‘‘STUDY OF MICROALBUMINURIA IN NON DIABETIC PATIENTS WITH ACUTE MYOCARDIAL INFARCTION ’’

BY

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DOCTOR OF MEDICINE

IN

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UNDER THE GUIDANCE OF

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LIST OF ABBREVIATIONS USED

AF	.....	Atrial fibrillation
CAD	.....	Coronary artery disease
ATP	.....	Adenosinetriphosphate
VT	.....	Ventricular tachycardia
VF	.....	Ventricular fibrillation
ECG	.....	Electrocardiogram
IHD	.....	Ischemic heart disease
CCF	.....	Congestive cardiac failure
LVF	.....	Left ventricular failure
JVP	.....	Jugular venous pressure
MAU	.....	Microalbuminuria
ACLS	.....	Advanced cardiac life support
FLP	……	Fasting lipid profile

ABSTRACT

Introduction.

Microalbuminuria has been an established indicator for micro and macrovascular pathology in diabetics. But there is growing evidence that microalbuminuria may be an important indicator of future chance of developing coronary arterial disease. This study was conducted to establish a relationship between microalburminuria and Ischemic cardiac Disease in non-diabetics.

Objective:

This is an observational study designed to study of microalbuminuria in non diabetic patients with acute myocardial infarction.

Methods:

`50 randomly selected non-diabetic patients with Ischemic Heart Disease who fulfilled the criteria for the study were evaluated for traditional risk factors and microalbuminuria in **BLDE (DEEMED TO BE UNIVERSITY) Shri B.M Patil Medical college Hospital and Research center ,Vijayapura** from November 2018 to June 2020.Information was collected through prepared proforma from each patient. All patients were interviewed as per the prepared proforma and then complete clinical examination was done.

Results:

Mean age of patients was 59.5±12.8 years. There were 44 male patients and 18 female patients in the study group. The predominant type of MI is inferior wall MI followed by anterior wall MI and lateral wall MI. Microalbuminuria was present significantly in 39 (62.9%) patients. MAU is also seen independent of smoking status, BMI, total cholesterol in patients of myocardial infarction with significant p value. Also in our study more common presentation was anterolateral wall MI but there was no significant correlation.

Conclusion:

From the above findings, our patients with ischemic heart disease had a significantly positive association with microalbuminuria. Hence, microalbuminuria can be regarded as an additional risk factor for ischemic heart disease.

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INTRODUCTION

Coronary heart disease (CHD) has been defined as impairment of heart functioning because of inadequate blood supply than its demand secondary to obstructive alteration in coronary flow. In year 2000, CHD contributed to 15.3 million deaths, equivalent to 30% of the global mortality. Of these 9.77 million deaths were across developing nations. The 5.52 million deaths across developed nations amounted to 76% more deathswhen compared to their population.[1]

The Indians and its diaspora across the world have one of the highest rates of CHD. Indian urban dwellers have as high as 10-12% prevalence of coronary artery disease (CAD).[2]Generally,they have more advanced presentation at first diagnosis, as compared to whites or other Asians. The affected Indians are mostly younger working population with a significant overall social and economic impact.[2, 3]. The decline in CAD related mortality and morbidity across western world, is not reciprocated in India.[3]The etiological factor for CAD, atherosclerosis, develops and progresses for decades prior to acute myocardial infarction (AMI).[4]Factors such as age, diabetes mellitus (DM), prior angina, heart failure, microalbuminuria (MAU),and depressed left ventricular function adversely affect prognosis of AMI.

Microalbuminuria was first designated as a risk factor for chronic renal failure in diabetic patients.[5] It was also established as responsible factor for vascular damage.[6] The MAU correlate with left ventricular wall thickness independent of blood pressure. It has been documented that there is increased prevalence of MAU in patients with AMI.[7]Among the manifestations of AMI, microalbuminuria (MAU)is associated with increased risk for in-hospital mortality.[7]The MAU predicts all-cause mortality in diabetics as well as general population.[5], [8], [9], [10]

A better understanding of the mechanisms of MAUdevelopment may assist in designing novel therapies. Microalbuminuria is result of an increased leakage of albumin through the complex glomerular sieve, which is called as the glomerular filtration barrier. Theleakage is secondary to alteration in the physio-chemical characteristics of theglomerular filtration barrier. However, the enhanced glomerular permeabilityin absence of explicit histological changesand suggestmore subtle ultrastructurealteration as the pathological mechanism. The epidemiological data indicate a close association between systemic endothelial dysfunction and vascular disease in MAU, suggesting major role of glomerular endothelial dysfunction in MAU.[11]

AIMS AND OBJECTIVES

1. To estimate microalbuminuria in non-diabetics having evidence Ischemic heart Disease.
2. To study the relation of micro albuminuria with Ischemic heart Disease in these subjects.

REVIEW OF LITERATURE

Blood supply of the heart

The heart's metabolic needs are very high. Unfortunately it holds limited energetic reserves to endure its immense workload. It totally depends on the coronary arterial network for maintaining its blood supply to sustain proficient cardiac muscle function.

Origin and course of coronary Arteries

The heart receives its blood supply from the right and left coronary arteries. These arteries arise from anterior aortic and left posterior aortic sinus respectively. The coronary arterial network originates just above the aortic valve, where the right and left main coronary arteries connect to the ascending aorta. These arteries branch out into smaller-diameter arterioles that connect to capillaries, where oxygen exchange takes place (Figure 1).[12]

After arising from the anterior sinus, right coronary artery passes between the right auricular appendage and the infundibulum of the right ventricle. Then it turns backwards at the inferior border of the heart and goes posteriorly. It gives branches to both atria and ventricles along the way vertically downwards. At the inferior border, the marginal branch goes to the left along the right ventricle. The inferior interventricular branch is given off on the diaphragmatic surface that passes along the interventricular groove to the apex of the heart. There is anastomoses of terminal part with the terminal arterioles of the coronary artery at the lower part of the leftatrium.[12]

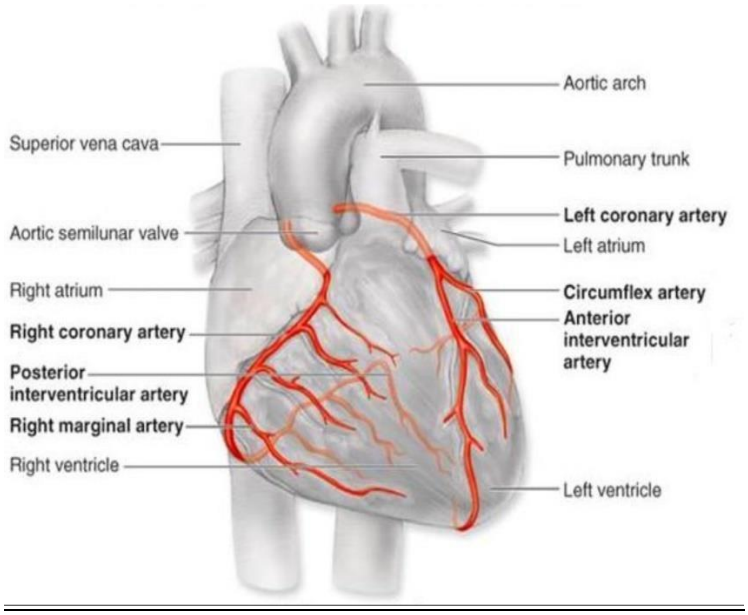


Figure 1: Blood supply to the heart

The left coronary artery at its origin bifurcates into anterior descending artery and left circumflex artery. The anterior descending artery travels in the interventricular groove to anastomose at the apex with the end artery branches of the inferior interventricular artery.

The left circumflex gives rise to branches to the posterior wall of the left ventricle and goes ahead to anastomose with the termination of the right coronary artery, below the coronary sinus. In about 40% of the subjects, it gives off a large branch, whichgoes over the posterior surface of the left atrium to end in the auricular appendage of the right atrium at the sino-atrial node. [(21)]

Anastomoses of Coronary Arteries

The anastomoses are situated between the distal end of the right and left ventricles of the atrrioventricular groove. The floor anastomosis areinsignificant.Intercoronary anastomoses are found freely at arteriolar level, between the inter-ventricular arteries. If the intraventricular arteries meet at the apex, this leads to large anastomosis. If the union site of the intraventricular arteriesare

inadequate to reach the apex, leading to potential reduction in the anastomotic area. In about 10% of the people the inferior as well as the anterior interventricular artery is a branch of the left coronary. These individuals do not have any anastomosesbetween thecoronary arteries. (12)

The chances of anastomoses also exist between the coronary arteries and pericardial arteries derived from the pericardiophrenic, the bronchial and the internal thoracic arteries. In very rare instances, one of these may open to replace a coronary artery.

Distribution of the Coronaries

The right coronary arteryprovides blood supply toright ventricle except at the upper margin of its anterior surface, where anterior interventriculararteries takes the role of blood supply. The left coronary artery provides blood supply to left ventricle except for a narrow strip of the diaphragmatic surface where it is supplied by the inferior interventricular artery. The two interventricular arteries share the area of blood supply to the interventricular septum, usually aboutequally.

Right coronary artery provides blood supply to the anterior surface of the right atrium.Left coronary artery provides blood supply to the posterior surface and the auricular appendage of the left atrium.(12)

SA Node: A branch of right coronary artery provides blood supply to SA Node in 60% of individuals and left coronary artery provides blood supply to40% of the individuals. The inferior interventricular artery provides blood supply toAV node and bundle of His, which arises in 90% of cases from the right coronary and in only 10% from the left coronary.

Dominant Arteries: In 67% of the people right coronary is dominant andin 15% of people it is the left coronary that is dominant. Whereas about 18% of individuals there is a balanced coronary arterial supply.

Physiology of Coronary Circulation

Although anatomically there are numerous intercoronary anastomoses, functionally, both the right and left coronary arteries behave as end arteries. Only the inner 75-100 microns of the endocardium can obtain significant amount of nutrition directly from the blood in the cardiac chamber.

Normal Coronary Blood Flow

The average resting coronary blood flow in human beings is about 225 ml/ min or 0.7-0.8 ml/G of heart muscle or 4.5 percent of the total cardiac output. During exercise, about 4 to 5 fold increase can occur.The heart requirement is the highest per gram oxygen consumption as compared to any organ (~50–100 μL O_2/min/g). It extracts ~70% to 80% of delivered oxygen even under resting conditions (coronary venous PO_2 ~18–20 mmHg). [12]

Phasic Changes in Coronary Blood Flow

During the contraction of heart, there is squeezing of the blood out of the cardiac musclesresulting in decreased blood in the cardiac muscle tissue and vice versa during diastole. This results in decreased bloodflow during systole that increases during diastole. The cardiac muscle tissue of left ventricle is more affected than the right because of its thickness (Figure 2).[12]

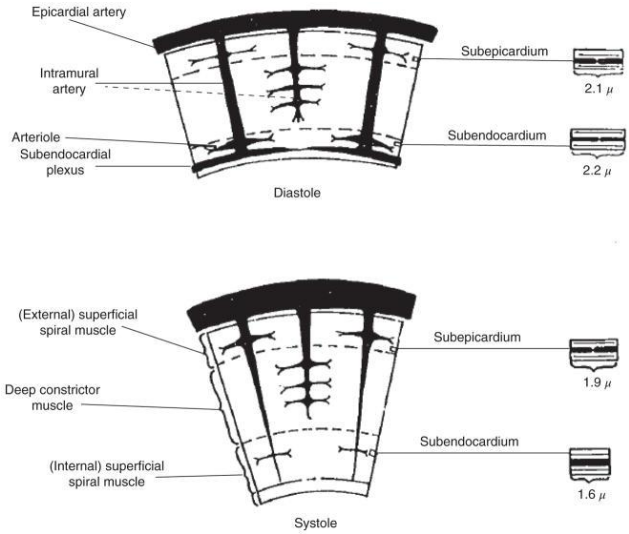


Figure 2: Schematic cross-section of the myocardial wall at end-diastole and end-systole[12]

The intramyocardial pressures compress the subendocardial blood vessels more than the outer vessels, which hamper its blood supply. Therefore,to compensate for reduced blood supply, the subendocardialvessel is much larger as compared to the nutrient arteries in the middle and outer layers of the heart. The arrangement allows increase in the blood flow during diastole as required.[12]

Control of Coronary Blood Flow

Over centuries of dedicated research has provided insights that coronary blood flow is regulated by extremely complex multiple mechanisms. These include extravascular compressive forces (tissue pressure), coronary blood pressure, myogenic, local endothelial, metabolic, as well as neural and hormonal factors. All these mechanisms have significant influence over myocardial blood supply. These mechanisms collectively regulate coronary vascular resistance and work to ensure that the myocardial demands for oxygen and substrates are adequately fulfilled by the coronary circulation largely through effects on end-effector ion channels (Figure 2). [12]

1. Local metabolism ofmyocardium – A primecontroller
2. Nervous control

1) Local metabolism of myocardium: The rate of flow increases with the vigor of contraction and decreases with decrease in activity[12]. The factors responsibleare:

a) **Oxygen Demand**:

A major factor of all: As oxygen extraction is near complete in resting state only, increase in oxygen demand has to be met with by increasing the blood flow. This is achieved probably by the following mechanisms[13]:

1. **Vasodilator Theory**: Anoxia will liberate many vasodilator materials from myocardial cells which increase the bloodflow[14]:
   i) Adenosine from theATP
   ii) Potassiumion
   iii) Hydrogenion
   iv) Carbon dioxide
   v) Bradykinin andpossibly
   vi) Prostaglindins

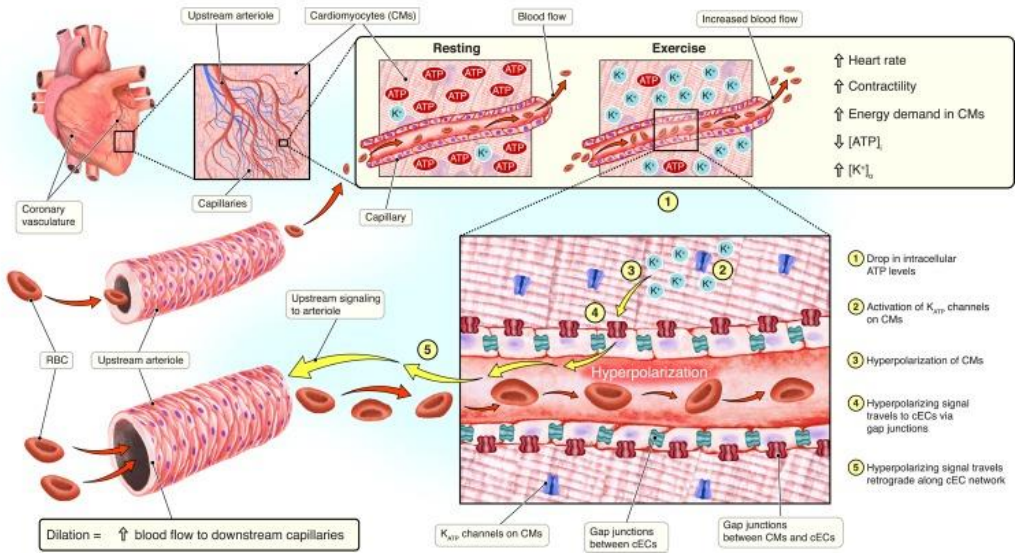


Figure 3: Metabolic–electrical signaling in the coronary vasculature(13)

During resting phase, cardiomyocytes (CMs) have high levels of intracellular ATP ($[ATP]_i$) and low levels of extracellular K^+ ($[K^+]_o$). During myocardial contraction, levels of $[ATP]_i$ are lowered and $[K^+]_o$ increases. Reduced $[ATP]_I$ levels stimulates the activation of K_{ATP} channels expressed in the CM plasma membrane. Efflux of K^+ ions induces hyperpolarization of CMs. Hyperpolarizing current passes to electrically coupled capillary endothelial cells (cECs) via gap junctions. The hyperpolarizing signal then travels in a backward direction along the cEC network to an upstream arteriole. This hyperpolarizing signal causes relaxation of the smooth muscle cells in the coronary arteries (Figure 3).[14]

Zhao et al. demonstrated that adenine nucleotide-mediated pathway helps in regulation of coronary blood flow (Figure 3). The authors demonstrated that K_{ATP} channels, expressed on CM, represent the metabolic sensor. K_{ATP} channels are opened by a fall in intracellular ATP ($[ATP]_i$) concentrations. Consequently, any decrease in $[ATP]_i$ will result in an efflux of K^+ from cardiomyocytes and subsequent hyperpolarization. Since $[ATP]_i$ levels drop during increased metabolic activity in cardiomyocytes, K_{ATP} channels provide the necessary link between metabolism and the production of an electrical signal.[14], [13]

2. **Arterial Smooth Muscle Relaxation Theory**: Reduction in oxygen supply causes anoxia of coronary arterial smooth muscle cells, which loses their tone thus getting the artery dilated. Factors that determine the oxygen consumptionare[12]:
    a) Higher the workload, higher is the oxygen consumption, within the physiologicallimitations.
    b) Oxygen consumption is proportionate to peak myocardial muscletension.
        i) Increased arterial pressure, increases the workload and hencetension.

ii) Dilatation of the heart increases the tension development in myocardium to pump the blood according to Laplace law, which states that tension required to generate a given pressure increases in proportion to the diameter of theheart.

c) Other factors which increase the oxygen consumption like stimulation of the heart by epinephrine and norepinephrine, thyroxine, digitalis, calcium ions, increased temperature of heart, will increase the oxygen consumption.

d) Reactive hyperemia: Anoxia brings about increase flow because of coronary dilatation after a brief period of coronaryocclusion.

2) Nervous Control

a) **Indirect**: Sympathetics increases the heart rate and contractility, through the local metabolic mechanisms, and hence increases the coronaryflow.Parasympathetics decrease the heart rate anddepresses the myocardium and hence brings about coronaryconstriction.[12]

b) **Direct Effect:**

Parasympathetics: As the vagal supply to ventricles is negligible, except for slight dilatation which may occur, there is no effect of its stimulation.**Sympathetics**: Epinephrine and norepinephrine through their receptors in coronary vessels usually bring about vasoconstriction or no change. When alpha effect dominates, severe constriction occurs which may bring about anginal attack.[12]

Epidemiology of coronary heart disease

After gaining tremendous insights on the prevention, diagnosis and management of atherothrombosis, cardiovascular disease (CVD) continues to be a critical cause of disability and premature death around the world. In the year 2010, an

estimated 16.7 million deaths were recognized to be due to CVD; with projections revealing anastounding 23.3 million by 2030 worldwide.[15] Coronary heart disease (CHD) is the most frequent cause of global mortality. In the United States, CHD accounts for 375,295 deaths with an estimated 635,000 incidence of coronary events (defined as first hospitalized MI or CHD death) annually.[15] In 2014, an estimated 2.3 million individuals had CHD accounting for about 69,000 deaths (15% of male deaths and 10% of female deaths) inUnited Kingdom (UK). [16]Most of CVD can be prevented by modifying the lifestyle risk factors such as smoking, unhealthy diet and obesity, sedentary lifestyle and excess intake of alcohol.

