STUDY OF C-REACTIVE PROTEIN IN DIABETIC AND NON-DIABETIC PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

By

Dr. SHASHANK J SHIROL

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In

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Under the guidance of

Dr. S. S. DEVARMANI M.D.

PROFESSOR

DEPARTMENT OF GENERAL MEDICINE

B.L.D.E.U.'S SHRI B.M.PATIL MEDICAL COLLEGE

HOSPITAL & RESEARCH CENTRE, BIJAPUR

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Date:
Place: Bijapur

Dr. SHASHANK J SHIROL
Post Graduate Student,
Department of General Medicine,
B.L.D.E.U.'s Shri B M Patil Medical College, Hospital & Research Centre,
Bijapur

B.L.D.E.UNIVERSITY'S

SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE, BIJAPUR

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Date:

Place: Bijapur

Dr. S S DEVARMANI$_{M.D.}$

Professor
Department of General Medicine,
B.L.D.E.U.'s Shri B. M. Patil
Medical College, Hospital &
Research Centre, Bijapur

B.L.D.E.UNIVERSITY'S
SHRI B.M.PATILMEDICALCOLLEGE, HOSPITAL &
RESEARCH CENTRE, BIJAPUR

ENDORSEMENT BY THE HEAD OF DEPARTMENT

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Date:
Place: BIJAPUR

DR.M S MULIMANI$_{M.D.}$
Professor and Head
Department of General Medicine,
B.L.D.E.U.'s Shri B. M.Patil Medical College, Hospital & Research Centre,
Bijapur

B.L.D.E.UNIVERSITY'S

SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE, BIJAPUR

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Date:
Place: Bijapur.

DR. M. S. BIRADAR M.D.
Principal,
B.L.D.E.U.'s, Shri B.M.Patil
Medical College, Hospital &
Research Centre, Bijapur.

B.L.D.E.UNIVERSITY'S

SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE, BIJAPUR

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Date:

Place: Bijapur

Dr. SHASHANK J SHIROL

Post Graduate Student,
Department of Community Medicine,
B.L.D.E.U.'s Shri B. M. Patil
Medical College, Hospital &
Research Centre, Bijapur

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Date: **Dr. SHASHANK J SHIROL**

Place: Bijapur

ABSTRACT

BACKGROUND: Acute myocardial infarction is associated with rise in serum levels of markers of acute inflammation like C-Reactive Protein. CRP is an indicator of underlying coronary inflammation as well as the extent of myocardial necrosis. Diabetes is an independent risk factor for atherosclerosis. It is considered to be a state of low grade inflammation. CRP levels have been reported to be augmented in diabetic patients. We evaluated the prognostic role of CRP separately in diabetic and non-diabetic patients with acute myocardial infarction.

Aim and Objective: To determine the CRP level at the time of admission as a strong predictor of hospital mortality and morbidity in patients with diabetes mellitus as well as in patients without diabetes who had acute myocardial infarction.

Materials and methods: This was a longitudinal study which consisted of 168 patients with acute myocardial infarction, out of which 86 were diabetic and 82 were non diabetic patients. CRP levels were estimated immediately after admission by immunoturbidimetry method and all the cases were followed till discharge.

Results: Significant differences were found in CRP levels with 48.05±37.40mg/l in diabetic patients as compared with 18.05±14.02mg/l in non diabetic patients with acute myocardial infarction. The morbidity and mortality were high in diabetic group than in the other group.

Conclusion: It can be concluded that CRP on admission is a strong predictor for hospital mortality and morbidity and these higher in diabetic group than in the non diabetic group with acute myocardial infarction.

LIST OF ABBREVIATIONS

AMI	–	Acute myocardial infarction
APC	–	Atrial premature complex
AF	–	Atrial fibrillation
AVB	–	Atrio ventricular block
BFB	–	Bifascicular block
CAD	–	Coronary Artery Disease
CRP	–	C reactive protein
CCF	–	Congestive cardiac failure
CHB	–	Complete heart block
CHD	–	Coronary Heart Disease
CKMB	–	Creatine kinase –MB
CVD	–	Cardiovascular diseases
DM	–	Diabetes mellitus
ECG	–	Electrocardiogram
IHD	–	Ischemic heart disease
LBBB	–	Left bundle branch block
LVF	–	Left ventricular failure
MI	–	Myocardial Infarction

MR	–	Mitral regurgitation
NSTEMI	–	Non ST elevation Myocardial Infarction
PSVT	–	Paroxysmal supra ventricular tachycardia
RBBB	–	Right bundle branch block
STEMI	–	ST elevation Myocardial Infarction
UA	–	Unstable Angina
VF	–	Ventricular fibrillation
VPC	–	Ventricular premature complex
VT	–	Ventricular tachycardia

TABLE OF CONTENTS

LIST OF TABLES

LIST OF GRAPHS

INTRODUCTION

Atherosclerosis remains the major cause of death and premature disability in developed societies. Moreover, current predictions estimate that by the year 2020 cardiovascular diseases, notably atherosclerosis, will become the leading global cause of total disease burden[1]. Atherosclerosis has been reported to be associated with chronic low-grade inflammation of the vascular structure and the endothelial cells[2].

Acute myocardial infarction is a serious complication of atherosclerotic coronary artery disease which may prove to be fatal or cause disability due to comprised LV function. The true incidence of acute myocardial infarction is difficult to judge because of varied reporting pattern of death certification and several systems of medicine being practiced in our country. This is further compounded by the fact that vast majority of cases die at home even before they reach the hospital and even without having been examined by a qualified practioner. Having said this, acute myocardial infarction remains a leading cause of death in developed and developing countries including India[3].

Inherent to the inflammatory process is the occurrence of an acute phase response. This response is induced by pro inflammatory cytokines which are released from the inflamed tissue by inflammatory and/or parenchymal cells. These in turn stimulate the liver to synthesize a number acute phase proteins. C-Reactive Protein(CRP), being one among them, synthesized by the liver in response to factors released by adipocytes[4]. CRP is a marker for inflammation and is enhanced in both atherosclerosis and in coronary artery disease. They reflect the extent of myocardial necrosis and co-relate with cardiac outcomes following acute myocardial infarction.

Diabetes mellitus is the single most important metabolic disease recognised worldwide as one of the leading cause of death and disability, its incidence being the highest in developing countries than developed countries. Today, India is the leading country in the world with largest number of diabetic subjects as compared with any given country. Currently estimated diabetic population of India is 31.7 million individuals and this number is expected to reach 79.4 million by the year 2025. The World Health Organisation (WHO) has already declared India as the global capital of diabetes. Diabetes mellitus is an independent risk factor for atherosclerosis. It is considered to be a state of low-grade inflammation. CRP levels have been reported to be augmented in diabetic patients[5].

Recent studies have shown CRP to be a risk predictor for the future myocardial infarction, stroke and coronary heart disease in apparently healthy persons2,7. This study is aimed at determing the role of CRP in the patients with myocardial infarction and at comparing the results between diabetic and non-diabetic patients as studies have shown importance of CRP levels on admission with regard to the hospital outcome of diabetic and non-diabetic patients. The excessive risk of mortality in patients with diabetes and elevated CRP will require an intensification of strategies to overcome the poor prognosis.

AIMS AND OBJECTIVES OF THE STUDY

To determine the CRP level at the time of admission as a strong predictor of hospital mortality and morbidity in patiens with diabetes mellitus as well as in patients without diabetes mellitus who had acute myocardial infarction.

REVIEW OF LITERATURE

HISTORICAL REVIEW

The history of ischemic heart disease is relatively brief and represents a very convincing example of the rapid development of cardiology as a scientific discipline.[13,14.] Bonetas (1700) made the earliest correlation of the clinical picture of coronary artery disease. William Herberden described angina pectoris and later published his paper in1772. John Hunter described the clinical description and clinical features in 1773

In 1799, Caleb Parry proposed that angina may be due to inefficient delivery of blood to heart muscles, particularly during exercise[15].

In 1845, Leipzig, Vogel discovered cholesterol as major constituent in atheromatous plaque[16].

It was James. B. Herrick in 1912, who described the symptomatology, diagnosis and treatment of obstruction of the coronary arteries. The experimental study of blood lipids and atherosclerosis started in 1913 by Anitschkow.[17].

In 1920, Pardee first recognized the electrocardiographic curve of acute stage of myocardial infarction. William Enthoven invented ECG[17].

Ladue Wrobleuski and Karmen introduced estimation of the SGOT enzyme levels in1954. The value of LDH estimation was introduced in 1955 and CPK by Dreyfuss in1960.

On the therapeutic side, Kobnson used streptokinase for thrombolysis in 1959. In1977, Mc-curtly Gruntzing introduced the technique of PTCA. Surgical reperfusion by CABG has been undertaken with variable success since early 1970's.[17]

Numerous articles have been published about the risk factors in IHD. In 1938,cigarette smokers were shown to die at an early age. It was estimated that the smoking directly contributes to 3, 25,000 premature deaths in America.[43]

CRP was discovered by Tillet and Francis in 1930.Lofstrom detected CRP in non-infectios as well as infectious condition, and the acute phase reaction, in which the concentration of certain plasma proteins increases, is now recognised as a general and nonspecific response to most forms of infective and non-infective inflammatory processes,cellular and /or tissue necrosis and malignant neoplasia[9].

CRP is not only an excellent biomarker of inflammation but it is also a direct participant in atherogenesis. It provides a valuable tool for identifying patients at risk of cardiovascular events in primary prevention in conjunction with lowering LDL-cholesterol and may also have utility in the treatment of acute coronary syndrome and with percutaneous coronary intervention therpy. CRP provides as a readily accessible marker for further testing of inflammatory hypothesis in atherosclerosis. Jupiter study has shown that in patients with raised CRP without hyperlipidemia, administration of rosuvstatin to decrease CRP levels have helped in decreasing the incidence of cardiovascular events in such groups.

The study of the Munich Myocardial Registry demonstrates that CRP on admission is a strong predictor for hospital mortality in both diabetic and non-diabetic

subjects. A cut off of 7mg/l for CRP levels on admission is suggested for patients with acute myocardial infarction.

Previously Lim, et-al. suggested CRP levels of 10mg/l and Dibra, et-al suggested CRP levels above 12mg/l to detect AMI patients at increased risk for short and long term mortality[10,11].

Diabetic patients presented with higher CRP levels compared to non-diabetic subjects. In the Munich myocardial Infarction Registry, the combined presence of diabetes and CRP levels in the two upper quintiles demonstrated that the rate of mortality was 6 to 7 fold higher as compared to diabetic patients, who presented with CRP-levels in the lowest quintile. The relationship between atherothrombosis, inflammation and diabetes is supported in the clinical setting of a registry[12].

EPIDEMIOLOGY

Coronary artery disease is a worldwide disease. Cardio vascular diseases rank number one in the United States in causing morbidity and mortality. Although CAD is considered a disease of industrialized western world, now it has brought this problem to the door step of the third world countries.[18]

Epidemics of CHD began at different times in different countries. In developed countries, where epidemic began earlier (1920's), started declining now.[19] The decline in CHD in various countries is due to changes in the life style and related risk factors –diet, diet related serum cholesterol, cigarette use, exercise habits and better control of hypertension .[20]

Coronary artery disease was a rare cause of death in US at the beginning of 20th century, accounting for less than 10% of all deaths in 1910. By 1965 coronary artery disease mortality rate rose to 55% of all deaths. The last three decades saw annual decline in coronary artery diseases in US.

From the 1960's to the 1990's the coronary artery disease prevalence increased two folds (from 2% to 4%) in rural India and three folds (3.45% to 9.45%) in urban India. The prevalence is even higher in South India (13% in urban and 7% in rural). In 1990 higher mortality of 25% deaths in India were attributed to cardiovascular diseases, compared to 9% to diarrhoeal diseases, 12% to respiratory infections and 5% due to tuberculosis.[21]

ISCHEMIC HEART DISEASE

Patients with ischemic heart diseases fall into two large groups [22]:

1. Stable angina secondary to chronic coronary artery disease
2. Acute coronary syndromes

Acute coronary syndromes are classified in to:

A) Acute Myocardial Infarction with ST segment elevation (STEMI)

B) Unstable angina and Non ST segment elevation Myocardial Infarction (UA/NSTEMI)

DEFINITIONS

Acute coronary syndromes is composed of patients with acute myocardial infarction (MI) with ST segment elevation on their presenting electrocardiogram (STEMI) and those with unstable angina (UA) and non-ST-segment elevation MI (NSTEMI).[23]

STEMI is due to the formation of occlusive thrombosis at the site of rupture of an atheromatous plaque in a coronary artery.

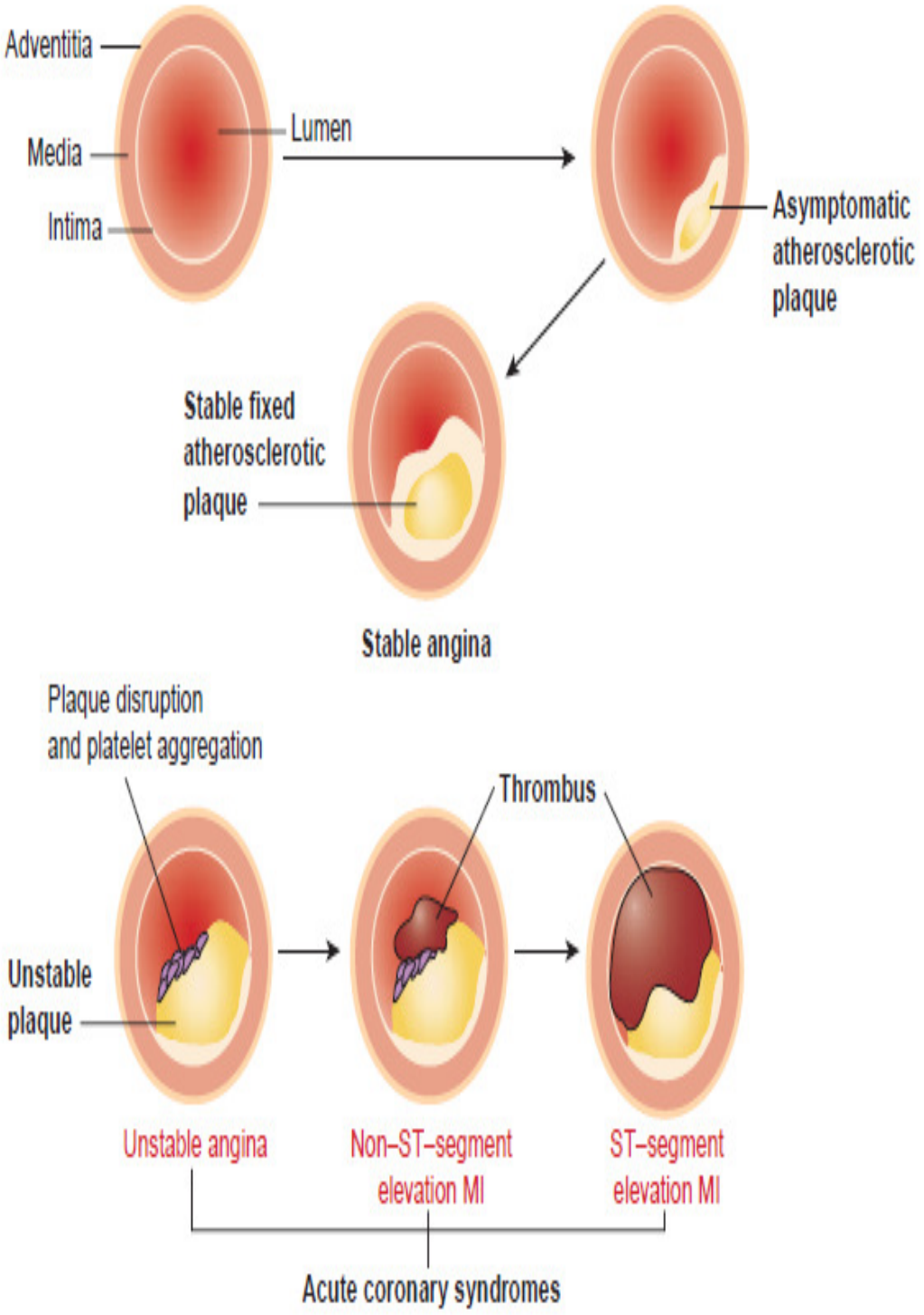
UA is defined as angina pectoris or equivalent ischemic discomfort with at least one of the three features-

1) It occurs at rest (or with minimal exertion); usually lasting > 10 min.

2) It is severe and of new onset,

3) It occurs with a crescendo pattern.

The diagnosis of NSTEMI is established if a patient with clinical features of UA develops evidence of myocardial necrosis, as reflected in elevated cardiac enzymes. UA/NSTEMI is usually associated with severe coronary obstruction but not total occlusion of the culprit artery. Among patients with UA/NSTEMI, between 40 to 60% have evidence of myocardial necrosis with elevated enzymes.[24]


Adventitia
Media
Intima
Lumen
Asymptomatic atherosclerotic plaque
Stable fixed atherosclerotic plaque
Stable angina
Plaque disruption and platelet aggregation
Thrombus
Unstable plaque
Unstable angina
Non–ST–segment elevation MI
ST–segment elevation MI
Acute coronary syndromes

ANATOMY OF CORONARY ARTERIES [25,26]

There are two coronary arteries, which arise from coronary sinuses at the beginning of ascending aorta

1) Right coronary artery

2) Left coronary artery

1. Right coronary artery (RCA):

It arises from anterior aortic sinus and passes between right auricle and infundibulum of right ventricle, then runs downwards in AV groove and then runs backwards. Its branches are:

1. Conus artery:

   It anastomoses with similar branch of left coronary artery and forms anastomatic ring around pulmonary trunk. It supplies right ventricular outflow tract.

