbuminuria is clearly associated with increased cardio vascular (CV)) risk in hypertension and predicts nephropathy progression in type 1 diabetes. Indeed, international abstracts demonstrate a strong, linear relationship between severity of angiographic coronary artery disease and albuminuria[2-4].

The pathophysiologic processes that link microalbuminuria and Cardio vascular disease CVD are unclear. Microalbuminuria could be a cause or a consequence of vascular disease. In the STENO hypothesis put forward by Deckert et al [5] albumin leakage into the urine is a reflection of widespread vascular damage. In a sense, the kidney is the window of the vasculature. In view of these considerations, endothelial function and chronic inflammation have been suggested as possible candidates to explain the association between microalbuminuria and CVD[6,7]. However, there are many inconsistencies in the literature. It is true that low-grade inflammation can be both a cause and a consequence of endothelial dysfunction, and some studies used markers of inflammation such as C-reactive protein, IL-6, and TNF- , which indicate that low-grade inflammation is associated with the occurrence and the progression of microalbuminuria and with an associated increased risk for atherosclerotic disease[8-10].

Microalbuminuria is associated with several cardiovascular risk factors such as aging, male gender, hypertension, diabetes, smoking, obesity, and dyslipidemia, it is clear that these explain, at most, a very small part of the association between microalbuminuria and atherosclerotic events. As with measures of endothelial function and inflammation, it is possible that this is related to inadequate quantification of these exposures, or there could be confounding by other risk factors that might cause both the microalbuminuria and the associated CVD[11].

The purpose of this study is to investigate whether urinary albumin excretion is a sign of atherosclerotic involvement of coronary artery in the general population.

MATERIALS AND METHODS

The present study was carried out in the Department of Biochemistry, Dr. D.Y.Patil Education Society's Medical College and Hospital, Kolhapur. This study was approved by Institutional ethical committee. In this study a total number of 200 subjects between age 40 yrs to 60 yrs matched with age and sex were included. They were distributed in controls and four groups.

Controls	Normal Healthy controls- 100 cases
Group- I	Patients with CAD and DM- 25 cases
Group- II	Patients with CAD – 25 cases
Group- III	Patients with DM – 25 cases
Group- IV	Patients with CAD and DM + Other risk factors- 25 cases

All controls were from the same age groups as patients, not showing any clinical signs and symptoms suggestive of CAD. They were having normal blood pressure (BP), ECG, blood sugar level and apparently no other cardiac risk factors. Group-I contained patients diagnosed to have CAD (based on angiography) with confirmed DM and were receiving treatment for the same Group- II contained patients with CAD but no DM Group-III contained Type II DM patients receiving treatment for DM, and were not showing any complications of DM, and had normal ECG and BP. Group- IV contained patients with CAD and DM along with other risk factors. (Such as smoking, hypertension, family history of CAD, obesity etc.)

Sample collection- Urine sample was collected at early morning for estimation of microalbuminuria.

Inclusion Criteria

A) Control group: 100 age matched healthy subjects were included in the control group. The subjects were selected after screening for any prior history of cardiovascular disease or any other disease. B) CAD Patients: Angiographically proven patients by the cardiologists with relevant coronary artery disease showing greater than 50% stenosis in at least one major coronary artery at the time of diagnostic catheterization were enrolled in this study. Each subject was screened by a complete history, physical examination and laboratory analysis. C) Diabetic Patients with CAD: Clinically diagnosed patients whose fasting blood glucose level was above 125 mg/dl.

Exclusion Criteria

The patients with hemodynamically significant valvular heart disease undergoing catheterization, surgery or trauma, known cardiomyopathy, known cancer, abnormal hepatic and renal function, past or concurrent history of any disease and taking any medication that could influence the oxidant and antioxidant status and endothelial functions were exuded from the study group.

RESULT

Levels of microalbuminuria in (mg/ l) in control subjects and different study groups

Groups	Microalbuminuria (mg/l)
Control	7.4 ± 10.07
Group I (CAD with DM)	21.6 ± 13.12 *
Group II (CAD with out DM)	31.6 ± 21.68 * #
Group III (DM with out CAD)	42.9 ± 22.2 * ♣ ♠
Group IV (CAD with DM with other risk factors)	29.4 ± 19.71 * $ ♦

Values are expressed as mean ± SD, * P<0.001 All four Groups as compared to control, # P<0.001 Group II as compared to Group I, ♣ P<0.001 Group III as compared to Group I, $ P<0.05 Group IV as compared to Group I, ♠ P<0.05 Group III as compared to Group II, ♦ P<0.001 Group IV as compared to Group III

In the present study significant Microalbuminuria was observed in all four groups of patients as compared to control. Similarly significant change was seen when the patient groups were compared with each other.

