RELATIONSHIP OF MICROALBUMINURIA WITH ACUTE MYOCARDIAL INFARCTION IN NONDIABETIC NORMOTENSIVE PATIENTS

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ABSTRACT

BACKGROUND

Microalbuminuria (MAU) is defined as an urinary albumin excretion rate between 30-300 mg/day. It is a surrogate marker for endothelial dysfunction and is independently associated with atherosclerosis in diabetic and in nondiabetic patients.

Microalbuminuria (MA) has important correlations with the development of CAD. It is increasingly being believed to be an emerging risk factor of this disease.

AIMS AND OBJECTIVES

Therefore, the present research was done;

1. To evaluate the prevalence of microalbuminuria in nondiabetic and non-hypertensive subjects who had an acute myocardial infarction.
2. Short-term outcomes and its prognostic importance as indicator of cardiovascular-related complications.
3. To evaluate the relationship between Microalbuminuria and Acute Myocardial Infarction in nondiabetic and non-hypertensive patients admitted in CCU of Cardiology Department, TMU, Moradabad.

MATERIALS AND METHODS

A cross-sectional and hospital-based study was performed. A total of 150 patients who were neither hypertensive nor diabetic and who had an acute myocardial infarction were included in this study. Microalbuminuria was determined by immunoturbidimetric method. Serum glucose and urea were measured by enzymatic method. Serum creatinine was measured by kinetic colorimetric method.

RESULTS

A significant Microalbuminuria was found in patients of AMI who were nondiabetic and non-hypertensive. The mortality in short-term outcome was also significantly increased in patients having MA, which highlights the significance of Microalbuminuria as an important prognostic biomarker.

CONCLUSION

Microalbuminuria has an important association with acute myocardial infarction in the absence of traditional risk factors like Hypertension and Diabetes.

KEYWORDS

Coronary Heart Disease; Acute Myocardial Infarction, Stable Angina, Unstable Angina, Microalbuminuria.

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INTRODUCTION: Coronary heart disease has been defined by WHO as Impairment of heart function due to inadequate blood flow to the heart compared to its needs caused by obstructive changes in coronary flow.

Acute Myocardial Infarction (AMI) is one of the commonest diseases amongst hospitalised patients globally. The mortality rate of AMI is approximately 30% and for every 1 in 25 patients who survive the initial hospitalisation dies in the first year after AMI.[1]

It is expected that CAD will become the most common cause of death in human history all over the world by the year 2020.[2]

Comprehensive research in the field has emerged with multiple new biomarkers and inflammatory markers of CAD such as increased lipoproteins (a) levels, total plasma homocysteine, elevated plasma fibrinogen levels, Plasminogen Activating Inhibitor (PAI), C-Reactive Protein (CRP), different cytokines and microalbuminuria.

Microalbuminuria was first defined by Mogensen[3] and others as 30-300 mg urinary albumin excretion per 24 hrs. Microalbuminuria (MA) is also defined as the urine albumin to the Urine Creatinine Ratio (UACR) of 30-300 mg/g of creatinine. According to ADA, Microalbuminuria is defined as levels of albumin ranging from 30 to 300 mg in a 24 hrs. urine collection.[4]

Overt albuminuria, macroalbuminuria or proteinuria is defined as a urinary albumin excretion of ≥300 mg/24 hrs. Urinary albuminuria comprises 20-70% or urinary total protein excretion. Albuminuria can be measured in several ways as measurement of albumin-to-creatinine ratio (ACR) in a random or first morning spot collection, 2) 24 hrs. urine collection with measurement of creatinine to verify adequacy of the collection and 3) timed (4 hrs. or overnight) urine collections.[4] Although, the 24 hrs. urine collection would overcome issues of diurnal variation in albumin excretion, it is subject to collection errors. The Kidney Disease Outcomes Quality Initiative Guidelines state that ACR measurement in a first-morning spot urine collection is adequate and a timed urine collection is not necessary.[5]

However, because women excrete less creatinine than men and microalbuminuria is based on a fixed amount of urinary albumin excretion per day, the definitions of microalbuminuria are different in men and women when using ACRs.[6]

The presence of albuminuria is a powerful predictor of renal and cardiovascular risk in patients with type 2 diabetes and hypertension. In addition, multiple studies have shown that decreasing the level of albuminuria reduces the risk of adverse renal and cardiovascular outcomes. The pathophysiology is not definitively known, but is hypothesised to be related to endothelial dysfunction, inflammation or possibly abnormalities in the renin-angiotensin-aldosterone system.