2. SA nodal artery:

   It forms ring around the termination of the superior vena cava. It supply SA node in 60% individuals.

3. Right marginal artery:

   It arises at inferior border and supply right ventricular free wall.

4. Posterior descending artery and posterolateral branch:

   These supply base, middle and inferior wall, basal inferior septum, right bundle, AV node, HIS bundle, posterior portion of left bundle branch and posteromedial mitral papillary muscle. Sometimes it gives AV nodal artery which supply AV node

2. Left coronary artery:

It arises from left posterior aortic sinus. It emerges between left auricle and infundibulum of right ventricle. After a short course it divides into circumflex and anterior descending artery.

Branches:

a) Left anterior descending artery (LAD):

It courses in anterior interventricular groove, wraps around cardiac apex and travels a variable distance along inferior interventricular groove towards base

b) Septal perforating branches:

These supply anterior septum, apical septum. First perforator supplies His bundle branch.

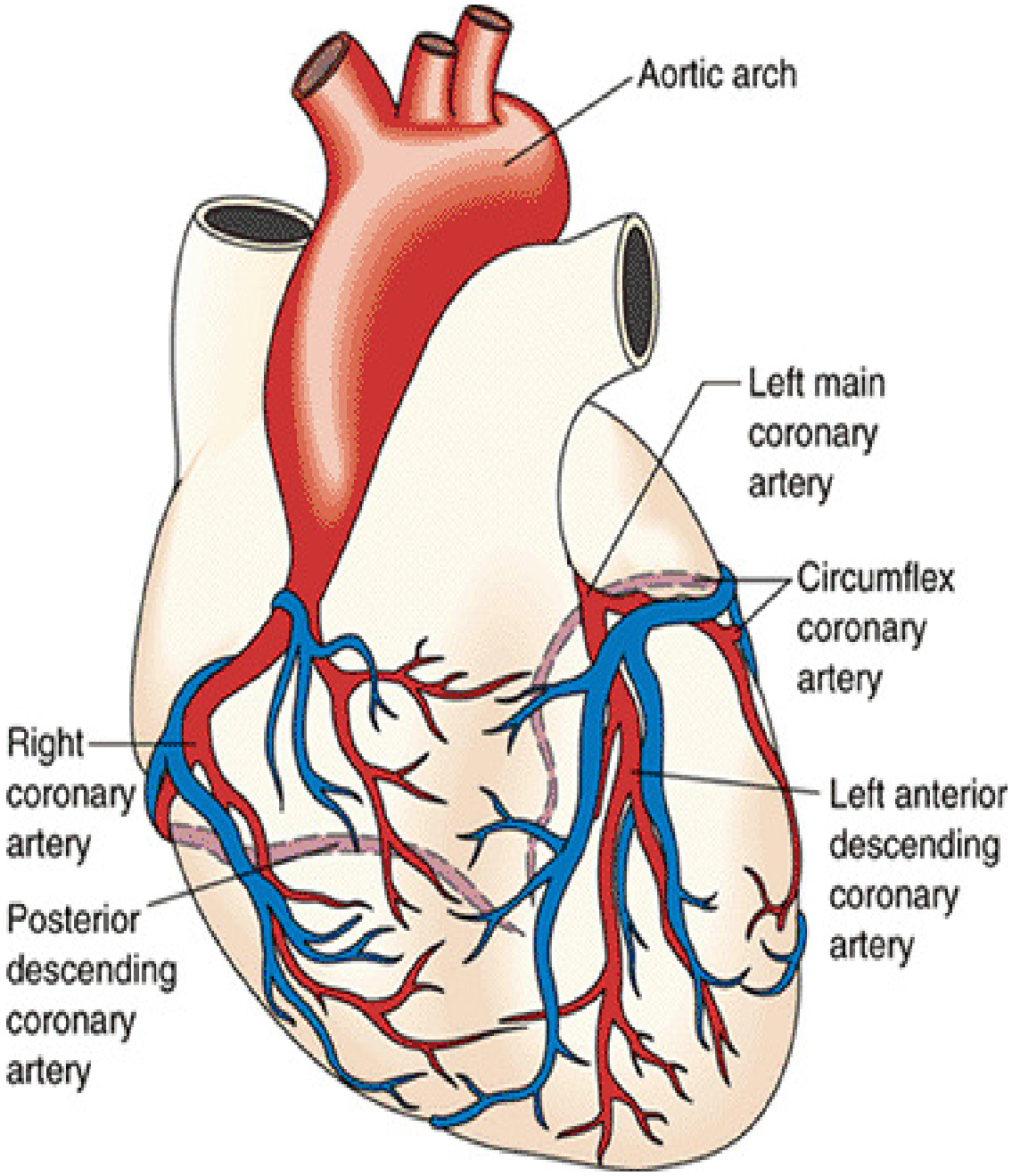
c) Diagonal branches:

These supply anterior left ventricle, free wall part of anterolateral mitral papillary muscle, medial 1/3rd of anterior right ventricular wall.

d) Left circumflex artery (LCX):

It courses in left AV groove and terminates just beyond its large obtuse marginal branch.

1. In 40% patients, it gives SA nodal branch
2. Obtuse marginal branch: It supplies lateral left ventricular free wall and portion of anterolateral mitral papillary muscle.


Aortic arch
Left main coronary artery
Circumflex coronary artery
Left anterior descending coronary artery
Right coronary artery
Posterior descending coronary artery

PATHOGENESIS

The dominant influence in the causation of the ischemic heart disease (IHD) syndromes is diminished coronary perfusion relative to myocardial demand, owing largely to a complex and dynamic interaction among fixed atherosclerotic narrowing of the epicardial coronary arteries, intraluminal thrombosis overlying a disrupted atherosclerotic plaque, platelet aggregation and vasospasm.

More than 90% of patients with IHD have atherosclerosis of one or more of coronary arteries. The clinical manifestations of coronary atherosclerosis are generally due to progressive encroachment of the lumen leading to stenosis or to acute plaque disruption with thrombosis which compromises blood flow. A fixed obstructive lesion of 75% or greater generally produces ischemic symptoms on exertion. A 90% stenosis can lead to inadequate coronary blood flow even at rest. Slowly developing occlusion may stimulate collateral vessels over time, which protects against distal myocardial ischemia and infarction even with an eventual high-grade stenosis.

Clinically significant plaques can be located anywhere within the major coronary epicardial vessels, but tend to predominate in the first several centimeters of LAD and LCX and along the entire length of RCA. Sometimes major epicardial branches are also involved but the atherosclerosis of the intramural branches is rare. The onset of symptoms and prognosis of IHD depend not only on the extent and severity of fixed, chronic anatomic disease but also critically on dynamic changes in coronary plaque morphology.[27]

ROLE OF ACUTE PLAQUE CHANGE :

In most of the patients the myocardial ischemia underlying the acute coronary syndromes is precipitated by abrupt plaque change followed by thrombosis. Most often the initiating event is disruption of previously only partially stenosing plaque with any of the following:

- Rupture/ Fissuring, exposing the highly thrombogenic plaque constituents.
- Erosion/ ulceration, exposing the thrombogenic subendothelial basement membrane to blood.
- Hemorrhage in to the atheroma, expanding its volume.

The events that trigger abrupt changes in plaque configuration and superimposed thrombosis are complex and poorly understood. Influences both intrinsic (e.g. plaque structure and composition) and extrinsic (e.g. blood pressure, platelet reactivity) are important.

The structure and composition of plaque are dynamic and contribute to the propensity for disruption. Plaque that contain large areas of foam cells and extracellular lipids, and those whose fibrous caps are thin or contain few smooth muscle cells or have cluster of inflammatory cells, are more likely to rupture, and are called " Vulnerable Plaques". Fissures frequently occur at the junction of fibrous cap and the adjacent normal plaque free arterial segment, a location at which blood flow inducing mechanical stresses within the plaque are highest and the fibrous cap is thinnest. It is now recognized that the fibrous cap can undergo continuous remodeling. The balance of synthesis and degradation of collagen, which is the major structural component of fibrous cap, accounts for its mechanical strength and determines plaque

stability and prognosis. Collagen is produced by smooth muscle cells and degraded by the action of metalloproteinases, enzymes elaborated by macrophages in atheroma.

Thus the inflammation destabilizes the mechanical integrity of the plaques. Extrinsic influences are also important. Adrenergic stimuli can elevate physical stresses on the plaque through systemic hypertension, or local vasospasm. Indeed the adrenergic stimulation associated with awakening and arising induces a pronounced circadian periodicity for the time of onset of acute myocardial infarction, with a peak incidence between 6 AM and 12 Noon, concurrent with a surge in the blood pressure and immediately following heightened platelet activity. Intense emotional stress can also contribute to the plaque disruption.

It is now recognized that the preexisting culprit lesion in patients who develop myocardial infarction and other acute coronary syndromes is not necessarily a severely stenotic and hemodynamically significant lesion prior to its acute change. Approximately two thirds of the plaques that rupture with subsequent occlusive thrombosis caused occlusion of only 50% or less before plaque rupture, and 85% had initial stenosis less than 70%.

ROLE OF INFLAMMATION

Inflammation plays an important role at all stages of atherosclerosis from its inception to the development of complications. The establishment of the initial lesion requires the interaction between endothelial cells and circulating leukocytes, leading to accumulation of T cells and macrophages in the arterial wall. Entry of leukocytes in to the wall is a consequence of the release of chemokines by endothelial cells and the increased expression of adhesion proteins (ICAM-1, VCAM-1, E-Selectin, PSelectin)

in these cells. T cells located in the arterial wall produce cytokines such as TNF, IL-6, and IFN gamma that stimulate endothelial cells and activate macrophages, which become loaded with oxidized LDL. During plaque rupture there will be release of metalloproteinases by macrophages. These enzymes weaken the plaque by digesting collagen at the fibrous cap or the shoulder of the lesion.

ROLE OF CORONARY THROMBUS

Partial or total thrombosis associated with disrupted plaque is critical to the pathogenesis of acute coronary syndromes. In acute transmural MI, thrombus superimposed on a disrupted but previously only partially stenotic plaque converts it to a total occlusion. In contrast, with unstable angina or acute subendocardial infarction the extent of luminal obstruction by thrombosis is usually incomplete and may wax and wane with time. Thrombus is a potent activator of multiple growth related signals in smooth muscle cells, which can contribute to the growth of atherosclerotic lesion.

ROLE OF VASOCONSTRICTION

Vasoconstriction compromises the lumen size, and by increasing the local mechanical forces, can potentiate plaque disruption. Vasoconstriction at the site of atheroma is stimulated by:

- Circulating adrenergic agonists
- Locally released platelet contents
- Impaired secretion of endothelial cell relaxing factors relative to contracting factors (e.g. endothelin) due to atheroma associated endothelial dysfunction .
- Mediators released from perivascular inflammatory cells.[28]

RISK FACTORS [29-33]

Risk factor reduction is the primary clinical approach to prevent coronary artery disease (CAD) morbidity and mortality. The concept of risk factor identification and modification is based on the fact that exposure to certain host and environmental factors increases the statistical risk for developing a disease and that alteration of these conditions reduces the risk. Thus identifying risk factors may possibly retard the formation and growth of an atherosclerotic plaque.

The Framingham study was first of its kind to describe the primary and secondary risk factors like hypertension, diabetes mellitus, hypercholesterolemia, cigarette smoking, obesity, race, family history of coronary artery disease, physical inactivity, personality type etc.

The Risk factors for CAD are divided into-

1. **Modifiable risk factors**

   A) Major

   1) Cigarette smoking.

   2) Hypertension.

   3) Diabetes mellitus.

   4) Hyperlipidemia.

   5) Obesity.

   B) Minor risk factors

   1. Oral contraceptives.
   2. Physical activity.
   3. Personality.
   4. Socioeconomic status (SES) and psychosocial factors
   5. Others–Alcohol, Hyperuricemia, Coffee consumption, Deficiency of trace elements, Low circulating levels of antioxidants etc.

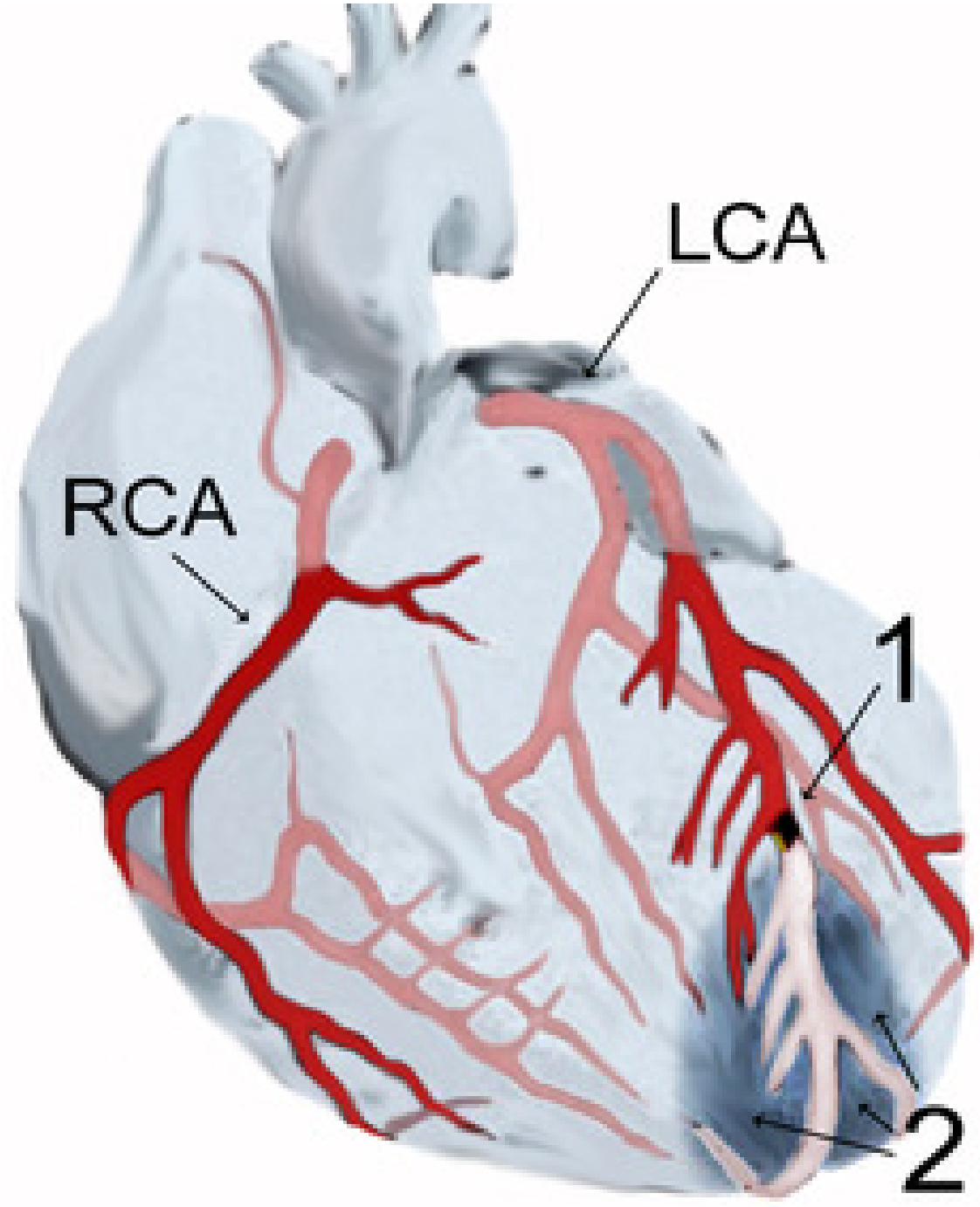
2. **Non modifiable :**

   1. Age

   2. Race

   3. Family history

   4. Male gender



1. SITE OF OCCLUSION

2. AREA OF MYOCARDIAL DAMAGE

ST-ELEVATION ACUTE MYOCARDIAL INFARCTION

HISTORY:

In up to 50% of cases precipitating factor is present before STEMI, such as vigorous exercise, emotional stress or a medical or surgical illness. Although seen at any time the peak incidence is seen between 6AM to 12 Noon. This is due to both increased sympathetic tone and increased tendency to thrombosis at this time.[34]

CLINICAL FEATURES [35]

Chest pain is the most common presenting symptom. Seen in 80-85% of cases. It is similar as angina but lasts longer. In 30% of cases pain radiates (left arm, epigastrium, back, jaw, neck) Weakness, sweating, nausea, vomiting & sense of impending doom accompany it. The incidence of painless infarctions is common in diabetics. Nausea and vomiting occur in 50% of patients with transmural infarction and is more common with inferior wall infarctions.

Sudden onset breathlessness, which may progress to pulmonary edema, may be the presenting feature. Palpitations and Syncope are the other features in patients with arrhythmias. Less commonly loss of consciousness and confusional states, sensation of profound weakness, evidence of peripheral embolism may be present.

