



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

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### 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 microalbuminuric 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 angiographic severity of CAD to microalbuminuria<sup>1</sup>.

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 cardiovascular (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<sup>2-4</sup>.

The pathophysiologic processes that link microalbuminuria and Cardiovascular 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<sup>5</sup> 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<sup>6,7</sup>. 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- $\alpha$ , 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<sup>8-10</sup>.

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<sup>11</sup>.

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 excluded 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<sup>12,13</sup>. Microalbuminuria is not only an established marker of diabetic nephropathy but<sup>14</sup> also has been shown to predict macrovascular complications in non- insulin dependent diabetes<sup>15-17</sup>. Proteinuria is the hallmark of renal disease

in diabetes and is now recognized as an independent risk factor for cardiovascular disease<sup>18</sup>. 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<sup>19</sup>. Microalbuminuria is associated with wide spread abnormalities in the vasculature that may manifest as altered vascular reactivity and endothelial dysfunction<sup>19</sup>. Stehouwer et al<sup>20</sup> has shown that both endothelial dysfunction and inflammation are involved in the pathogenesis of MAU and poor glyceemic controls was associated with increase in markers of endothelial dysfunction and inflammatory activity. They observed that HbA<sub>1c</sub> 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<sup>21</sup>. Changes in the quality of the extracellular matrix<sup>22-23</sup> and proliferation of mesangial and myomedial cells<sup>24</sup> have been reported. Similar changes in the extracellular matrix of vessel walls have also been found in atherosclerosis<sup>25</sup>. It has been suggested that microalbuminuria is a marker of vascular damage and thus is an early finding in atherosclerosis<sup>26</sup>. The increased microalbuminuria observed in our study points towards the vascular damage in the patients with CAD as well as diabetes mellitus.

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