



## ACUTE CORONARY SYNDROME; MICROALBUMINURIA AS ATHEROSCLEROTIC RISK FACTOR AND ITS ASSOCIATION

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**ABSTRACT:** Microalbuminuria is a strong and independent indicator of increased cardiovascular risk among individuals with and without diabetes and hypertension. The pathophysiologic mechanism underlying the association between albumin excretion and cardiovascular disease (CVD) is that microalbuminuria can be a predictor of CVD risk as it reflects the vascular damage in kidneys. It also shows endothelial damage predicting CV disease risk. Based on this theory, periodic screening for microalbuminuria could allow early identification of vascular disease and help stratify overall cardiovascular risk, especially in patients with risk factors such as hypertension or diabetes. Therefore microalbuminuria can be used for stratification of risk for cardiovascular disease. Once microalbuminuria is present, cardiovascular risk factor reduction should be aggressive. **Objectives:** The objective of the study was to determine the role of microalbuminuria as an atherosclerotic risk factor and its association with coronary artery disease. **Study Design:** Cross-sectional study. **Duration of Study:** Duration of study was 6 months with first patient enrolled on 16-03-2007 and last patient enrolled on 15-09-2007. **Setting:** Medical Unit-III and CCU Allied Hospital, Faisalabad. **Subjects:** 300 patients with acute coronary syndrome, admitted in Allied hospital Faisalabad were enrolled. **Methods:** 300 patients diagnosed as having acute coronary syndrome admitted in Allied hospital Faisalabad, were included in the study. Early morning urine as well as 24 hour urine had been collected in sterilized urine bags and microalbuminuria was tested. **Results:** In this study 300 patients having acute coronary syndrome were enrolled. Microalbuminuria was positive in 66 (22%) patients and 234 (78%) patients had no microalbuminuria. There was significant association between microalbuminuria and atherosclerotic coronary artery disease. **Conclusion:** It is concluded that microalbuminuria is an atherosclerotic risk factor and it is strongly associated with coronary artery disease.

**Key words:** Microalbuminuria, Cardiovascular Disease, Acute Coronary Syndrome.

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### INTRODUCTION

It has been proposed that microalbuminuria is useful prognostic factor which predicts cardiovascular(CV) mortality & morbidity in people with diabetes mellitus and also in people without diabetes mellitus.<sup>1</sup> However, it is controversial that microalbuminuria can predict mortality in people without diabetes mellitus with acute coronary syndrome in a hospitalized setting.<sup>2</sup> Diabetes mellitus is a common denominator of microalbuminuria and acute coronary syndrome, it is quite possible that its presence can be associated with both these conditions as a confounding factor. In addition, very little is known about its predictive role and consequently risk stratification in CV disease.

Acute coronary syndrome is one of the top causes of morbidity and mortality worldwide. Diabetes mellitus and hypertension are some of the most important risk factors of acute coronary syndrome.<sup>3</sup> People with diabetes mellitus are 2-4 fold more prone to cardiovascular disease over people without diabetes mellitus.<sup>4</sup> Several primary and secondary interventions have been proposed to reduce cardiovascular risk and mortality. These include optimum smoking cessation, serum lipid profiles, glycemic control and postmyocardial infarction  $\beta$ -blockade, weight reduction, and diet modification, blood pressure control, ACE inhibitor for left ventricular (LV) dysfunction.<sup>5</sup> Despite these guidelines, CV disease diabetic patients more than those without diabetes.<sup>6</sup>

Increased attention has been given to the role of microalbuminuria as a cardiovascular risk indicator particularly in patients with diabetes and hypertension. In many studies it has been demonstrated that 20-40% people with diabetes mellitus have microalbuminuria as compared to 10-15% in people without diabetes mellitus. Microalbuminuria is an independent predictor of myocardial infarction, cerebrovascular Accident (CVA) and death.<sup>7</sup> Microalbuminuria increases the risk of cardiovascular disease twice than for those with normal albuminuria in people with diabetes mellitus. Drugs used for treatment of microalbuminuria decreases progression to overt nephropathy, their efficacy in lowering subsequent cardiovascular risk have yet to be determined.

CV-risk and microalbuminuria association is difficult to establish because numerous risk factor can interact, modify and contribute to CV risk. It is imperative to study the association to exactly know the role of drugs that changes albumin levels. Furthermore, the microalbuminuria is defined as ability to predict diabetic nephropathy rather than on CV mortality and morbidity.

In order to reduce risk of CV disease, researchers are exploring preventive measures which is only possible after early detection of risk of atherosclerosis.