Previous studies have shown that MA is associated independently with cardiovascular morbidity and mortality in diabetic and hypertensive patients.[7-11] Accordingly, the national and international guidelines recommend the screening for MA in patients with diabetes or hypertension.[12]

Prevalence of MAU: The prevalence of MAU among nondiabetic patients with essential hypertension ranges from around 5 to 40%. For this high variability in prevalence, number of factors are responsible like level of blood pressure control, associated dyslipidaemia, biases in inclusion criteria of patients like age, race, associated renal diseases, sample size, technique used for detection of MAU, day-to-day variability in albumin excretion.[13]

Pathophysiology: Vascular injury is in the centre of pathophysiology of microalbuminuria complications in patients with or without diabetes or associated hypertension, but the mechanism differs.[14-16] Patients with MAU have an increased rate of albumin escape from capillaries. Such patients also have cluster of metabolic and non-metabolic risk factors for CAD like hypertension, insulin-resistance dyslipidaemia, etc.[17,18]

The pathophysiological mechanism associated with MAU are multiple and complex. It involves local changes in the kidneys like increased intraglomerular pressure, increased shunting of albumin through glomerular membrane pores and loss of glomerular membrane charge; systemic factors like activation of inflammatory mediators, increased escape rate of albumin through capillaries and vascular endothelial dysfunction.[14-19]

Clinical Implications: MAU signifies abnormal vascular permeability. It has important implications as a marker of target organ damage from cardiovascular disease. Along with that, it is also helpful in evaluating severity of disease, risks involved and future prognosis.[16] MAU gains further importance in the presence of coexisting inflammatory conditions like CAD, acute conditions like trauma, sepsis, surgery, etc. The amount of MAU too has been shown to be in proportion to the severity of associated conditions.[18]

MAU has also been found in acute coronary syndrome and peripheral vascular disease. It has been found to be proportional to the size of the infarct and claudication pain.[15][20] Hence, early recognition of microalbuminuria has beneficial influence on the management and outcome of these diseases.

Investigators have postulated that MA maybe a marker of risk even in apparently healthy people because it reflects vascular damage in the kidneys and in the systemic endothelial dysfunction.[12,13,14]

So, this study was planned to see the association of microalbuminuria in nondiabetic and non-hypertensive patients with myocardial infarction.

MATERIALS AND METHODS: A cross-sectional and hospital-based study was performed. A total of 150 patients who were neither hypertensive nor diabetic who had an acute myocardial infarction were included in this study.

Subjects were considered being diabetic when they positively answered the question whether they had a physician diagnosis of diabetes regardless of the type of antidiabetic treatment. Those patients were excluded from our study.

Those who reported taking antihypertensive or lipid lowering medication were regarded as hypertensive and hyperlipidaemic, respectively. They were also excluded from our study. Subjects were classified as smokers if they reported smoking or having smoked cigarettes during the previous 5 years.

Exclusion Criteria: Age <20 and >70 years, diabetes mellitus, history of hypertension, congestive cardiac failure, renal disease, macroalbuminuria, females taking oral contraceptives, hypertensive at the time of admission.