GENERAL EXAMINATION:

- Patient may be anxious and restless.
- Pallor associated with sweating and cold peripheries.
- About 1/4th of patients with anterior wall MI have manifestations of sympathetic over activity (tachycardia/hypertension).

- About 50% of patients with inferior wall infarctions have parasympathetic over activity (bradycardia /hypotension).
- Raised JVP and clear chest is a feature of right ventricular infarction.

Temperature elevation up to 38 degrees may be observed during the first week.

PRECORDIAL EXAMINATION:

Precordium is usually quiet and apical impulse may be difficult to localize. In patients with anterior wall MI, abnormal systolic pulsations caused by dyskinetic bulging of infracted area may develop in periapical area.

Auscultation may reveal muffled heart sounds, may be paradoxical splitting of S2, or S3/S4 may be heard. There may be transient apical systolic murmur due to papillary muscle dysfunction. Pericardial rub is common in transmural MI.

There may be bilateral basal crepitations on chest auscultation in left ventricular failure and pulmonary edema.

LABAROTARY INVESTGATIONS:[36]

The laboratory tests in confirming the diagnosis are divided in to four groups:

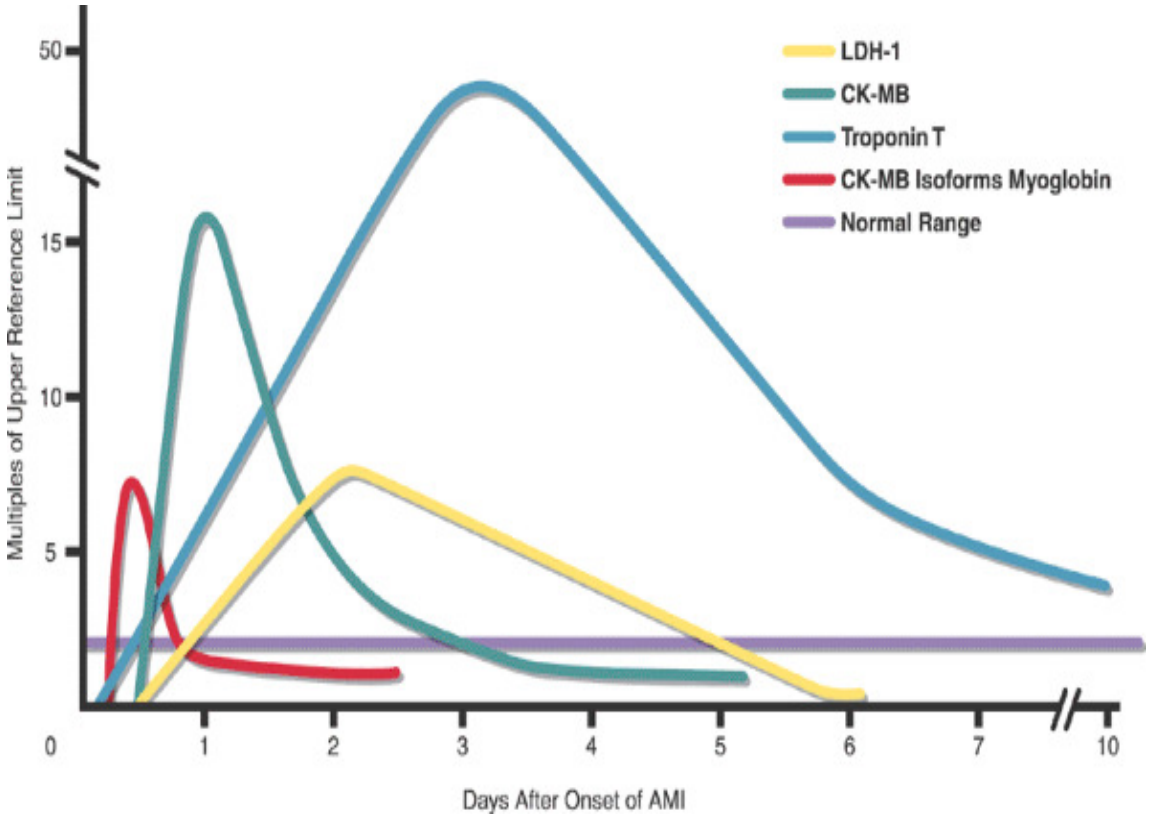
1] Electrocardiogram

2] Serum cardiac biomarkers

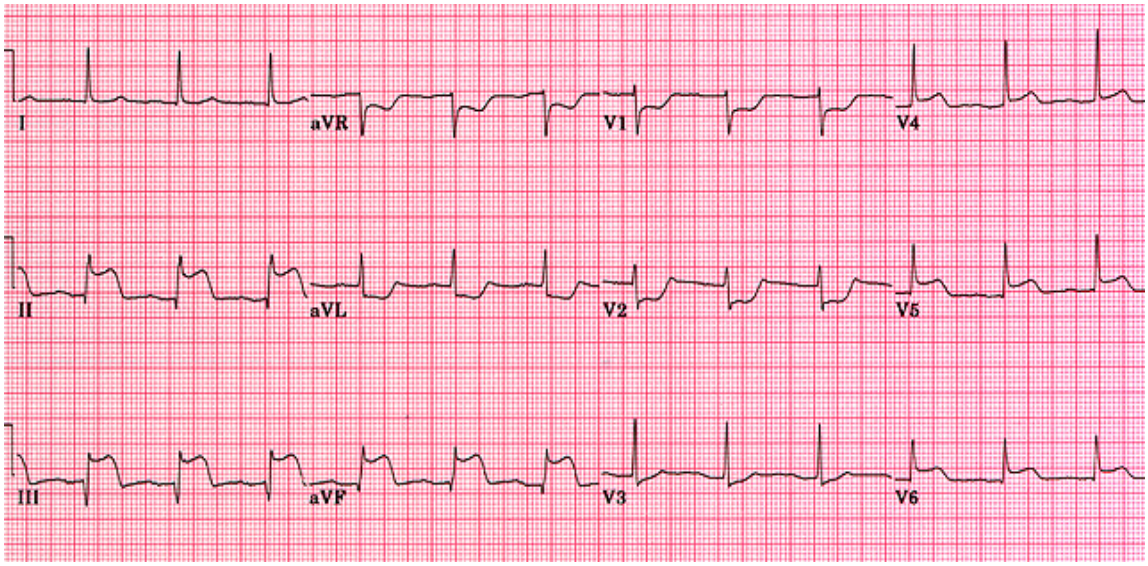
3] Cardiac imaging

4] Others

CARDIAC BIOMARKERS



ECHOCARDIOGRAPHIC CHANGES IN INFERIOR WALL MI



1] ELECTROCARDIOGRAM (ECG)

The infarction process evolves through three easily recognizable phases,

1] Hyperacute phase

a) Slope elevation of ST segment

b) Tall and wide T waves

c) Tall R waves

d) Increased ventricular activation time

2] Fully evolved phase

a) Pathological Q waves or QS complex

b) Coved and elevated ST segment

c) Loss of R wave amplitude

d) Symmetrical, inverted T waves

3] Chronic stabilized phase:

ST segment returns to base line. T waves regains positivity, Q waves may persist.

Localization of myocardial infarction

The electrocardiographic features of myocardial infarction may be localized to the following principal regions of left ventricular cone.

1] The Anterior wall

2] The Inferior wall

3] The Posterior wall

1] The Anterior wall MI:

It is further divided in to 4 categories:

A] Extensive anterior wall:

Reflected by the typical infarction pattern in lead I, lead AVL and all the Precordial leads.

B] Anteroseptal wall:

It is reflected by the typical infarction pattern in leads V1 to V4

C] Anterolateral wall:

It is reflected by the typical infarction pattern in Lead I, Lead AVL and Leads V4 to V6.

D] Apical wall:

Typical pattern appears predominantly in leads V5 and V6.

2] The Inferior wall MI:

Inferior wall of the left ventricular cone is oriented to standard leads II, III and AVF. So inferior wall infarction is reflected by the typical infarction pattern in these leads. In fully evolved phase lead III commonly reflects a QS complex; standard Lead II and AVF however usually reflect Qr complexes.

An inferolateral infarction (inferoapical infarction) is reflected by the infarction pattern in leads II, III and AVF, as well as in leads V5 and V6.

3} Posterior wall MI:

There is no conventional electrode which is directly oriented to the posterior wall of the heart. Infarctions of the posterior wall must consequently be diagnosed by the inverse or the mirror image changes, which will be reflected by electrodes oriented in the same plane to the uninjured anterior myocardial wall. The right

precordial leads V1 to V3 and especially lead V2 are oriented to the anterior wall and reflect the inverse changes or mirror image. Thus-

1. The mirror image of QS complex is reflected by the tall and slightly widened R wave.
2. The mirror image of the coved and elevated ST segment is theoretically reflected by a depressed concave upward ST segment. (This finding is not commonly seen).
3. The mirror image of the inverted symmetrical T wave is reflected by an upright, widened and usually tall or relatively tall T wave. This upright T wave is an essential characteristic of posterior wall infarction, and the diagnosis should not be entertained without it.

ECG manifestations of right ventricular infarction

1. Right ventricular infarction should be strongly suspected if, in the clinical setting of acute inferior wall infarction, there is ST segment elevation of 1mm or more in lead V1, lead V4R or any one of right precordial leads. V4R is the most sensitive. An ST segment higher in V4R than in leads V1 to V3 offers the highest specificity and efficiency in diagnosis.
2. ST segment elevation in lead V2 which is 50% (or less) the magnitude of the ST segment elevation in lead AVF indicates Right ventricular infarction.
3. Occasionally Right ventricular infarction may be associated with ST segment elevation in lead V1 as well as several other precordial leads. It thus mimic

anterior wall MI. However in case of Right ventricular infarction, ST elevation is maximum in lead V1.

4. When there is ST elevation in V1 and ST depression in V2, a discordant relationship- also suggests right ventricular infarction.
5. Lewis and associates reported the hyperacute phase of Right ventricular infarction, this manifests principally with slope elevation of ST segments in V1 or V4R or only in lead V4R.

2] CARDIAC MARKERS

Certain proteins, called serum cardiac markers are released into the blood in large quantities from necrotic heart muscle .

1. Creatinine Phosphokinase:

It starts rising within 4-8 hrs and peaks at 24 hrs and returns to normal by 48hrs. The isoenzyme CKMB is more specific for myocardium.

2. Lactate dehydrogenase:

It starts rising after 24-48 hrs and peaks at 3-6 days and returns to normal by 8-14 days.

3. Myoglobin:

It is earliest to be released in to the serum (1-4 Hrs). It lacks cardiac specificity and is rapidly excreted in urine and blood levels returns to normal within 24 hrs.

4. Cardiac specific troponin (cTnT and cTnI) :

These have high specificity for myocardium. Both quantitative and qualitative tests are approved for diagnosis of acute myocardial infarction. CTnT assays are produced by a single manufacturer, leading to relative uniformity of cut-off values, where as multiple manufacturers produce cTnI assays. Both of these typically increase

more than 20 times above the reference range. Elevation of cTnI may persist for 7-10 days after acute myocardial infarction; elevation of cTnT may persist for up to 10-14 days. This makes late diagnosis possible.

3] CARDIAC IMAGING:

Echocardiography helps by detecting wall motion abnormalities. It also helps in deciding about reperfusion therapies, localizing the site of infarction, determining left ventricular function, detection of ventricular aneurysm, pericardial effusion and left ventricular thrombus. Doppler echocardiography helps in detection and quantitation of a ventricular septal defect and mitral regurgitation. Radionuclide studies like Technetium 99m and Thallium 201 help in diagnosis and localizing infarction.

CORONARY ANGIOGRAPHY

Coronary angiography is helpful in localization of obstruction in coronary artery and to assess extent of myocardial infarction.

TREATMENT OF ACUTE MYOCARDIAL INFARCTION [37,38,39]

A] Aspirin:

All patients with definite or suspected myocardial infarction should receive aspirin at a dose of 162 mg or 325 mg at once. Chewable aspirin provides rapid blood levels. Patients with definite aspirin allergy may be treated with clopidogrel 300mg.

B] Thrombolytic therapy: Thrombolytic therapy reduces mortality and limits infarct size in patients with acute myocardial infarction associated with ST segment elevation (defined as more than or equal to 0.1 mV in two inferior or lateral leads or in two

contiguous precordial leads), or with LBBB. The greatest benefit occurs if treatment is initiated within 6 hrs of onset of chest pain, when up to 50% reduction in mortality rate can be achieved. The magnitude of benefit declines thereafter, but a 10% relative mortality reduction can be achieved up to 12 hrs after the onset of chest pain. The survival benefit is greatest in patients with large, usually anterior infarctions. Patients without ST elevation do not benefit and may derive harm from thrombolysis.

Thrombolytic Agents:

1. Streptokinase: 1.5 million units infused over 30- 60 minutes.
2. Alteplase: 15 mg bolus followed by 50 mg infused over next 30 minutes, and 35 mg over following 60 min.
3. Reteplace: 10 units as a bolus over 2 minutes, repeated after 30 minutes.
4. Tenecteplace: 40 mg (0.5 mg/ kg) bolus.

C] Primary percutaneous coronary intervention (PCI):

Immediate coronary angiography and primary PCI (including stenting) of infarct related artery have been shown to be superior to thrombolysis when done by experienced operators in high volume centers with rapid time from first medical contact to intervention (“ door to balloon”). US and European guidelines call for door to balloon time of less than 90 minutes.

D] General measures:

1. Continuous ECG monitoring

2. Activity initially limited to bed rest but can be advanced within 24 hrs. Progressive ambulation should be started after 24 to 72 hrs, if tolerated.

E] Oxygen therapy:

If oxygen saturation falls <90%, arterial hypoxemia is clinically evident or if pulmonary edema is present, delivery of 2-4 L/min of 100% oxygen is considered.

F] Control of chest pain:

Morphine is the preferred drug to control the chest pain. 4-8 mg given intravenously and dose of 2-8 mg can be repeated at 5-15 minutes intervals until pain is controlled.

G] Beta-Adrenoreceptor Blockers:

These drugs relieve pain, reduce need for analgesics in many patients and reduce infarct size. Metaprolol is given in three 5 mg iv bolus doses. Patient is observed for 2-5 min between each dose. If heart rate falls< 60/min or Systolic Blood pressure falls < 100mm Hg, no further drug is given. If hemodynamic stability continues 15min after the last dose, oral metaprolol 50 mg sixth hourly for 2 days, then switched over to 100mg twice daily.

H] Nitrates

These reduce ischemic pain and relieve pulmonary congestion, and reduce blood pressure. It can be given sublingually or intravenously at 5-10 micrograms/min.

I] Angiotensin converting enzyme inhibitors

Should be prescribed within 24 hrs to all patients with STEMI and continued indefinitely in patients who have congestive heart failure, decreased LV function, large regional wall motion abnormalities or those who are hypertensives.

UNSTABLE ANGINA AND NON ST-ELEVATION MYOCARDIAL INFARCTION (UA/NSTEMI) [40]

Unstable angina is defined as angina pectoris or equivalent ischemic discomfort with at least one of the three features

1. It occurs at rest (or with minimal exertion) usually lasting more than 10 minutes.
2. It is severe and new of onset.
3. it occurs with a crescendo pattern .

The diagnosis of NSTEMI is established if a patient with the clinical features of unstable angina develops evidence of myocardial necrosis, as reflected by elevated cardiac biomarkers.

PATHOPHYSIOLOGY:

Following contribute to the development of Unstable angina:

1. Plaque rupture or erosion with superimposed non-occlusive thrombus, believed to be the most common cause.
2. Dynamic obstruction (e.g. coronary spasm, as in Prinz-metal angina)
3. Progressive mechanical obstruction (e.g. rapidly advancing coronary atherosclerosis or restenosis following percutaneous coronary intervention.) and
4. Secondary Unstable angina related to increased myocardial oxygen demand and/or decreased supply (e.g. Anemia)

More than one process may be involved in many patients.

HISTORY AND PHYSICAL EXAMINATION:

Chest pain:

Located in the substernal or epigastrium, frequently radiates to neck, left shoulder, and left arm.

Anginal "Equivalents" such as dyspnea and epigastric discomforts may also occur. Examination may be unremarkable or in large NSTEMI may include sinus tachycardia, pale cool skin, S3 or S4, basilar rales and sometimes hypotension.

ECG:

In unstable angina, ST segment depression, transient ST segment elevation, and/or T wave inversion occurs in 30-50% of patients.

CARDIAC BIOMARKERS:

Elevated markers (CK-MB or Troponin) distinguish patients with NSTEMI from those with Unstable angina.

TREATMENT:

Bed rest and continuous ECG monitoring is recommended as general measures.

Anti-ischemic treatment:

To provide relief and prevent recurrence of chest pain. Initial treatment should include nitrates and beta-blockers. Nitrates are given either sublingually or as buccal spray. If pain persists after 3 doses given 5 minutes apart, intravenous nitroglycerin is recommended.

Beta blockers given intravenously followed by orally, targeted to maintain heart rate of 50-60 per min, is recommended. Verapamil and diltiazem are recommended in patients who have persistent or recurrent symptoms with nitroglycerine and beta blockers. Morphine can be used if pain persists.