The mechanism of association between CV disease and albumin excretion is not fully defined. Microalbuminuria may be a marker of CV Disease risk because of similar mechanism to renal vascular damage and damage to micro vessels in rest of body. It indicates systemic endothelial dysfunction leading to CV events.<sup>8</sup> Periodic microalbuminuria screening allows and help to stratify overall CV risk. Therefore microalbuminuria can be utilized as an important tool to stratify CV disease risk.

## OBJECTIVES

The objective of the study was to determine the association of microalbuminuria with atherosclerosis risk and its association with

coronary artery disease.

## HYPOTHESIS

Microalbuminuria is a strong and independent predictor of increased cardiovascular risk among individuals with and without diabetes and hypertension and it has strong association with atherosclerosis risk which is strongly associated with coronary artery disease.

## OPERATIONAL DEFINITIONS

### Micro albuminuria

Microalbuminuria is an abnormal urinary excretion of 30–300 mg of albumin/24hours (20–200 $\mu$ g/minute) in a 24 hour sample, or an albumin to creatinine ratio greater than 30 mg/g in a first morning midstream sample.

### Acute coronary syndrome

Acute myocardial infarction (MI) patients with ST segment elevation (STEMI) on their presenting ECG, unstable angina (UA) and non-ST segment elevation MI (NSTEMI).

## MATERIAL&METHODS

### Sampling

Non-probability purposive sampling technique was used for selection of patients

### Sample Size

300 patients with acute coronary syndrome, admitted in Allied hospital Faisalabad were enrolled. The expected frequency of microalbuminuria among acute coronary syndrome was taken as 25%. A confidence interval of 22 – 28 % was used. The calculated sample size was 267, which has been rounded off to 300.

### Setting

Coronary Care Unit and Medical Unit III, Allied Hospital, Faisalabad.

### Study Design

Cross-sectional study

### Inclusion Criteria

300 patients with acute coronary syndrome

diagnosed on clinical and ECG criteria were included in the study.

### Exclusion Criteria

Patients having gross nephropathy with raised urea and creatinine, macro albuminuria (>30–300 mg of albumin/24hours), cardiac failure, pyrexial or viral illness and pregnancy were excluded from study.

### Method

Informed consent was obtained from all patients fulfilling the inclusion criteria before enrolling in the study. 300 patients admitted in Allied hospital were diagnosed as acute coronary syndrome on basis of history, examination and investigations including ECG, Troponin T and cardiac enzymes obtained from hospital laboratory. Albumin to creatinine ratio (ACR) was calculated as mg/g. The findings were recorded on a proforma and data was analysed according to SPSS version 16.

The quantitative variables like age, 24 hour urinary albumin were presented as Mean  $\pm$  SD.

The qualitative variables; Sex, Diabetes mellitus, Troponin T and ECG findings were presented as percentage. The SPSS version 20 was used for data analysis.

## RESULTS

In this study total 300 patients of acute coronary syndrome were included. Out of these 300 patients 67 (22.33%) patients were having age up to 40 years. One hundred and four (34.67%) were having age from 41-50 years and 88 patients (29.33%) were having their ages between 51-60 years. 41 patients (13.67%) were having ages between 61-70 years (Table-I). Out of total 300 patients, 176 patients (58.7%) were males and 124 (41.3%) were females (Figure-1). Out of total 300 patients, 172 patients (57.3%) were nondiabetic while 128 patients (42.7%) had diabetes mellitus. In this study, there were three types of acute coronary syndrome (ACS). Among them Acute STEMI was the most common consisting of 137 (45.7%) patients out of total 300 patients. Next common type was unstable angina

(UA) 83 (27.7%). Non-ST-segment elevation MI (NSTEMI) was the least common type of acute coronary syndrome in this study, only 80 (26.7%) patients in this type. (Table-II). Out of total 137 patients with ST segment elevation MI, 28 patients (20.4%) had microalbuminuria. Out of 83 patients with unstable angina, 21(25.3%) had microalbuminuria and out of 80 patients with non ST elevation MI, 17 (21.3%) had microalbuminuria (Table-III). Microalbuminuria was positive in 66 patients (22%) and 234 patients (78%) had no microalbuminuria (Figure-2). Frequency of microalbuminuria was higher in patients with diabetes mellitus than non-diabetics. Out of 172 non diabetic patients, microalbuminuria was positive in 32 patients (18.6%), whereas out of 128 diabetics, 34 patients (26.6%) had microalbuminuria.

