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Relationship of Microalbuminurea in Non-Diabetic and Non-Hypertensive Patients with Acute Myocardial Infarction

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Abstract

Background and objective: Microalbuminuria (MA) has implications on the development of CHD and it is emerging as a new risk factor of this disease. The aim of the present study was to assess the prevalence of microalbuminuria in non-diabetic and non-hypertensive subjects suffering from acute myocardial infarction, short term outcome and its prognostic importance as indicator of cardiovascular morbidity and mortality. To evaluate the relationship between Microalbuminuria and Acute Myocardial Infarction in Non-diabetic and non- hypertensive patients admitted in CCU Cardiology Department LUMHS Hyderabad.

Material and methods: A cross-sectional and hospital based study. 126 consecutivenon diabetic non hypertensive patients of acute myocardial infarction were included in this study. Microalbuminuria was determined by immunoturbedimeteric 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 non diabetic and non-hypertensive. The mortality and morbidity in short term outcome was also significantly increased in patients having MA, indicating the significance of Microalbuminuria as powerful prognostic biomarker.

Conclusion: Microalbuminuria may have an association with acute myocardial infarction in absence of traditional risk factors like Diabetes and Hypertension.

Keywords: Coronary heart disease; Stable angina; Unstable angina; Myocardial infarction; Micro-albuminuria

Introduction

The terms coronary artery disease (CAD), ischemic heart disease (IHD) and coronary heart disease (CHD) are synonymous but the common form of heart disease is CHD. This is always due to atherosclerosis of coronary arteries long before it manifests as angina pectoris, unstable angina, myocardial infarction and chronic IHD with heart failure [1]. Despite of adopting, the preventive measures and the treatment against established risk factors i.e. smoking, obesity, physical inactivity, diet, hypercholesterolemia, diabetes mellitus and hypertension, the incidence of the CHD is still on rise. It is expected that CHD will become the most common cause of death in human history all over the world by the year 2020 [2]. At present the countries like India, Pakistan, Bangladesh, Sri Lanka and Nepal has the highest incidence of CHD when compared globally. Moreover most of the studies on CHD have been conducted in Bangladesh, India and Pakistan [3,4]. Comprehensive research in the field has emerged with multiple new biomarkers and inflammatory markers of CHD such as, increased lipoproteins (a) levels, total plasma homocysteine, elevated plasma fibrinogen levels, plasminogen activating inhibitor (PAI), C-reactive protein (CRP), different cytokins and microalbuminuria. The excretion of albumin in urine, in the range of 20-200 µg/min (30-300 mg/day) is called Microalbuminuria. This range of albumin is not detected in routine urine tests. Microalbuminuria has been known to be associated with Diabetes Mellitus (Type 1 and 2) over periods of time. Microalbuminuria is defined as the UAER between 30-300 mg/24 hour [5]. Microalbuminuria (MA) as a biomarker now a day is also considered a risk marker for CHD in diabetics and non-diabetics. Patients with microalbuminuria and concomitant diabetes have higher rate of mortality due to the development of CHD. In clinically healthy subjects the levels of atherogenic risk factors are increased if they have associated problem of microalbuminuria. It is also noticed that the patients with MA have more severe angiographic CAD than those without MA [6]. There is increased atherogenic risk factor pattern even in normotensive persons with MA. So it may be taken as a marker for CHD in such patients although it is not certain that the associated metabolic changes of atherosclerosis are due to MA or results from some other metabolic disturbances such as insulin resistance [7]. Moreover MA is independently associated with cardiovascular morbidity, after adjusting the known cardiovascular risk factors of the prevalence of CVD in men and women. It may be a useful indicator of an absolute high cardiovascular risk in the community; yet prospective data is needed to establish its independent predictive value for future events. Where persistent microalbuminuria in diabetic patients is considered a risk factor for renal disease, there it can also be the cause of morbidity and death. Even microalbuminuric individuals without diabetes tend to have increased cardiovascular morbidity in the heart patients. Furthermore the established cardiovascular risk factors are more frequent in diabetic individuals with persistent MA than in normal buminuric diabetic individuals of the same age and sex. About 50% of the albuminuric patients will die due to cardiovascular causes

well before the development of the progressing end stage renal disease. Even in non-diabetic patients, MA has been noticed as factor for the premature atherosclerosis [8]. CAD coexisting with MA is the main cause of morbidity and mortality in patients with PAD. Clinical evaluation and non-invasive tests have limitations for the detection of CAD in patients with PAD [9]. Furthermore MA is the early predictor of death and morbidity in patients suffering from diabetes and hypertension which confirmed the involvement of albuminuria as risk factor for deaths due to heart diseases in future, which is independent of hypertension and diabetes mellitus [10]. In a prospective study non diabetic and hypertensive patients were screened for MA by reagent strips which revealed that MA identifies hypertensive patients, particularly at risk of cardiovascular disease. High sensitivity C-reactive protein has also been found raised in the serum of general population having microalbuminuria, marking microalbuminuria as useful indicator representing low grade systemic inflammation and also a risk factor for cardiovascular system in apparently healthy individuals [11]. The frequency of MA has been found 37% in non-diabetic patients and it was highest in elderly patients [12]. Keeping in view the present perspective this study has been conducted to evaluate the association and prognostic importance of Microalbuminuria in non-diabetic, non-hypertensive patients who have suffered from acute myocardial infarction.

