IMPACT OF HBA1C ON ACUTE CARDIAC STATE BOTH IN DIABETIC AND NON-DIABETIC PATIENTS

By

Dr. GOUS MOHIDDIN FARASH

Dissertation submitted to

BLDE University, Bijapur

In partial fulfillment of the
requirements for the degree of

MD

in

GENERAL MEDICINE

Under the guidance of

Dr. S.S. DEVARMANI M.D

Professor,

Department of Medicine,

Shri B.M. Patil Medical College, Bijapur.

2014

BLDE University
Bijapur, Karnataka State

DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation/thesis entitled "**IMPACT OF HBA1C ON ACUTE CARDIAC STATES BOTH IN DIABETIC AND NON-DIABETIC PATIENTS**" is a bonafide and genuine research work carried out by me under the guidance of **Dr. S.S. Devarmani**, **M.D.**, Professor, Department of Medicine, Shri B.M. Patil Medical College, Bijapur

Date:
Place: Bijapur **Dr. Gous Mohiddin Farash**

BLDE University

Bijapur, Karnataka State

CERTIFICATE BY THE GUIDE

This is to certify that the dissertation entitled "**IMPACT OF HBA1C ON ACUTE CARDIAC STATES BOTH IN DIABETIC AND NON-DIABETIC PATIENTS**" is a bonafide research work done by **Dr Gous Mohiddin Farash** in partial fulfillment of the requirement for the degree of MD in General Medicine.

Date:
Place: Bijapur

Dr. S.S. Devarmani M.D.
Professor,
Department of Medicine

BLDE University

Bijapur, Karnataka State

ENDORSEMENT BY THE HOD, PRINCIPAL / HEAD OF THE INSTITUTION

This is to certify that the dissertation entitled "**IMPACT OF HBA1C ON ACUTE CARDIAC STATES BOTH IN DIABETIC AND NON-DIABETIC PATIENTS**" is a bonafide research work done by **Dr Gous Mohiddin Farash** under the guidance of **Dr. S.S. Devarmani**, **M.D.**, Professor, Department of Medicine, Shri BM Patil Medical College, Bijapur.

Seal & Signature of the
HOD of Medicine

Seal & Signature of the prinipal

Dr M. S.Mulimani
M.D. (Medicine)
BLDEU's Shri B.M. Patil
Medical College, Hospital
and Research Centre, Bijapur.

Date:
Place: Bijapur

Dr M.S.Biradar
M.D. (Medicine)
BLDEU's Shri B.M. Patil
Medical College, Hospital
and Research Centre, Bijapur.

Date:
Place: Bijapur

COPYRIGHT

DECLARATION BY THE CANDIDATE

I hereby declare that the BLDE University, Karnataka shall have the rights to preserve, use and disseminate this dissertation / thesis in print or electronic format for academic / research purpose.

Date:
Place: Bijapur **Dr. Gous Mohiddin Farash**

ACKNOWLEDGEMENT

I have got no words to express my deep sense of gratitude and regards to my guide **Dr. S.S. Devarmani M.D.,** Professor of Medicine, under whose inspiring guidance & supervision, I am studying and continuing to learn & master the art of medicine. His deep knowledge, logical approach, devotion to work and zeal of scientific research makes him a source of inspiration not only for me but for others too. It is because of his generous help, expert and vigilant supervision, that has guided & helped me to bring out this work in the present form.

I would also like to express my sincere thanks to **Dr. M.S. Mulimani M.D.,** Professor and Head of Department of Medicine, for all his help and guidance. I am thankful to the Principal **Dr. M.S.Biradar M.D,** for his kind support.

I am also thankful for the support extended by **Dr. V.G.Warad M.D, Dr. Anand Choudhary M.D,**

I am also grateful to my other teachers **Dr R.C.Bidri, Dr. S.R. Badiger M.D** , **Dr. L.S. Patil M.D** and **Dr S.N.Bentoor** Professors of Medicine**.**

My sincere thanks to all the **staff** of the **Department of Biochemistry, the Department of Pathology,** Shri B.M. Patil Medical College Hospital & Research Centre, Bijapur who helped me in the laboratory investigation work. I would also thank **Mrs. Vijaya M Sorganvi M.Sc.,** Statistician, Department of Community Medicine, Shri B.M. Patil Medical College Hospital & Research Centre, Bijapur who kindly obliged & helped me with the statistical work.