DISCUSSION

Microalbuminuria (MAU) is a persistent, increased urinary excretion of albumin[12,13]. Microalbuminuria is not only an established marker of diabetic nephropathy but[14] also has been shown to predict macrovascular complications in non- insulin dependent diabetes[15-17]. Proteinuria is the hallmark of renal disease in diabetes and is now recognized as an independent risk factor for cardiovascular disease[18] In the present study significant Microalbuminuria was observed in all four groups of patients as compared to control. Similarly significant change was seen when the patient groups were compared with each other. Diabetes is a chronic condition which poses risk for nephropathy because of increased vascular permeability. Increased Urinary albumin (Microalbuminuria) gives an early signal of incipient diabetic nephropathy. Microalbuminuria is an early feature of excessive capillary leakage[19]. Microalbuminuria is associated with wide spread abnormalities in the vasculature that may manifest as altered vascular reactivity and endothelial dysfunction[19]. Stehouwer et al[20] has shown that both endothelial dysfunction and inflammation are involved in the pathogenesis of MAU and poor glycemic controls was associated with increase in markers of endothelial dysfunction and inflammatory activity. They observed that HbA_1c was consistently positively associated with longitudinal development of markers of inflammatory activity and endothelial dysfunction. Microalbuminuria is associated with the accumulation of extracellular matrix in glomeruli and large vessel walls[21]. Changes in the quality of the exteracellular matrix[22-23] and proliferation of mesagial and myomedial cells[24] have been reported. Similar changes in the exteracellular matrix of vessel walls have also been found in atherosclerosis [25]. It has been suggested that microalbuminuria is a marker of vascular damage and thus is an early finding in atherosclerosis[26]. The increased microalbuminuria observed in our study points towards the vascular damage in the patients with CAD as well as diabetes mellitus.

REFERENCES

1. Magda S, Jussara, C, Ronivan, L,Vanessa, D.Fatty acid composition of serum lipid fractions type 2 diabetic patients with microalbuminuria. Diabetes Care,2003, Vol-26,No-3.
2. Kaushik Bhowmick, AVM Kutty, Shetty H.V. Glycemic control modifies the association between microalbuminuria and C-reactive protein in type 2 diabetes mellitus. Indian Journal of Clinical Biochemistry, 2007:22, 2, 53-59.
3. De Jong P.E, Curhan G.C. Screening, monitoring, and treatment of albuminuria: Public health perspectives. J Am Soc Nephrol, 2006. 17 :2120 –2126.
4. Doqi K. Clinical practice guidelines on hypertension and antihypertensive agents in chronic kidney disease. Am J Kidney Dis, 2004. 43 :S1 –S290.
5. Deckert T, Feldt-Rasmussen B, Borch-Johnsen K, Jensen T, Kofoed- Enevoldsen A: Albuminuria reflects widespread vascular damage. The Steno hypothesis. Diabetologia, 1989. 32 :219 –226.
6. Stehouwer C.D, Henry R.M, Dekker J.M, Nijpels G, Heine R.J, Bouter L.M: Microalbuminuria is associated with impaired brachial artery, flow-mediated vasodilation in elderly individuals without and with diabetes: Further evidence for a link between microalbuminuria and endothelial dysfunction—The Hoorn Study. Kidney Int Supp, 2004, l92 :S42 –S44.
7. Stehouwer C.D, Smulders Y.M. Microalbuminuria and risk for cardiovascular disease: Analysis of potential mechanisms. J Am Soc Nephrol, 2006, 17 :2106 –2111.
8. Jager A, van H, V, Kostense P.J, Emeis J.J, Nijpels G, Dekker J.M, Heine R.J. Bouter LM, Stehouwer CD: C-reactive protein and soluble vascular cell adhesion molecule-1 are associated with elevated urinary albumin excretion but do not explain its link with cardiovascular risk. Arterioscler Thromb Vasc Bio, 2002, l22 :593 –598.
9. Stehouwer C.D, Gall M.A, Twisk J.W, Knudsen E, Emeis J.J, Parving H.H. Increased urinary albumin excretion, endothelial dysfunction, and chronic low-grade inflammation in type 2 diabetes: Progressive, interrelated, and independently associated with risk of death. Diabetes, 2002, 51 :1157 –1165.