Antithrombotic Therapy:

Combination of Aspirin and clopidogrel is recommended for all patients with Unstable Angina and Non ST-Elevation myocardial infarction (UA/NSTEMI) who are not at excessive risk for bleeding.

Unfractioned heparin (UFH) or Low Molecular Weight Heparin (LMWH) should be added to aspirin and clopidogrel.

Invasive Strategy:

Following treatment with anti-ischemic and anti-thrombotic agents, coronary arteriography is carried out within 48 hrs of admission, followed by PCI or CABG.

LONG TERM MANAGEMENT:

Risk factor modification:

Smoking cessation, achieving optimal body weight, daily exercise, following an appropriate diet, blood pressure control and lipid management.

Drugs:

Beta-blockers are appropriate anti-ischemic therapy. Statins and ACE inhibitors are recommended for long-term plaque stabilization. Aspirin and clopidogrel for at least 9 to 12 months, with aspirin continued thereafter.

COMPLICATIONS AND MANAGEMENT [41,42]:

These are divided into mechanical complications, electrical complications and others.

I] MECHANICAL COMPLICATIONS

Myocardial dysfunction:

The severity of cardiac dysfunction is proportionate to the extent of myocardial necrosis but is exacerbated by preexisting dysfunction and on-going ischemia. Patients who have normal blood pressure, no signs of heart failure, and normal urine output have good prognosis. Those with hypotension or evidence of more than mild heart failure should have bedside right heart catheterization and continuous measurement of arterial pressure. These measurements permit the accurate assessment of cardiac function; facilitate correct choice of therapy, and important prognostic information.

Acute left ventricular failure:

Basilar rales are common in acute myocardial infarction, but dyspnea, more diffuse rales and arterial hypoxemia usually indicate left ventricular failure. Since both the physical examination and chest x-ray correlate with hemodynamic measurements and since the central venous pressure doesn't correlate with pulmonary capillary wedge pressure (PCWP), right heart catheterization may be required in monitoring therapy. General measures include oxygen supplementation and trunk elevation. Diuretics should be used unless right ventricular infarction is present. Morphine is valuable in acute pulmonary edema.

Diuretics are usually effective; however, since most patients with acute infarction are not volume overloaded, the hemodynamic response may be limited and may be associated with hypotension. Vasodilators will reduce PCWP and improve cardiac output by combination of venodilation and arteriolar dilation. In mild heart failure, sublingual isosorbide dinitrate or nitroglycerine ointment may be adequate to lower PCWP. In more severe failure, especially if cardiac output is reduced, sodium nitroprusside is the preferred agent. Intravenous nitroglycerine (starting at 10micro gram/min) is usually less effective but may lower PCWP with less hypotension. Oral or transdermal vasodilator therapy with nitrates or angiotensin converting enzyme inhibitors is often necessary after the initial 24-48 hours.

Inotropic agents should be avoided if possible, because they often increase heart rate and myocardial oxygen requirement. Dobutamine has the best hemodynamic profile, increasing cardiac output and moderately lowering PCWP, usually without excessive tachycardia, arrhythmia or hypotension. Dopamine is more useful in presence of hypotension since it produces peripheral vasoconstriction but it has less beneficial effect on PCWP. Amrinone is a positive inotrope and vasodilator that produces hemodynamic effects similar to those of dobutamine but with greater decrease in PCWP, however its longer duration of action makes it less useful in unstable situations. Milrinone is a more potent and newer congener of amrinone with fewer side effects.

Hypotension and shock:

Patients with hypotension (systolic blood pressure <100 mm Hg, individualized depending on prior blood pressure) and signs of diminished perfusion (low urine output, confusion and cold extremities) should be hemodynamically

monitored. Up to 20% will have findings indicative of intravenous hypovolemia (due to diaphoresis, vomiting, decreased venous tone, drug such as diuretics, nitrates, morphine, betablockers, calcium channel blockers and thrombolytic agents and lack of oral intake).

These should be treated with successive boluses of 100 ml normal saline until PCWP reaches 15-18 mm Hg to determine whether cardiac output and blood pressure respond. Pericardial tamponade must be ruled out.

Most hypotensive patients will have moderate to severe left ventricular dysfunction; pathologic studies indicate that more than 20% of the left ventricle is infracted (>40% in cardiogenic shock). If hypotension is only modest and PCWP is elevated, diuretics and initial trial with nitroprusside are indicated. If blood pressure falls inotropic support has to be added. Such patients may also be treated with intra aortic balloon counter pulsation (IABC). This device unloads the left ventricle during systole and increases diastolic coronary artery filling pressure. It often facilitates the use of vasodilators in patients who previously did not tolerate them.

Dopamine is the most appropriate pressor for cardiogenic hypotension. It should be initiated at the rate of 2-4 micrograms/kg/min and increased at 5 minutes interval to the appropriate hemodynamic end point. Norepinephrine (0.1-0.5 micrograms/kg/min) is the usual pressor of last resort, since isoproterenol and epinephrine produce less vasoconstriction and do not increase coronary perfusion pressure (aortic diastolic pressure), and both tend to worsen the balance between myocardial oxygen delivery and utilization.

Patients with cardiogenic shock not due to hypovolemia have a poor prognosis, with 30-day mortality rates 50-80%. If they do not respond rapidly, IABC should be instituted. Surgically implanted ventricular assist device may be used in extreme cases. Early cardiac catheterization and coronary angiography followed by percutaneous or surgical revascularisation offer the best chance of survival, particularly in patients under 75 years of age.

Right ventricular Infarction:

Approximately 1/3rd of patients with infero-posterior infarction demonstrate at least minor degree of RV necrosis. Clinically significant RV infarction causes signs of RV failure [Raised JVP, Kussmal's sign, Hepatomegaly] with or without hypotension. ST segment elevation in right-sided precordial leads especially V4R are frequently present in first 24hrs. 2D-ECHO and catheterization of right side of heart often help. Therapy consists of volume expansion to maintain adequate RV preload and efforts to improve LV performance with attendant reduction in pulmonary capillary wedge and pulmonary arterial pressures.

Mitral regurgitation:

It is due to ischemia or rupture of the papillary muscles recognized by the systolic murmur at the apex. Severe mitral regurgitation can produce life threatening left ventricular failure and cardiogenic shock and may warrant coronary angiography followed by bypass surgery and mitral valve replacement.

Ventricular septal defect:

It is due to infarction of interventricular septum. Clinically detected by pansystolic murmur at the left sternal border, or may be diagnosed by 2D-ECHO.

VSD produces severe left ventricular dysfunction and needs immediate surgical treatment.

Cardiac Rupture:

It is the most serious complication. It results in cardiogenic shock and results in almost 100% mortality. Rare cases have been saved by emergency surgery.

Left ventricular aneurysm:

The term ventricular aneurysm is used to describe dyskinesis or local expansile paradoxical wall motion. The complications of aneurysm usually do not occur for weeks to months after STEMI. Complications include: congestive heart failure, arterial embolism, and ventricular arrhythmias. Apical aneurysms are the most common and easily detected by clinical examination (double, diffuse, and displaced apical impulse). These can be easily detected by 2D-ECHO, which may reveal mural thrombus in the aneurysm.

ELECTRICAL COMPLICATIONS

The mechanism responsible for infarct related arrhythmias include, autonomic nervous system imbalance, electrolyte disturbance, ischemia, slowed conduction in zones of ischemic myocardium.

Ventricular Premature Contractions (VPC):

Infrequent sporadic VPC occur in almost all patients with STEMI and do not require therapy. Beta-blockers are effective in abolishing ventricular ectopic activity and in prevention of ventricular fibrillation. So these agents must be used routinely in patients without contraindications. In addition hypokalemia and hypomagnesemia are risk factors for ventricular fibrillation.

Ventricular Tachycardia and Fibrillation (VT/VF):

Within first 24hrs of STEMI VT/VF can occur without prior warning. Sustained VT that is well tolerated hemodynamically should be treated with intravenous amiodarone (bolus of 150 mg over 10 min, followed by infusion of 1 mg/min for 6 hrs and then 0.5 mg/min.) or procainamide; if it does not stop promptly electroversion should be used.

Accelerated Idioventricular Rhythm:

It is ventricular rhythm with a rate of 60 to 100 bpm, occur in 25% of patients with STEMI. It often occurs transiently during fibrinolytic therapy at the time of reperfusion. Most episodes do not require treatment if patient is carefully monitored, as degeneration in to more serious arrhythmias is rare, and if occurs, can be generally treated readily with a drug that increases sinus rate.

Supraventricular arrhythmias:

Sinus tachycardia is the most common form. If it occurs due to some secondary cause (anemia, fever etc) the main cause has to be treated first. If it is due to sympathetic over-stimulation then treatment with beta-blockers is indicated. Other common arrhythmias in this group are atrial fibrillation or flutter. Digoxin is the drug of choice if heart failure is present otherwise beta-blockers or diltiazem or verapamil can be used.

Sinus Bradycardia:

Treatment is indicated if hemodynamic compromise results from slow heart rate. Atropine is the drug of choice. Persistent bradycardia despite atropine therapy is treated with electrical pacing.

Atrio-Ventricular Conduction Disturbances:

Complete AV block associated with anterior wall MI carries higher mortality than that associated with inferior wall MI. Temporary electrical pacing is recommended.

OTHER COMPLICATIONS:

Recurrent chest discomfort:

Recurrent angina is seen in 25% of patients with STEMI. As this may indicate extension of the original infarction or a recurrent infarction, these patients should undergo coronary angiography and revascularization.

Pericarditis:

Percardial friction rubs and/or pericardial pain are frequently encountered in patients with STEMI. This complication is usually managed with aspirin (650 mg, qid). Anticoagulants can cause tamponade in presence of acute pericarditis. One week to 12 weeks after infarction, Dressler's syndrome (post myocardial infarction syndrome) develops in 5% of patients. This is an autoimmune phenomenon and presents as pericarditis with associated fever, leukocytosis, and occasionally pericardial or pleural effusion. A short course of steroids may help if NSAIDs do not relieve symptoms.

Thromboembolism:

Clinically apparent thromboembolism complicates STEMI in about 10% of cases. Thromboembolism typically occurs in presence of large infarct (especially anterior), and congestive heart failure. When a thrombus has been clearly demonstrated by ECHO or other techniques or when a large area of regional wall motion abnormality is seen even in the absence of detectable mural thrombus, systemic anticoagulation should be undertaken.

CORONARY ARTERY DISEASE IN DIABETES MELLITUS

Atherosclerosis accounts for 65% to 85% of all deaths among North American patients with diabetes. A two to fourfold excess in mortality due to coronary artery disease(CAD) among individuals with diabetes has been noted in a number of prospective studies encompassing a variety of ethnic and racial groups. A meta analysis of several studies estimated the risk of death from CAD in patients with diabetes at 2.58 in men and 1.85 in women[77]. Factors associated with an increase in mortality rates among those with diabetes include male gender, black race, longer duration of diabetes, and insulin use[78].

Mukamal et al studied 1935 patients hospitalized with an acute MI and found that the mortality among those with diabetes in the short term period was similar to that of patients without diabetes who had suffered their first acure coronary event[79].

Malmberg evaluated the findings of OASIS(organization of assess strategies for ischemic syndromes) registry and found that patients with diabetes hospitalized for unstable angina or non-Q wave MI had the same long term morbidity and mortality as patients without diabetes with established cardiovascular disease. These data suggest that individuals with T2DM should be treared as if they had experienced an MI[80].

T2DM increases relatively cardiovascular risk and is particularly high in women. The protection against atherosclerosis in premenopausal women is almost completely lost in women with diabetes[81].

C-REACTIVE PROTEIN

CRP was discovered by Tillet and Francis in 1930[8]. They were investigating serological reactions in pneumonia with various extracts of pneumococci and observed that a non type specific somatic polysaccharide fraction, which they designated fraction C, was precipated by the sera of acutely ill patients. After the crisis, the capacity of the patients sera to precipitate C polysaccharide(CPS) rapidly disappeared and the C-reactive material was not found in sera from normal healthy individuals.

Avery and his collaborators characterized the C-reactive material as a protein which required calcium ions for its reaction with CPS and introduced the term “acute phase” to refer to serum from patients acutely ill with infectious disease and containing the CRP[45,46].

Lofstrom independently described a non-specific capsular swelling reaction of some strains of pneumococci when mixed with acute phase sera and subsequently showed that the substance responsible was CRP[47]. He detected CRP in non-infectious as well as infectious conditions, and the acute phase reaction, in which the concentration of certain plasma proteins increases is now recognized as a general and non-specific response to most forms of infective and non-infective inflammatory processes, cellular and/or tissue necrosis and malignant neoplasia.

A feature of most forms of inflammation, infection and tissue damage is the increase in the circulating concentrations of various plasma proteins known as acute phase reactants[48]. These reactants are mainly produced by hepatocytes and the increased expression of acute phase protein genes is driven by cytokines, which are

produced by activated macrophages and other cells. During inflammation the plasma concentration of CRP can rise upto 1000 fold[49]. The plasma concentration of CRP is determined only by its production rate, which provided liver function is normal depends on the concentration of cytokines and other mediators that reach the hepatocytes. Concentration of CRP is directly correlated with the presence and seberity of coronary, cerebral and peripheral atherosclerosis.

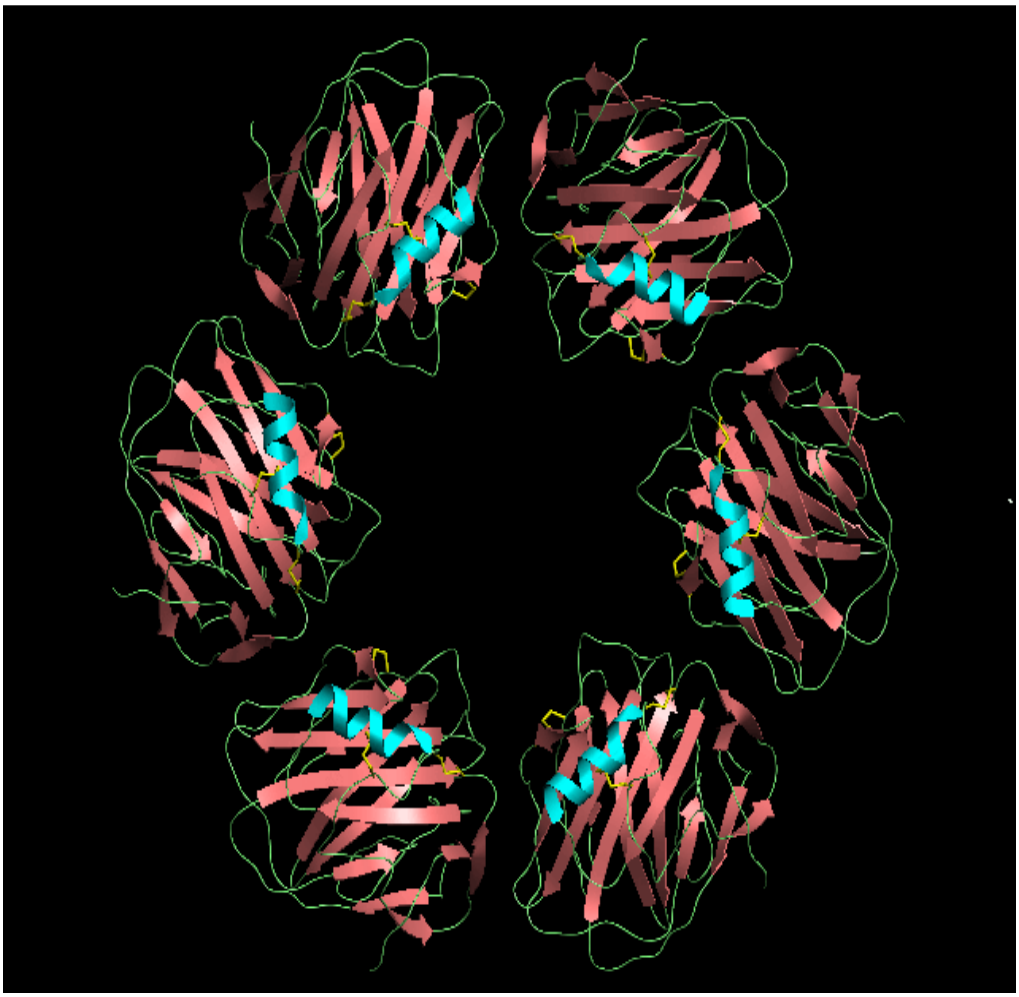
Synthesis, structure and binding properties of CRP:

CRP is synthesized by hepatocytes[50] and is normally present as a trace constituent of the plasma. The median circulating concentrations of CRP is 0.8mg/dl. Normal range may be as low as 0.07mg/dl and among apparently healthy individuals 90% have less than 3mg/dl and 99% have less than 10mg/dl[51].

The rate of CRP synthesis and secretion increases within hours of an acute injury or the onset of inflammation[52], probably under the influence of humoral mediators such as leucocyte endogenous mediator (endogenous pyrogen)[53] and prostaglandin PGE. The serum CRP concentration may reach peak levels as much as 300mcg/ml within 24-48hrs. CRP belongs to the pentroxin family of proteins with a molecular weight of 1,05,500. It consists of five, identical non-glycosylated polypeptide subunits, which are noncovalently associated in a disc like configuration with cyclic pentameric symmetry[54]. This arrangement and the amino acid sequence of the subunit are distinct from all other known proteins, with the exception of serum amyloid P component[55].