Materials and Methods

A Cross-sectional and hospital based study conducted at CCU, Depart Cardiology, Liaquat University Hospital, Hyderabad.

Characteristics	Frequency/%
Mean ± S. deviation	42.5 ± 10.8 years
Range	20-80 years

Table 1: Age distribution of patients (N=126).

Smoker (n=82)		Nonsmoker (n=44)	
Male	**Female**	**Male**	**Female**
76/(60.4%)	06/(4.7%)	24/(19.0%)	20/(15.9%)

Table 2: Smoking history of the cases (N=126).

Data collection procedure

Total 126 patients with Acute Myocardial Infarction were admitted to Coronary Care Unit Cardiology Department, Liaquat University Hospital Hyderabad. All clinical and laboratory data was collected during the first week of hospitalization. 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. The left ventricle ejection fraction and other aspects of heart after myocardial infarction were estimated by echocardiography in first week of admission. A blood pressure was measured using a standard mercury sphygmomanometer and an appropriately sized cuff. Detailed history of patients regarding presence of risk factors was noted. A written informed consent was taken from patients or attendant of the patients on informed consent Proforma after full explanation of procedure in relation to the study and all the data of the study was recorded on the pre-designed proforma. All the data were analysed on SPSS version 16.0.

Results

Total 126 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 80 years (Table 1).

According to the gender distribution male were found in majority 79.3% and females were found 20.7% (Figure 1).

After diagnosis out of 126 patients 77 patients, found with microalbuminuria, furthermore 50% male and 11.11% female were with microalbuminuria. In our study 82 patients were smokers; while 60% male were smoker and 4.7% female were smoker (Table 2).

In the present study cardiac enzyme CK-MB was seen raised in 98 patients, out of them 63/50.0% were fund with MA. Troponin T was positive in 108 cases, out of them 68/53.9% were with MA (Table 3).

TROPT (n=126)			CKMB n=126	
	Positive	**Negative**	**Raised**	**Normal**
MA	68/53.9%	09/7.2%	63/50.0%	14/11.11%
NMA	40/31.7%	09/7.2%	35/27.7%	13/10.3%

Table 3: Distribution of cardiac enzymes (n=126).

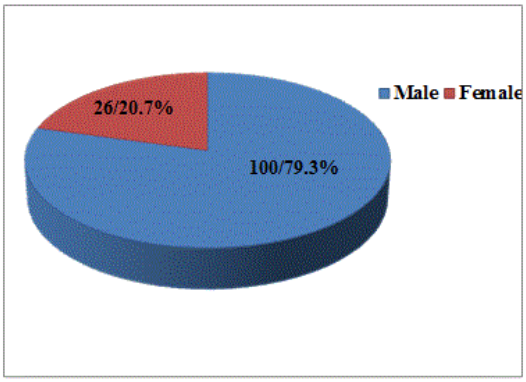

Figure 1: Gender distribution (N=126).

Blood urea was raised in 20 patients, from them 17/13.4% having MA. Raisedserum creatinine was found in16 of cases, out of them 12/9.5% were noted with MA (Table 4).

Based on ECG (electrocardiogram) findings,Anterior wall MI was found in 51 cases, NSTEMI in 34 cases and Inferior wall MI was found in 26 patients, from these most common findings MA was found in 36/28.5%, 20/15.8% and 17/13.4% respectively (Table 5).

In this study complications associated with acute myocardial infarction were noted as Extension of MI, Re MI, Arrhythmias, Post myocardial angina, Shock, Heart block, Pericarditis, Heart failure, and Mechanical complications (VSR, Acute MR) The complications like

Re-MI, Extension of MI, Arrhythmias, Post-MI angina, Shock, And mechanical complication were more associated in group of patients having Microalbuminuria while complications like Heart block and heart failure were more seen in group of patients of Normoalbuminuria.

UREA (n=126)			Creatinine (n=126)	
	Raised	Normal	Raised	Normal
MA	17/13.4%	60/47.6%	12/9.5%	65/51.5%
NMA	03/2.3%	46/36.5%	04/3.1%	45/35.7%

Table 4: Distribution of the blood urea and creatinine (n=126).

Findings	MA	NMA
Anterior wall MI	36/28.5%	15/11.9%
Inferior wall MI	17/13.4%	9/7.2%
Inf+RV MI	10/7.9%	8/6.3%
Lateral wall MI	3/2.3%	1/0.7%
Posterior wall MI	1/0.7%	2/1.5%
NSTEMI	20/15.8%	14/11.11%

Table 5: Distribution of the cases according to Base on ECG (electrocardiogram) (n=126).