Currently India is going through an epidemic of cardiovascular diseases, especially coronary heart disease (CHD). As per the Registrar General of India, CHD is responsible for 17% of total deaths and 26% of adult deaths in 2001-2003, which increased to 23% of total and 32% of adult deaths in 2010-2013.

The World Health Organization (WHO) and Global Burden of Disease Study have projected increasing trends in years of life lost (YLLs) and disability-adjusted life years (DALYs) from CHD in India. Epidemiological studies in India have reported increasing CHD prevalence over the last 60 years, from 1% to 9%-10% in populations living in cities and <1% to 4%-6% in populations residing in rural areas. The prevalence of CHD in India ranges from 1%-2% in rural populations and 2%-4% in urban populations when more stringent criteria (clinical ± Q waves) are used to define CHD, which reflects a more realistic prevalence.The significant risk factors for CHD in Indian population are diabetes, hypertension, abdominal obesity, dyslipidemias, smoking, psychosocial stress, unhealthy diet, and physical inactivity. It is a urgent requirement to have practical preventive strategies overcome this epidemic.[17]

Among patients suffering from AMI, 70% of fatal events are due to occlusion from atherosclerotic plaques. As atherosclerosis is the predominant cause of acute myocardial infarction, risk factors for atherosclerotic disease are often alleviated in the prevention of disease. Modifiable risk factors account for 90% (men) and 94% (female) of myocardial infarctions.[18]

Indeed, through early diagnostic strategies, advanced medical treatment, lifestyle modification and risk factor reductions, UK age-standardised CHD death rates declined by 73% for all ages, and 81% for those dying before the age of 75, between 1974 and 2013.[16] Nonetheless, with falling CHD mortality rates, an increasing number of people live with CHD and may need support to manage their symptoms and improve prognosis.

Pathophysiology of acute myocardial infarction

Acute myocardial infarction (AMI) is among the most serious and disastrous of acute cardiac disorders, resulting in large number of deaths every year globally. Although the incidence of AMI has been decreasing in some countries, heart disease is still continues to be the leading cause of deaths in adults. In majority cases of AMI, the underlying pathology is acute intraluminal coronary thrombus formation within an epicardial coronary artery leading to total or near total acute coronary occlusion.[4]

Acute myocardial infarction defined as myocardial necrosis due to a lack of oxygen because of interruption in the blood supply to cardiac tissue as a result of partial or complete blockage of branches of coronary arterial network. In other words AMI is caused by an acute imbalance in the ratio of cardiac tissue blood supply to cardiac oxygen demand in the heart. So when there is an acute coronary thrombosis, to leads to acute drop in blood flow, resulting in myocardial necrosis in the myocardial segment supplied by the involved coronary artery. It may lead to impairment in

diastolic and systolic function and making the patient susceptible to development of arrhythmias. Additionally, an AMI can cause several serious complications. This clinical evidence of AMI is clinically diagnosed by the presence of patient's symptoms, acute electrocardiograph (ECG) findings, or other evidence indicating a new cardiac wall movement irregularity in a segment of the myocardium.[19]

Coronary pathophysiology

The fundamental pathophysiologic mechanisms in AMI commences with the development of atherosclerosis, which evolves and progresses for decades before the occurrence of the acute event.Atherosclerosis refers to a low-grade inflammatory condition of the intima (inner lining) of medium-sized arteries, wherein there is accumulation lipids, cholesterol and other substances in leading to the formation of plaque, which can restrict blood flow. It that is enhanced by risk factors such as hypertension, high lipid levels, smoking, diabetes, and genetic abnormalities.

When atherosclerosis commences in coronary arteries, initially it is slow progression leading to the gradual thickening of the inner layer, which gradually narrow the lumen of the artery to significantly. Atherosclerosis leading to the AMI has a preference for the proximal segments of the major coronary arteries frequently at arterial bifurcation points that modify flow in the artery.[20]This gradual progression of atherosclerosis may be interrupted by one or more cycles of rapid progression resulting in one of eithercourses: either plaque disruption with formation of a non-occlusive intraluminal thrombus without any symptomatic or plaque hemorrhage (Figure 4).

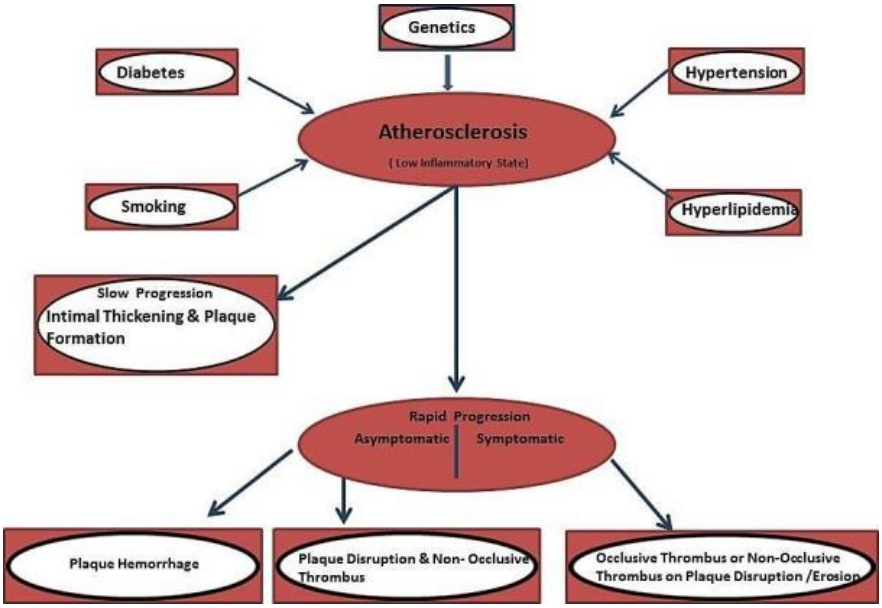


Figure 4: Pathophysiological progression of atherosclerosis

Asymptomatic plaque disruption

An atherosclerotic plaque is consist of inflammatory cells, cellular debris, smooth muscle cells (SMCs), and different quantity of cholesterol and cholesterol ester, some of which are present as cholesterol crystals. This lipid core is developed in some plaques beneath a fibrous cap made up of collagen, SMCs, and elastin. On its luminal side, the cap is enclosed by a single layer of endothelial cells. Large amount of inflammatory cells, derived foam cells arising from circulating monocytes travel into the arterial wall and may weaken and thin out the fibrous cap. These plaques are called as thin-capped fibroatheromas (TCFA) (Figure 5) which can ultimately disrupt revealing the thrombogenic lipid core. This lipid core on exposure to the flowing blood, results in the development of an intraluminal coronary thrombus. The fate of this thrombus is decided by several factors. These factors are:

a) Plaque composition, and volume

b) Degree of luminal narrowing

c) Size of the cap tear, and

d) Thrombotic milieu (a complicated interaction of different forces that ultimately determine how prothrombotic the blood is)

The thrombus may meet one of the following fates[21]:

a) Break spontaneously
b) Remain as it is
c) Later get incorporated into the wall of the artery (further narrowing the lumen)
d) Grow and progress to total or near coronary occlusion
e) Symptomatic acute coronary event

Depending on pathologic assessment of patients with AMI, there are could be many episodes of asymptomatic coronary thrombus that have been incorporated into the arterial wall prior to the final fatal event.[22]

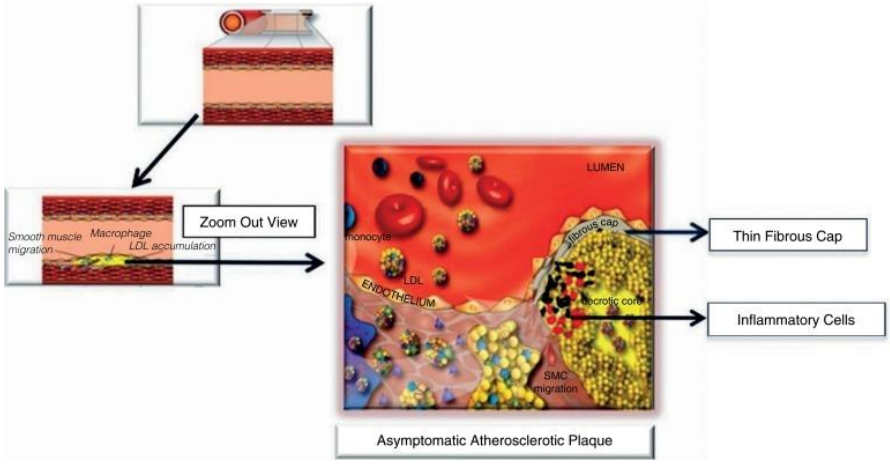


Figure 5: Formation of an asymptomatic atherosclerotic plaque (Thin-capped fibroatheroma)

Intraluminal coronary thrombus formation can also result from plaque erosion. The site of plaque erosion acts as site where the thrombus forms in the endothelial layer. Inflammation may or may not be present. The cap is generally thick. The prothrombotic milieu is a critical factor in the progression. The plaque erosions are common in smokers and in women < 50 years of age. Majority of the insight on

plaque erosion are obtained from symptomatic patients with an acute coronary event and it is not whether these changes occur in asymptomatic patients. [4]

Plaque hemorrhage

The thick intima of an artery needs to be nourished by sufficient blood supply which by the small vessels or vasa vasorum. This intimal blood supplier generally grows from the adventitia or outer layer of the artery into the media and intima providing the required nutrients. Vasa vasorum are thin-walled, and their endothelial integrity is not always maintained. They are quite vulnerable to rupture into the intima leading to enlargement the plaque size by the blood accumulation. Moreover, the erythrocyte cell membrane is rich in lipids which increase the lipid and inflammatory cell composition of the the.[23]Thus, intermixed slow progression and rapid progression cycles causes the growth of plaque. However, as the plaque increase in size, it does not necessarily result in the narrowing arterial lumen. There is remodelling of arterial wall and when plaque volume approaches 40%, it starts narrowing of the arterial lumen.[24]This phenomenon is called as Glagovian or positive remodeling, is partly responsible for the angiographic finding that plaques ultimately result in acute coronary events which are often non-obstructive (<50% diameter stenosis) in the weeks to month prior to the event.[25]

It is feasible to view the inside of the artery with the help of angiogram but not possible to assess the arterial wall. Large and bulky plaque are ultimately responsible for the acute event (usually termed vulnerable or high-risk plaques). Owing to remodelling process, the lumen of artery may appear normal or only mildly narrowed on the angiogram.[4]

Symptomatic coronary occlusion

In most cases intraluminal coronary thrombus formation is responsible for symptomatic coronary occlusion. This was based on post-mortem pathologic assessment of patients with a fatal coronary thrombosis. The plaque rupture is usually found in about 66% to 75% of cases.[26]In 84% of cases presenting with ST segment elevation on their ECG, angiograms carried out within 4 hours of the onset of AMI symptoms revealed total occlusion of the coronary artery and the remaining patients had almost a near total occlusion with some flow to the distal branches.[27]

In large number of patients, the thrombus that is found is older than the clinical presentation of the AMI. When thrombus was removed from the involved coronary at the acute presentation during percutaneous coronary intervention (less than 12 hours after the onset of symptoms), partially organized thrombus was found in about 50% of patients. This indicates that it formed before the onset of symptoms.[28]

The pathophysiology involved in AMI seems to be little dissimilar when examined in the living patient. Moreover it also isbe determined by the type of AMI. Clinically, AMI can be classified based on the ECG as ST elevation myocardial infarction (STEMI) and non-ST elevation myocardial infarction (NSTEMI). Generally, STEMI mostly involves presents with total coronary occlusion and the grade of myocardial necrosis (or the myocardial risk of necrosis) is greater as compared to NSTEMI.

There is lower incidence of total coronary occlusion in NSTEMI, nevertheless if the artery lumen is not completely blocked; there is involvement of more than one artery. These involved arteries demonstrates a severe blockage (>70% diameter stenosis) with an intraluminal coronary thrombus. Differences in STEMI and NSTEMI pathophysiology have been reported during evaluation with intracoronary

devices at the time of acute presentation to the catheterization laboratory for coronary intervention. Ocular coherence tomography when used to evaluate intraluminal pathology, plaque rupture was reported in 72% of STEMI and 32% of NSTEMI. There was plaque erosion reported in 28% of patient with STEMI and 48% of patients with NSTEMI. Calcified nodules could be also the cause forNSTEMI, although not commonly found (<10%). They may be responsible for the underlying mechanism in fatal coronary thrombus.[29]

Another study using intraluminal catheterduring the acute presentation of AMI demonstrated the presence of lipid-rich plaque in patients presenting with STEMI. Intense yellow plaques (a sign indicating plaque lipid) were found in 19 of 20 patients with an acute coronary occlusion.[30]

Assessment of patient with vulnerable plaque

The vulnerable or high-risk plaques are the thrombosed plaque that is likely to progress in the future resulting in acute coronary events. Diagnosis based only on symptoms alone is not useful asmajority of the patients do not have occlusion of coronary artery and are asymptomatic in the weeks prior to the event. However, there no consensus on the ideal and most cost-effective methods to prevent future acute coronary events. It is not clear whether identification of the responsible plaque or focusing on the high-risk or vulnerable patient likely to develop the acute clinical event is more helpful.

Detection of vulnerable plaque can be made by a device, either invasive or (preferably) non-invasive. Both types of devices have certain limitations. In case an invasive methodology is that all of the detectors are focusing on finding the responsible TCFA and do not consider the plaque erosion. Non-invasive detectors of a vulnerable plaque are inadequate and need more prospective evaluation for validation.

The vulnerable plaque detection and management are really challenging and efforts should be focused on the high-risk or vulnerable patient.However it is difficult to identifypatients who will ultimately develop AMI. Traditional risk factor scores are inadequate because although those individuals are at highest risk, they are more likely to develop adverse events. Most adverse events on follow-up do not occur in these patients, but in the middle- or lower-risk populations. Those at middle- or lower-risk are much larger in numbers than the high-risk populations.[31]

Researcher around the world are evaluating various methods of risk evaluation in primary prevention, that include intimal-medial thickness of the carotid artery, and iliofemoral atherosclerosis by ultrasound and coronary calcification by computed tomography scanning. These efforts are to identify those subgroups that might require intensive medical treatment to decrease subsequent risk.

Clinical features of acute myocardial infarction

History and Physical

The medical disease history and physical examination are often inconsistent during the evaluation ofAMI. Thehistory should concentrate on the onset, quality, and associated symptoms. Current data indicate that diaphoresis and bilateral arm radiating pain are most often associated with myocardial infarction in men. [32]Associated symptoms consist of:

- Anxiety
- Lightheadedness
- Choking sensation
- Cough
- Wheezing
- Diaphoresis

- Irregular heart rate

Physical examination essentially should include a note vital signs and patient's appearance, such as diaphoresis, along with lung findings, and cardiac auscultation. The common signs and symptoms observed in patients with AMI include:

- Tachycardia, atrial fibrillation or ventricular arrhythmia
- Unequal pulses suggest aortic dissection
- High blood pressure or hypotension if the patient is in shock
- Neck veins may be distended indicating right ventricular failure
- Heart: lateral displacement of apical impulse, soft S1, palpable S4, new mitral regurgitation murmur. A loud holosystolic murmur radiating to the sternum may be indicative of ventricular septal rupture.
- Tachypnea and fever are not uncommon
- Wheezing and rales in case of presence of pulmonary edema
- Cold extremities, edema, cyanosis

Assessment and diagnostic workup

Every patient presenting with chest pain should be subjected to early and rapid ECG testing. Atypical symptoms like abdominal pain or dizziness are often seen in women. They may also present without any chest pain. Patients in the geriatric age group frequently present with shortness of breath for myocardial infarction (MI). Therefore all such atypical presentations should be indications for ECG testing.[33] Although ECG is has very high specificity for MI (95% to 97%), the sensitivity is low (about 30%). The ECG sensitivity can be enhanced by right-sided, posterior lead placement, and repeat ECG testing. Peaked T-waves on ECG, called as "hyperacute T waves," generally suggests early ischemia and will evolve into ST elevation. The

presence of ST-elevations greater than 2 mm in two contiguous leads on ECG (inferior: leads II, III, aVF; septal equal V1, V2; anterior: V3, V4; lateral: I, aVL, V5, V6) are indicators of an ST-elevation MI. Frequently, there are ST depressions that are seen in opposite anatomical areas of the heart.(32)

Sometimes the diagnosis of STEMI can be challenging with ECG, especially in individuals with a left bundle branch block and pacemakers. Sgarbosa has defined criteria that can aid the doctors in diagnosing STEMI in these individuals. In the appropriate clinical setting, isolated ST-elevations in aVR suggest of left main coronary artery occlusion. Deeply biphasic T waves in V2, V3, are frequently predictive of an impending proximal left anterior descending artery occlusion, which could result in severe anterior wall MI.(32)

It is not necessary that all the patients presenting with MI have diagnostic ST-elevation ECG abnormalities. Whenever patients present with typical chest pain, they should be investigated for NSTEMI with subtle abnormalities on ECG, including ST-depressions and T wave changes. Sometime serial ECGs can aid in understanding the dynamic alteration. ECG free of acute changes or any abnormalities is frequently observed in NSTEMI.(32)

There are several guidelines led down for diagnostic purpose that can help the physicians in finding out whether further testing is required in diagnosing patients with NSTEMI. Owing to the poor sensitivity of ECG for STEMI, troponins are also commonly utilized for patients with a doubtful clinical history. The HEART score is also frequently used which has been validated and disseminated for use in suspicious cases and in those patients with risk factors. ECG and troponin level to are useful in deciding the “risk level” of the patient. (32)

Laboratory features

Following laboratory blood investigation are carried out in patients with presentation of AMI:

- Cardiac troponins should be the only marker ordered
- CBC
- Lipid profile
- Renal function
- Metabolic panel

B-type natriuretic peptide (BNP) not generally carried out as a marker for AMI, but it is of significance to stratify risk, especially in patients who progress to develop heart failure followingAMI.

Cardiac Imaging

Cardiac angiography is carried out to perform percutaneous coronary intervention (PCI) and determination of obstructions in the coronary vessels.An echocardiogram is utilized in the assessment of wall motion, valvular abnormality, ischemic mitral regurgitation (MR), and presence of cardiac tamponade.[32]

Treatment / Management

The goal of management is to reperfuse the cardiac tissue by restoring the blood supply. The earlier the intervention (< 6 hours from symptom onset), the better is the prognosis.

All patients with STEMI and NSTEMI should be treated as follows [32], [34],:

- Immediately chewed aspirin 160 mg to 325 mg
- Oxygen supplementation if oxygen saturation is less than 91%
- Opioids may be used for pain control
- Sublingual nitroglycerin if the blood pressure is adequate

- Intravenous access for drug and fluid admiration

The STEMI should be managed with immediate reperfusion preferably with emergent percutaneous coronary intervention (PCI). Prior to PCI, patients should be given dual antiplatelet agents, including intravenous heparin infusion as well as an adenosine diphosphate inhibitor receptor (P2Y2 inhibitor), most commonly ticagrelor. Additionally, glycoprotein IIb/IIIa inhibitor or direct thrombin inhibitor may be administered during percutaneous intervention.(32) In case percutaneous intervention is not within 90 minutes of the diagnosis of STEMI, reperfusion should be carried out by administration of intravenous thrombolytic agent.