In addition to the reaction with the pneumococcal C-polysaccharide by which it was discovered, CRP also undergoes calcium dependent binding to choline phosphatides such as lecithin, lysolecithin and sphingomyelin to some other lipids

which donot contain phospharyl choline (PC) to PC containing and non PC containing microbial polysaccharides and peptidopolysaccharides, which are present in diverse bacteria, fungi and parasites and to poly anions including nucleic acids, heparin and dextran sulphate. Although CRP does bind materials lacking PC, free PC is the best inhibitor of all these reactions and is itself bound by CRP with very high affinity. In addition CRP binds in the absence of calcium ions to poly cations, including histones, leucocyte cationic protein, myelin basic protein and protamine. The binding site for poly cations seems to be distinct from the calcium dependent site for PC but the two sites interact[56,57].



STRUCTURE OF C-REACTIVE PROTEIN

Functional properties of CRP:

CRP precipitates soluble ligand and agglutinates particulate ligands[58,59]. Once complexed via either its calcium dependent or its poly cations binding sites, it becomes a potent activator of the classical complement pathway starting C1q. Complement activation proceeds as efficiently as with IgG antibody and leads to fixation of C4b and Cab, which can mediate the important complement dependent adherence reactions and to fixation of the terminal complex C5b-C9, causing lysis if the ligand is on a cell surface. Complement split fragments, active in the fluid phase, are also generated. CRP like antibodies can thus bind to ligands, opsonise materials for phagocytosis and initiate cell damaging and inflammatory reactions.

Other activities which have been ascribed to CRP include:

- Selective binding to T-lymphocytes and modification of some of their functions[60].
- Suppression of platelet aggression and activation reaction[61].
- Enhancement of the activity and motility of phagocytic cells.

However, none of these observations have proved reproducible with highly purified CRP, either in the laboratories, which originally reported them or elsewhere[62]. CRP complexed in a suitable way may bind to lymphocyte bracing FC(y) receptors both in vivo and in vitro, but the functional significance of this is not known[63,64].

The role of CRP in vivo is not known although under some circumstances it can cause inflammation. For example, intracutaneous injections of CPS in acutely ill patients elicits a characteristics immediate wheal and flare reaction, followed by a more extensive edematous erythema which is maximal at 6-10 hours. Local

deposition of CRP may contribute to the chronicity of the lesions of cutaneous vasculitis[65].

The complement mediated hemolysis, which sometimes follows the bite of the brown recluse spider (loxosceles recluse)depends on CRP.

CRP may play a part in the pathogenesis of the many inflammatory conditions, in which its circulating concentrations is elevated. It seems unlike that this is its major role or that it has been conserved in evolution for this reason. Probably the normal function of CRP is generally beneficial to the organisms as a whole and this may be acting as an easily broad spectrum recognition mechanism for the products of pathogenic microorganisms.

On the other hand increased CRP production is a feature of non infective as well as infective disease and CRP binds to a wide range of autogenous products. Lipids and phospholipids, polycations and polyanions all of which are constituents of cells and likely to be abnormally exposed in or released from damaged tissues. In vivo binding of CRP to necrotic cells has been described and contribute to resolution and repair. However, the main role of CRP, for which it evolved and has been conserved is to recognize in the plasma the potentially toxic autogenous materials released from damaged tissues to bind them and thereby to detoxify them and/or facilitate their clearance[66].

Clinical applications of measurements of serum CRP:

The CRP response is non-specific and can therefore never be precisely diagnostic but there are important differential patterns in certain diseases. Also CRP production per se is not suppressed or modified by any drugs or other therapies

currently in use unless these effect the underlying pathological process, which has provoked the acute phase reaction. The only condition which interferes with normal CRP response is severe hepatocellular impairment. CRP levels thus usually provide an objective index of the presence and activity of disease of response to treatment. By virtue of its speed and extended dynamic range, the CRP response yields valuable information, which when interpreted at the bedside together with all other available clinical and laboratory results can contribute significantly to the management of wide range of conditions[51].

It can be used for :

1. Screening for organic diseases: CRP production is very sensitive index of organic disease and raised CRP is unequivocal of active disease.
2. Monitoring the extent and activity of disease: Serial measurements reflects activity and response to treatment and can be used for monitoring.

Detection and management of intercurrent infection:

A raised level is a useful guide to the possible presence of infection in otherwise normal subjects or individuals with primary condition, which predisposes to infection. Effective antimicrobial therapy of infection is always associated with a prompt fall in CRP while persistent CRP elevation indicates continuing infection and/or activity of the underlying disease. There is no other objective test which yields this sort of information so accuretly and changes in results of clinical examination and tests of organ function usually lag hours or days behind the CRP response[51].

Conditions associated with major elevation of CRP:

1. Allergic complications of infection: erythema nodosum leprosum, rheumatic fever
2. Inflammatory disease: rheumatoid arthritis, juvenile arthritis, systemic vasculitis, polymyalgia rheumatica, ankylosing spondylitis, psoriatic arthritis, reiter's disease, crohn's disease, familial Mediterranean fever.
3. Allogrft rejection: renal transplantation
4. Malignant neoplasia: lymphoma, sarcoma
5. Necrosis: myocardial infarction, tumor embolization, acute pancreatitis
6. Trauma: surgery, burns, fractures[51].

Conditions associated with minor elevation of CRP:

1. SLE
2. Systemic sclerosis
3. Dermatomyositis
4. Ulcerative colitis
5. Leukemia
6. Graft versus host disease[51]

Several studies have shown that CRP can be used for diagnosis and assessing prognosis with acute acute coronary syndromes.

Kushner et al[62] studied 19 patients with mild or extensive MI. An increase in CRP was seen in all patients. The rate of increase in concentration was found to be exponential with a mean hourly rate constant for the entire group of patients of 0.085(doubling time 8.2 hour). Patients with extensive infarction attained mean serum CRP levels about 4 times as great as did patients with mild infarction. 7 out of 10

patients with presumed unstable angina showed no rise in CRP concentration while, a small increase was noted in 3 patients. They suggested that acute tissue injury such as MI rapidly leads to acceleration in synthesis of CRP and that the duration of this period of acceleration related to the extent of tissue injury.

De Beer F C[67] et al measured CRP and creatine kinase MB levels in patients with definite MI, patients with spontaneous or exercise induced angina, subjects undergoing coronary arteriography and patients with non- cardiac chest pain. They found that all individuals with infarction developed raised CRP levels and there was a significant correlation between the peak CRP and CKMB levels. In 20 patients who recovered uneventfully , CRP levels fall returning to normal about seven days after infarction in 4 cases who were followed to this point. In 8 complicated cases including 4 who died within the first 10 days, the CRP level remained high. Increased CRP production is a non specific response to tissue injury and raised CRP levels in cases of chest pain, with a normal CKMB indicated a pathological process other than MI. Regular monitoring of CRP levels may also assist in early recognition of intercurrent complications occurring after MI.

Ridker[68] et al measured CRP in 543 apparently healthy men and followed them up for a period exceeding 8 years. They found that the baseline plasma CRP concentrations were higher among men who went on to have MI. They also found that the reduction associated with the use of aspirin in the risk of a first MI appears to be directly related to the level of CRP raising the possibility that anti-inflammatory agents may have clinical benefits in preventing cardiovascular disease.

Haverkate[69] et al measured CRP in 2121 outpatients with angina enrolled in ECAT angina pectoris study and followed them upto 2years. They found that raised

circulated concentrations of CRP are predictors of coronary events in patients with stable or unstable angina. There was a two fold increase in the risk of coronary events in patients whose CRP concentration was >3.6mg/dl.

Thomas[70] et al estimated baseline CRP in 3043 patients with angina pectoris and followed them up to 2 years. He found that CRP concentration was directly correlated with the incidence of coronary events with increasing levels of CRP and fibrinogen.

Anzal T et al in 1997 studied CRP as a predictor of infarct expansion and cardiac rupture after a first Q-wave acute MI. He concluded that CRP responses after acute MI predict clinical outcome such as 6months mortality, irrespective of infarct size. Thus CRP response after acute MI cannot simply reflect the extent of myocardial necrosis.

Lagrand WK et al in 1997 studied the local inflammatory action of CRP in the setting of acute MI. They found that CRP localizes with complement in human heart during acute MI.

Voulgari[71] et al measured CRP in 17 patients with MI. CRP was elevated in all patients. A raised serum CRP level was found on admission in four patients before a rise in CKMB. The peak CRP level was reached on the third post infarct day. They found that serial monitoring of serum CRP in parallel with cardiac proteins of short life (CKMB) and long half life (tropomyosin) provides maximal information for diagnosis and for detecting post infarct complications.

Berk[72] et al measured CRP in 37 patients with unstable angina, 30 patients with non ischemic illness and 32 patients with stable coronary artery disease. CRP

levels were significantly elevated in 90% of the unstable angina group compared to 20% in patients with non ischemic illness and 13% of stable angina group. They concluded that an inflammatory component in active angina may contribute to the susceptibility of these patients to vasospasm and thrombosis.

Diabetic patients presented with higher CRP levels compared to non-diabetic subjects. In the Munich myocardial Infarction Registry, the combined presence of diabetes and CRP levels in the two upper quintiles demonstrated that the rate of mortality was 6 to 7 fold higher as compared to diabetic patients, who presented with CRP-levels in the lowest quintile. The relationship between atherothrombosis, inflammation and diabetes is supported in the clinical setting of a registry[12].

CRP levels were found to be related to insulin resistance, obesity and endothelial dysfunction in a cross-sectional study by Yudkin et al[73]. Data derived from the women's healthy study showed elevated levels of CRP predict the development of T2DM[74].this was confirmed by the data from the nurses health study[75].

In a cross-sectional study in urban North Indians of 2520 urban subjects with 1410 type 2 diabetes patients and 1110 non-diabetic subjects, carried out with assessment of 18 metabolic traits, it was found that in type-2 diabetes patients, there was a statistically significant positive correlation between hsCRP and all the indices of obesity, hyperglycemia, insulin resistance and dyslipidaemia except high-density lipoprotein cholesterol and a negative correlation with creatine. The strongest correlation of hsCRP was observed with BMI, triglycerides, and HbA1c[76].

MATERIALS AND METHODS

SOURCE OF DATA:

The material for the present study will be collected from patients who are admitted in ICU in BLDEU'S Shri B M PATIL medical college hospital and research centre, Bijapur.

Period of study will be from January 2013 to July 2014.

STUDY DESIGN:

This is a longitudinal study, in which patients suffering from acute myocardial infarction, venous blood will be collected on admission and sent for required investigations mentioned. A cutoff of 3mg/l for CRP have been shown to indicate an increase in cardiovascular risk and a cutoff of 7mg/l for C-reactive protein on admission is suggested for patients with acute myocardial infarction[12].

METHOD OF COLLECTION OF DATA:

By detail history

By detail examination

By relevant investigations like ECG changes, lipid profile, CPKMB enzyme levels, blood glucose levels (FBS/PPBS) and C-reactive protein.

The patient will be followed till discharge and all complications like arrhythmias, failure and outcome noted.

Estimation of C Reactive Protein level by turbidimetric immunoassay:

Patients venous blood is collected at the time of admission and serum is separated.

25mcl of sample is mixed with 500mcl of buffer and is incubated for 5 minutes. Then 50mcl of antiserum is added to this mixture and calibrated using Mispa UNO semi auto analyzer at 340nm and the readings read after 300 sec.

INCLUSION CRITERIA:

- Patients of any age who are admitted in ICU in BLDEU's Shri B M Patil medical college hospital and research centre, Bijapur between January 2013 to July 2014
- The non-ST segment elevation MI, ST segment elevation MI are selected on basis of history, examination and relevant investigations (WHO criteria).
- Patient is considered to be diabetic if patient was informed of the diagnosis earlier or was on prescribed anti-diabetic treatment (ADA criteria).

EXCLUSION CRITERIA:

- Renal failure
- Inflammatory bowel disease
- Non cardiac chest pain
- Recent infections
- Immunologic disorder
- Known or suspected neoplastic disease
- Recent(less than 3 month old)

  Major trauma

  Surgery

  Burns
- Re-infarction patient

SAMPLE SIZE:

The prevalence of coronary artery disease in India is 37 per 1000(PARK textbook of community medicine, 21st edition). At 95% confidence interval and at 20% of clinical expected variation , the sample size is 164 using the statistical formula

$$n = \frac{(2\ SD)^2 \times p \times q}{l^2}$$

p = prevalence of CHD

q = (100 – p)

l = clinical expected variation

STATITICAL ANALYSIS:

- Data will be presented with

  MEAN +_SD

- Results will be compared by X^2 test and other necessary statistical tests.
- Correlation will be found by logistic regression(if necessary)

INVESTIGATIONS REQUIRED

COMPLETE BLOOD COUNT

BLOOD SUGAR

SERUM CREATININE

BLOOD UREA

ECG

CPKMB

C-REACTIVE PROTEIN

LIPID PROFILE

OBSERVATION AND RESULTS

Total of 168 patients were included in the study and out of which 82 subjects were non diabetic and 86 patients were diabetic.

These patients have been divided in two groups:

Group A: diabetic patients.

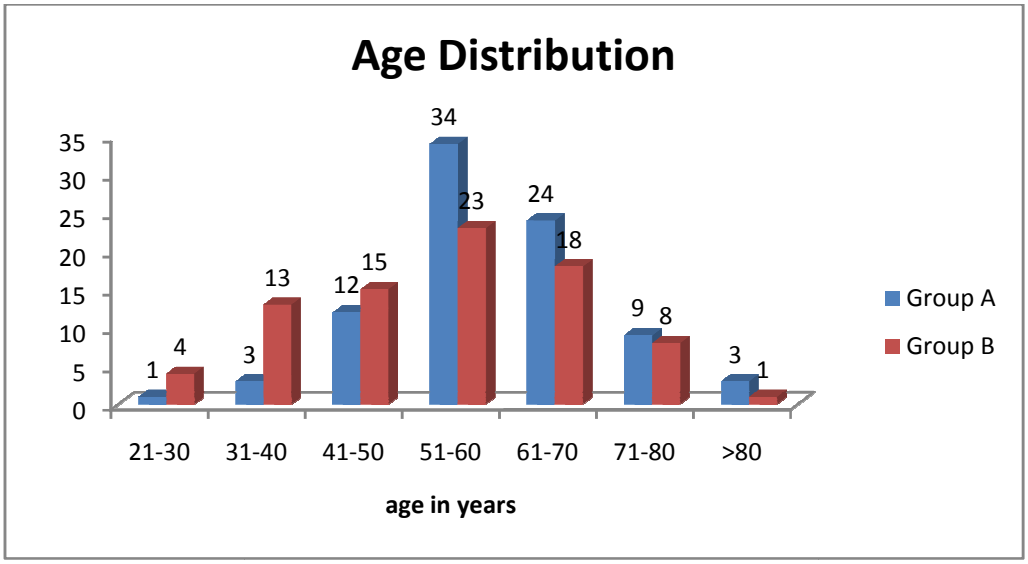
Group B: non diabetic patients.

Age distribution:

The below table showing age distribution of cases in each group.

Table 1. Age Distribution

Age(in years)	Group A N=86	Group B N=82	Total
21-30	1 (1.1%)	4 (4.8%)	5 (2.97%)
31-40	3 (3.4%)	13 (15.85%)	16 (9.52%)
41-50	12 (13.9%)	15 (18.29%)	27 (16.07%)
51-60	34 (39.53%)	23 (28.04%)	57 (33.9%)
61-70	24 (27.90%)	18 (21.95%)	42 (25%)
71-80	9 (10.4%)	8 (9.75%)	17 (10.11%)
>80	3 (3.4%)	1 (1.2%)	4 (2.38%)



Graph 1. Age Distribution in diabetic and non diabetic

The youngest patient was aged 24 years and the eldest patient being 96 years.

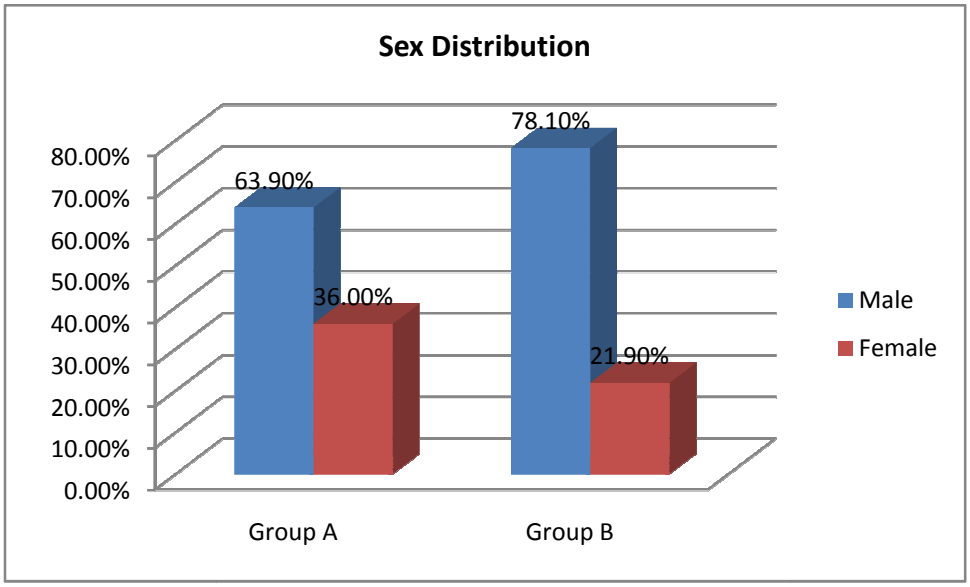
The maximum number of patients were between the age group of 51-70years (58.9%).