Urinary Albumin Measurements: Morning Urinary Albumin Concentration (MUAC) was determined by a commercial immunoturbidimetry assay with sensitivity of 2.3 mg L^{-1} and inter- and intra-assay coefficients of variation of 4.4 and 4.3%, respectively (Dade Behring Diagnostics). Microalbuminuria is conventionally defined as a urinary albumin excretion between 30 and 300 mg per 24 hrs. for timed 24 hrs. urine collections. Microalbuminuria can be defined for untimed samples as urinary albumin excretion between 20 and 200 mg L^{-1}. Subjects with the morning urinary albumin concentration of 10-20 mg L^{-1} were considered to have 'high-normal' albuminuria and those with less than 10 mg L^{-1} were regarded to have 'low-normal' albuminuria.

All clinical and laboratory data was collected during the first week of hospitalisation. The diagnosis of Acute Myocardial Infarction was based on the presence of chest pain, electrocardiographic alterations and significant elevations of cardiac enzymes (biomarkers) especially Troponins. Patients were divided into two groups A and B.

Patients with normoalbuminuria were included in Group A and patients with Microalbuminuria were included in Group B. Urinary albumin concentration was measured using 24-hour urine collection.

Detailed history of patients regarding presence of risk factors was noted. Blood pressure was measured using a standard mercury sphygmomanometer and an appropriately-sized cuff. A written informed consent was taken from patients or attendant of the patients on informed consent. All the data were analysed on SPSS version 16.0.

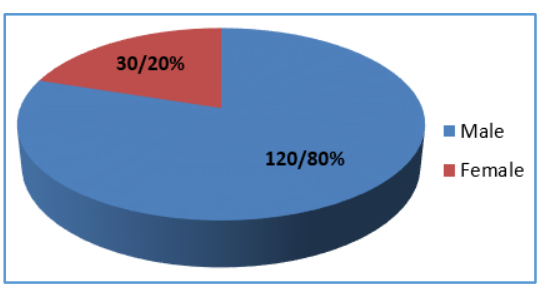

Fig. 1: Sex Wise Distribution of Patients

Characteristics	Frequency/%
Mean±S. deviation	42.5±10.8 years
Range	20-70 years

Table 1: Age Distribution of Patients (N=150)

Smoker (n=97)		Nonsmoker (n=53)	
Male	**Female**	**Male**	**Female**
77/(79%)	20/(20.61%)	30/(56.6%)	23/(43.3%)

Table 2: Smoking History of the Cases (N=150)

RESULTS: Total 150 patients with acute MI were included in this study, patients age distribution was with mean±SD of 42.5±10.8 with range of 20 to 70 years (Table 1).

According to the gender distribution, male were found in majority 80% and females were found 20% (Figure 1).

After diagnosis, out of 150 patients, 87 patients found with microalbuminuria. Furthermore, 50% male and 11.11% female were with microalbuminuria. In our study, 97 patients were smokers, while 79.3% male were smoker and 20.6% female were smoker (Table 2).

In the present study, cardiac enzyme CK-MB was seen raised in 111 patients. Out of them, 70/50.0% were found with MA. Troponin T was positive in 129 cases. Out of them, 77/60% were with MA (Table 3).

	TROPT (n=150)		CK-MB n=150	
	Positive	**Negative**	**Raised**	**Normal**
MA	77/60%	10/7%	70/50.0%	18/16.2%
NMA	52/40.3%	10/7%	44/27.7%	18/16.2%

Table 3: Distribution of Cardiac Enzymes N=150

	UREA (n=150)		CREATININE n=150	
	Raised	**Normal**	**Raised**	**Normal**
MA	18/12%	72/42%	13/10%	66/52.2%
NMA	4/3%	55/37%	5/4%	54/36%

Table 4: Distribution of Blood Urea and Creatinine Levels

Blood urea was raised in 22 patients; from them, 18/12% having MA. Raised serum creatinine was found in 16 of cases; out of them, 12/9.5% were noted with MA (Table 4).