Gender Distribution

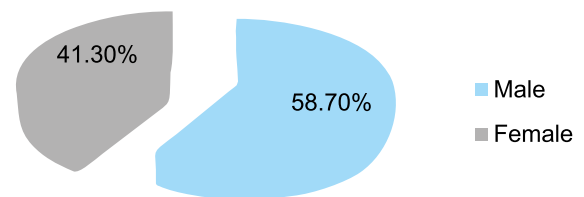


Figure-1. Gender Distribution of Study Population

Microalbuminuria

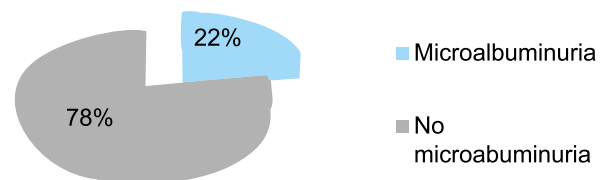


Figure-2. Microalbuminuria

Out of 176 male patients microalbuminuria was present in 42 patients (23.9%), whereas out of 124 female patients 24(19.4%) patients had microalbuminuria. So frequency of microalbuminuria was higher in male patients than in the female patients (Table-IV).

Age Range (years)	No. of Patients	Percentage (%)
≤40	67	22.33
41-50	104	34.67
51-60	88	29.33
61-70	41	13.67
<b>Total</b>	<b>300</b>	<b>100</b>

**Table-I. Age Distribution of Patients**

Type	No. of Patients	Percentage
ST-Segment Elevation Myocardial Infarction (STEMI)	137	45.7
Unstable angina (UA)	83	27.7
Non-ST-segment elevation MI (NSTEMI)	80	26.7
<b>Total</b>	<b>300</b>	<b>100</b>

**Table-II. Type of Acute coronary syndrome (Frequency Distribution)**

Type of ACS	Total number of Patients	Patients with microalbuminuria	Percentage
ST-Segment Elevation Myocardial Infarction (STEMI)	137	28	20.4%
Unstable angina (UA)	83	21	25.3%
Non-ST-segment elevation MI (NSTEMI)	80	17	21.3%
<b>Total</b>	<b>300</b>	<b>66</b>	<b>22%</b>

**Table-III. Association between type of ACS and microalbuminuria distribution**

Sex	Total number of Patients	Patients with microalbuminuria	Percentage
Male	176	42	23.9%
Female	124	24	19.4%
<b>Total</b>	<b>300</b>	<b>66</b>	<b>22.0%</b>

**Table-IV. Association between sex and microalbuminuria distribution**

## DISCUSSION

This study was conducted to determine microalbuminuria role as an atherosclerotic risk factor and its association with CV disease. In this study 300 patients with ACS, admitted in Allied hospital Faisalabad were enrolled.

Yudkin et al first reported association between microalbuminuria and the prevalence of CV disease and peripheral arterial disease (PAD). After this, several studies demonstrated the association between microalbuminuria and cardiovascular risk factors like (age, hyperglycaemia, obesity, hypertension, dyslipidemias, smoking) as well as new CVD risk factors like (insulin resistance, high C-reactive protein, endothelial dysfunction, hyperinsulinaemia, high-fibrinogen levels, hyperhomocysteinaemia and others).<sup>9</sup>

It was suggested long ago that microalbuminuria is an independent risk factor for cardiovascular disease with or without diabetes mellitus in various populations of the world. Presence of microalbuminuria has been linked with increasing risk of CV events and mortality and it is directly proportional to amount of proteinuria in type I and type II diabetes.

Many studies supported these findings showing independent associations between microalbuminuria and CV or total mortality. Microalbuminuria was demonstrated as a strong independent risk factor for cardiovascular disease.

Data from the Framingham Offspring Study shows that cardiovascular disease risk factors are more likely to be present with microalbuminuria.

In a 9 year follow up study, Stehouwer et al. demonstrated presence of markers of chronic endothelial inflammation and dysfunction in 328 patients with type II diabetes mellitus.<sup>10</sup> Endothelial dysfunction, chronic inflammation markers and microalbuminuria have been found to be interrelated present concomitantly and were related to mortality.<sup>11</sup>

Study by Festa et al., (Insulin Resistance Atherosclerosis Study), contained patients with and without type 2 diabetes mellitus and demonstrated association between elevated CRP and microalbuminuria and fibrinogen.<sup>12</sup>

No such study was found in Pakistan in literature review. However, this study was comparable to a cross sectional study in India. They measured the carotid intima-media thickness (IMT) and microalbuminuria with or without CAD. Microalbuminuria was associated with increased intima media thickness.<sup>13</sup>

## CONCLUSION

Microalbuminuria has been found associated with an increased cardiovascular disease risk, and is an independent predictor. Microalbuminuria can be very useful for cardiovascular disease risk stratification. Presence of microalbuminuria is an indication for prompt aggressive reduction of cardiovascular disease risk factors. However, association of microalbuminuria to CV risk is **unclear**.

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