In diabetic group 39.53% of patients were in the age group of 51-60years and 28.04% of patients in non-diabetic were in the age group of 51-60years.

Sex distribution:

Table 2. Sex Distribution in each group

Patients	Group A N=86	Group B N=82	Total N=168
Male	55(63.9%)	64 (78.1%)	119 (70.9%)
Female	31 (36.0%)	18 (21.9%)	49 (29.1%)



Graph 2. Sex Distribution

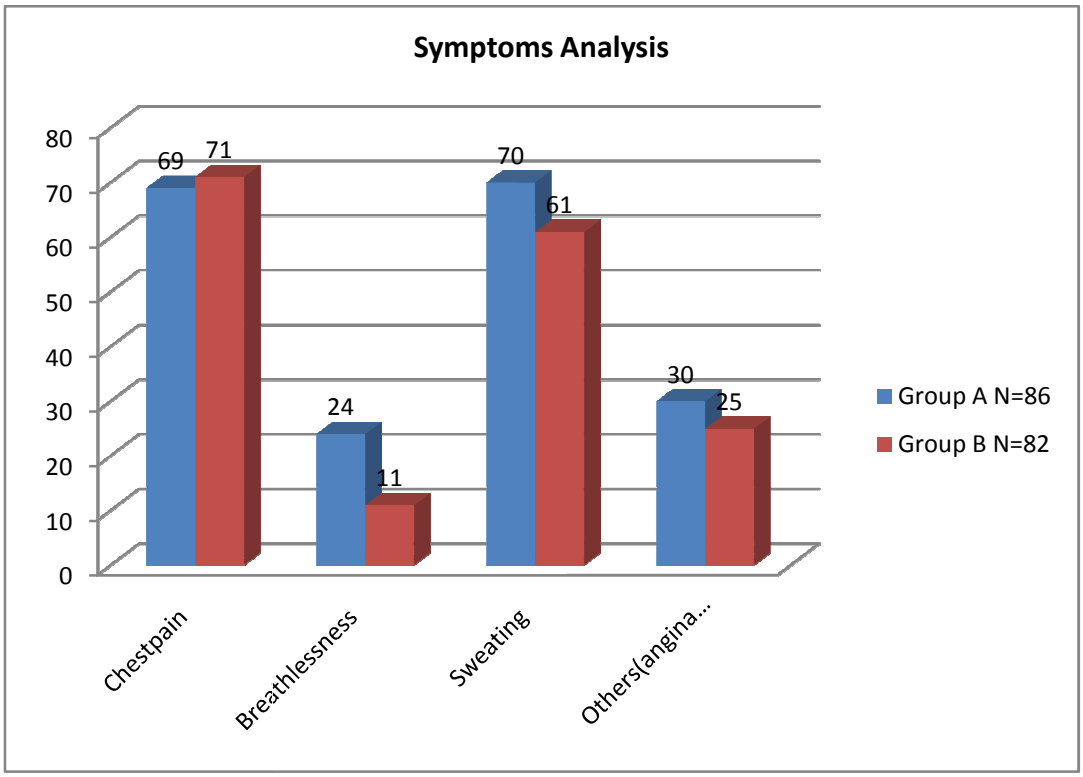
Out of 168 patients 119(70.9%) were male and 49(29.1%) patients were female. In diabetic group 63.9% were males and in non diabetic group 78.1% were males.

Symptoms:

The presenting feature are shown below:

Table 3. Presenting complaints

Complaints	Group A N=86	Group B N=82	Total N=168
Chestpain	69(80.23%)	71(86.58%)	140(83.33%)
Breathlessness	24(27.9%)	11(13.4%)	35(21.42%)
Sweating	70(81.39%)	61(74.39%)	131(77.97%)
Others (angina variant, vomiting, giddiness,)	30(34.88%)	25(30.48%)	55(32.73%)



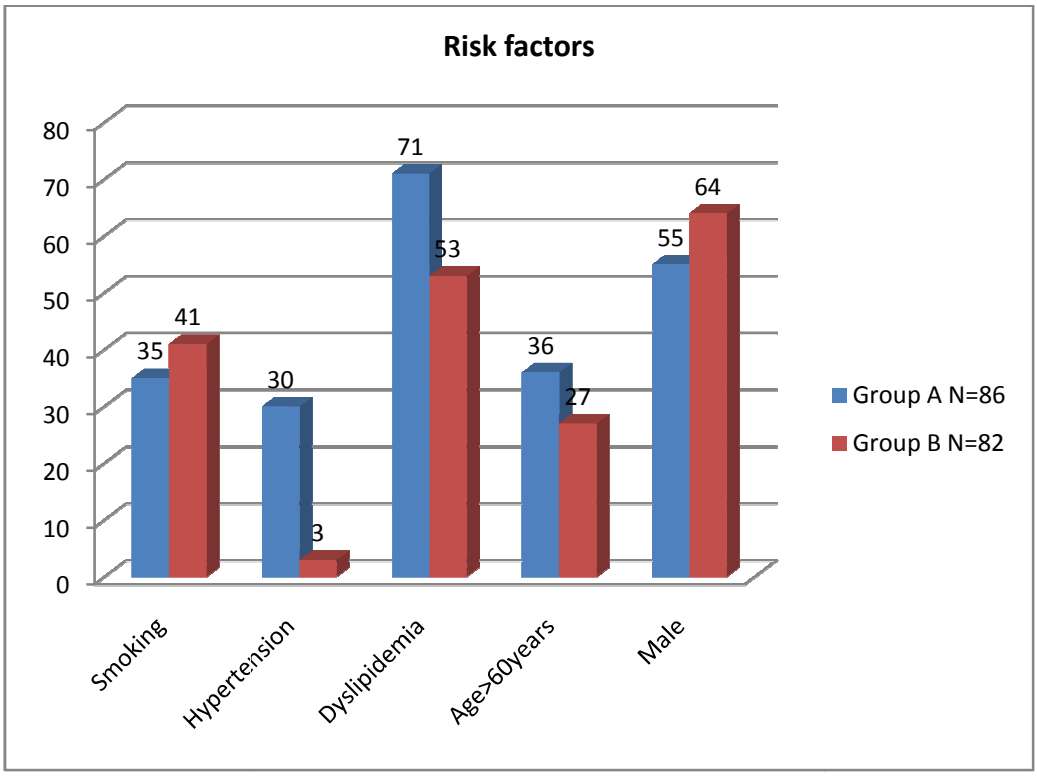
Graph 3. Symptom analysis

Chestpain is the most commonest symptoms occurring in 140(83.33%) patients, followed by sweating in 131(77.97%), and breathlessness in 35(21.42%) patients of acute myocardial infarction.

Risk factors:

Table 4. Risk Factors

Risk factors	Group A N=86	Group B N=82	Total N=168
Smoking	35(40.69%)	41(51.21%)	76(45.23%)
Hypertension	30(34.88%)	3(3.65%)	33(19.64%)
Dyslipidemia	71(82.55%)	53(64.63%)	124(73.80%)
Age>60years	36(41.86%)	27(32.92%)	63(37.5%)
Male	55(63.95%)	64(78.04%)	119(70.83%)



Graph 4. Risk Factors

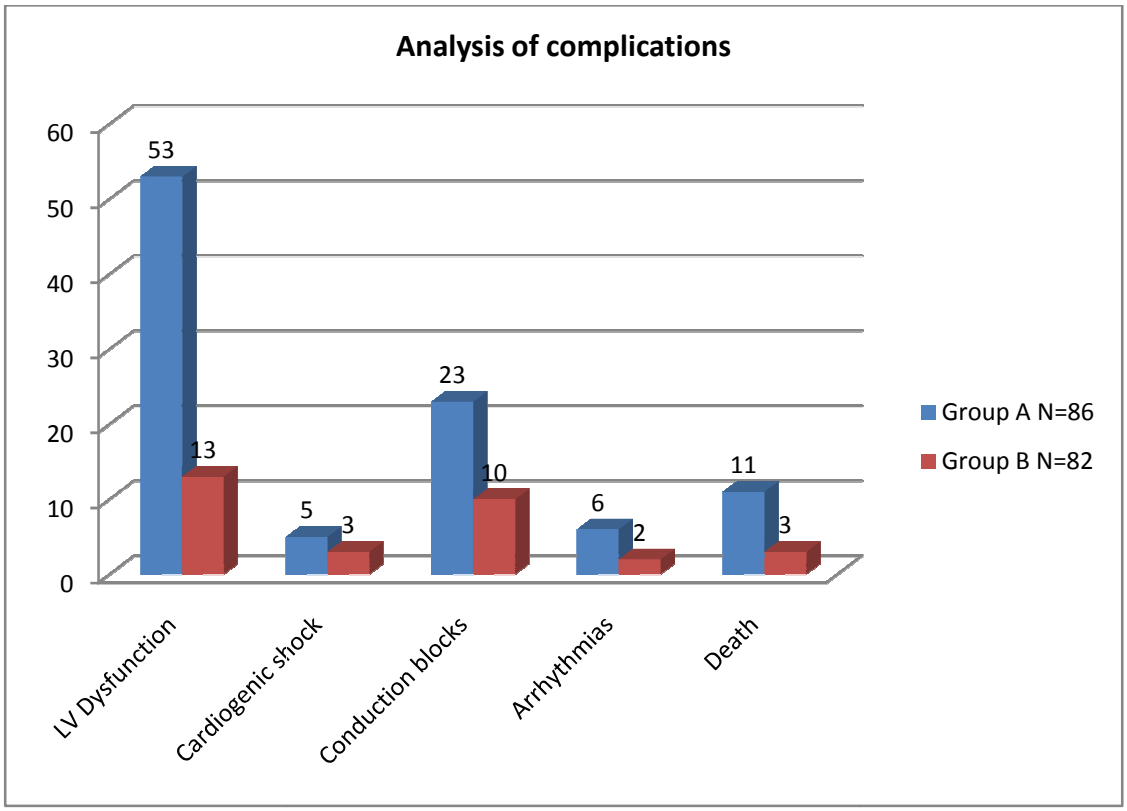
In this study, the most common non-modifiable risk factor is male sex accounting for 70.1% of all the cases followed by age >60years(37.5%).

The most common modifiable risk factor is dyslipidemia accounting for about 73.8% followed by smoking (45.23%), and hypertension(19.64%)

Analysis of complications:

Table 5. Analysis of complications

Complication	Group A N=86	Group B N=82	Total N=168
LV Dysfunction	53(61.62%)	13(28.04%)	66(39.28%)
Cardiogenic shock	5(5.81%)	3(3.65%)	8(4.76%)
Conduction blocks	23(26.74%)	10(12.19%)	33(12.31%)
Arrhythmias	6(6.97%)	2(2.43%)	8(4.76%)
Death	11(12.79%)	3(3.65%)	14(8.33%)



Graph 5. Analysis of complications

Left ventricular dysfunction was the most common complication seen in 66(39.28%) patients, followed by conduction blocks in 33(12.31%) patients, cardiogenic shock in 8(4.76%) patients, arrhythmias in 8(4.76%) patients and death occurred in 14(8.33%) patients.

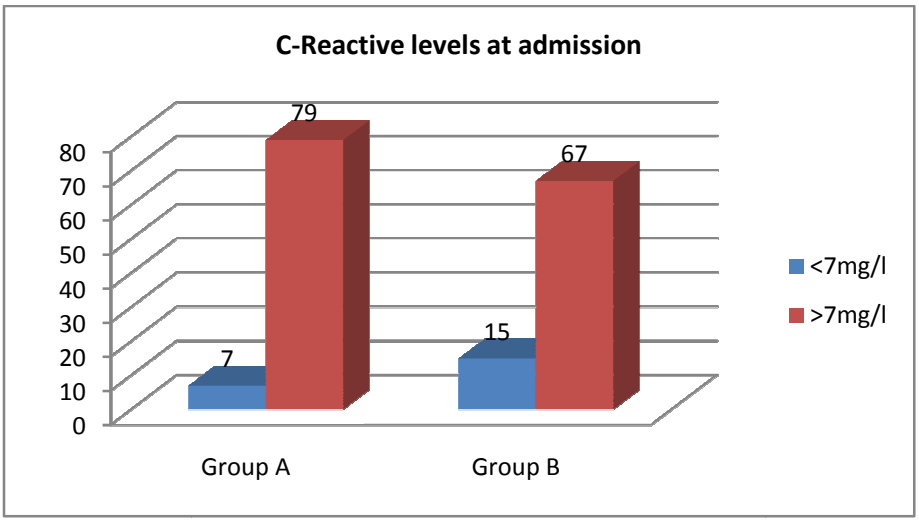
C-Reactive levels at admission:

In our study CRP level of 7mg/l is taken as cut off valueAmong the study groups 146(86.90%) patients had CRP of more than 7mg/l, and 22(13.09%) patients had CRP of less than 7mg/l.

The following table shows CRP level in diabetic and non diabetic patients with acute myocardial infarction.

Table 6. CRP levels in each group with acute myocardial infarction

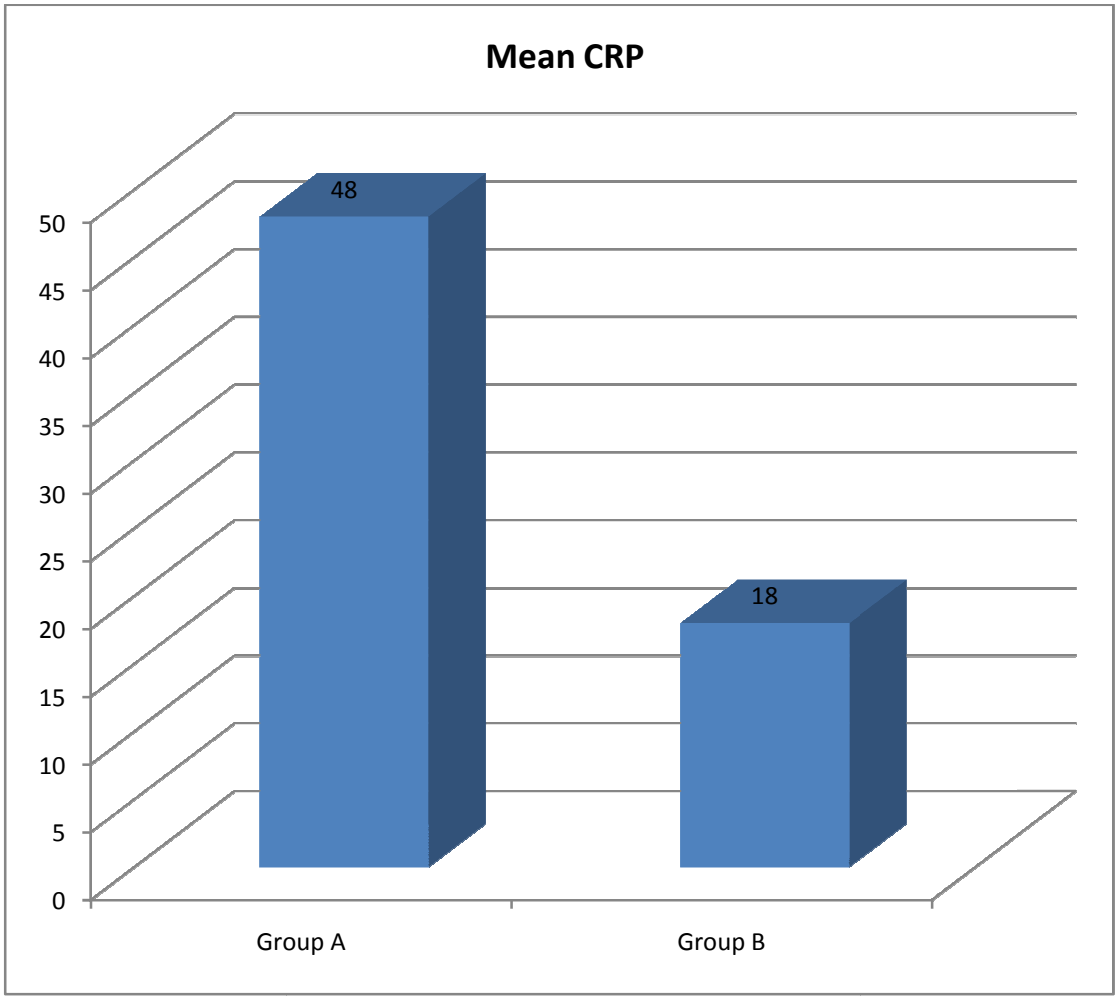
CRP levels	Group A	Group B	Total
<7mg/l	7(8.13%)	15(18.28%)	22(13.09%)
>7mg/l	79(91.86%)	67(81.70%)	146(86.90%)



Graph 6. CRP levels at admission

Table 7. Mean CRP levels in diabetic non diabetic group.