I would be failing in my duty, if I would not acknowledge my thanks to all the patients who were kind enough to help for this study.

I would also like to thank my parents **Shri Mohammed Ishaq Farash** & **Smt. Mehrunissa Farash**; without their constant encouragement & moral support, my studies would have been a distant dream.

Finally, I would like to thank the **Almighty GOD** who gave me the energy, skill and the enthusiasm to complete this as well as the other tasks in my life & also for continuing to shower his blessings upon me.

Dr Gous Mohiddin Farash

LIST OF ABBREVIATIONS USED

ACS	Acute Coronary Syndromes
Acc HTN	Accelerated Hypertension
CBC	Complete blood count
CHD	Coronary Heart Disease
CVD	Cardiovascular disease
FBS	Fasting blood sugars
HBA1c	Glycosylated Hemoglobin
HDL	High Density Lipoprotein
LDL	Low Density Lipoprotein
PPBS	Post Prandial Blood Sugar
NSTEMI	Non-ST Segment Elevation Myocardial Infarction
STEMI	ST Segment Elevation Myocardial Infaction
TC	Total Cholesterol
TG	Triglycerides
VLDL	Very Low Density Lipoprotein
WHO	World Health Organisation

ABSTRACT

Back ground & Objectives:

Acute cardiac states are the commonest and most important cause for premature death in both developed and developing countries. The present study was planned to assess diagnostic and the prognostic importance of HbA1c in acute cardiac states and to find the incidence of various complications in acute cardiac states , thereby permitting early initiation of appropriate preventive measures

Methods:

This study was carried out in B.L.D.E.U's Shri B.M. Patil Medical College Hospital and Research Centre, Bijapur during the period from October 2011 to July 2013. A total of 156 patients (111 males & 45 females) with acute cardiac state who satisfied the inclusion criteria were included in the study.

Results

A highly significant (<p0.01) correlation exists between HBA1c >7% and complications in acute cardiac states. This indicates that, the patients with HBA1c >7% in acute cardiac states are prone for going in to complications and there is increased rate of mortality in patients with HBA1c >7%.

Conclusion

The findings of this study illustrate the valuable additional information that can be provided by HbA1c about the adverse outcomes in acute cardiac states , besides its primary role in monitoring long-term glycemic control. This study also emphasizes that persons with high levels of HbA1c should be monitored for complications in acute cardiac states and managed accordingly.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

INTRODUCTION

The 20th century saw major changes in the pattern of cardiovascular diseases .In the developed world, syphilitic and tuberculous involvement of the cardiovascular system became rare and the incidence of rheumatic disease declined considerably. Myocardial and conducting tissue diseases on the other hand were diagnosed with increasing frequency and the importance of arterial hypertension became well established.

Coronary artery disease emerged as the major cardiovascular disorder of the era, becoming the most common cause of premature death. In the new millennium coronary artery diseases showed signs of loosening its grip on the developed world. But in developing countries like India, its prevalence is in step ascent, and threatening to over take malnutrition and infectious diseases as the major cause of death.

Acute coronary syndromes are the commonest and most important cause for premature death in both developed and developing countries. It is the cause for 25% of deaths in female and 30% of deaths in male, and cuts short the life expectancy ranging from 3.4 to 9.4 years[1].

Recently, it has reached an endemic proportion. The Global Burden of Diseases (GBD) study reported the estimated mortality from coronary artery disease(CHD) in India as 1.6 million in the year 2000.Extrapolatation of these numbers estimates the burden of CHD in India to be more than 32 million patients. Hospital statistics reveal that 20-25% of all medical admissions are due to CHD [2].

Acute coronary syndromes indicate myocardial impairment due to many factors. However most common cause is atherosclerotic disease of coronary arteries impairing the delicate balance of "supply and demand." [3,4]

Acute cardiac states which include unstable angina, NSTEMI, STEMI, accelerated hypertension and cardiomyopathies has become one of the most common illnesses in the today's world with acute myocardial infarction presenting as emergent manifestation having significant mobidity and mortality and complication rate. Various indicators have been proposed to predict the severity and complications of an episode of acute cardiac state for example clinical profile, electrocardiogram changes, hemodynamic parameters, cardiac size, metabolic acidosis and cardiac enzymes. Elevated free fatty acids, cortisol and catecholamines and depressed insulin secretion have also been characterized in patients with myocardial infarction.