Majority of the deaths was seen in the patients with Microalbuminuria 12.8% while in the patients with Normoalbuminuria were with mortality of 7.5% (Table 6).

Days	Normoalbuminuria n=(49)				Microalbuminuria n=(77)			
	Survival		Death		Survival		Death	
	N.of pt	%	N.of pt	%	N.of pt	%	N.of pt	%
1-15	70	55.55%	1	6.15%	52	91.42 %	3	8.57%
16-30	66	52.38%	4	9.23%	45	85.71 %	7	5.71%

Table 6: Short term survival of the patients (n=126).

Discussion

In the study of Palwasha Sahibzada et al. [13,14] reported that total of 45.1% patients were with STEMI, from them 29% were anterior wall myocardial infarctions and 16% were inferior wall MI, 29% patients suffered NSTEMI and 29% were diagnosed as ACS. Similarly in this study on ECG and cardiac biomarkers findings 38% were noted with anteriolateral wall MI, 30.0% with inferior wall MI. Posterior wall MI,LWMI, NSTEMI, a VR MI with percentage of 1.5%, 2.0%, 35.0% and 1.5% respectively. In the study of Singh et al. [15] reported that troponin T test was positive in the 100% cases with acute MI. According to AlaHussain Abbase Haider [16], level of CK-MB divided into two groups, group with elevated CK-MB patients 35.7% and group with normal CK-MB patients 64.3%. In our study cardiac enzyme CK-MB was seen raised in 76% and Troponin T was positive in 81% of the cases. In our study complications associated with acute myocardial infarction were noted as Extension of MI, Re MI, Shock, Arrhythmias, Post myocardial angina, Heart block, pericarditis were more common in patients having Microalbuminuria. Majority of the cases in our study (79%) had normal renal function (<30 mg/dl), creatinine ≤ 1.1 mg/dl. Microalbuminuria in these patients was therefore not related to renal dysfunction. Our study in this respect agrees with Peter Gosling, who considered it to be a sensitive indicator of non-renal disease [17]. Haffner et al. [18] considered Microalbuminuria as a cardiovascular risk factor in the non-diabetic patients. Gosling et al. [19,20], also considered it to be an emerging cardiovascular risk factor though he felt more studies are required to come to conclusion. Our study agrees with these observations as it shows a significant Microalbuminuria in the acute myocardial infarction patients and they are non-diabetic. Hypertension can also lead to Microalbuminuria [21]. It is to be seen how Microalbuminuria is related to cardiovascular diseases in those who are non-diabetic and non-hypertensive. Studies indicate that Microalbuminuria occurs in the non-diabetic, non-hypertensive population and that it is an independent risk factor in this group of patients for cardiovascular diseases. Hillege et al. [22] demonstrated Microalbuminuria prevalence rate of 6.6% in diabetic non-hypertensive patients. However Romaunstadt et al. [23] considered other risk factors and other markers to be influencing Microalbuminuria in non-diabetic and non-hypertensive individuals with high risk of cardiovascular diseases compared to those with low total risk. Our study has shown Microalbuminuria in 77 of patients out of 126 patients. Therefore our study agrees with the fact that Microalbuminuria does occur in non-diabetic, non-hypertensive patients, but it does not agree with the percentage of patients (Prevalence rates) of Microalbuminuria found in other studies. The higher values in our study might be due to effect of smoking which was present in 65% (82/126) of our study patients. The results of our study indicate that there is highly significant Microalbuminuria in non-diabetic, non-hypertensive acute myocardial infarction patients and significance of Microalbuminuria in our study was comparable to that observed other international studies. [24,25] The level of Microalbuminuria in acute myocardial infarction in our study was significantly correlated with cardiac markers.. In Our study the mortality in the patients with Microalbuminuria was 12.8% whiles in the patients with Normoalbuminuria the mortality was 7.5%. Therefore our study agrees with Klausen et al. [26], study where they found Microalbuminuria to be independent risk factor of CVD and death, independent of renal insufficiency, diabetes and hypertension. Thus the major pathophysiologic cause of Microalbuminuria in our clinical setting seems to be a systemic inflammatory response. This leads to an increased capillary permeability to proteins. This effect is amplified by kidneys and manifests as Microalbuminuria. However a tubular dysfunction leading to tubular reabsorption cannot be ruled out.

Conclusion

In our study we found a significantly high Microalbuminuria levels in non-diabetic, non-hypertensive acute myocardial infarction patients. The level of significance of Microalbuminuria in our patients was comparable to the conventional cardiac markers like TROP-T and CK-MB. In the absence of renal insufficiency Microalbuminuria is a non-specific yet highly sensitive marker of myocardial infarction. Since the Microalbuminuria is simple investigation and relatively inexpensive test, we propose the use of Microalbuminuria as an

adjunct biochemical parameter in non-diabetic, non-hypertensive acute myocardial infarction patients.

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