Generally, NSTEMI patients are stable, asymptomatic and may not benefit from emergent percutaneous coronary intervention. They should be treated with antiplatelet agents. Percutaneous coronary intervention can be carried out within 48 hours of admission to improve in-hospital survival and reduce length of hospital stay. In case NSTEMI with refractory ischemia or ischemia and hemodynamic or electrical instability patient should be subjected to emergent PCI.[32]

Universally, prior to discharge patients with acute MI, should be always prescribed aspirin, high-dose statin, beta-blocker, and/or ACE-inhibitor.

If PCI is planned, it should be carried out within 12 hours. If fibrinolytic therapy is considered, it should be administer within 120 minutes. All patients should receive parenteral anticoagulation, in addition to antiplatelet therapy.[32]

Differential Diagnosis

- Pericarditis
- Aortic dissection
- Myocarditis
- Acute cholecystitis

- Acute gastritis
- Asthma
- Pneumothorax
- Pulmonary embolism
- Esophagitis

Prognosis

Most deaths in AMI patients occur before arrival to the hospital. About 5%-10% of survivors die within the first 12 months after the AMI. Nearly half of the survived patients require hospitalization within 12 months. The overall prognosis is determined by the extent of muscle damage. Favourable outcomes are observed in thoseindividuals who undergo early perfusion- thrombolytic therapy within 30 minutes of arrival or PCI within 90 minutes. Moreover,chances of survival is better if the ejection fraction is preserved and there is early initiation of aspirin, beta-blockers, and ACE inhibitors therapy.[32]

Factors that adversely affect the outcomes are:

- Advanced age
- Diabetes
- Delayed reperfusion
- Prior MI, peripheral vascular disease (PVD), or stroke
- Elevated C-reactive protein and BNP levels
- Diminished ejection fraction (the strongest predictor)
- Presence of congestive heart failure (CHF)
- Depression

Complications

The complications of AMI include

- New-onset mitral regurgitation
- Ventricular septal rupture
- Left ventricular aneurysm
- Arrhythmias
- Emboli

Microalbuminuria

Mogensen was the first to highlight the significance of Microalbuminuria (MAU) as a renal risk factor and also as a dominant predictor of cardiovascular (CV) mortality among diabetic patients.[5] Since then, MAU has been an useful toolas a prognostic marker for CV or renal risk or both, even in non-diabetic population.[35]Accumulating data suggest a strong relationship between urinary albumin excretion (UAE) and cardiorenal risk, similar to the relationship between blood pressure (BP) and risk of CV events.[36]

The significance MAU as an independent predictor of progressive renal disease and cardiovascular mortality demonstrated in several prospective and epidemiological studies especially in diabetic and hypertensive population.[37], [38]At present the association between MAU, CVD, and progressive renal disease is well established in patients with systemic diseases such as diabetes. In the general population, MAU has also emerged as a significant risk factor for the development of CVD, and the all-cause mortality. With the increasing prevalence of obesity, type 2 diabetes and metabolic syndrome, screening for MAU appears to an important strategy to detect and prevent CVD.[11]

The term ‘Microalbuminuria’ is a relative misnomer: it implies ‘small size’ but actually refers to the presence of a relatively ‘small quantity’ of protein in the urine. The term was first used nearly 30 years ago when referring to urinary protein excretion of 30–300 mg per day or an albumin: creatinine ratio of 2.5 to 25 mg/mmol in men and 3.5 to 25 mg/mmol in women. [39]

Microalbuminuria is now defined as a urine albumin excretion (UAE) between 20 and 200 μg/min or 30 to 300 mg in an overnight or 24-h collection. This range of UAE, although used in the pediatric population, is derived from population studies in adults.[11]MAU is used by physicians for screening and diagnosis of diabetic nephropathy.

There are various methods for analysis of the presence of MAU. The urine dipstick method for analysis of albuminuria has low sensitivity. It gives positiveresult only when albumin excretion exceeds 300 to 500 mg/day. Normally, UAE is < 30 mg/day and when it oscillates between 30 and 300 mg/day in a 24-hour urine collection or 30 to 300 mg/g of creatinine (urine albumin-to-creatinine ratio, or UACR) in a first morning sample, it is referred as MAU, also known as “moderately increased albuminuria”. Increased albuminuria to > 300 mg/dayis considered macroalbuminuria.[40] The gold standard for the detection of MAU is 24-hour urine collection however screening can be carried out from a first morning urine sample or at any time. Recently, the albumin-to-creatinine ratio (ACR) from spot urine, ideally that first morning voided sample should considered similar to the values of a 24-hour urine collection.

Prevalence of Microalbuminuriainacute myocardial infarction

As perthe third National Health and Nutritional Examination Survey (NHANES), the prevalence of AMI is 7.8% (6.1% in males and 9.7% in females), which progressively increasing with age.[41]The prevalence of MAU among non-diabetic population with arterial hypertension varies from 5 to 40 %. Several factors are liable for this high capriciousness such as quality of blood pressure control and associated lipid abnormalities. The studies also may have patient eligibility biases such as age, race, coexisting renal disease. The method utilised in the tests to detect MAU, sampling size, and day to day variability of albumin excretion involve some of the variables impacting the prevalence.[42]

Pathophysiology

The exact pathophysiological role of MAU as the contributor or accelerator of the atherosclerosis is unclear. The present insights indicate that vascular injury associated with MAU differ between those with or without diabetes with hypertension. Patients with MAU also have an increased transcapillary escape rate of albumin and number of other metabolic morbidities such as dyslipidemia, and insulin resistance. Thereare non- metabolic risk factors associated with CVD as well, such as arterial hypertension.In non-diabetics patients with MAU, an increase in vascular permeability is produced by changes in the extracellular matrix. This leads to endothelial dysfunction which is responsible for lipid influx into the vessel wall resulting in atherosclerotic lesions.In several acute and chronic health disorders, MAU is associated with enhancedvascular permeability as the final common pathway. Theseare associated with complement activation and activation of neutrophil granulocytes, macrophages, and endothelial cells by participation of various inflammatory mediators.[42]

In non-diabetic individuals, the role of albumin in the pathogenesis of vascular disease could be different from those with diabetes. In diabetic individuals, the glycation of albumin into an antigenic molecule triggers a several cellular and immune reactions, such as activation of polymorphonuclear leukocytes. Additionally, there is direct injury to glomerular membrane selectivity.(42)

Microalbuminuriaas a marker of generalized endothelial damage

Endothelial dysfunction plays a key role in the pathophysiology of CVD, including hypertension, coronary artery disease (CAD), chronic heart failure (CHF), peripheral artery disease (PAD), diabetes, and chronic renal failure (CRF). Adverse changes in endothelial function commences prior to the start of morphological atherosclerotic changes and contributes in the development of lesions and following clinical complications. These pathological changes begin early in childhood. (11)

MAU along with von Willebrand Factor levels, a marker of endothelial dysfunction, can predict endothelial dysfunction development. The link between endothelial dysfunction and MAU seems to be important in predicting the development of diabetic nephropathy and susceptibility to micro- and macrovascular disease.(11)

Endothelial dysfunction, as critical precursor of MAU, provides a logical explanation for the association between MAU and vascular disease in diabetes. It is responsible for producing a breach in the sieving action of kidney leading to MAU.Glomerular structural alteration typical of glomerular diseases like diabetic nephropathy include an increase in glomerular size, thickening of the GBM, expansion of the mesangium, and effacement of podocyte foot processes. The

enhancement in glomerular size is result of both mesangial expansion and enlargement in glomerular capillaries due to hemodynamic changes.[11]

Although not a very reliable predictor of protein excretion, effacement of podocyte foot processes is suggestive of podocyte injury. Nevertheless, proteinuria can found even in absence of structural changes in podocytes as evidenced in diabetic MAU associated with type 2 diabetes.This could be because of lower proportion of podocytes observed in early disease. As an increase in mesangial and endothelial cells sets in early while podocyte loss occurs at a later stage. The glomerular endothelial glycocalyx play acritical role in the pathogenesis of MAU. GBM thickening alone, without change in composition, does not significantly affect its protein permeability characteristics.[11]

Major risk factors for acute myocardial infarction in relation to microalbuminuria

The presence of MAU is an indicator of widespread vascular disease. It is associated with the presence of unfavourable risk profile and target organ damage.

Hypertension:Many studies have demonstrated the amount of MAU present in a patient is proportional to the blood pressure. Circadian blood pressure variations, as observed in (non-dippers) individuals, who are known to be at high risk for AMI, have also been found in patients with MAU. The relative risk of having an elevated systolic blood pressure among men with MAU is a greater as compared to women with MAU. More over the association of MAU and hypertension in diabetics is higher than in non-diabetics.[42]

Hyperinsulinemia: In non-diabetics, presence of both hyperinsulinemia and MAU have been shown to enhance CVD risk. It is even greater when other risk

factors for atherosclerosis such as dyslipidemia, arterial hypertension, and obesity are also present. These risk factors when present together are called syndrome X or cardiometabolic syndrome.(42)

Endothelial dysfunction: Several endothelial components of extracellular matrix and different proteins are involved in vascular and renal function. Endothelial dysfunction which leads to the disruption of its antithrombotic and vasodilatory propertiescontributes to pathological factors involved inatherogenesis. It is postulated that, an increased endothelial permeability may be responsible for MAU in the general population and those with arterial hypertension and diabetes.Endothelial dysfunction plays a pivotal role in non-diabetic glomerulosclerosis and atherosclerosis. Enhanced endothelial permeability of the endothelium permits atherosclerotic lipoprotein particles (oxidized LDL and others) to penetrate into the vessel wall and facilitate the development and progression of atherosclerotic plaques.(43)

Endothelial dysfunction biochemical indices such as increased von-Willebrand-Factor (VWF) and platelet adhesiveness have been associated with MAU. Increased levels of VWF were found in patients with MAU and a direct correlation between these two variables has been demonstrated. Increased plasma concentrations of angiotensin II, tissue type plasminogen activator inhibitor-1, and endothelin-1 are the other biochemical indices of endothelial dysfunction, associated with MAU.(43)

Dyslipidemia: An association between MAU and abnormalities in serum lipoproteinssuch as low levels of HDL as well as high levels of LDL, total triglycerides and lipoprotein have been demonstrated by several studies. The most frequent association between lipid abnormalities and MAU is decrease in thelevel of HDL.(43)

Clinical implications

The occurrenceof MAU is of abundant diagnostic value as it signifies a very sensitive index of abnormal vascular permeability. Its usefulness as a marker of target organ damage from CVD disease includes risk assessments, evaluation of disease severity and prognosis. The current evidence suggests that assessment of MAU is a very sensitive tool when acuteinflammatory reactions are evidence in condition such as AMI, trauma, sepsis and surgery. The amount of MAU is proportional to the severity of the disease state. Ischemia and reperfusion are other conditions which are also associated with MAU.[44] The presence MAU in AMI peripheral vascular diseaseis proportional to the severity of the infarct size or claudication.[45]Early detection of MAU is of immense importance as it may impact the aggressiveness of management and consequently the outcome of the health condition.

Correlation of microalbuminuriain acute myocardial infarction

In addition to being a marker of renal disease, MAUis also useful in the predictionof coronary heart disease (CHD) and mortality. However,confounding role of renal dysfunction in the association continues to be debatable.[11]

There are several studies indicating that MAU is associated with the commencement and advancement of CHD, and cardiovascular disease (CVD). Data from Rancho Bernardo Study demonstrated that MAU along with metabolic parameters, is a more powerful predictor of CVD mortality than either alone in women but not in men. Screening for MAU in older women may identify women at high risk for CVD mortality, beyond those conferred by risk factors included in the metabolic syndrome.[46]

On the contrary, another study has suggested that MAU could not predict the development of CVD and associated mortality.[47] These controversial results may

bebecause of differences in the ethnic groups and the wide range of age of patients included in different studies. Therefore, it is still not clear whether MAU is an independent risk factor for cardiovascular or all-cause mortality.

There is increasing evidence suggesting the relationship between MAU and cardiovascular (CV) risk. Several clinical trial data indicate that an incremental increase in MAU, even when albuminuria is within the normal range is associated with an increased rate of CV events in adult population.[11]This was also confirmed in a recent, meta-analysis of 105,872 subjects, which showed that the hazard ratio for all-cause and CV mortality (adjusted for age, genetics, history of CV disease, systolic BP, diabetes, total cholesterol and smoking,) rises progressively with increase in UAE well below the MAU range, increasing to 1.83 with MAU in individuals with normal renal function.[48]

A positive and independent association between MAU and AMI has been demonstrated. Jensen et al conducted follow-up analyses as a part of the 3rd Copenhagen City Heart Study. This study was carried out at Denmark between 1992-1994, and included 2,613 participants aged 30-70 years, and without DM, renal or urinary tract disease or haematuria. It was found thatamong the participants, 3.6% had AMI. There was a positive association between urinary albumin excretion rate (logarithmically transformed) and acute myocardial infarction (odds ratio 1.35, 95% confidence interval 1.08 to 1.70, n = 2, 613; P = 0.01), which was independent of age, sex conventional atherosclerotic risk factors, and glomerular filtration rate. The odds ratio for AMI associated with MAU was 2.06 (95% confidence interval 1.20 to 3.55, n = 2,613; P = 0.009).[49]

Microalbuminuria is an early response to acute myocardial infarction

Increased urinary protein excretion was found to be an early and proportional response to AMI. Goslinget al studied 96 patients with suspected AMI of which 44 had confirmed AMI and remaining 52 were used as a control group. Urinary albumin and IgG were measured by automated immunoturbidimetry and expressed as the protein creatinine ratio in mg.mmol-1. The log mean (SD) albumin creatinine ratios for the first urine passed in the myocardial infarction and non-myocardial infarction patient groups were 6.2(4.2) and 1.3(3.4) respectively. The difference in log mean albumin creatinine ratio was 4.9 mg.mmol-1, (95% CI 3.4 to 6.2 mg.mmol-1; t = 6.127 df = 94, P< 0.0001). The median IgGcreatinine ratio for the first urine passed after admission in AMI patients was 1.0 mg.mmol-1 (95% CI 0.5 to 1.2) and for non-AMI patients 0.3 (95% CI 0.2 to 0.4).[45]

Microalbuminuria in non-diabetic STEMI is found to be an independent predictor for acute kidney injury. Lazzeri et al carried out a study to evaluate the impact of MAU on development of acute kidney injury. They investigated its prognostic role at long term follow-up in 526 consecutive patients with ST elevation myocardial infarction without previously known diabetes. They found that patients with MAU were older ($p = 0.013$). They showed higher values of peak glycemia ($p = 0.017$), peak Tn I ($p < 0.001$), NT-pro BNP ($p = 0.020$), ESR ($p = 0.003$), CRP ($p = 0.020$), and leukocyte count ($p < 0.001$). Lower eGFR was observed in patients with MAU both on admission and during intensive care unit stay ($p = 0.048$ and $p = 0.003$, respectively). A positive correlation was observed between CRP and MAU (Spearman's rho 0.114, $p = 0.024$). The composite end point was observed in 73 patients (18 patients died and 59 patients developed acute kidney injury). At multivariable regression analysis, MAU was an independent predictor of acute kidney

injury. At follow-up Kaplan-Meier curve analysis showed that patients with MAU had a lower survival rate in respect to patients without MAU. Moreover MAU was an independent predictor of long term mortality (HR: 1.089; 97% CI 1.036-1.145; p < 0.001).Furthermore, MAU identifies a subset of patients at higher risk for long term mortality.(50)

Association of Microalbuminuria in non-diabetics with acute myocardial infarction

The MAU is significantly associated with in non-diabetic non-hypertensive AMI. It is observed in younger population with AMI and is significantly associated with male sex. MAU is strongly associated with smoking, high body mass index and high total cholesterol. MAU is seen independent of smoking status, BMI, total cholesterol in patients of myocardial infarction.AbhijitBasu*etal*conducted a study to evaluate the association of MAU in non-diabetic and non-hypertensive 50 patients with AMI and to determine whether MAU is an independent marker of AMI in non-diabetic and non-hypertensive patients. They found that 66% (n=33) patients had MAU. The difference was statistically significant P <0.001. MAU was found in lower age group (48.76 ± 6.97) cases as compared to controls (54.5 ± 4.12) (P <0.05). Among 83.33% of the males had MAU (P <0.05). Smokers and patients with high cholesterol had higher MAU (P <0.001). About 80.76% patient with BMI >25 had MAU.(1)

Lazzeri*etal*carried out a study to determine whether MAU, in the early phase, has a prognostic role for in-hospital mortality or complications (acute pulmonary edema and arrhythmias) in 242 consecutive hypertensive, non-diabetic patients with STEMI diabetes, all submitted to mechanical revascularization. The patients were allocated to two groups as per MAU excretion: group A (MAU within the normal

range); group B (MAU above the normal range).The incidence of MAU was 52.1% (126/242). No significant difference was detectable in the incidence of in-hospital mortality and complications between the two groups. Patients with MAU had a larger infarct size as evidenced by the higher values of troponin I. Moreover, MAU was associated with higher levels of glucose and insulin resistance suggesting thatthese finding could be related to the metabolic response to AMI.(51)

Taskiran*et al* studied the association of MAU with mortality in patients with AMI in a ten-year follow-up study. They followed 151 patients from 1996 to 2007 to evaluate if MAU is a risk factor in patients with AMI. Fifty percent of patients had MAU and it was associated with increased all-cause mortality. Thus, 68% of the patients with MAU versus 48% of the patients without MAU had died during the 10 years of follow-up (P=0.04). The crude hazard ratio for death associated with MAU was 1.78 (CI: 1.18-2.68) (P=0.006), whereas the gender- and age-adjusted hazard ratio was 1.71 (CI: 1.03-2.83) (P=0.04). They also recommendedMAU evaluation to be included as a baseline risk factor in patients with AMI.(52)

Impact of microalbuminuriainacute myocardial infarction

Congestive heart disease

Yuyun MF *et al* examined the relation between MAU and incident CHD (1993-2002) in a population-based British cohort of 22,368 men and women aged 40-79 years without prevalent baseline CHD and evaluated its prognostic significance in 1,596 participants with baseline CHD. During an average of 6.4 years of follow-up, 800 primary CHD events were registered. The multivariate hazard ratio for incident primary CHD was 1.36 (95% confidence interval (CI): 1.12, 1.64) for MAU and 1.59 (95% CI: 1.10, 2.37) for macroalbuminuria. Among participants with established

baseline CHD, the independent risk of all-cause mortality associated with MAU was 1.61 (95% CI: 1.19, 2.07).(53)A meta-analysis was carried out 23,238 patient data, which included 889 cases of CHD. A total of 2,837 (12.2%) had MAU at baseline. The Figure 6 illustrates the pooled RR for CHD of 1.41 (95% CI 1.17-1.69) in a fixed-effect model. No significant heterogeneity between studies was observed (I^2=50.3%; *P*=0.156). (54)

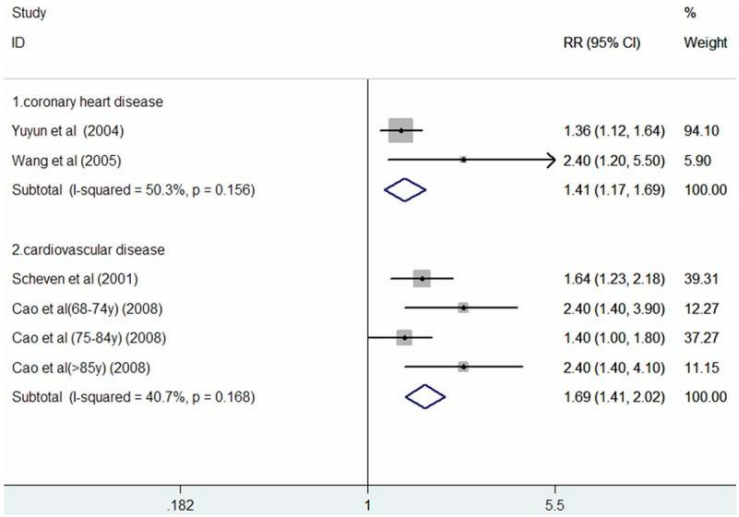


Figure 6: RR and 95% CI from the eligible studies of coronary heart disease and cardiovascular disease comparing the MAU to without MAU in a random effect model.