Hyperglycemia is common in patients of acute myocardial infarction in the initial phase and appears to be related to stress mechanism and is a reflection of relative insulin deficiency, associated with elevated free fatty acids. Previous reports of relationship between admission plasma glucose levels and development of cardiac failure have been found.

Elevated admission glucose level is a very strong predictor of short term adverse outcome in patient with acute cardiac state. Numerous trials have shown that blood glucose concentration on admission is a good prognostic factor of short and long term mortality in acute cardiac state in all individuals irrespective of diabetic status . Although admission glucose level has good prognostic value on outcome in acute cardiac state ,it may be affected by meals , circadian cycle and also stress response . Glycated HbA1c is a good reflect of plasma glucose concentration over 8 to 12 weeks with no effect from meals or circadian cycle .[5]

Therefore, the present study was planned to assess diagnostic and the prognostic importance of HbA1c in acute cardiac states and to find the incidence of various complications in acute cardiac states , thereby permitting early initiation of appropriate preventive measures.

AIMS AND OBJECTIVE

1) To find out the level of HbA1c in acute cardiac state.
2) To find out the correlation between HbA1c levels and the severity and complications in the patients admitted with acute cardiac state admitted in intensive coronary care unit .

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.[6,7.] 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 8.

In 1845, Leipzig, Vogel discovered cholesterol as major constituent in atheromatous plaque 9.

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.[10]

In 1920, Pardee first recognized the electrocardiographic curve of acute stage of myocardial infarction. William Enthoven invented ECG.[10]

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.[10,11,12]

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. [13]

Elizabeth Mani et al conducted a prospective study in 2006 in which 166 patients admitted to ICU with acute cardiac state (unstable angina , acute myocardial infarction , accelerated hypertension , cardiomyopathy) were studied. They concluded that there was a significant direct correlation between HbA1c and severity and complications of heart disease .A large number of patients presenting with acute cardiac states i.e 97.2% had HbA1C values >=5.[14]

Chi Yuen chan et al conducted a retrospective study in 317 patients admitted with acute cardiac state . They concluded that majority of these patients had higher value of HbA1c and higher values of HbA1c are associated with increased short term complications .[15]

Stamler J Vaccaro et al conducted a study between 1973 to 1975, concluding that individuals with acute cardiac conditions had higher value of HbA1c and had increased rates of complications of acute cardiac state .[16]

Kelly J hunt et al conducted a study in 4996 peoples and concluded that increased levels of HbA1c in acute cardiac state were associated with increased rates of complication in acute cardiac state.[17]

EPIDEMIOLOGY

Coronary artery disease is a world wide 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 20thcentury, 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% inrural). 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]

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%.

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. Some times 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.

   Artery which gives rise to posterior descending branch is called dominant 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. Some times 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

A) Oral contraceptives.

B) Physical activity.

C) Personality.

D) Socioeconomic status (SES) and psychosocial factors

E) 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

ST SEGMENT 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

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 Prinzmetal 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 betablockers.

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 out put 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 out put 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 out put 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 out put, 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 out put 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 angigraphy follow percutaneous or surgical revascularisation offer the best chance of suvival, particularly in patients under 75 years of age.

Right ventricular Infarction:

Approximately 1/3rd of patients with inferoposterior infarction demonstrate atleast 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.

GLYCOSYLATED HAEMOGLOBIN

History

Hemoglobin A1c was first separated from other forms of hemoglobin by Huisman and Meyering in 1958 using a chromatographic column.43 It was first characterized as a glycoprotein by Bookchin and Gallop in 1968.[44] Its increase in diabetes was first described in 1969 by Samuel Rahbar et. al.45 The reactions leading to its formation was characterized by Bunn and his co-workers in 1975.46 The use of hemoglobin A1c for monitoring the degree of control of glucose metabolism in diabetic patients was proposed in 1976 by Anthony Cerami, Ronald Koenig and coworkers.47

Clinical Significance of HbA1c

HbA1c is a widely used marker of chronic glycemia, reflecting average blood glucose levels over a 2 to 3-month period of time. The test is widely used as the standard biomarker for the adequacy of glycemic management. Patient's daily blood glucose tests provide only a snapshot of glycaemic control at the moment of testing. The HbA1c test,

on the other hand, gives the big picture by showing how patient blood glucose control has been over the previous couple of months. HbA1c tests are helpful to physician because they give an immediate indication of patient blood glucose control.[48,49]

Haemoglobin: [50-53]

The red pigment of the erythrocyte is the conjugated protein hemoglobin. The normal concentration of hemoglobin in an adult is 14 – 16g/dL of blood, all confined to erythrocyte. It is estimated that there is about 750g of hemoglobin in total circulating blood of a 70kg man and destroyed each day.