10. Schram M.T, Chaturvedi N, Schalkwijk C.G, Fuller J.H, Stehouwer C.D Markers of inflammation are cross-sectionally associated with microvascular complications and cardiovascular disease in type 1 diabetes: The EURODIAB Prospective Complications Study. Diabetologia, 2005, 48 :370 –378.
11. De Zeeuw D, Parving HH, Henning RH: Microalbuminuria as an early marker for cardiovascular disease. J Am Soc Nephrol, 2006,17 :2100 –2105.
12. De Jone P.E, Curhan G.C Screening, monitoring, and treatment of albuminuria: Public health perspectives. J. Am Soc Nephrol 17: 2120-2126
13. Doqi K. Clinical practice guidelines on hypertension and antihypertensive agents in chronic Kidney disease. Am J Kidney Dis, 2004, S1-S290.
14. Viberti GC, Jarrett RJ, Mahmud U, Hill RD, Argypailos A, Keen H. Microalbuminuria as a predictor of clinical nephropathy in insulin – dependent diabetes mellitus. Lancet, 1982; 1: 1430 – 1432.
15. Mogenesen C.F. Microalbuminuria predicts clinical proteinuria and early mortality in maturity – onset diabetes mellitus. N Engl J Med, 1984; 310: 356 – 360
16. Mogenesen C E, Damsguard EM, Froland A, Nielsin S. Microalbuminuria is non – insulin – dependent diabetes mellitus. Clin Nephrol, 1992; 38 (suppl 1): S 28 – S 39.
17. Mattock MB, Morrish N J, Viberti GC, Keen H, Fitzgerald AP, Jackson G.Prospective study of microalbuminuria as predictor of mortality in NIDDM. Diabetes 1992; 4 : 735 – 741.
18. Keane WF, Eknoyan G, Proteinuria, albuminuria, Risk assessment. Detection, Elimination (PARADE) : A position paper of the national kidney foundation.
19. Stenhouwer C.D, Naut J.J, Zeldenrust G.C, Hackeng W.H, Donker A. J. Urinary albumin excretion, cardiovascular disease and endothelial dysfunction in non – insulin dependent Diabetes Mellitus
20. Lancet 1992; 340: 319 – 23.
21. Stehouwer C, Gall M, Twisk J, Knudsen E, Emeis J, Parving H. Increased Urinary albumin excretion, endothelial dysfunction and chronic low grade inflammation in type 2 diabetes: Progressive interrelated and independently associated with risk of death. Diabetes 2002; 51: 1157 – 1165.
22. Osterby R, Parving HH, Hommel E, Jorgensen HE, Lokkegaard H. Structure and function in diabetic nephropathy; early to advance stages. Diabetes, 1990: 39: 1057 – 1063.
23. Shimomura H, Spiro R.G. Studies on macromolecular component of human glomerular basement membrane and alterations in diabetes: decreased levels of heparin sulfate proteoglycan and laminin. Diabetes, 1987; 36 : 374 – 381.
24. Dybdahl H, Ledet T. Diabetic macroangiopathy: quantitative histopathological studies of the extramuaral coronary arteries from type – 2 diabetic patients. Diabetologia, 1987, 30: 882 – 886.
25. Castellot J.J, Hoover R.J, Garper P.A, Karnovsky M.J. Heparin and glomerular epithelial cellsecreted heparin like species inhibit mesangial – cell proliferation. Am J Pathol. 1985: 20; 427 – 435.
26. Hillmann J, Schmidt A, Von Bassewitz D.B, Byddecke F. Relationship of sulfated glycosaminoglycans and cholesterol content in normal and arteriosclerotic human aorta. Arteriosclerosis, 1989; 9: 154 – 158.
27. Deckert T, Kofoed – Enevoldsen A, norgaard k, Borch – Jonensen K. Feldt –Rasmusse B, Microalbuminuria : implications for micro and macro vascular disease. Diabetes Care, 1992; 15 : 1181 – 1191.

Source of support: Nil, Conflict of interest: None Declared

QUICK RESPONSE CODE	ISSN (Online) : 2277 –4572
	Website http://www.jpsionline.com

How to cite this article:
Suvarna Tryambak Jadhav, Ajit V Sontakke, Bipin M Tiwale, Nilima Patil, Smita Patil. Study of levels of microalbuminuria in coronary artery disease and diabetes mellitus. J Pharm Sci Innov. 2015;4(3):180-182 http://dx.doi.org/10.7897/2277-4572.04340