	Mean CRP in mg/l	P value
Group A	48.05±37.40	<0.0001
Group B	18.05±14.02	



Graph 7. Mean CRP

In our study group, 91.86% of diabetic patients were found to be having CRP level >7mg/l as compared to 81.70% of non diabetic patients in acute myocardial infarction. The mean CRP in diabetic group was 48.05±37.40mg/l as compared to 18.20±14.02mg/l in non diabetic group which statistically significant (p=0.0001).

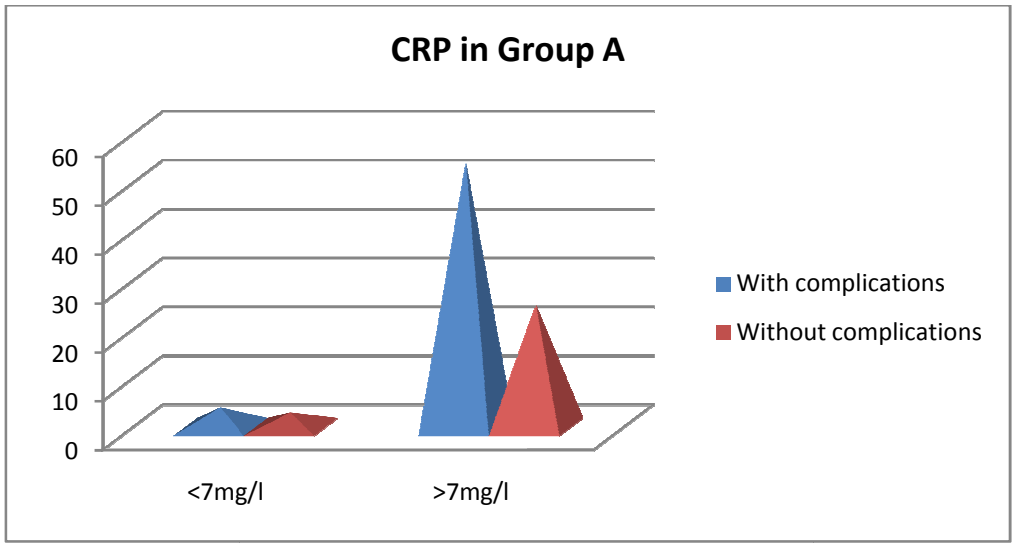
On applying appropriate statistical test there was significant correlation between CRP level and diabetes in patients with acute myocardial infarction.

CRP levels on admission were higher in diabetic patients than in non diabetic patients with the median value of CRP in diabetic patients is 39mg/l as compared to 14mg/l in non diabetic patients with acute myocardial infarction.

CRP in diabetic patients:

Table 8. CRP levels in Group A

CRP Levels	With complications	Without complications
<7mg/l	4(4.65%)	3(3.48%)
>7mg/l	54(62.79%)	25(29.09%)

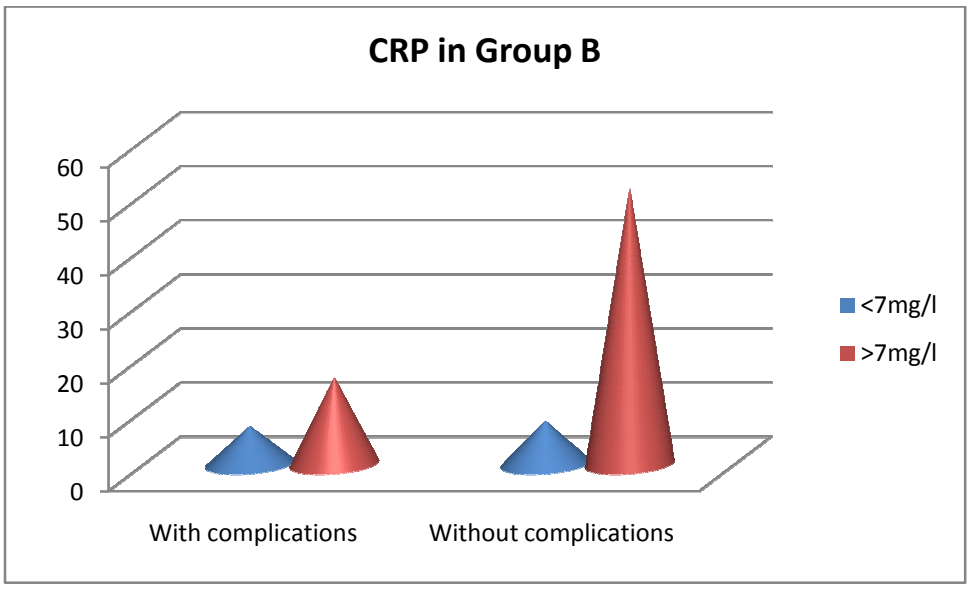


Graph 8. CRP levels in Group A

CRP in non diabetic patients:

Table 9. CRP levels in GoupB

CRP levels	With complications	Without complications
<7mg/l	7(8.53%)	8(9.75%)
>7mg/l	16(19.51%)	51(62.19%)



Graph 9. CRP levels in Group B

The diabetic patients with higher CRP levels had high incidence of mortality and morbidity as compared to non diabetic patients.

Diabetic patients who died in the hospital presented with higher plasma levels on admission as compared to non diabetic patients who had mortality with median CRP level of 76mg/l in diabetic as compared to 24mg/l in nondiabetic.

DISCUSSION

A total of 168 patients with acute myocardial infarction were included in this study, and these subjects were divided into diabetic group (n=86) and non diabetic group (n=82).

In our study the maximum number of patients were between the age group of 51-70 years (58.9%) with the mean age of 57.6 years in diabetic and 57.55years in non diabetic. The youngest being 24years of age and eldest being 96 years of age. Out of total patients 70.9% of the subjects were male and 29.1% of the patients were female.

The most common non-modifiable risk factors is male sex accounting for 70.1% of all the cases followed by age >60 years.

The most common modifiable risk factor other than diabetes is dyslipidemia accounting for about 73.8% followed by smoking (45%).82.1% of diabetic patients had dyslipidemia whereas 64.6% of non diabetic patients had dyslipidemia.

In this study CRP levels were classified in two groups <7mg/l and >7mg/l in our study. Out of 168 subjects, 146(86.90%) patients had CRP of more than 7mg/l, and 22(13.09%) patients had CRP of less than 7mg/l. The mean CRP level in patients with acute myocardial infarction is 33.48±32.11mg/l. Out 146 subjects (CRP>7mg/l), 79 patients were diabetic and 67 were non diabetic.

Similar study done by Kushner et al[62] showed that myocardial infarction results in rapid exponential increase in serum concentration of CRP, and this increase usually begins within a few hours after chestpain, and that its magnitude is related to the degree of tissue injury. The study done by De Beer FC[67] et al found that all

individuals with infarction or raised CPKMB levels showed a rise in CRP concentration.

Thompson et al found that the concentrations of CRP were on an average 20.2% higher in the patients who had coronary events than in those without such events, after adjustment for other risk factors and higher levels predict poor outcomes in patients with coronary artery disease[84].

Liuzzo et al[85] showed that in 31 patients with severe unstable angina and no evidence of myocardial necrosis, as documented by the absence of increased cardiac enzymes, hs-CRP concentrations >3mg/l at admission were associated with an increased incidence of recurrent angina, coronary revascularization, MI and cardiovascular death. The same group later demonstrated that hs-CRP >3mg/l at discharge in 53 unstable angina patients was associated with increased readmission for recurrent instability and MI.

In a similar study, Ferreiros et al[85] concluded that the prognostic value of CRP measured at discharge was better than that determined at admission in predicting adverse events at 90 days. Data from the Thrombolysis In Myocardial Infarction 11A, a study of unstable angina and non Q wave MI, showed that markedly increased hs-CRP(15.5mg/l) at admission was a good predictor of 14 day mortality in that population.

Similar results were found in the studies conducted by Nikfardjam et al[86], Dibra et al[11], Voulgari et al[87] and Lim et al[10].

In this study CRP levels on admission were higher in diabetic patients than in non diabetic patients with the median value of CRP in diabetic patients was 39mg/l as

compared to 14mg/l in non diabetic patients with acute myocardial infarction. The mean CRP level in diabetic group was 48.05±37.40mg/l as compared to 18.20±14.02mg/dl in non diabetic group which was highly significant (p=0.0001).

The diabetic patients with higher CRP levels had high incidence of mortality and morbidity as compared to non diabetic patients. Left ventricular dysfunction was the most common complication seen in 39.2% of individuals, followed by conduction blocks (12.31%), cardiogenic shock (4.76%), arrhythmias (4.76%) and death (8.33%). 12.7% of diabetic patients had mortality as compared with 3.6% in non diabetic group.

Diabetic patients who died in the hospital presented with higher plasma levels on admission as compared to non diabetic patients who had mortality with median CRP level of 76mg/l in diabetic as compared to 24mg/l in non-diabetic.

The study done W Otter et al[12] also showed high CRP levels in diabetic parients with acute myocardial infarction with median valve of 8mg/l in diabetic as compared to 6mg/l in non diabetic. In their study, the diabetic patients who died had a median CRP value of 23mg/l as compared with 16mg/l in non diabetic subjects who had mortality.

In Munich myocardial infarction Registry, the combined presence of diabetes and CRP levels in the two upper quintiles demonstrated that the rate of mortality was 6 to 7 fold higher as compared to diabetic patients, who presented with CRP levels in the lowest quintile[12].

In a study done by Dombal A[82] et al the mean hs-CRP value in diabetic patients with acute myocardial infarction was 7.71mg/l as compared to 6.30mg/l in non diabetic patients.

The significant difference in CRP can attributed to low grade inflammation in the pathogenesis of type-2 diabetes mellitus. Studies in non diabetic patients and in subjects with impaired glucose tolerance or impaired fasting glucose have confirmed that high concentrations of inflammatory markers predict the development of type-2 diabetes mellitus and closely linked to insulin resistance.

Hyperglycemia directly induces apoptosis and myocyte necrosis , which in turn leads to systolic and diastolic dysfunction [74] . The United kingdom Prospective Diabetes study (UKPDS) showed that by maintaining intensive glycemic control, there was a 16% reduction in the risk of myocardial infarction , but this correlation was not statistically significant. It also reported that control of other cardiovascular risk factors, such as hypertension, dyslipidemia in persons with diabetes was of particular benefit in preventing adverse macrovascular outcomes(32% reduction diabetes related deaths). [64]

The Hoorn study showed an association between CRP and cardiovascular mortality in patients with type-2 diabetes, but the association was not independent of other CHD risk factors . In patients with type-2 diabetes who had acute coronary syndrome, CRP seemed to be an independent predictor for cardiovascular death. In the Honolulu Heart Program, the association with elevated CRP and MI was weaker in diabetic than in non-diabetic men. It is possible that other CHD risk factors typical for patients with type-2 diabetes like high triglyceride level, low HDL cholesterol level, hypertension and hyperglycemia per se partially masks the role of hs-CRP as a

risk factor for CHD in this population. In non-diabetic subjects, increased level of hs-CRP seems to be a strong risk factor in apparently healthy individuals, but it also seems to predict future outcomes in patients with established CHD. Several studies have found that diabetes does not significantly affect the prognostic value of hs-CRP in population studies but such data in patients with acute coronary syndrome are lacking.[83]

CONCLUSION

The present study results demonstrated that CRP on admission is a strong predictor for hospital morbidity and mortality in both diabetic and non diabetic patients with acute myocardial infarction.

Diabetic patients presented with higher CRP levels compared with those in non diabetic patients with acute myocardial infarction.

CRP may serve as marker in predicting the hospital mortality in patients with acute myocardial infarction.

It can also be concluded that significant high values of CRP in diabetics may signal a considerable damage to the vascular endothelium, which could play a role in the causation of cardiovascular events.

Limitations of the study:

1. The sample size was small.
2. The severity of diabetes was not considered.
3. The extent of infarction was not considered.
4. The role of thrombolysis was not highlighted.
5. Other risk factors of CVD also played a role in the cardiac events.

SUMMARY

The aim of this study was to determine the CRP level at the time of admission as a strong predictor of hospital mortality and morbidity in patients with diabetes mellitus as well as in patients without diabetes mellitus who had acute myocardial infarction.

A total of 168 patients with acute myocardial infarction were included and out of which 86 patients were diabetic and 82 patients were non diabetic.

Immediately after admission, venous sample was drawn sent for blood glucose, CRP levels, and other required investigations.

Outcome of the patients in the hospital including complications like arrhythmias, shock, conduction blocks, and deaths were documented and these data were correlated with the diabetic status and CRP levels.

After statistical analysis, our study showed that there was significant correlation between CRP levels and diabetic status in patients with acute myocardial infarction.

In this study CRP levels on admission were higher in diabetic patients than in non diabetic patients with the median value of CRP in diabetic patients was 39mg/l as compared to 14mg/l in non diabetic patients with acute myocardial infarction.the mean CRP level in diabetic group was 48.05±37.40mg/l as compared to 18.20±14.02mg/dl in non diabetic group which was highly significant (p=0.0001) 12.7% of diabetic patients had mortality as compared with 3.6% in non diabetic group. Diabetic patients who died in the hospital presented with higher plasma levels

on admission as compared to non diabetic patients who had mortality with median CRP level of 76mg/l in diabetic as compared to 24mg/l in non-diabetic.

Thus, this study reveals that CRP can be used as a prognostic marker in diabetic patients with acute myocardial infarction.

BIBLIOGRAPHY

1. Fauci AS, Kasper DL, Hauser SL, Lango DL,Jameson JL, Loscalzo. Ischemic heart disease. In - Harrison's principles of internal medicine, 18th Ed,: Mc Graw Hill; 2012. 1998.
2. Ridker PM, Cushman M, Stampfer MJ, Tracy RP, Hennekens CH. Inflammation, asprin, and the risk of cardiovascular disease in apparently healthy men. N Engl J Med 1997: 336; 973-979.
3. Dev BP, Siddarth NS, M Paul A, Aspi RB, Sandhya AK, Dilip RK, et-al. ST-elevation myocardial infarction. In API textbook of medicine, 8th edition, 2008.520.
4. Lau DC, Dhillon B, Yan H, Szmito PE, Verma S. Adipokines: molecular links between obesity and atherosclerosis. Am J Physiol Heart Circ Physiol 2005; 288(5):H2031-41.
5. Pai JK, Pischon T, Ma J, Manson JE, Hankinson SE, Joshipura K, Curhan GC, Rifai N, Cannuscio CC, Stampfer MJ, Rimm EB. Inflammatory markers and the risk of coronary heart disease in men and women. N Engl J Med 2004;351:2599-2610.
6. Otter W, Kleybrink S, Doering W, Standl E, Schnell O. Hospital outcome of acute myocardial infarction in patients with or without diabetes mellitus. Diabet Med 2004;21:183-187.
7. Kuller LH, Tarcy RP, Shaten J, Meilahn EN. Relation of C-reactive protein and coronary heart disease in the MRFIT nested case control study. Am J Epidemiol 1996; 144: 537-47.
8. Tillet WS, Francis T. Serological reactions in pneumonia with a non protein somatic fraction of pneumococcus. J Exp Med 1930;52:561-571.

9. Lofstrom G. Comparison between the reactions of acute phase serum with pneumococcus C-polysaccharide and with pneumococcus type 27. Br J Exp Pathol 1994;25:21-26.
10. Lim SY, Jeong MH, Jeong MH, Bae EH, Kim W, Kim JH, Hong YJ, et-al. Predictive factors of major adverse cardiac events in acute myocardial infarction patients complicated by cardiogenic shock undergoing primary percutaneous coronary intervention. Circ J 2005;69:154-158.
11. Dibra A, Mehilli J, Schwaiger M, Schuhlen H, Bollewein H, Braun S, Neverve J, Schomig A, Kastrati A. predictive value of basal C-reactive protein levels for myocardial salvage in patients with acute myocardial infarction is dependent on the type of reperfusion treatment. Eur Heart J 2003;24:1128-1133.
12. Otter W, Winter M, Doering W, Standl E, and Schnell O. C-reactive protein in diabetic and non diabetic patients with acute myocardial infarction. Diabetes Care 2007;30(12):3080-3082
13. Braunwald E. The Simon Dack lecture. Cardiology: The past, the present, and the future. J Am Coll Cardiol 2003; 42:2031-41.
14. Stanek V, Progress in the therapy of ischemic heart disease, Kapitoly z kardiologie 2002; 4:3-11.
15. Waters DD**.** Acute coronary syndrome: Unstable angina and non-ST-elevation myocardial infarction,**.** . In; Cecil's textbook Of Medicine 22nd eds. Philadelphia, WB Saunders; 2004:400-409.
16. Paul Durrington: Hyperlipidemias-Diagnosis and Management 2000:232-236
17. Burton ES**:** ST-elevation Myocardial Infarction. In; Cecil's textbook Of Medicine 22nd eds Philadelphia, WB Saunders; 2004.410-17.