Dilute acid will readily split hemoglobin into the protein globin and its prosthetic group haeme (haematin). The hydrochloride of haeme called haemin can easily be prepared in crystalline form. Haeme is an iron porphyrin. Globin, the protein moiety of hemoglobin, consists of 4 subunits i.e it has the structure of a tetramer. Each subunit consists of polypeptide chains. Two of the chains having identical aminoacids composition are designated as alpha, the other two also identical with another are beta chains. Adult human hemoglobin therefore possesses two α and two β chains. Each of the four chains has an associated haeme group.[50]

A haeme group consists of an iron (Fe) ion held in a heterocyclic ring, known as a porphyrin. The iron ion, which is the site of oxygen binding, co ordinates with the four nitrogens in the centre of the ring, which all lie in one plane. The iron is also bound strongly to the globular protein via the imidazole ring of the F8 histidine residue below the porphyrin ring. A sixth position can reversibly bind oxygen by a coordinate covalent bond, completing the octahedral group of six ligands. Oxygen binds in“end on bent”

geometry where one oxygen atom binds Fe and the other protrudes at an angle, when oxygen is not bound, a very weakly bonded water molecule fills the site, forming a distorted octahedron. The iron ion may either be in the Fe2+ or Fe 3+ state, but ferrihaemoglobin (methaemoglobin) (Fe3+) cannot bind oxygen. In binding, oxygen temporarily oxidizes (Fe2+) to (Fe3+), so iron must exist in the +2 oxidation state in order to bind oxygen. The enzyme methaemoglobin reductase reactivates hemoglobin found in the inactive (Fe3+) state by reducing the iron center.[51]

During fetal life, hemoglobin that is produced is different from hemoglobin A (HbA) produced during adult life. This fetal hemoglobin (HbF) has two α chains but there are two γ chains instead of β chains as in hemoglobin A.

An α chain has 141 amino acids. Valine is the N - terminal and arginine is the C - terminal amino acid. The β chain also has 146 amino acids but glycine is the N – terminal and histidine is the C – terminal amino acid. The γ chain also has 146 amino acids but glycine is the N – terminal and histidine is the C – terminal amino acid.

The α chain has a molecular weight of 15,126 daltons, the β chain has a molecular weight of 15,866 daltons. Considering the fact that there are two α chains and two β chains in the entire globin molecule, it may be concluded that it contains a total of 574 amino acids, which, with four haeme prosthetic groups (one for each chain) gives the haemoglobin molecule a molecular weight of 64,650 daltons. Ultracentrifugal determinations of the molecular weight of haemoglobin had suggested a weight of 64,500 daltons.