Cardiovascular mortality and all-cause mortality

Two studieshave reported the risk estimates of developing cardiovascular disease.(55), (56)The total number of patients in this meta-analysis was 11,468, which included 1,959 cases of CVD. A total of 759 (6.62%) had MAU at baseline. As shown in Figure 6, the pooled RR for cardiovascular disease was 1.69 (95% CI 1.41-2.02) in a fixed-effect model. No significant heterogeneity between studies was observed (I^2=40.7%; *P*=0.168).(54)

Four studies reported the relative risk of developing cardiovascular

mortality.(46),(47), (57), (58),

Jassal SK *etal*evaluated the usefulness of MAU versus the metabolic syndrome as a predictor of cardiovascular disease in women and men>40 years of age (from the Rancho Bernardo Study). At baseline, 267 participants had the Adult Treatment Panel III metabolic syndrome, 151 had MAU, and 34 had both. During follow-up, there were 180 CVD deaths, including 83 CHD deaths. In women, MAU was associated with a twofold increased risk of CVD and CHD mortality (p<or=0.01). Women with both MAU and the metabolic syndrome (n=18) had a threefold increased risk of CVD mortality and a fivefold increased risk of CHD mortality compared with women without either (n=657). A significant interaction existed between MAU and the metabolic syndrome in the prediction of both CVD and CHD (p=0.02). In men, neither the combination of the metabolic syndrome and MAU (n=16), nor either alone, significantly increased the risk of CVD or CHD mortality.(46)

Muntner P *et al* studied the association between renal insufficiency and increased CVD -related and all-cause mortality rates during 16 year of follow-up monitoring was examined among participants who were 30 to 74 year of age at the baseline examinations in 1976 to 1980, with urinary protein dipstick measurements (n = 8786) or serum creatinine levels of <or=3.0 mg/dl (n = 6354), from the Second National Health and Nutrition Examination Survey Mortality Study. Cardiovascular disease-related mortality rates were 6.2, 17.9, and 37.2 deaths/1000 person-year among subjects with urinary protein levels of <30, 30 to 299, and >or=300 mg/dl and were 4.1, 8.6, and 20.5 deaths/1000 person-year among patients with estimated GFR of ≥ 90, 70 to 89, and <70 ml/min, respectively. After adjustment for potential confounders, the relative hazards (and 95% confidence intervals) for CV -related death were 1.57 (0.99 to 2.48) and 1.77 (0.97 to 3.21) among subjects with urinary

protein levels of 30 to 299 and ≥ 300 mg/dl, respectively, compared with <30 mg/dl (P trend = 0.02). The corresponding relative hazards for all-cause-related death were 1.64 (1.23 to 2.18) and 2.00 (1.13 to 3.55; P trend < 0.001). Compared with subjects with estimated GFR of ≥ 90 ml/min, those with estimated GFR of <70 ml/min exhibited higher relative risks of death from CVD and all causes [1.68 (1.33 to 2.13) and 1.51 (1.19 to 1.91), respectively.(47)

Hillege*et al* examined the relationship between urinary albumin excretion and all-cause mortality and mortality caused by cardiovascular (CV) disease and non-CV disease in the general population during period 1997 to 1998 in Netherlands. They found a positive dose-response relationship between increasing UAC and mortality. A higher UAC increased the risk of both CV and non-CV death after adjustment for other well-recognized CV risk factors, with the increase being significantly higher for CV mortality than for non-CV mortality (P=0.014). A 2-fold increase in UAC was associated with a relative risk of 1.29 for CV mortality (95% CI 1.18 to 1.40) and 1.12 (95% CI 1.04 to 1.21) for non-CV mortality.[57]

Yuyun MF *et al*carried out a prospective population-based cohort study of 20 911 individuals aged 40-79 years recruited in 1993-1997 for the EPIC-Norfolk Study (UK) and followed-up for an average of 6.3 years**.** During follow-up, 934 deaths were registered. Age-adjusted all-cause mortality rate increased significantly across categories of baseline albuminuria (5.3, 5.2, and 6.3/1000 person years (pyrs) across tertiles of normoalbuminuria, 8.7/1000 pyrs for MAU, and 18.4/1000 pyrs for macroalbuminuria, P < 0.001 for trend); CVD, 1.6, 1.7, 2.1, 4.3, 12.6/1000 pyrs (P < 0.001); and non-CVD, 3.7, 3.5, 4.2, 4.4, 5.8/1000 pyrs (P = 0.052) respectively. The multivariate hazard ratio for all-cause mortality associated with MAU was 1.48 (95% CI: 1.20, 1.79), and CVD 2.03 (95% CI: 1.55, 2.67). The association with non-CVD

mortality was only significant in men.[58]

The above 4 studies were included in the meta-analysis carried on the data of 73,310, which included 1,886 cases of cardiovascular mortality.[46], [47], [57], [58] A total of 7,224 (9.85%) had MAU at baseline. As shown in Figure 7, the pooled RR for cardiovascular mortality was 1.57 (95% CI 1.20-2.06), with evidence of significant heterogeneity (I^2=73%; P=0.005).(54)

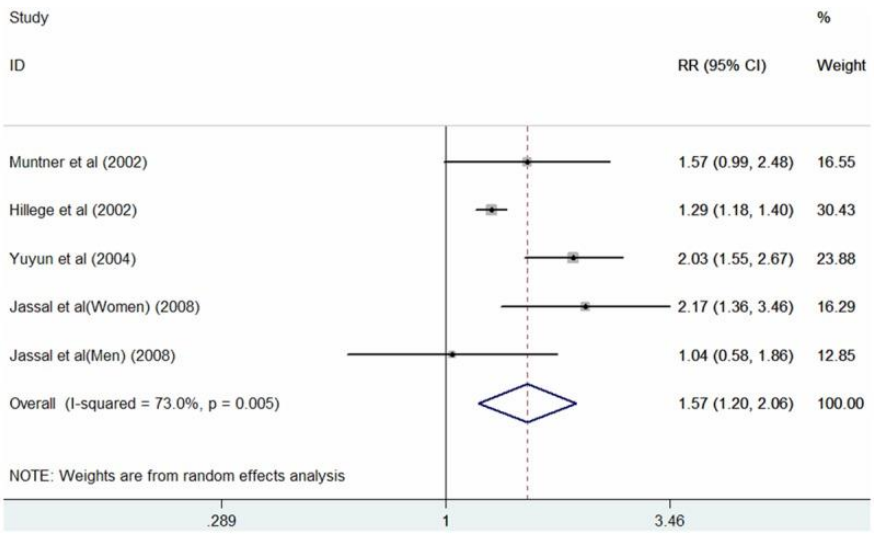


Figure 7: RR and 95% CI from the eligible studies of cardiovascular mortality comparing the MAU to without MAU in a random effect model.

Four studies reported the relative risk of developing all-cause mortality. (55), (47), (58), (59)

Cao JJ et al evaluated UAE in 3112 participants of the Cardiovascular Health Study who attended the 1996-1997 examination and had median follow up of 5.4 years. The prevalence of elevated UAE was 14.3%, 17.1% and 26.9% in those aged 68-74, 75-84 and 85-102 years, respectively. CVD incidence and all-cause mortality were doubled (7.2% and 8.1% per year) in those with microalbuminuria and tripled (11.1% and 12.3% per year) in those with macroalbuminuria compared to those with normalurinary ***albumin excretion*** (UAE)(3.3% and 3.8% per year). The increased

CVD and mortality risks were observed in all age groups after adjustment for conventional risk factors. The adjusted population attributable risk percent of CVD and all-cause mortality for elevated UAE was 11% and 12%, respectively. When participants were cross-classified by UAE and Framingham Risk Score categories, the 5-year cumulative incidence of coronary heart disease among participants with elevated UAE and a 5-year predicted risk of 5-10% was 20%, substantially higher than 6.3% in those with UAE <30m µg/mg.(55)

SolfridRomundstad S et al carried out a study to examine the association between MA and all-cause mortality in nondiabeticnonhypertensiveindividuals.They found a positive association between all-cause mortality and MA. The lowest ACR level associated with increased RR for mortality was the 60th percentile (≥ 6.7 µg/mg[0.76 mg/mmol]; RR, 2.4; 95% confidence interval, 1.1 to 5.2), applying 3 urine samples with an ACR greater than the cutoff level. It was found that there was a positive association between mortality and increasing numbers of urine samples with an ACR greater than different cutoff levels, in which 3 urine samples were superior. Results persisted after adjusting for several confounders and excluding individuals with untreated hypertension (BP ≥ 140 90 mm Hg) and those who died during the first year of follow-up.(59)

Above 4 studies reported were included in the meta-analysis. (55), (47), (58), (59)The total number of participants included in this meta-analysis was 40,519, which included 3609 cases of all-cause mortality. A total of 3,076 (7.59%) had MAU at baseline. As shown in Figure 8, the pooled RR for all-cause mortality was 1.65 (95% CI 1.45-1.88) in a fixed-effect model. No significant heterogeneity between studies was observed (I^2=37.1%; P=0.145).(54)

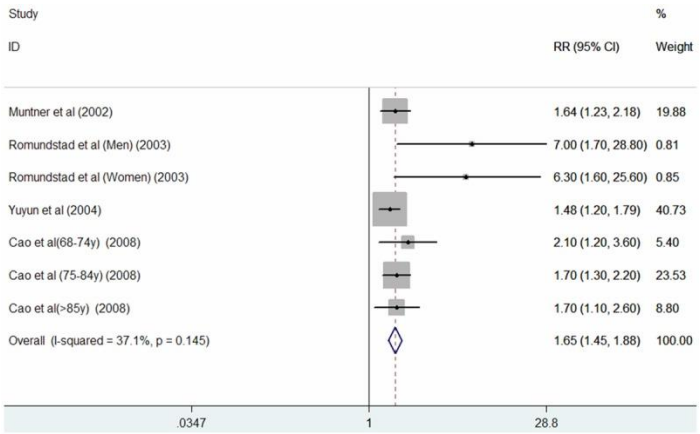


Figure 8: RR and 95% CI from the eligible studies of all-cause mortality comparing MAU to without MAU in a fixed-effect model.

Prognostic significance of microalbuminuria in acute myocardial infarction

Microalbuminuria is a significant predictor of in-hospital morbidity and mortality in non-diabetic patients with acute myocardial infarction.

Lekatsas Iet al performeda study to examine whether the presence of MAU (20-200 µg/mg/min) can predict in-hospital morbidity and mortality in non-diabetic patients with acute myocardial infarction in 223 (172 men and 51 women) non-diabetic patients with AMI. A significant proportion of patients (33.6%) had MAU. Thirty four percent patients developed an in-hospital event (fatal or non-fatal). Six patients (2.7%) with acute myocardial infarction died in the hospital. Patients with MAU had a higher mortality rate in comparison with normoalbuminuric patients (6.6% vs. 0.68%, $p = 0.01$). For non-fatal events, the incidence of pulmonary edema and ventricular arrhythmias was significantly higher in patients with MAU (14.6% vs. 3.4%, $p < 0.001$ and 12% vs. 3.4%, $p = 0.01$, respectively). The combined end-point of the total number of fatal and non-fatal events was significantly higher in patients with MAU (57.3% vs. 22.3%, $p < 0.001$). In multiple logistic regression analysis, MAU ($p < 0.001$) and ejection fraction ($p = 0.01$) were independently related to the

occurrence of major in-hospital events.(60)

G Berton *et al* carried out a prospective cohort study to examine whether urinary albumin excretion has predictive power for 1-year mortality after AMI in 432 patients with AMI. The incidence of mortality was related to the baseline urinary albumin:creatinine ratio. The best cut-off for total mortality approximated to 50 mg x g(-1)on the first day after myocardial infarction, 30 mg x g(-1)on the third day, and to 20 mg x g(-1)on the seventh day. At multivariable Cox analysis, the albumin:creatinine ratio was the strongest among several independent predictors of mortality (adjusted relative risks: 3.6 (95% CI, 2.1--6.2) on the first day, 4.9 (95% CI, 2.9--8.2) on the third day and 4.0 (95% CI, 2.3--6.8) on the seventh day). Independent determinants of urinary albumin were plasma aldosterone on the first day, and inflammatory markers on the third and seventh days. Urinary albumin assessed in the first week after AMI is a strong prognostic marker for 1-year mortality.(61)

Microalbuminuria has been reported to occur in patients with AMI and is associated with worse outcome. Apostolovic S et al conducted prospective analysis to examine the predictive power of MAU for 6-month mortality and re-hospitalization for CVD in 130 patients. A high proportion of study patients (27.7%) had MAU and 8.5% had overt albuminuria (UACR over 25 mg/mmol in men and over 35 mg/mmol in women) at the time of urine examination. During the hospital stay (average 7.6 +/- 3.0 days) 4 patients (3.1%) died from cardiovascular complications and all had MAU. In this study a high percentage of patients with in-hospital nonfatal complications had MAU but it did not have positive predictive association with the occurrence. During a 6-month follow-up period, 8 patients died from cardiovascular cause. In-hospital and total mortality (in-hospital and the during six-month follow-up) were significantly frequent in patients with MAU ($p < 0.05$). During a six-month follow-up period, 24

patients (18.5%) were re-hospitalized for cardiovascular disease and, among them, 54.2% had MAU. In univariant regression analysis MAU increased the risk for re-hospitalization, but multiple analysis didn't show the significance.(62)

W Otter*et al* performed a study to assess hospital mortality and morbidity in 330 diabetic and non-diabetic patients with AMI. Of those, 126 (38%) were diabetic and 204 (62%) were non-diabetic patients. Mortality within 24 h after admission was 13.5% in diabetic patients and 5.4% in non-diabetic patients (P<0.01). Mortality during entire hospitalization was higher in diabetic than in non-diabetic patients (29.4% vs. 16.2%; P=0.004). Diabetic patients were resuscitated more frequently than non-diabetic patients were (24% vs. 11%, P<0.01). In diabetic patients, heart rate at admission was increased (91 +/- 27 vs. 82 +/- 23/min; P<0.01) and presence of angina pectoris was reported less frequently (59% (n=72) vs. 82% (n=167); P<0.001). Preceding myocardial infarction, MAU, peripheral artery disease and arterial hypertension were more frequent in diabetic than in non-diabetic patients. Diabetic patients demonstrated higher C-reactive protein (CRP) levels than non-diabetic patients (91.4 +/- 78.2 mg/l vs. 45.2 +/- 62.4 mg/l; P<0.001).(63)

Microalbuminuria is considered a major risk factor predisposing to cardiovascular morbidity and mortality. Admission MAU MA levels are associated with impaired myocardial flow and poor prognosis in STEMI patients undergoing primary PCI**.** Outcomes after percutaneous coronary intervention (PCI) for patients with (AMI) complicated by MA have been well described. Chen JW*et al* carried out a study to evaluate the effects of admission MA on coronary blood flow and prognosis in STEMI patients undergoing primary PCI in 247 patients. Patients were divided into 2 groups according to admission urinary albumin extraction rate (UAER): (1) an MA group (UAER 20-200 μg/min), and (2) a normoalbuminuria (NA) group (UAER < 20

µg/min).MAU was observed in 108 patients. Univariate analyses showed statistical differences between the NA and MA groups in serum creatine level, plasma glucose level, and peak creatine kinase level on presentation. Thrombolysis In Myocardial Infarction (TIMI) flow grades (TFGs) 0-2 in the MA group were more frequent (9.4% vs 21.2%, $P < 0.05$) than in the NA group, and corrected TIMI frame count was higher (23.9 ± 18.5 vs 29.8 ± 23.5, $P < 0.05$). Admission MA was an independent predictor of poor myocardial perfusion (adjusted relative risk: 3.14, 95% confidence interval: 0.99-6.78) and a higher rate of 6-month mortality in STEMI patients undergoing primary PCI (adjusted relative risk: 1.58, 95% confidence interval: 0.74-3.39).(64)

SpyridonKoulouris*et al* carried out a study to evaluate the significance of MAU as a 3-year prognostic index in nondiabetic 175 patients with AMI. Forty-two patients (24%) developed a new cardiac event during the follow-up. MAU ($P < .001$), pulmonary edema during initial hospitalization ($P < .001$) and postinfarction angina ($P = .0364$), advanced age ($P = .001$), severe atherosclerosis (high Gensini score) ($P = .036$), ejection fraction <50% ($P = .0013$), history of bypass surgery ($P = .0265$), and early conservative management ($P = .0214$) were all associated with adverse prognosis. Cox proportional hazards regression analysis showed that MA was an independent predictor of 3-year adverse prognosis in all the models tested, with an adjusted relative risk for the development of a cardiac event ranging from 2.1 to 4.3.**It was concluded that**innondiabetic patients with AMI, MAU is a strong and independent predictor of an adverse cardiac event within the next 3 years.(65)

Jin L *et al* performed a study to investigate the impact of metabolic syndrome (MetS) with MAU on the improvement of cardiac function after AMI.A total of 530 ST-Elevation Myocardial Infarction (**STEMI**) patients were included (average age =

66.6 years). Analysis of covariance showed that Left ventricular ejection fraction (**LVEF**)recovery in the normoalbuminuria/no MetS group was better than that of the normoalbuminuria/MetS, MAU/no MetS, and MAU/MetS groups (49.22% vs. 48.92% vs. 47.48% vs. 46.99%, respectively, $p < 0.001$) when acute phase LVEF was the covariable. The NT-proBNP level of the normoalbuminuria/no MetS group at the 6-month follow-up was lower than that of the MAU/MetS group ($p < 0.001$). Further regression analysis revealed that there was a lower probability of complete cardiac function recovery after 6 months in patients with MAU (odds ratio: 0.455) than in patients without MAU (95% CI: 0.316-0.655, $p < 0.001$).**It was concluded that** although post-AMI cardiac function in MetS patients with MAU can be improved after revascularization, the improvement is not as good as that of patients without MAU, suggesting that clinical attention should be paid to this subgroup.(66)

MATERIALS AND METHODS

This is an observational study among the patients admitted with acute coronary syndrome in the dept. of medicine in Shri. B. M. Patil Hospital, Vijayapur, from December 2018 to April 2020.