18. Gunda H R Rao, White JG. Coronary Artery Disease – An Overview of Risk 73Factors. Indian Heart J 1993; 45(3):143-153.
19. Rose, G .Coronary artery disease In: Oxford Text Book of Public Health, 1985; (4):133.
20. Stamler J. Coronary artery disease N Engl J Med.1988; 312:1053
21. Ridker M Paul, Marrow A David; "Prevention of cardiovascular diseases, C reactive protein, inflammation and coronary risk"; Cardiology clinics Aug; 2003;
22. Kasper DL, Fauci AS, Longo DL, Braunwald E, Hauser SL, Jameson JL, Harrison's principles of internal medicine; 16th Ed; New York: Mc Graw Hill ;2005; 1444
23. Cannon CP, Braunwald E: Unstable angina and non-ST-elevation myocardial infarction, in Harrison's principles of internal medicine,16th Ed, Kasper et al (eds).McGraw Hil,NewYork;2005.1444-47.
24. Cannon CP, Braunwald E: Unstable angina and non-ST-elevation myocardial infarction. In: Hurst's The Heart, 11th Ed. O'Rourke et al (eds) McGraw-Hill, New York 2005. 1243-1263.
25. Chumny S. "Blood supply of heart"; Lasts anatomy- regional and applied; 10th Ed; 2000; 197- 198.
26. Johanson D, Shah P, Collins P, Wigley C. Heart and great vessels. In: Susan, Standring. Gray's Anatomy. The anatomical basis of clinical practice.32nd Ed, Elsevier 2005. 1014-1018.
27. Kumar V, Abbas AK, Fausto N, Pathologic basis of diseases; 7th Ed; Philadelphia: Elsevier; 2004. 572-581

28. Barkhoff D, Weisfeldt ML. Cardiac Function and its Circulatory Control. In; Cecil's textbook Of Medicine 22nd Ed Philadelphia, WB Saunders; 2004. 254-260.
29. Kannel WB, Dannenburg AL, Abott RD. Unrecognized Myocardial Infarction and Hypertension. The Framingham Study. Am Heart J 1985; 109:581-85
30. Antaman EM, Braunwald E: Acute myocardial infarction. In: Braunwald's heart disease. A text book of cardiovascular medicine, 7th Ed, DP Zipes et al (eds).Philadelphia, WB Saunders; 2005. 1167-1226.
31. Kannel WB. Smoking and hypertension as predictors of cardiovascular risk in population studies. J Hypertension Suppl-8:S3, 1990.
32. Sigurdsson G. Interaction between a polymorphism of the apo A-I promoter region and smoking determines plasma levels of HDL and apo A-I. Arterio-Scler. Thromb 1992; 12:1017.
33. Sugiishi M, Takatsu F. Cigarette smoking is a major risk factor for coronaryspasm. Circulation 1993; 87:76-79.
34. Leo Schamroth, An Introduction to electrocardiography; 7th Ed; Delhi; Oxford university press; 1990. 131-155
35. Peter J. Zimetbaum et al; "Use of electrocardiogram in acute MI". N Engl J Med 2003; 348; 933-940
36. Tierney LM Jr, Mc Phee SJ, Papadakis MA; CMDT 2005; 44th Ed; New York; Mc Graw Hill; 2005. 346-355
37. R. Wayne Alexander, "Diagnosis and management of patients with acute myocardial infarction"; Hurst's The Heart; 9th Ed; Chap-47. 1375-1377.

38. Pahlajani DB. Myocardial infarction. In.: Shah SN.API text book of medicine.7th revised ed: The association of physicians of India, Mumbai; 2006:441-446.
39. Schamorath L. Myocardial infarction. In: Schamorath C. An introduction to electrocardiography. 7th Ed Oxford: Black well science; 1990. 131-155
40. Kasper DL, Fauci AS, Longo DL, Braunwald E, Hauser SL, Jameson JL, Harrison's principles of internal medicine; 16th Ed; New York: Mc Graw Hill ; 2005. 1444-1448
41. Kasper DL, Fauci AS, Longo DL, Braunwald E, Hauser SL, Jameson JL, Harrison's principles of internal medicine; 16th Ed; New York: Mc Graw Hill ;2005. 1455-1459
42. Pearl R. Tobacco, smoking and longevity. Science 1938; 87:216.
43. Luce BR, Schweitzer SO. Smoking and Alcohol Abuse: A Comparison of their economic consequences. N Engl J Med 1978; 298:569-71.
44. Tillet WS, Francis T. Serological reactions in pneumonia with a non protein somatic fraction of pnemococcus. J Exp Med 1930; 52:561-571.
45. Abernethy TJ, Avery OT. The occurrence during acute infectious protein not normally present in the blood. First distribution of reactive protein in patients sera and effect of calcium ions on the flocculation reaction with C-polysaccharide of pnemococcus. J Exp Med 1941; 73:173-177.
46. Macleod CM, Avery OT. The occurrence during acute infections of a protein not normally present in the blood II isolation and properties of reactive protein. J exp Med 1941; 73:183-187.

47. Lofstorm G.Comparison between the reactions of acute phase serum with pnemococcus C-polysaccharide and with pnemococcus type-27. Br. J. Exp. Pathol 1944; 25: 21-26.

48. Pepys MB, Baltz ML.Acute phase proteins with special reference to C-reactive pritein and related proteins and serum amyloid A protein. Adv Immunol 1983; 34: 141-152.

49. Shine B, De Beer FC, Pepys MB. Solid phase radioimmuno assays for C-reactive protein. Clin chem Acta 1981; 117: 13-23.

50. Hurlimann J, Thosbeeks G, Hochwald G. The liver as the site of C-reactive protein formation. J Exp Med 1996; 123: 65-78.

51. Pepys MB. The acute phase response and C-reactive protein. chapter 11, 13.3 in Oxford Textbook of Medicine, 3rd Edition, weahurall DJ, Ledingham JGG, Warrell DA, Tokyo; Oxford University Press 1906. 1527-1533.

52. Kushner I, Feld man G. Control of acute phase response- Demonstration of C-reactive protein synthesis by hepatocytes during acute inflammation in rabbit. J Exp Med 1978; 148: 466-77.

53. Merriman CR, Pulliam LA, Kampschmidist RF. Effect of leukocytic endogenous mediator on C-reactive protein in rabbits. Proc Soc Exp. Bio Med 1975; 149: 782-84.

54. Osmand AP, Friedenson B, Gewurtz H, Painter RM, Hoffmann T, Shelton E. Characterization of C-reactive protein and the homologous proteins displaying cyclic pentamuric symmetry (Pentraxins). Proc Nat Acad Sci, USA 1977:739-43.

55. Oliveria EB, Gotschilch EC, Liu T. Primary structure of human C-reactive protein. Proc Nat Acad Sci USA 1977; 74: 3148-51.

56. Oliveria EB, Gotschlich EL, Liu TY. Comparative studies on the binding of human and rabbit C-reactive protein. J Immunol 1980; 124: 1396-402.

57. Tsujimoto M, Inoue K, Nojima S. C-reactive protein induced agglutination of lipid suspensions prepared in the presence an absence of phospotidyl choline. J. Biochem 1980; 87: 1531-37.

58. Osmand AP, Mortensen RF, Siegal J, Gewurtz H.Interactions of C-reactive protein with the complement system 111. Complement dependent passive hemolysis initiated by CRP. J Exp Med 1975; 142: 1065-72.

59. Mortnson RF, Osmand AP, Gewurz H. Effect of C-reactive protein on the lymphoid system I, Binding to thymus dependent lymhocytes and alteration of their functions. J Exp Med 1975; 141:821-39.

60. Fiedle BA, Gewurz H. Effects of C-reactive protein on platelet functions –I. Inhibition of platelet aggregation and release reactions. J Immunol 1976; 116: 1289-94.

61. Hokama Y, Nagasaw LS, Uchida DA, Morita AM, Abad MA, Michimoto. suppression of arachidonic acid and endoperoxide analog stimulated platelet aggregation by sodium azide and protection of this effect by C-reactive protein. Fed Proc 1978; 37:1455.

62. James K, Hansen B, Gewurz H. Further studies of binding of C-reactive protein to human Lymphocytes; Development of a radio assay and requirement for a multivalent binding specificity. Fed. Proc 1980; 39: 945-49.

63. Williams RC JR, Kilpatrick KA, Kassoby M, Abdin ZN. Lymphocytes binding C-reactive protein during acute rheumatic fever. J Clin Invest 1978; 61:1384-93.

64. Parish WE. Studies in vasculitis VII C-reactive protein as a substance perpetuating chronic vasculitis. Occurance in lesions and concentrations in sera. Clin Allergy 1976; 6: 543-50.

65. Pepys MB. C-reactive protein fifty years on. Lancet 1981; 653-6.

66. Irving Kushner, Border ML. Control of the acute phase response serum C-reactive protein kinetics after acute myocardial infarction. The Journal of clinical investigations 1978; 61: 235-42.

67. De Beer FC, Hind CR, Fox KM. Measurement of serum C-reactive protein in myocardial ischemia and infarction. Br Heart J 1982; 47: 239-43.

68. Ridker PM, Cushman M, Stampfer MJ. Inflammation aspirin and risk of cardiovascular disease in apparently healthy man. New Eng J Med 1996; 336: 973-9.

69. Haverkate F, Thomson SG, Pyke SD, Gallimore JR, Pepys MB. Production of C-reactive protein and risk of coronary events in stable and unstable angina. Lancet 1997; 349: 462-66.

70. Thomson SG. Hemostatic factors and the risk of myocardial infarction or sudden death in patients with angina pectoris. N Engl J Med 1995; 332: 635-641.

71. Vulgari F, Cummins P. serum levels of acute phase and cardiac proteins after MI, surgery and infection. Br Heart J 1982; 48: 352-6.

72. Berk BC, Weintraub WS et al. Elevation of C-reactive protein in active coronary artery disease. Am J Cardiol 1990; 65: 168-72.

73. John S. Yudkin; C. D. A. Stehouwer; J. J. Emeis; S. W. Coppack C-Reactive Protein in Healthy Subjects: Associations With Obesity, Insulin Resistance, and Endothelial Dysfunction. ATVG 1999; 19:972-978.

74. Aruna D P, JoAnn E; Nader R, Julie E B, Paul M R. C-Reactive Protein, Interleukin 6, and Risk of Developing. T2DM; JAMA.2001; 286: 327-334.

75. Frank B. Hu, James B. Meigs, Tricia Y. Li1, Nader Rifai, and JoAnn E.Manson Inflammatory Markers and Risk of Developing T2DM in Women. Diabetes 2004; 53:693-700.

76. Anubha Mahajan, Rubina Tabassum, Sreenivas Chavali, Omprakash D, Bharadwaj M, Tandon N, et al. High-Sensitivity C-Reactive Protein Levels and T2DMin Urban North Indians. The Journal of Clinical Endocrinology & Metabolism 2008; 94: 6 2123-2127.

77. Lee WL, Cheung AM, Cape D, Zinman B. Impact of diabetes on coronary artery disease in women and men: a meta-analysis of prospective studies. Diabetes Care.2000; 23:962–968.

78. Gu K, Cowie CC, Harris MI. Mortality in adults with and without diabetes in a national cohort of the U.S. population, 1971–1993. Diabetes Care 1998;21: 1138–1145.

79. Mukamal K, Nesto R, Cohen M, Muller J, Maclure M, Sherwood J, Mittleman M. Impact of diabetes on long-term survival after acute myocardial infarction: comparability of risk with prior myocardial infarction. Diabetes Care 2001; 24:1422–1427.

80. Malmberg K, Yusuf S, Gerstein H, Brown J, Zhao F, Hunt D, et al. Impact of diabetes on long-term prognosis in patients with unstable angina and non-Qwave myocardial infarction: results of the OASIS (Organization to Assess Strategies for Ischemic Syndromes) Registry. Circulation 2000; 102:1014–1019.

81. Nathan DM. Long-term complications of diabetes mellitus. N Engl J Med 1993; 328:1676–1685.

82. Dambal A, Padaki S, Herur A, Kashinakunti S, Manjula R (2012) High Sensitivity C-Reactive Protein in Patients of Acute Myocardial Infarction with Type-2 Diabetes Mellitus-A Cross-Sectional Study. Open access scientific reports 2012; 12: 1-4.

83. Jager A, van Hinsbergh VW, Kostense PJ, Emeis JJ, Yudkin JS, et al. (1999) von Willebrand factor, C-reactive protein, and 5-year mortality in diabetic and nondiabetic subjects: The Hoorn Study. Arterioscler Thromb Vasc Biol 19: 3071- 3078.

84. Thompson S G, Kienast J, Stephen, Pyke, Havarkate F, Jurgen C W, et al. Hemostatic factors and the risk of myocardial infarction or sudden death in patients with angina pectoris. N Engl J Med 1995; 332 : 635-641.

85. Liuzzo G, Biasucci LM, Gallimore JR, et al. The prognostic value of C-reactive protein and serum amyloid A protein in severe unstable angina. N Engl J Med 1994;331:417-24.

86. Nikfardjam M, Mullner M, Schreiber W, Oschatz E, Exner M, Domanovits H, et al. The association between C-reactive protein on admission and mortality in patients with acute myocardial infarction. Journal of internal medicine 2000; 247: 341-345.

87. Voulgari F, Cummins P, Gardecki T, Beeching N, Stone W, Stuart J. Serum levels of acute phase and cardiac proteins after myocardial infarction, surgery, and infection. Br Heart J 1982; 48: 352-356.

ANNEXURE – I

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

PROFORMA

CASE NO :

NAME :

AGE/SEX :

I.P NO :

DATE OF ADMISSION :

DATE OF DISCHARGE :

OCCUPATION :

ADDRESS :

1) CHIEF COMPLAINTS :

2) HISTORY OF PRESENT ILLNESS:

3) PAST HISTORY:

4) FAMILY HISTORY:

5) PERSONAL HISTORY:

1. GENERAL PHYSICAL EXAMINATION:

   Weight: Height: BMI:

   Temp:

   Pulse:

   B.P:

   R.R:

   Pallor: icterus: clubbing: cyanosis:

   Generalized lymphadenopathy: edema:

5) SYSTEMIC EXAMINATION :

- CARDIOVASCULAR SYSTEM:

- RESPIRATORY SYSTEM:

- PER ABDOMEN:

CENTRAL NERVOUS SYSTEM:

INVESTIGATIONS:

HB%		RBC count	
Total count		PCV	
Neutrophils		MCV	
Lymphocytes		MCH	
Eosinophils		MCHC	
Monocytes		PLATLET COUNTS	
Basophils		ESR	

FBS		T. CHOLESTEROL	
PPBS		HDL	
S. CREATININE		LDL	
BLOOD UREA		VLDL	
CPKMB		TRIGLYCERIDES	
CRP			

ECG:

2D ECHO:

Complications:

ANNEXURE – II

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

CONSENT FORM

TITLE OF RESEARCH: "STUDY OF C-REACTIVE PROTEIN IN DIABETIC AND NON-DIABETIC PATIENTS WITH ACUTE MYOCARDIAL INFARCTION"

Principle Investigator	:	DR.SHASHANK J SHIROL
P.G. Guide Name	:	DR.S S DEVARMANI M.D (MEDICINE)
Ethical committee chairman	:	DR TEJASWINI V

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

I) INFORMED PART

i. Purpose of study

I have been informed that this is the study of C-reactive protein in diabetic and non-diabetic patients with acute myocardial infarction. This method requires hospitalization.

ii. Procedure: I will be selected for the treatment after the clinical study of my age, chief complaints and general physical examination. I will be admitted immediately. I will have to attend follow-up to OPD regularly.

iii. Benefits

I understand that my participation in this study will have no direct benefit to me other than the potential benefit of treatment which is planned to prevent further morbidity or mortality in me.

iv. Confidentiality

I have been assured that all information furnished to the doctor by me regarding my medical condition will be kept confidential at all times and all circumstances except legal matters.

v. Requirement of more information

It has been made clear to me that I am free at all time under any circumstances to touch based with doctor by directly approaching or otherwise to satisfy any query, doubt regarding any aspect of research concerns.

vi. Refusal or withdrawal of participation

It has been made clear to me that participation in this medical research is solely the matter of my will and also that right to withdraw from participation in due course research at any time.

II) CONSENT BY PATIENT

I, the undersigned have been explained by Dr SHASHANK J SHIROL in the language understood by me. I have also been explained that participation in this medical research is solely the matter of my will and also that I have the right to withdraw from this participation at any time in due course of the medical research.

Signature of participant/patient Date: Time:

Signature of witness: Date: Time:

ANNEXURE – III

ETHICAL CLEARANCE CERTIFICATE

Institutional Ethical Committee
BIJAPUR-586 103.
OUTWARD
No. 0466/2012
Date 18/10/12
B.L.D.E. University's Shri.B.M.Patil Medical College

B.L.D.E. UNIVERSITY'S
SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR-586 103
INSTITUTIONAL ETHICAL COMMITTEE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 18-10-2012 *at* 3-30pm *to scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected & revised version synopsis of the Thesis has been accorded Ethical Clearance.*

Title "Study of c-reactive protein in diabetic and non-diabetic patients with acute myocardial infarction"

Name of P.G. student Dr. Shashank J Shirol
Medicine

Name of Guide/Co-investigator Dr S.S. Devarmani
Prof of Medicine

DR.TEJASWINI. VALLABHA
CHAIRMAN
INSTITUTIONAL ETHICAL COMMITTEE
BLDEU'S, SHRI.B.M.PATIL
MEDICAL COLLEGE, BIJAPUR.

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 – IV

KEY TO MASTER CHART

M	–	Male
F	–	Female
n	–	No
y	–	Yes
d	–	Dyslipidemia