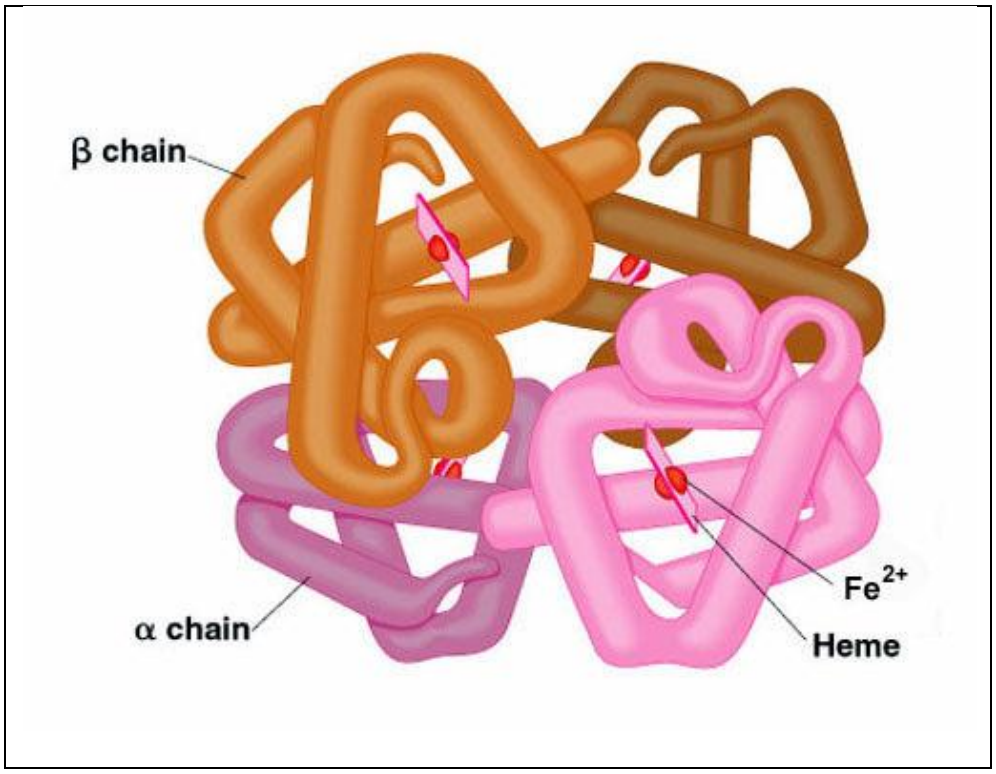


Fig 1: STRUCTURE OF HAEMOGLOBIN

The iron contained in each haeme group is coordinately bound to 2 histidine residues, probably at positions 58 and 87 in the α chains and at positions 63 and 92 in the β chains. It has been suggested that one of the imidazole bonds (possibly histidine 58 in α chain and histidine 63 in the β chain) is reversibly displaced by oxygen when haemoglobin is oxygenated.

The confirmation of the tetrameric structure of haemoglobin depicts the α and the β chains with their N and C terminals indicated as well as the approximate portions of the haeme porphyrin residues. The positively charged (cationic) N –terminal ammonium group of one α chain is close to the negatively charged (anionic) C- terminal group of the second α chain. A similar relationship exists between the β chains. The resultant

electrostatic attraction is of considerate importance in the maintenance of the quaternary structure of the protein.[52]

The most characteristic property of haemoglobin is its ability to carry oxygen to form oxyhaemoglobin. The combination takes place with increasing tensions of oxygen, and the sigmoidal curves of oxyhaemoglobin formation can be drawn at varying tensions of oxygen (O2) and of carbon dioxide (CO2). The effect of CO2 on oxygen combination with haemoglobin the so called Bohr Effect is due to changes in pH in the medium surrounding the red cell. The combination of oxygen with haemoglobin is reversed merely by exploring oxyhaemoglobin to lowered oxygen tensions. At oxygen tensions of 100 mm Hg or more, haemoglobin is virtually 100% saturated, and approximately 1.34mL of oxygen is then combined with each gram of haemoglobin.