SOURCE OF DATA:

- The study is among the patients with acute coronary syndrome admitted in BLDE Hospital Vijayapur
- The patients will be informed about study in all respects and informed consent will be obtained.
- Period of study will be from DECEMBER 2018 TO APRIL 2020

SAMPLE COLLECTION

Oral and written consent will be taken from the subjects prior to the collection of specimens

INCLUSION CRITERIA:

All the patients of either sex with acute coronary syndrome of middle age(30 to 60yrs) admitted in BLDE HOSPITAL

EXCLUSION CRITERIA:

1) Recent history of surgery or trauma within the preceding 2 months.
2) Renal insufficiency (serum creatinine>1.3).
3) Patients with CVA or previous history of CVA.
4) Malignancy.
5) Patients having evidence of infection, inflammatory disease, active hepatic disease, severe dehydration.

LIST OF INVESTIGATIONS

Complete haemogram,

Random blood sugar

serumhomocysteine levels.

Ecg

2d echo/echo doppler

Trop t, cpkmb

Chest xray

Lipid profile

Urinary microlbumin

Along With The Above Investigations Other Relevant Investigations will be performed if required.

Sample size calculation

With 95% confidence level and margin of error of ±10%, a sample size of 62 subjects will allow the study to assess the urinary microlbuminevel among ACS patients with finite population correction.

By using the formula:

$$n = \frac{z^2 p(1-p)}{d^2}$$

where

Z= z statistic at 5% level of significance

d is margin of error

p is anticipated prevalence rate

Statistical analysis used

All characteristics were summarized descriptively. For continuous variables, the summary statistics of mean± standard deviation (SD) were used. For categorical data, the number and percentage were used in the data summaries and diagrammatic presentation. Chi-square (χ^2) test was used for association between two categorical variables.

The difference of the means of analysis variables between two independent groups was tested by unpaired t test. The difference of the means of analysis variables between more than two independent groups was tested by ANOVA and F test of testing of equality of Variance.

If the p-value was < 0.05, then the results were considered to be statistically significant otherwise it was considered as not statistically significant. Data were analyzed using SPSS software v.23.0. and Microsoft office 2007.

RESULTS

The study of Microalbumnuria in non diabetic patients with acute myocardial infarction was done in patients admitted to ICCU of Shri. B. M.Patil Medical College and Research Centre from December 2018 to April 2020. Total of 62 patients were admitted with acute coronary syndrome, who fulfilled the inclusion criteria.

Table1: Distribution of Cases according to Age

Age(yrs)	N	Percent (%)
≤40	7	11.3
41-60	28	45.2
61-80	24	38.7
>80	3	4.8
Total	62	100

In this study of 62 patients presenting with acute coronary syndrome between 40-80 years , age group of 41-60 years are affected more compared to other age groups

Figure1: Distribution of Cases according to Age

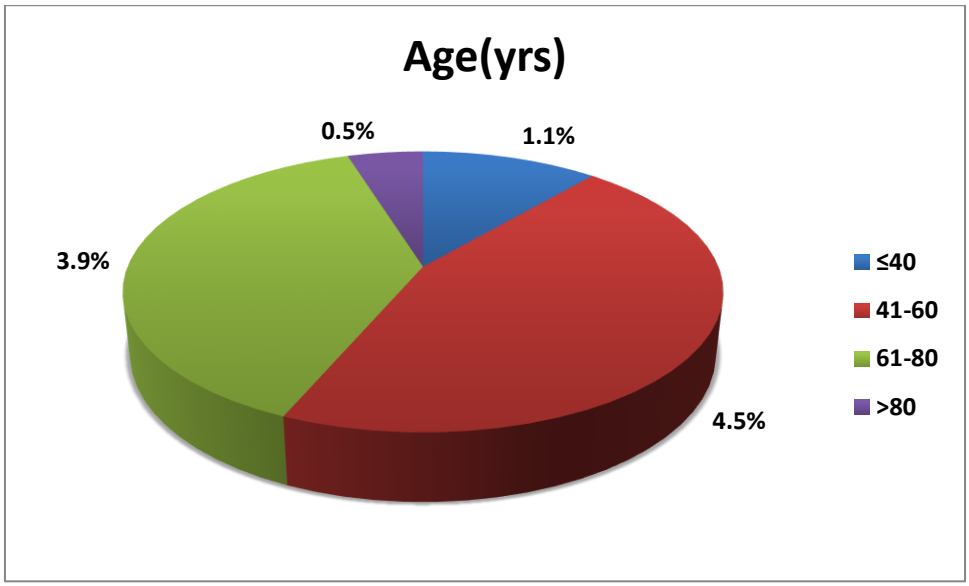


Table2: Distribution of Cases according to Sex

Sex	N	Percent (%)
Male	44	71
Female	18	29
Total	62	100

In this study of 62 patients, males were 44 patients and females were 18 patients

Figure 2: Distribution of Cases according to Sex

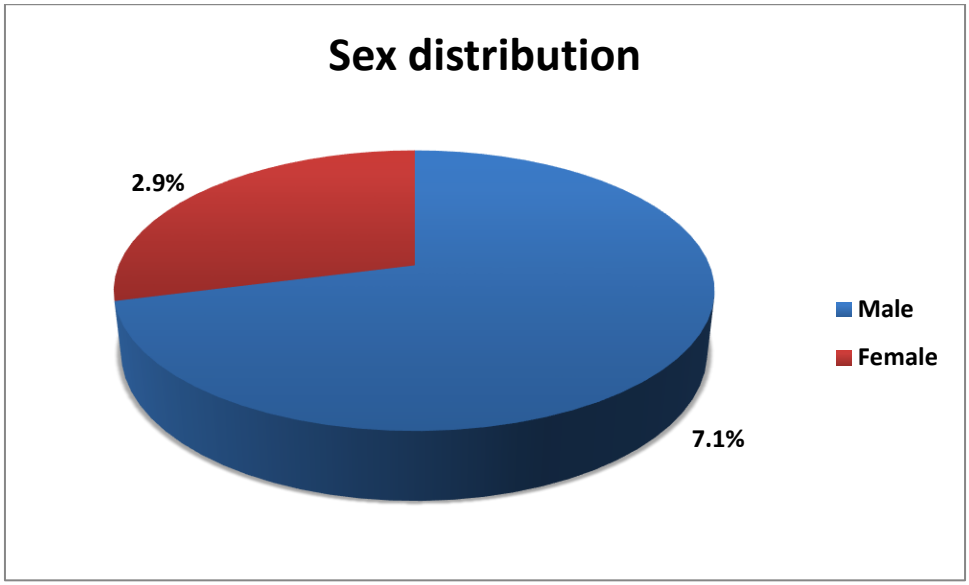


Table 3: Association of Age and Sex

Age(yrs)	Male		Female		p value
	N	%	N	%	
≤40	4	9.1%	3	16.7%	0.661
41-60	19	43.2%	9	50.0%	
61-80	19	43.2%	5	27.8%	
>80	2	4.5%	1	5.6%	
Total	44	100.0%	18	100.0%	

In this study, out of 62 patients, there were 4 male patients with age group less than 40yrs , 19 male patients with age group between 41 to 60 yrs and 19 male patients with age group between 61 to 80yrs and 3 female with age group less than 40 yrs , 9 females with age group between 41 to 60 yrs and 5 female patients with age group between 61 to 80 yrs , out of which 41 to 60 yrs age group were most commonly affected age group between male and female patients, however the difference is not statistically significant with p value 0.661

Figure 3: Association of Age and Sex

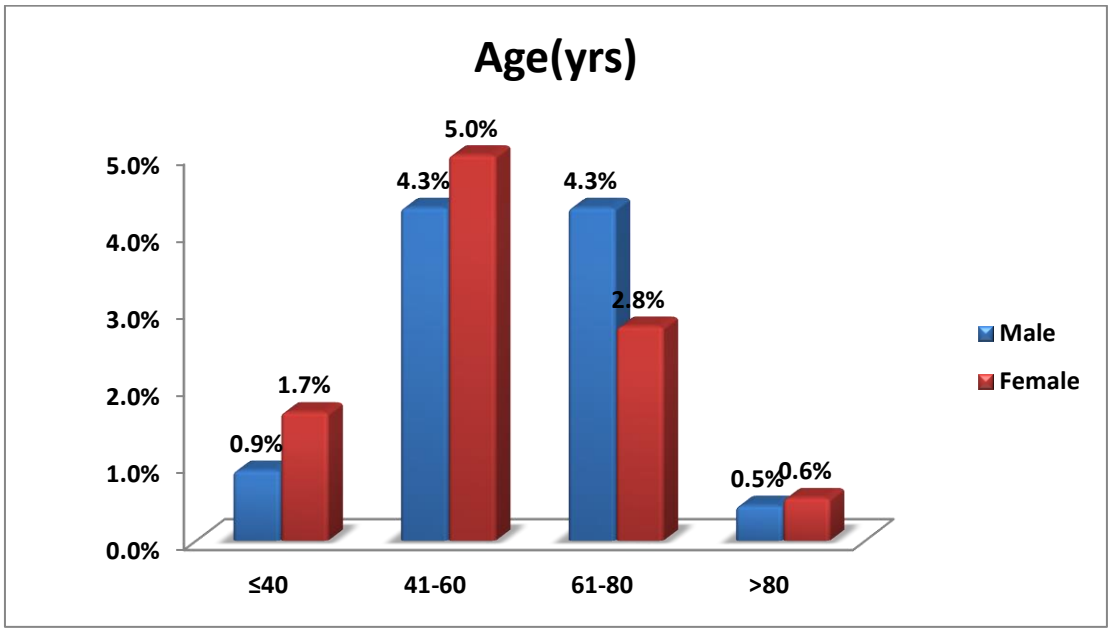


Table4: Distribution of Cases according to Microalbuminuria

Microalbuminuria	N	Percent(%)
Present	39	62.9
Absent	23	37.1
Total	62	100

In our study,microlbuminuria was present in 62.9 percent of patients with acute myocardial infarction

Figure4: Distribution of Cases according to Microalbuminuria

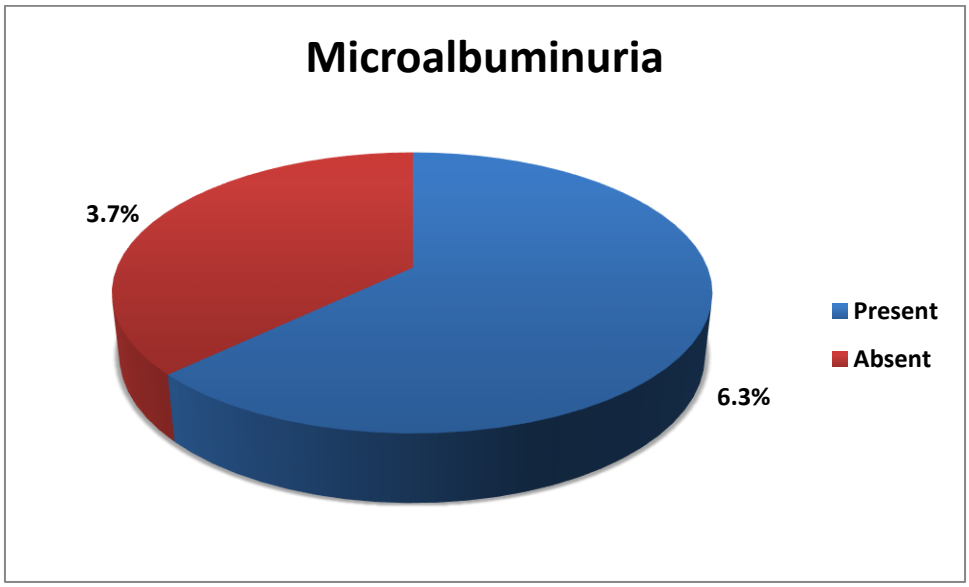


Table 5: Distribution of Age between Study Groups

Age(yrs)	Microalbuminuria		Normoalbuminuria		p value
	N	%	N	%	
≤40	4	10.3%	3	13.0%	0.707
41-60	18	46.2%	10	43.5%	
61-80	16	41.0%	8	34.8%	
>80	1	2.6%	2	8.7%	
Total	39	100.0%	23	100.0%	

In our study, microalbuminuria is present in most of patients (46.2 %) in the age group of 41 to 60 years who are most prone for acute coronary syndrome

Figure 5: Distribution of Age between Study Groups

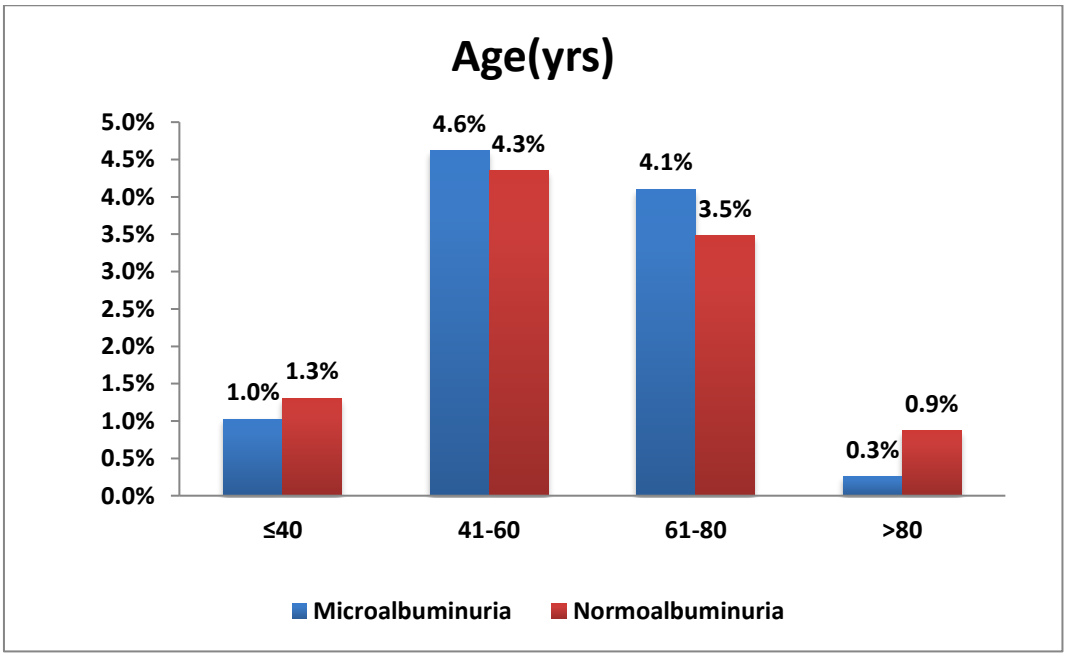


Table 6: Mean Age between Study Groups

Parameters	Microalbuminuria		Normoalbuminuria		p value
	Mean	SD	Mean	SD	
Age(yrs)	59.5	12.8	60.4	14.1	0.796

In this study of 62 patients presenting with acute coronary syndrome between 40-80 years , age group of 41-60 years are affected more compared to other age groups with mean range of 59.5 and SD OF 12.8 observed respectively.

Figure6 : Mean Age between Study Groups

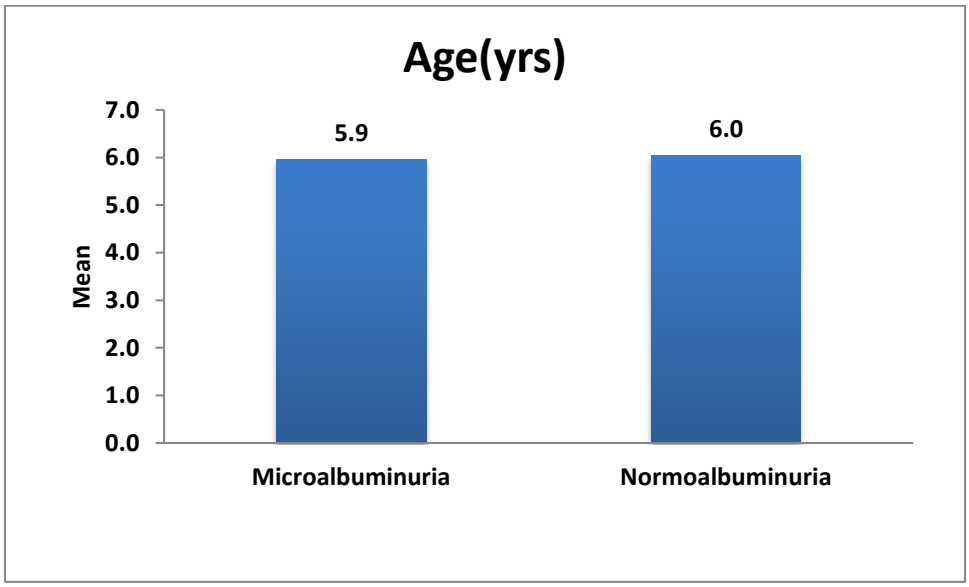


Table 7: Distribution of Sex between Study Groups

Sex	Microalbuminuria		Normoalbuminuria		p value
	N	%	N	%	
Male	26	66.7%	18	78.3%	0.331
Female	13	33.3%	5	21.7%	
Total	39	100.0%	23	100.0%	

In our study of 62 patients, 39 patients had microlbuminura where 26 (66.7%) were male and 13(33.3%) were female.

Figure 7: Distribution of Sex between Study Groups

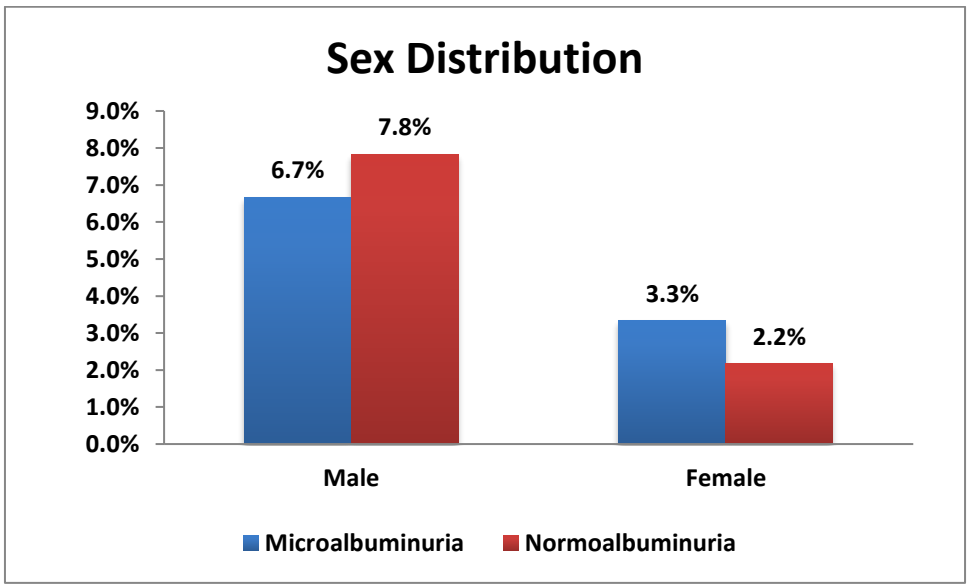


Table 8: Chief Complaints between Study Groups

Chief Complaints	Microalbuminuria		Normoalbuminuria		p value
	N	%	N	%	
Back Pain	0	0.0%	1	4.3%	0.517
Breathlessness	8	20.5%	3	13.0%	
Chest Pain	27	69.2%	18	78.3%	
Epiastric Pain	1	2.6%	1	4.3%	
Vomitting	2	5.1%	0	0.0%	
Weakness	1	2.6%	0	0.0%	
Total	39	100.0%	23	100.0%	

In our study of 62 patients, most of the patients came with complaints of chest pain 27 patients(69.2%) ,with next most common presenting complaints with breathlessness ,8 patients(20.5%).