Findings	MA	NMA
Anterior wall MI	40/26.6%	20/13.3%
Inf+RV MI	25/16.6%	11/ 7%
Inf+RV MI	10/7.9%	5/3%
Lateral wall MI	6/4%	2/1.5%
Posterior wall MI	1/0.7%	2/1.5%
NSTEMI	18/12%	10/6%

Table 5: Distribution of the Cases According to Changes in ECG

Based on ECG findings, anterior wall MI was found in 60 cases, NSTEMI in 28 cases and inferior wall MI was found in 36 cases. Amongst these, most common findings Microalbuminuria was found in 26.6% cases, Inferior wall MI in 16.65% cases and NSTEMI in 12% cases. In our study, complications which occurred following acute MI were acute MR, Ventricular septal rupture, Shock, Reinfarction, Arrhythmias and Heart block. Complications like Cardiogenic Shock, Reinfarction and mechanical complications were more associated with patients with microalbuminuria.

Majority of deaths were seen in patients with microalbuminuria 16% whereas in the normoalbuminuria group mortality was just 11.1.

Days	Normoalbuminuria n=(63)				Microalbuminuria n=(87)			
	Survival		Death		Survival		Death	
	No. of pt.	%	No. of pt.	%	No. of pt.	%	No. of pt.	%
1-15	30	47%	2	3%	43	49%	5	5%
16-30	20	31%	5	7%	30	2.9%	9	10%

Table 6: Short-Term Survival of the Patients

DISCUSSION: The data from our study clearly indicate that there is highly significant Microalbuminuria in Nondiabetic, Non-hypertensive patients who have had an acute myocardial infarction.

In a study conducted by PS Singh and et al[21] in the year 2013, Trop-T was found to be positive in 100% of cases with acute MI. Ala Hussain Abbas Haider[22] in the year 2010 divided the CK-MB level in two groups with elevated CK-MB patients 35.7% and group with normal CK-MB patients with 64.35%. In our study, CK-MB positive was seen in 74% cases and Trop-T was positive in 86% cases. Most of the cases in our study had normal renal profile (Cr Cl <30 mg/dL). Microalbuminuria in these patients were therefore was unrelated to renal dysfunction. In this respect, our study is in agreement with Peter Gosling and et al who have considered microalbuminuria to be a sensitive indicator towards non-renal pathology.

In a study by Sahibzada and et al[23] in the year 2008-2009, they found that among nondiabetic acute MI patients 22% had anterior wall MI, 38% had inferior wall MI, 8.4% had an posterior wall MI, 22% had NSTEMI.

Haffiner and et al[24] in the year 1990 reported microalbuminuria to be a potential marker for increased cardiovascular risk in nondiabetic subjects. Gosling and et al[25] in the year 1995 also conducted a similar study on the role of microalbuminuria as an important indicator for non-renal disease. However, they recommended further research to establish this fact.

Our study is almost in agreement with these previous observations. Various studies indicate that microalbuminuria may occur in nondiabetic and normotensive population and is an independent risk factor for cardiovascular diseases.

A cross-sectional study conducted by H.L. Hillege and et al[26] in the year 2001 reported the percentage of microalbuminuria in nondiabetic normotensives to be around 6.6%. Our study has shown microalbuminuria in 87 out of 150 patients. In this respect, our study agrees with the fact that microalbuminuria does in nondiabetic normotensive individuals, but it is different from some other studies in respect of prevalence. The higher values in our study was mainly due to culture of bidi smoking in this region of Uttar Pradesh, which was 79% in males and 20.615 in our female patients.

Coming to its correlation with cardiac biomarkers in Acute MI, we found that level of MA significantly correlated with cardiac biomarkers. In our study, mortality in patients with MA was around 16% where as in NA group, it was just 11.1%.

CONCLUSION: In our study, we found the level of microalbuminuria to be significant enough to be considered in nondiabetic normotensive individuals. It can be compared to conventional cardiac biomarkers like Troponins and Creatinine phosphokinases. In the absence of renal insufficiency, Microalbuminuria is a nonspecific yet highly sensitive marker of myocardial infarction and since testing for microalbuminuria is relatively simple and affordable investigation for resource poor centres, we highly recommend the use of Microalbuminuria as an adjunctive test in nondiabetic, non-hypertensive acute myocardial infarction patients.

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