Figure8 : Chief Complaints between Study Groups

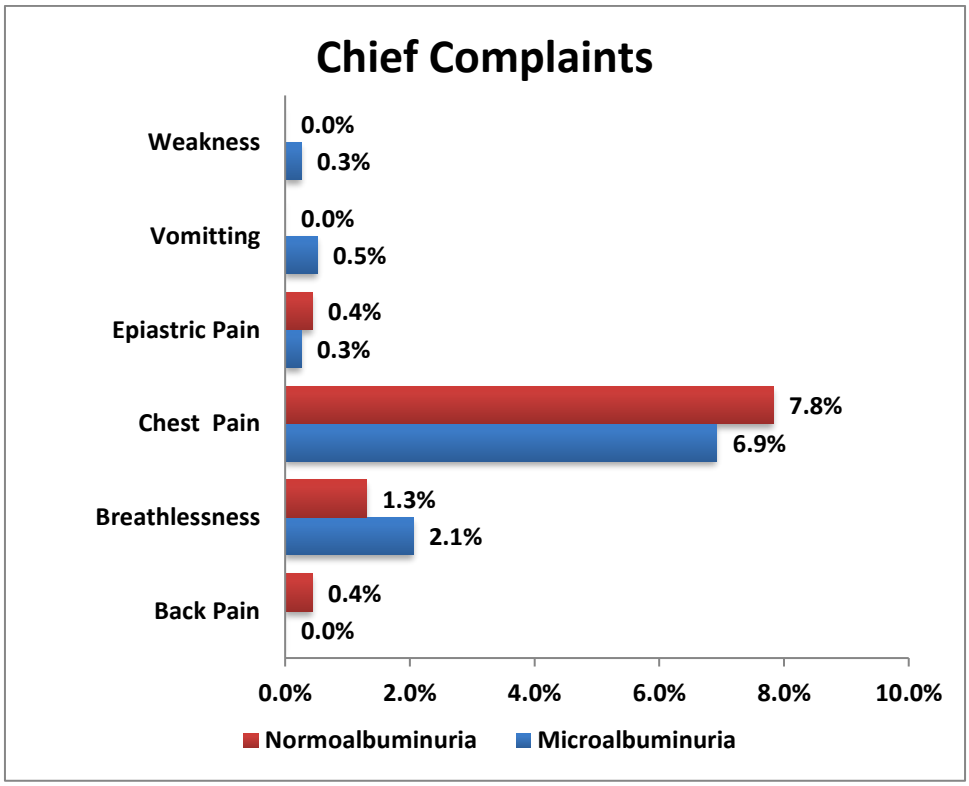


Table 10: Hypertension and Microalbuminuria in IHD Patients

HYPERTENSON	Microalbuminuria		Normoalbuminuria		p value
	N	%	N	%	
HYPERTENSIVE	8	20.5%	9	39.1%	0.112
NORMOTENSIVE	31	79.5%	14	60.9%	
Total	39	100.0%	23	100.0%	

In our study with 62 patients 17patients had hypertension among which 8(20.5%) had microalbuminuria and 31 (79.5%) of normotensive patients had microalbuminuria.

Figure10 :Hypertenson and Microalbuminuria in IHD Patients

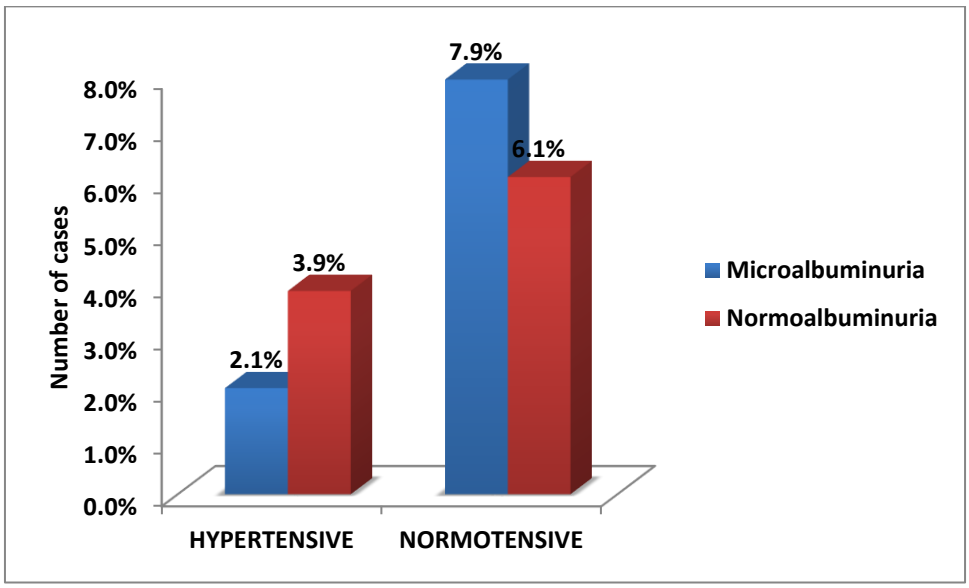


Table 11: Distribution of Smoking between Study Groups

Smoking	Microalbuminuria		Normoalbuminuria		p value
	N	%	N	%	
Absent	14	35.9%	16	69.6%	0.010*
Present	25	64.1%	7	30.4%	
Total	39	100.0%	23	100.0%	

Note: * significant at 5% level of significance (p<0.05)

In our study of 62 patients, 25 (64.1%) patients of the microalbuminuria group had history of smoking compared to the 7 (30.4%) patients in normoalbuminuria group which is statistically significant with p value of 0.010.

Figure11: Distribution of Smoking between Study Groups

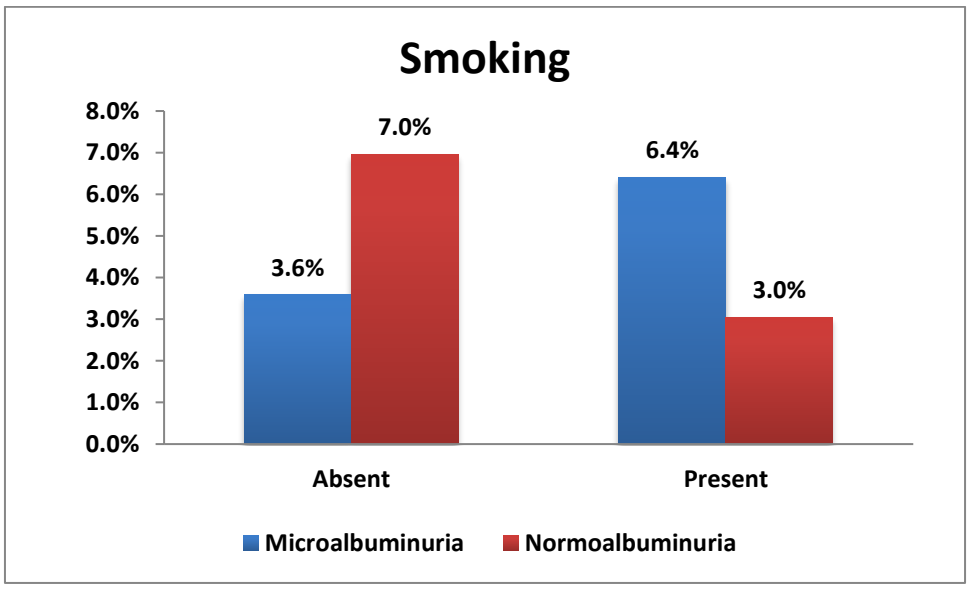


Table 12: Distribution of BMI between Study Groups

Overweight/Obese	Microalbuminuria		Normoalbuminuria		p value
	N	%	N	%	
Male	8	20.5%	4	17.4%	0.457
Female	13	56.5%	11	28.2%	0.049*
Total	21	53.8%	15	65.2%	0.052

In our study of 62 patients,21 (53.8%)patients were obese in the microalbuminuria group with 13 (56.5%) being females and 8 (20.5%) were males compared to the normoalbumnuria group 11(28.2%) were females and 4 (17.4%) were male which is statistically significant with p value 0.049.

Figure 12: Distribution of BMI between Study Groups

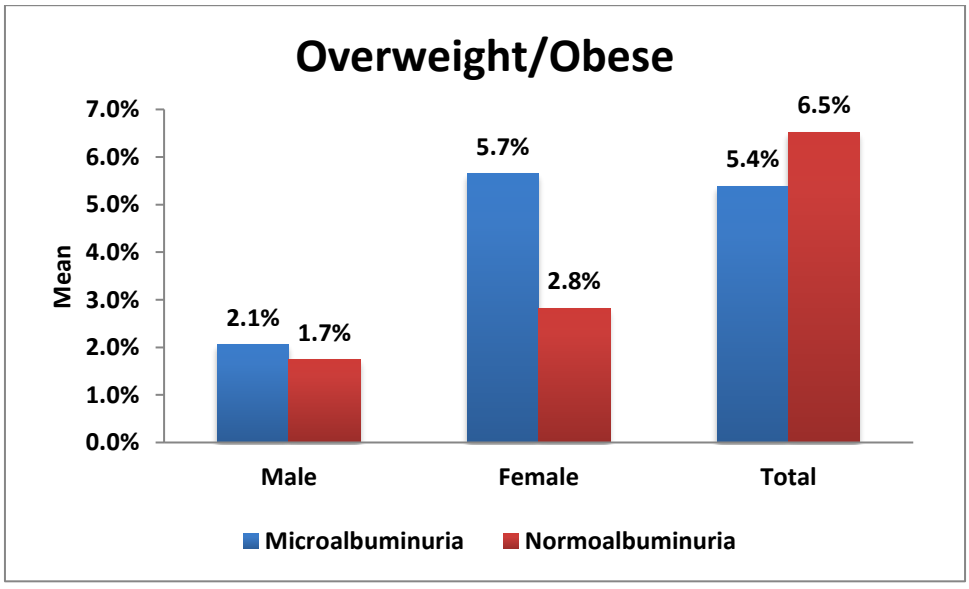


Table13: Diagnosis between Study Groups

Diagnosis	Microalbuminuria		Normoalbuminuria		p value
	N	%	N	%	
AWMI	12	30.8%	15	65.2%	0.028*
IWMI	18	46.2%	6	26.1%	
LWMI	9	23.1%	2	8.7%	
Total	39	100.0%	23	100.0%	

Note: * significant at 5% level of significance (p<0.05)

In our study of 62 patients inferior wall myocardial infarction was present in 46.2% in the microalbumnuria group as compared to normoalbumniuria group where anterior wall myocardial infacrtion was present in 65.2% which is statically significant with p value 0.028.

Figure 13: Diagnosis between Study Groups

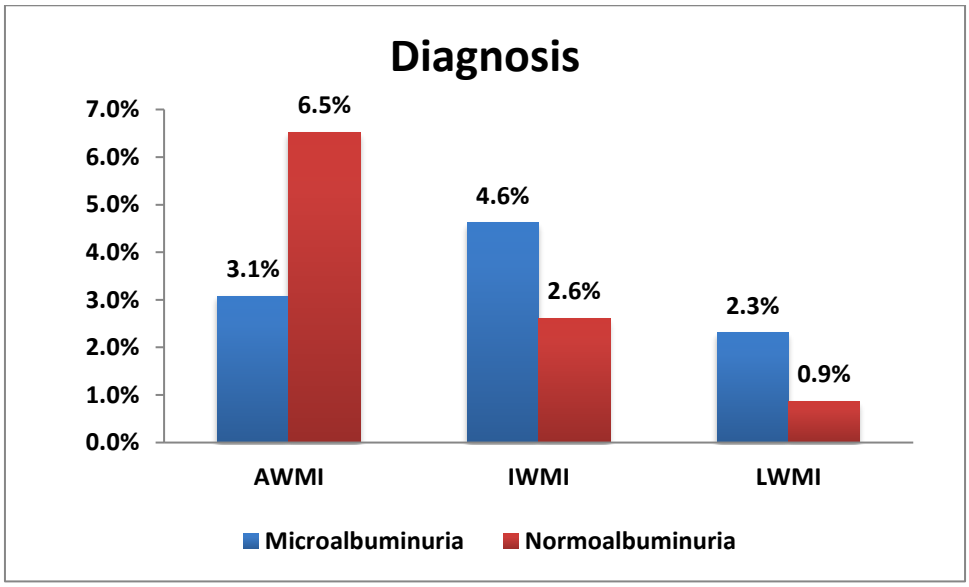


Table 14: Total Cholesterol between Study Groups

TOTAL CHOLESTEROL	Microalbuminuria		Normoalbuminuria		p value
	N	%	N	%	
<200	10	30.3%	9	69.2%	0.016*
≥200	23	69.7%	4	30.8%	
Total	33	100.0%	13	100.0%	

Note: * significant at 5% level of significance (p<0.05)

In our study of 62 patients microalbuminuria was present in 69.7% of hypercholesterolemia compared to 30.8% in normoalbumnuria which is found to be statiscally significant with p value of 0.016.

Figure 14: Total Cholesterol between Study Groups

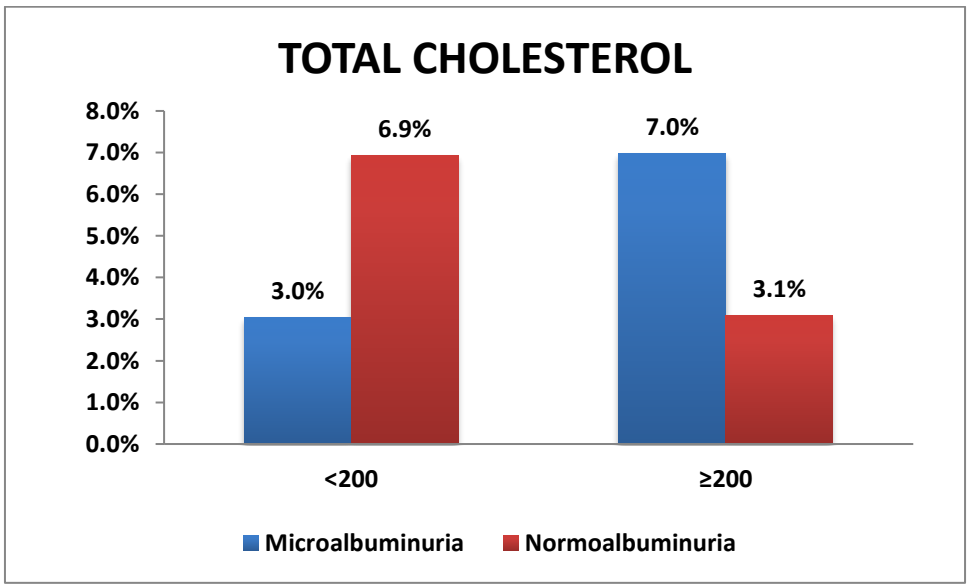


Table 15: Lab Parameters between Study Groups

arameters	Microalbuminuria		Normoalbuminuria		p value
	Mean	SD	Mean	SD	
TROP I	260.6	1272.1	12.4	30.5	0.355
CPK MB	54.3	68.3	37.0	20.1	0.262
RBS	116.6	18.6	113.6	17.4	0.531
CREATININE	0.8	0.2	0.8	0.2	0.648

In our study of 62 patients, the mean of Troponin I in microalbuminuria group was 260.6 with SD 1272.1 compared to mean of 12.4 with SD 30.5 and CPK MB, mean was 54.3 with SD 68.3 in microalbuminuria group compared to mean 37 with SD 20.1 in normoalbuminuria, both were found to be statistically insignificant.

Figure 15: Lab Parameters between Study Groups

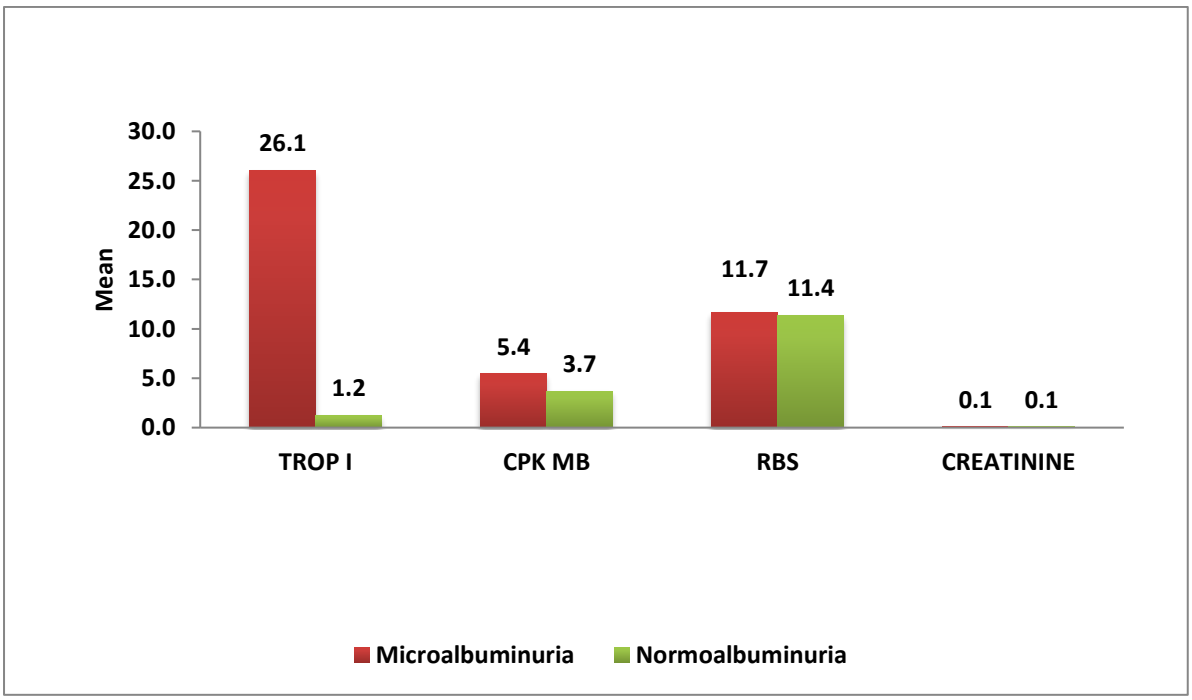


Table 16: Distribution of IHD LVEF between Study Groups

IHD LVEF	Microalbuminuria		Normoalbuminuria		p value
	N	%	N	%	
<30%	6	15.4%	2	8.7%	0.710
31%-59%	32	82.1%	20	87.0%	
≥60%	1	2.6%	1	4.3%	
Total	39	100.0%	23	100.0%	

In our study of 62 patients, 32 (82.1%0 had ejection fraction of 31 -59% and 6(30%) had ejection fraction less than 30% in the microlbumnuria group.

Figure 16: Distribution of IHD LVEF between Study Groups

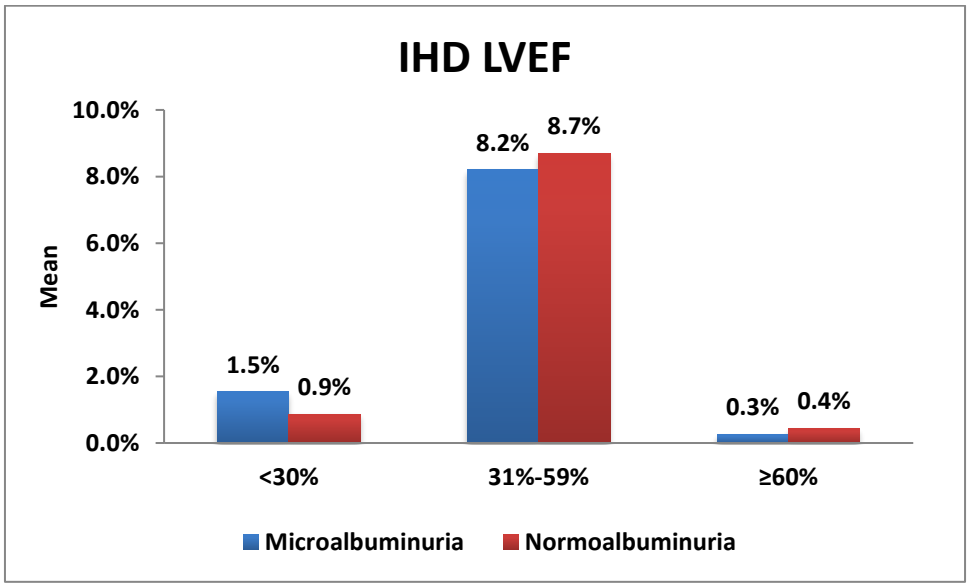
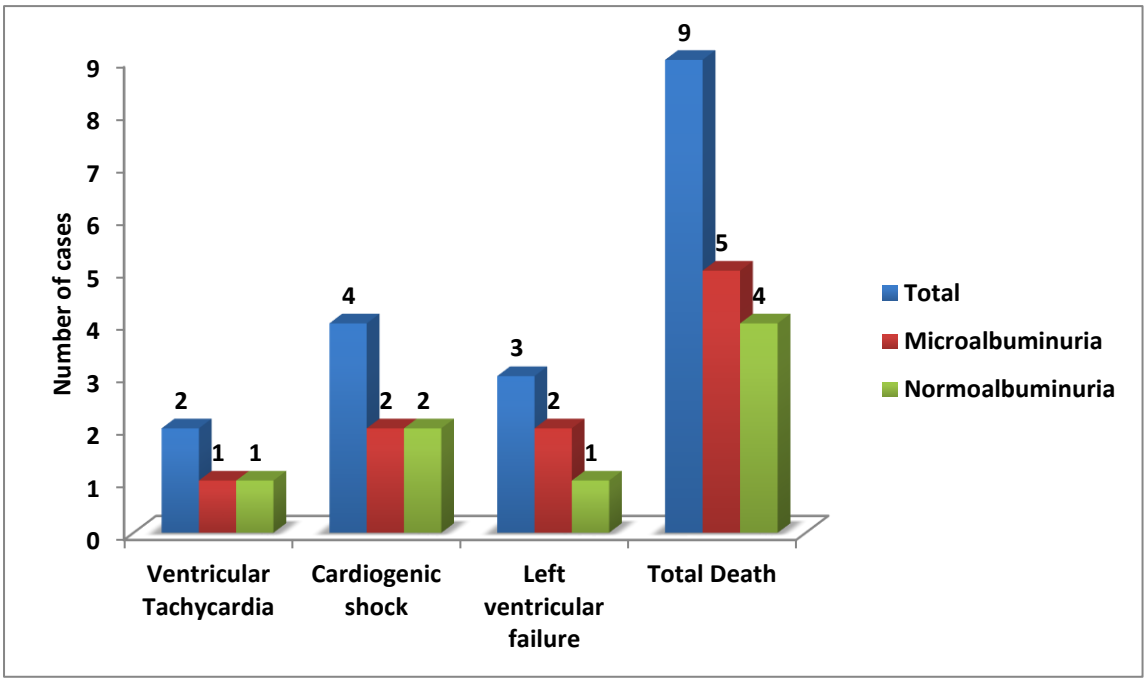


Table 17: OutcomeandMicroalbuminuria in IHD Patients

Outcome	Total		Microalbuminuria		Normoalbuminuria		p value
	N	%	N	%	N	%	
Ventricular Tachycardia	2	22.2%	1	20.0%	1	25.0%	0.894
Cardiogenic shock	4	44.4%	2	40.0%	2	50.0%	
Left ventricular failure	3	33.3%	2	40.0%	1	25.0%	
Total Death	9	100.0%	5	100.0%	4	100.0%	

Figure 17: Outcome and Microalbuminuria in IHD Patients



In our study out of 62 patients, 9 deaths happened secondary to complications of acute coronary syndrome including ventricular tachycardia, cardiogenic shock and left ventricular failure. Total number of deaths are observed to be more in microalbumniuria group with most common complication being cardiogenic shock(44%)

DISCUSSION

This study is an observational study conducted over a period of one and half years from December 2018 to April 2020 to study microalbuminuria in non diabetic patients with acute myocardial infarction. A total of 62 patients included in this study and were analyzed to study microalbuminria in acute coronary syndrome patients.

Cardiovascular diseases , especially coronary heart disease, have assumed epidemic proportions worldwide.To target preventive strategies, risk stratification of the population should be effective. There are many reports emanating from the western literature about micro albuminuria where it is already considered in many countries as an independent risk determinant for development of ischemic heart disease.(67)

Hitherto, microalbuminuria was considered as a marker of endothelial dysfunction in diabetes mellitus, but many studies have shown micro albuminuria has become an effective indicator of generalised vascular dysfunction even in non-diabetic population.(68,69)

In this present study, all the cases had no renal dysfunction (creatinine less than 1.1mg/dl).Microalbuminuria in these patients was not associated with renal dysfunction .our study agrees in this respect with Peter Gosling who considered it to be an sensitive indicator to non renal disease. (78)

This study was done to find out whether there is an association between IHD and MA in non-diabetic subjects.

This study had 71% male patients compared to 29% female patients. This is in accordance with the knowledge that males are more prone for ischemic heart disease than females.Also the EPIC NORFLOK study had higher male incidence which is in concordance with my study.(70)

In my study the mean age of the study group was 59.5 ± 12.8 years. All the females were in the post-menopausal age group, which shows that sex hormones have a protective effect as far as cardiovascular risk is concerned. This is in concordance with the fact that Roeste and Banga et al have demonstrated that urinary albumin excretion in significantly higher in non diabetic postmenopausal group when compared to pre menopausal group.(71)

In our study of 62patients , 27 patients (69.2%) had presented with chest pain , 8patients(20.5%) had breathlessness in the microlbumnuria group and 18 (78.3%) in the normolbumnuria group presented with chief complaint of chest pain . The common presenting symptom was chest pain (45 patients). Similarly in a study done by Goel PK et al [(79)] in 609 patients admitted with ACS for 1 year in 2008, they found that the most common symptom in patients with acute coronary syndrome was chest pain (84%), followed by breathlessness (8.7%).

In other study done by Conto J G et al[(80)] in 434877 patients admitted with acute myocardial infarction, they found that chest pain was present in 67% of patients which is same as that observed in this study and they all find out that most common presenting symptom is chest pain in acute coronary syndrome.

In this study, habit of smoking was there in 64.1% of the study subjects indicating that smoke abuse may be an important risk factor for IHD. Umesh N Khot et al.had found a prevalence of 41.6% in males and 29.5% in females in their study for smoking as a risk factor(72)

The BMI was > 25kg/m2 in majority of the study group. This prevalence was much higher than that obtained by Singh R.B. et al.(11.0% in rural and 27.2% in urban). (73)

In our study 45% of the patients in the microalbuminuria group

hadhypertriglyceridemia which was similar to that obtained by Voss and Cullen et al by the PROCAM study (39.6% of females and 34.1% of males had abnormal lipid parameters).(75,76)

The present study showed that 62.9% of the patients with ischemic heart disease had microalbuminuria which shows a positive association. The PREVEND trial has demonstrated that that in a multivariate adjusted scenario while taking in comparison established risk determinants, the prescence of microalbuminuria was by itself having an independent association with pattern of infarct , major type of ischemia and minor varieties of ischemia.(74)

The prevalence of Micro albuminuria was estimated in 15 % of a cohort of people in the HOPE(HEART OUTCOMES AND PREVENTION AND EVALUATION survey which was done in the years between 1998 and 2003.(68,71)This survey revealed that 20.6% of subjects with microalbuminuria were having a higher incidence of coronary artery disease, myocardial infarction and stroke when compared with 13.8% of those who did not have microalbuminuria.

With regard to PREVEND trial, 32.4% of ischemic coronary disease patients were described here, 20.8% of subjects with ischemic cardiac disease were having microalbuminuria as in comparison with 76% in this study.(74)

This was probably because, the present study had a cohort of IHD patients in whom micro albuminuria was estimated whereas the studies mentioned above was done on the general population.

The present trial design indicate that microalbuminuria may be used as a supplementary Cardiac risk determinant even among non-diabetics and in future may supplant existing markers currently used to quantify ischemic heart disease.(77)

LIMITATIONS OF MICROALBUMINURIA

Several limitations of microalbuminuria evaluations require consideration. In case ofacute infection or trauma there is non specific increase in inflammatory markers. Inpatients with known systemic inflammatory conditions microalbuminuria measurement should be avoided and at the time of infection or trauma as it may have limited clinical utility. Across different ethnic groups utility of testing microalbuminria is also uncertain.

CONCLUSION

The present study aimed at studying microalbuminuria in non diabetic acute myocardial infarction patients. A total of 62 cases of acute myocardial infarction were taken.

Mean age of patients was 59.5±12.8 years. There were 44 male patients and 18 female patients in the study group. Thepredominant type of MI is inferior wall MI followed by anterior wall MI and lateralwall MI.Microalbuminuria was present significantly in 39 (62.9%)patients.

The presence of MAU is an indicator of widespread vascular disease. It is associated with the presence of unfavourable risk profile and target organ damage. In the general population, MAU has also emerged as a significant risk factor for the development of CVD, and the all-cause mortality.

With the increasing prevalence of obesity, type 2 diabetes and metabolic syndrome, screening for MAU appears to an important strategy to detect and prevent CVD. Recent articles suggest role of microalbuminuria as risk factor for cardiovascular diseases including myocardial infarction in non diabetic as well.

MAU is strongly associated with smoking, high body mass index and high total cholesterol. MAU is also seen independent of smoking status, BMI, total cholesterol in patients of myocardial infarction.

The presence of microalbuminuria in the majority of patients with AMI suggests involvement of inflammation in the etiopathogenesis of MI and has prognostic utility in AMI.Microalbuminuria is associated with low-grade systemic inflammation and endothelial dysfunction.

In non-diabetics patients with MAU, an increase in vascular permeability is produced by changes in the extracellular matrix. This leads to endothelial dysfunction

which is responsible for lipid influx into the vessel wall resulting in atherosclerotic lesions.

Thus, our data are consistent with the hypothesis that glomerular endothelial dysfunction, as indicated by low-grade albuminuria, is an important marker of future CVD events even in non diabetic individuals.

In the absence of any renal insufficiency,microalbuminuria is non specific yet highly sensitive marker of myocardial infarction. Since microalbuminuria is simple investigation and is relatively inexpensive we propose the use of microlbuminuria as adjunct biochemical parameter in non diabetic myocardial infarction patients.

However more studies are required with larger sample size to ascertain whether microalbumnuriacan predict in hospital mortality and its pathophysiology in a clinical setting.

SUMMARY

A hospital based prospective, randomized study was conducted with sixty two patients with acute coronary syndrome, at B.L.D.E. U'S Shri. B.M. PatilMedical College Hospital and Research Centre, Vijayapura between December 2018 to april 2020.

1. Microlbuminuria was estimated on the first urine sample after admission by using immunoturbidometric method.
2. Most patients belonged to a age group of 41-60 with a mean age of 59.5 ± 12.8 years.
3. In the present study male patients (71%) were more common than female (29%).
4. Chest pain, dyspnea and sweating were the most common presenting symptoms.
5. Out of 62 patients, the common wall motion abnormality was inferior wall occurring in 29 patients.
6. 64.1% of the patients of acute myocardial infarction with microalbumnuria had history of smoking.
7. 53.8% of the patients of acute myocardial infacrtion with microalbumnuria had a BMI > 25 kg/m2
8. Microlbuminuria was present significantly (62.9%) in non diabetic patients with acute myocardial infarction. Hence is a non specific yet highly sensitive marker of myocardial infarction in non diabetic individuals.
9. We therefore propose the use of microalbuminuria as adjunct biochemical parameter in non diabetic, acute myocardial infarction patients.

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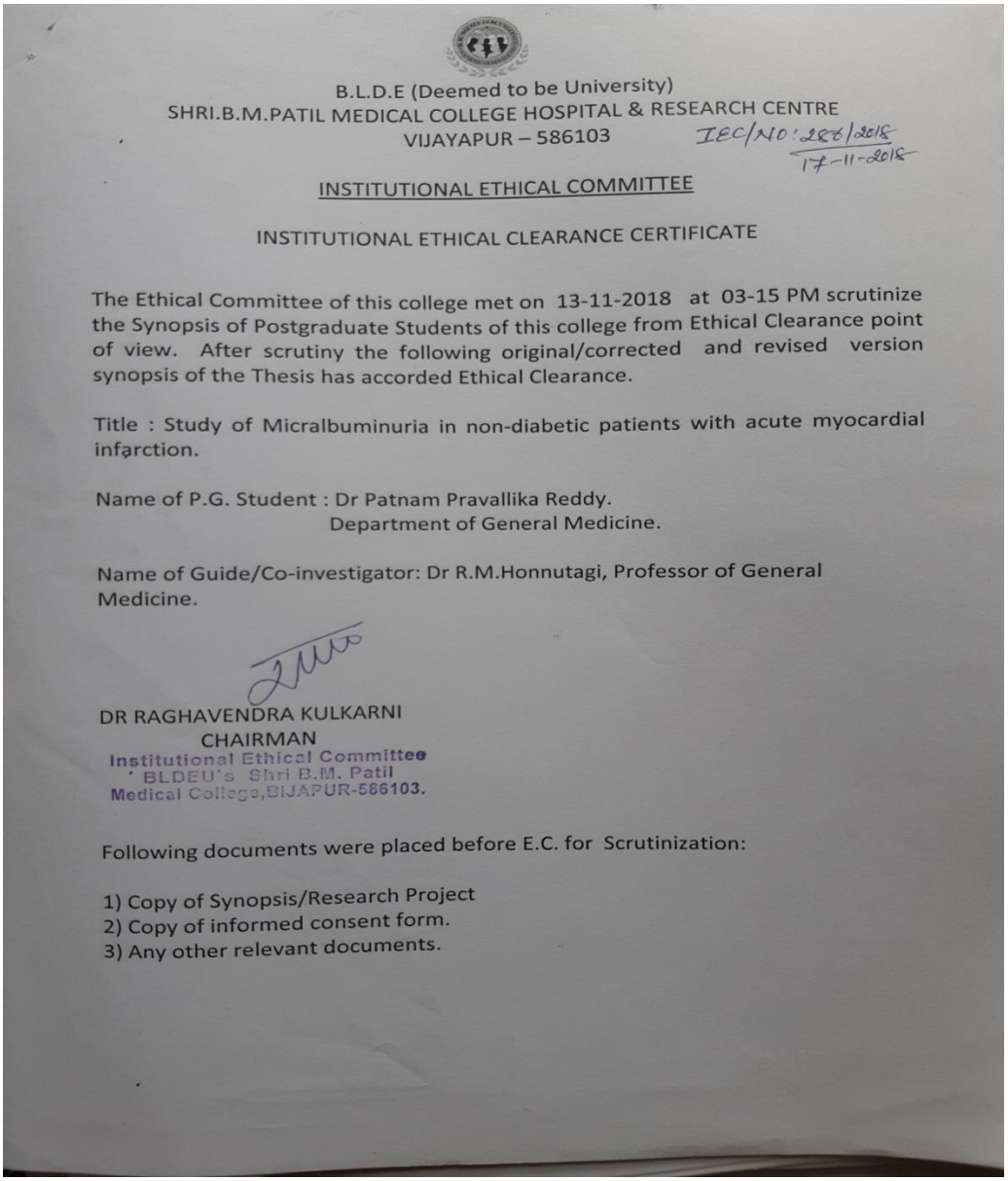
ANNEXURE-I

ETHICAL CLEARANCE CERTIFICATE



B.L.D.E (Deemed to be University)
SHRI.B.M.PATIL MEDICAL COLLEGE HOSPITAL & RESEARCH CENTRE
VIJAYAPUR – 586103

IEC/NO:288/2018
17-11-2018

INSTITUTIONAL ETHICAL COMMITTEE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 13-11-2018 at 03-15 PM scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has accorded Ethical Clearance.

Title : Study of Micralbuminuria in non-diabetic patients with acute myocardial infarction.

Name of P.G. Student : Dr Patnam Pravallika Reddy.
Department of General Medicine.

Name of Guide/Co-investigator: Dr R.M.Honnutagi, Professor of General Medicine.

DR RAGHAVENDRA KULKARNI
CHAIRMAN
Institutional Ethical Committee
BLDEU's Shri B.M. Patil
Medical College,BIJAPUR-586103.

Following documents were placed before E.C. for Scrutinization:

1) Copy of Synopsis/Research Project
2) Copy of informed consent form.
3) Any other relevant documents.

ANNEXURE II

INFORMED CONSENT FORM

BLDE (DEEMED TO BE UNIVERSITY)

SHRI B. M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, BIJAPUR- 586103

TITLE OF THE PROJECT

"STUDY OF MICROALBUMINURIA IN NON DIABETIC PATIENTS WITH ACUTE MYOCARDIAL INFARCTION."

PRINCIPAL INVESTIGATOR	-	Dr.Patnam Pravallika Reddy 9962757770
P.G.GUIDE NAME	-	Dr. R M HONNUTAGI PROFESSOR OF MEDICINE 9844088287
CHAIRMAN ETHICAL COMMITTEE		**Dr. TejaswiniVallabha** Professor and HOD, Department of General Surgery, B.L.D.E. (Deemed to Be University) Shri B. M. Patil Medical College, Hospital &Research Centre, Vijayapur.

All aspects of this consent form are explained to the patient in the language understood by him/her.

I) **INFORMED PART**

1. **PURPOSE OF RESEARCH:** I have been informed about this study. I have also been given a free choice of participation in this study.
2. **PROCEDURE:**I am aware that in addition to routine care received I will be asked series of questions by the investigator. I have been asked to undergo the necessary investigations and treatment, which will help the investigator in this study.
3. **RISK AND DISCOMFORTS:**I understand that I may experience some pain and discomfort during the examination or during my treatment. This is mainly the result of my condition and the procedure of this study is not expected to exaggerate these feelings that are associated with the usual course of treatment.
4. **BENEFITS:**I understand that my participation in this study will help to patients survival and better outcome.
5. **CONFIDENTIALITY:** I understand that the medical information produced by this study will become a part of Hospital records and will be subject to the confidentiality and privacy regulation. Information of a sensitive personal nature will not be a part of the medical records, but will be stored in the investigator's research file and identified only by a code number. The code-key connecting name to numbers will be kept in a separate location.

   If the data are used for publication in the medical literature or for teaching purpose, no name will be used and other identifiers such as photographs and audio or videotapes will be used only with my special written permission. I understand that I may see the photographs and videotapes and hear the audiotapes before giving this permission.

6. **REQUEST FOR MORE INFORMATION:** I understand that I may ask more questions about the study at any time.**Dr. Patnam Pravallika Reddy** is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of the study, which might influence my continued participation.

   If during the study, or later, I wish to discuss my participation in or concerns regarding this study with a person not directly involved, I am aware that the social worker of the hospital is available to talk with me. A copy of this consent form will be given to me to keep for careful reading.

7. **REFUSAL OR WITHDRAWAL OF PARTICIPATION:**I understand that my participation is voluntary and that I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice to my present or future care at this hospital. I also understand that **Dr Patnam Pravallika Reddy** may terminate my participation in the study after he has explained the reasons for doing so and has helped arrange for my continued care by my own physician or physical therapist, if this is appropriate.

8. **INJURY STATEMENT:**I understand that in the unlikely event of injury to me resulting directly from my participation in this study, if such injury were reported promptly, the appropriate treatment would be available to me, but no further compensation would be provided. I understand that by my agreement to participate in this study I am not waiving any of my legal rights.

   I have explained to _____the purpose of the research, the procedures required and the possible risks and benefits to the best of my ability in patient's own language.

_____ _____

Dr Patnam Pravallika Reddy

Date (Investigator)

II) **STUDY SUBJECT CONSENT STATEMENT:**

I confirm that Dr. Patnam Pravallika Reddy has explained to me the purpose of research, the study procedures that I will undergo, and the possible risks and discomforts as well as benefits that I may experience in my own language. I have read and I understand this consent form. Therefore, I agree to give consent to participate as a subject in this research project.

Participant / Guardian Date:

Witness to signature Date:

ANNEXURE III

CASE PROFORMA

Name of the patient :

Age in years :

Sex :

Address:

Religion:

Occupation:

IP no/OP no:

Presenting Complaints :

Past history:

Personal history:

1. Tobacco chewing

2. Smoking

3. Alcoholism

4. Diet- Veg/Mixed

5. No habits

Family history:

GENERAL PHYSICAL EXAMINATION :

Built :

Nourishment :

Ht(Cm) :

Wt(Kg) :

BMI:

Pallor

Icterus

Clubbing

Cyanosis

Edema

6. Vital parameters a. Pulse :

b. BP :

c. Respiratory rate :

d. Temperature

SYSTEMIC EXAMINATION:

ABDOMEN EXAMINATION

CARDIOVASCULAR SYSTEM

RESPIRATORY SYSTEM

CENTRAL NERVOUS SYSTEM

BIOCHEMISTRY

• Serum RBS levels • Serum homocysteine levels • Trop t • Cpk- mb • Lipid profile	

PATHOLOGY 1)Urine Routine	
Urine albumin	
Urine sugar Urine bile salts Urine bile pigments	
Urine microscopy RBC's Pus cells Cast's Epithelial cells	
2)Complete blood count:	
Hb	gm/dl
Total count	Cells/cumm
Differential count Neutrophils	%
Lymphocytes	%

Eosinophils	%
Basophils	%
Monocytes	%
ESR	At end of 1st hour.
Platelet Count	Lakhs/cumm

2D-ECHOCARDIOGRAPHY

LVIVSd : cm LVIDd : cm RVIDd:

cm LVPWd : cm LVISd : cm Aorta:

cm RVIDd : cm EF% : % PA : cm

VALVES :

Mitral Valve :

AorticValve :

Tricuspid Valve :

Pulmonary Valve :

CHAMBERS :

Left Ventricle :

Right Ventricle :

Left Ventricle :

Right Ventricle :

SEPTAE : GREAT ARTERIES

Aorta : Pulmonary Artery :

DOPPLER STUDY

Mitral Valve :

Aortic Valve :

Tricuspid Valve :

Pulmonary Valve :

REGIONAL WALL MOTION ABNORMALITIES :

PERICARDIAL EFFUSION :

CLOT/VEGETATION :

CONCLUSION :

ECG:

IMPRESSION AND CONCLUSION:

SIGNATURE

DATE:

MASTER CHART

NAME	AGE	SEX	IP NUMBER	CHIEF COMPLAINTS	HYPERTENSION	DIAGNOSIS	ALB TO CREAT RATIO	MICROALBUMINURIA	TROP I	CPK MB	RBS	CREATININE	ECG	2D ECHO	TOTAL CHOLESTEROL	SMOKING	BMI	COMPLICATIONS
SHIVAPPA BHIMASEE	65	M	14170	CHEST PAIN	YES	ALMI	21	ABSENT	0`82	21	87	0`7	T WAVE INVERSIONS V1-4	IHD LVEF 40		PRESENT	28	IMPROVED
TARABHAI	60	F	12626	CHEST PAIN	NO	IWMI	107	PRESENT	285	48	107	0`6	ST ELEVATION 2 3 AVF	IHD LVEF 50	191	ABSENT	21	IMPROVED
MUDAKAPPA BAJNTRI	55	M	14123	BREATHLESSNESS	NO	IWMI	73	PRESENT	9`44	33	120	0`9	ST ELEVATION 2 3 AVF	IHD LVF 35	208	PRESENT	30	IMPROVED
BHIMANNA	70	M	7554	WEAKNESS	YES	AWMI	168	PRESENT	0`13	36	134	0`8	ST ELEVATION V234	IHD LVEF 45	117	PRESENT	23	IMPROVED
LAXMAN RARTHOD	30	M	4773	CHEST PAIN	NO	LWMI	32	PRESENT	0`227	44	132	1`2	ST ELEVATION V345	IHD LVEF 50	201	ABSENT	26	IMPROVED
CHANDU TOPU	60	M	3057	CHEST PAIN	YES	IWMI	23	ABSENT	61`4		107	0`8	ST ELEVATION IMN 2 3 AVF	IHD LVEF 50		PRESENT	27	IMPROVED
BASSAMA ANNAYA	60	F	12956	CHEST PAIN	NO	ALMI	86`7	PRESENT	7866	235	100	0`8	ST ELEVATION V234	IHD LVEF 40		ABSENT	22	DEATH
ASHOK RAMMANA	41	M	12995	CHEST PAIN	NO	IWMI	8`7	PRESENT	286	15	121	1`1	ST DEPRESSION 2 3 AVF	IHD LVEF 45	202	PRESENT	28	IMPROVED
CHANDRABAGH SHANKAR	78	M	15050	CHEST PAIN	YES	IWMI	17	ABSENT	0`54	10	160	0`8	ST ELEVATION2 3 AVF	IHD LVEF 50	133	ABSENT	21`2	IMPROVED
SRIMANTH BARANANNA	72	M	12994	CHEST PAIN	NO	ALMI	194	PRESENT	1446	31	126	0`7	ST ELEVATION V234	IHD LVEF35	160	PRESENT	20	IMPROVED
GIRIMALLAYYA HIREMATH	70	M	18330	VOMITTING	NO	IWMI	167	PRESENT	42	300	117	0`8	ST ELEVATION 23AVF	IHD LVEF 45	131	PRESENT	22	IMPROVED
VITTAL BHIMAPPA	70	M	15565	CHEST PAIN	NO	IWMI	88`7	PRESENT	1`82	48	94	1`1	ST ELEVATION2 3 AVF	IHD LVEF 40	206	PRESENT	20	LVF
SHNATBAI KITTUR	60	F	19134	CHEST PAIN	NO	IWMI	222	PRESENT	0`792	15	110	0`5	ST ELEVATION2 3 AVF	IHD LVEF 60	212	ABSENT	27	IMPROVED
JAKAWWA SABU	67	F	19016	BACK PAIN	YES	NSTMI	20	ABSENT	5`43	32	112	0`8	NSTEMI	IHD LVEF30		ABSENT	30	IMPROVED
SUBHAS APPASAB	38	M	23697	CHEST PAIN	YES	ASMI	21`2	ABSENT	3`22		122	0`9	ST ELEVATION V345	IHD LVEF 50	167	PRESENT	27	IMPROVED
SHRISHAIL	55	M	24453	CHEST PAIN	YES	AWMI	21	ABSENT	137	35	131	0`8	ST ELEVATION V123	IHD LVEF35	177	PRESENT	29	IMPROVED
LALBI MAKANDHAR	60	F	17866	CHEST PAIN	NO	IWMI	17	ABSENT	0`225	30	138	1		IHD LVEF 45		ABSENT	31	IMPROVED
IRRAPPA CHANDAPPA	62	M	20994	CHEST PAIN	NO	IWMI	4	ABSENT	3`4	101	112	1	ST ELEVATION2 3 AVF	IHD LVEF35	119	PRESENT	24	IMPROVED
SATTEWAA BHIMAPPA	85	F	25080	CHEST PAIN	YES	IWMI	501	ABSENT	0`064	58	87	0`9	ST ELEVATION2 3 AVF	IHD LVEF 50	147	ABSENT	19	DEATH
YALAGURADAPPA	80	M	24691	CHEST PAIN	YES	ASMI	13`6	ABSENT	7`6	45	98	0`8	ST ELEVATION V234	IHD LVEF35	206	PRESENT	26	IMPROVED
SAYDHASHA GOUMOUDIN	63	M	26750	CHEST PAIN	YES	IWMI	2	ABSENT	0`029	48	94	1	ST ELEVATION2 3 AVF	IHD LVEF60	192	ABSENT	24	IMPROVED
HANUMANTAPPA BASAPPA	85	M	29677	CHEST PAIN	YES	AWMI	1`3	ABSENT	0`285	28	118	0`7	ST ELEVATION V234	IHD LVEF45		PRESENT	29	IMPROVED
SURESHGOUDA BIRADER	65	M	29120	CHEST PAIN	YES	ASWMI	5`7	ABSENT	0`103	12	137	0`7	ST DEPRESSION V234	IHD LVEF 45	156	PRESENT	26	IMPROVED
SANGEETA SHRIDHAR	36	F	29013	CHEST PAIN	NO	IWMI	225	PRESENT	11`9	21	99	0`7	ST ELEVATION 2 3 AVF	IHD LVEF 50	167	ABSENT	31	DEATH
ABDULRAZAK KHAZAK	56	M	28720	CHEST PAIN	NO	AWMI	4`2	ABSENT	2`2	32	107	1`4	ST ELEVATION V234	IHD LVEF 50		PRESENT	28	IMPROVED
SATTEWWA MAHADEV	60	F	27237	CHEST PAIN	NO	ASWMI	31	PRESENT	0`316	300	158	0`6	ST ELEVATION IN V2 V3 V4	IHD LVEF 30	221	ABSENT	29	IMPROVED
SABAWWA RAMAPPA	70	F	28358	VOMITTING	NO	IWMI	40	PRESENT	0`768	21	150	0`8	ST ELEVATION 2 3 AVF	IHD LVEF45	226	ABSENT	22	IMPROVED
ANAND RAO	58	M	22456	CHEST PAIN	NO	ASMI	66	PRESENT	12`2	52	127	0`7	ST ELEVATION V3 V4	IHD LVEF 50	155	PRESENT	28	VT
NINGAPPA	68	M	29564	CHEST PAIN	NO	IWMI	35	PRESENT	0`235	25	96	0`7	ST ELEVATION 2 3 AVF	IHD LVEF 40	200	PRESENT	27	IMPROVED

AMEERBEE DADAPEER	70	F	4465	CHEST PAIN	YES	IWMI	66	PRESENT	1`43	25	115	0`7	ST ELEVATION IN 2 3 AVF	IHD LVEF 35	220	ABSENT	32	IMPROVED
BASAPPA SNAGAPPA SOUNND	70	M	6654	CHEST PAIN	NO	IWMI	40	PRESENT	0`29	32	140	1	ST ELEVATON 2 3 VF	IHD LVEF 50	183	PRESENT	20	DEATH
SHANTAGOUDA BIRADER	60	M	6339	BREATHLESSNESS	YES	AWMI	60	PRESENT	4`484	29	85	1	ST ELEVATION V1 2	IHD LVEF 30	200	PRESENT	26	IMPROVED
DHARMANN DALAWAI	80	M	6180	BREATHLESSNESS	YES	AWMI	536	ABSENT	0`374	53	90	0`7	ST FLATTENNG V 1 2 3	IHD LVEF 40		PRESENT	27	IMPROVED
APPASAHEB ISHWERPPA	90	M	5490	BREATHLESSNESS	YES	LWMI	290	PRESENT	0`343	28	126	0`7	T WAVE INVERSIONS V4 TO6	IHD LVEF 55		PRESENT	21	LVF
BANGAREMM MALLEPA	70	F	6746	CHEST PAIN	NO	IWMI	40	PRESENT	9`13	26	140	0`7	ST ELEVATION 2 3 AVF	IHD LVEF 45	250	ABSENT	26	IMPROVED
SANGAPPA HADAPAD	68	M	10835	EPIASTRIC PAIN	NO	IWMI	72	PRESENT	9`4	59	145	1`5	Q WAVES IN 2 3 AVF	IHD LVEF 35	170	PRESENT	24	IMPROVED
SUNANDA MURUGAPPA	40	F	11591	CHEST PAIN	NO	LWMI	90	PRESENT	1`79	13	130	0`6	STT DEPRESSION V 4 5 6	IHD LVEF 35	115	ABSENT	28	IMPROVED
PARVATI SHIVAPPA	40	F	11791	CHEST PAIN	YES	AWMI	13	ABSENT	0`7	38	130	0`8	ST ELEVTION V 1 2 3	IHD LVEF 40	150	ABSENT	25	IMPROVED
BASAPP HANAMANTH	75	M	10702	CHEST PAIN	YES	AWMI	45	PRESENT	4`5	19	119	1`1	ST ELEVATON V 1 4	IHD LVEF 30		PRESENT	20	IMPROVED
PUTALABAI JETTAPAA	70	F	15280	CHEST PAIN	NO	LWMI	37	PRESENT	2`99	48	126	1	ST SEG ELEVATION V 4 5 6	IHD LVF 35	126	ABSENT	22	IMPROVED
SHIVANANDA PARANGOUDAPPA	50	M	14061	CHEST PAIN	NO	LWMI	78	PRESENT	13`6	63	118	0`9	ST SEG DEP I AVF	IHD LVEF 30	180	PRESENT	29	DEATH
TOPU MANSINGH	60	M	12684	BREATHLESSNESS	YES	ALMI	50	PRESENT	0`36	17	106	1`1	ST SEG DEP V 4 5 6	IHD LVEF 20		PRESENT	20	IMPROVED
SHANTABHI SIDDAYYA	55	F	10814	BREATHLESSNESS	YES	LWMI	2	ABSENT	0`46	32	113	1	ST DEP V 4 5 6	IHD LVEF 42		ABSENT	28	IMPROVED
ANNAPPA	56	M	15607	BREATHLESSNESS	NO	IWMI	56	PRESENT	106	52	106	1	ST ELEVATION 2 3 AVF	IHD LVEF 40	220	PRESENT	22	IMPROVED
SALEEM MTEBSB	49	M	15938	BREATHLESSNESS	YES	AWMI	20	ABSENT	9`6	23	112	0`7	ST ELE N V1 2 3	IHD LVEF 35		PRESENT	26	IMPROVED
SHANTABAI	58	F	15982	CHEST PAIN	YES	IWMI	33	PRESENT	2	53	86	1	ST ELEV N 2 3 AVF	IHD LVEF 40	346	ABSENT	28	IMPROVED
BASAVARAJ	40	M	15074	CHEST PAIN	YES	LWMI	12	ABSENT	11	21	112	0`7	ST ELEV IN V5 V6	IHD LVEF 55	136	PRESENT	24	IMPROVED
RAMAKRISHNA	35	M	10991	CHEST PAIN	NO	AWMI	36`5	PRESENT	0`966	13	103	0`7	ST ELEVTION V 1 2 3	IHD LVEF 35	201	PRESENT	27	DEATH
PUNDALIK	53	M	10885	CHEST PAIN	NO	IWMI	20`1	ABSENT	0`985	25	114	0`7	ST ELE N 2 3 AVF	IHD LVEF 40	340	PRESENT	29	IMPROVED
LAKSHMNAN	44	M	10257	BREATHLESSNESS	NO	AWMI	55	PRESENT	2`6	54	150	0`7	ST ELEV IN V123	IHD LVEFF 45		PRESENT	26	IMPROVED
KRISHNJI	51	M	10665	CHEST PAIN	YES	IWMI	29	ABSENT	6`3	25	112	0`6	ST ELE IN 2 3 VF	IHD LVEF 30	201	PRESENT	23	IMPROVED
SHANKREPPA	55	M	10552	CHEST PAIN	NO	IWMI	65	PRESENT	5`23	28	104	0`6	ST DEP 2 3 AVF	IHD LVEF 35	116	PRESENT	28	IMPROVED
LAXMI RATHOD	46	F	10668	CHEST PAIN	NO	LWMI	55	PRESENT	0`885	22	111	0`7	ST ELEV IN V 5 6	IHD LVEF 40	122	ABSENT	22	IMPROVED
RAMESH PUJARI	58	M	11257	CHEST PAIN	YES	IWMI	21	ABSENT	0`552	54	108	0`9	ST ELEV N 2 3 AVF	IHD LVEF 55	201	PRESENT	27	IMPROVED
MANJUNATH	44	M	11209	BREATHLESSNESS	YES	AWMI	55	PRESENT	12`3	22	117	0`8	ST DEP IN V 1 2 3	IHD LVEF 40	154	PRESENT	24	IMPROVED
GANAPAT BHATT	66	M	11328	CHEST PAIN	NO	IWMI	66	PRESENT	2`6	56	124	0`6	ST ELE IN 2 3 VF	IHD LVEF 35	226	PRESENT	26	DEATH
CHANANNAMA	55	F	11444	CHEST PAIN	NO	LWMI	54	PRESENT	0`964	26	96	0`7	ST ELEV IN V 5 6	IHD LVEF 40	196	ABSENT	32	IMPROVED
SANGAYYA HIREMATH	63	M	11421	BREATHLESSNESS	NO	AWMI	107	PRESENT	5`6	88	121	0`7	ST ELEV IN V 1 2 3	IHD LVEF 35	148	PRESENT	23	IMPROVED
SRINATH	44	M	11432	EPIASTRIC PAIN	YES	IWMI	21	ABSENT	32	54	112	0`9	ST ELEV IN 2 3 AVF	IHD LVEF 45		PRESENT	28	IMPROVED
OGEPPA	71	M	11541	CHEST PAIN	YES	LWMI	98	PRESENT	0`758	31	105	0`7	ST ELEV IN V5 V6	IHD LVEF 30	177	PRESENT	21	IMPROVED
SHARANAPPA SAMBANI	69	M	15274	CHEST PAIN	NO	IWMI	57	PRESENT	12`4	66	85	0`7	ST ELEV N 2 3 AVF	IHD LVEF 45		PRESENT	22	IMPROVED
NARAYANASWAMY	55	M	15214	CHEST PAIN	NO	LWMI	85	PRESENT	0`697	24	99	0`6	ST ELEV N V 4 5 6	IHD LVEF 40	187	PRESENT	23	IMPROVED