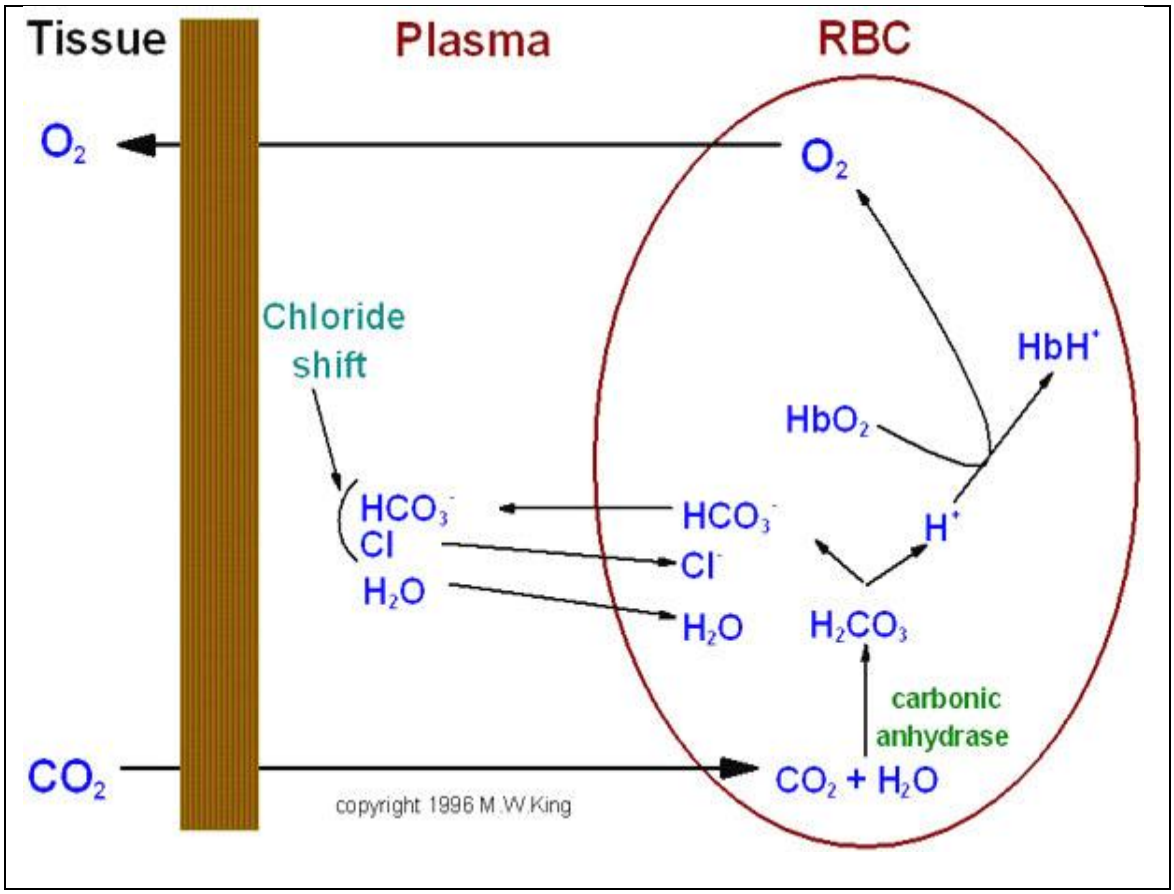


Fig 2: TRANSPORT OF CO2 AND THE BOHR EFFECT

The absorption spectra obtained when white light is passed through the solutions of haemoglobin or closely related derivatives are of value in distinguishing these compounds from one another. Oxyhaemoglobin or diluted arterial blood shows three absorption bands: a narrow band of light absorption at a wave length of λ = 578nm, a wider band at 542nm and a third with its centre at 425nm at the extreme violet end of the spectrum. Deoxygenated (i.e reduced) haemoglobin, on the other hand, shows only one broad band with its centre at 559nm. When blood is treated with ozone, potassium permanganate, potassium ferric cyanide, chlorates, nitrates, nitrobenzene, pyrogallic acid,

acetanilide or certain other oxidizing substances methaemoglobin is formed. In this compound, the iron which is in the ferrous state (Fe2+) in haemoglobin is oxidized to the ferric state (Fe3+) in which the haemoglobin cannot carry oxygen. In acid solution, haemoglobin has one absorption band with its centre at λ = 634nm.

Carbonmonoxide combines with haemoglobin even more readily than does oxygen. Carboxyhaemoglobin shows two absorption bands, the middle of the first at 570nm and the second at 542nm.Combinations of haemoglobin with hydrogen sulphide or hydrocyanic acid also gives characteristic absorption spectra. This provides a valuable means of detecting these compounds in the blood of individuals suspected of having been exposed to H2S or HCN.

The average life of a red blood cell in the human body in adult is about 120 days. When the red cells are destroyed, the porphyrin moiety of haemoglobin is broken down and thus forms the bile pigments biliverdin and bilirubin, which are carried through liver for excretion into intestine by way of the bile.[53]

GLYCOSYLATED HAEMOGLOBIN [54,55]

In adults and children above the age of 6 months, about 90% haemoglobin is HbA, HbF comprises 0.2% of the total. In addition of HbA which is the major haemoglobin of the normal adults, a minor glycosylated form of this haemoglobin is also found in the adult red blood cell. In normal individuals, it is present in concentrations of 3.5% of total haemoglobin. However in patients with diabetes, its concentration may be increased to as much as 6 – 15%. When haemolysate is chromatographed on cation exchange resins, negatively charged minor haemoglobins are eluded before the main HbA peak. This has been designated as HbA1a1, HbA1a2, HbA1b, HbA1c and these

comprise 0.2%, 0.2%, 0.2%, and 3% of the haemoglobin respectively. These minor haemoglobins are post translational modification of adult haemoglobin (HbA). These minor haemoglobins (particularly HbA1c) are increased two to three fold in the blood of diabetic patients.[54]

The glycosylation of haemoglobin A to form HbA1c occurs throughout the life of the erythrocyte, but it occurs 2.7 times faster in normal donor red cells given to diabetic recepients, the metabolic changes in the diabetic patient apparently accomplish glycosylation within red cells circulating in their blood faster than occurs when the transfused red cells circulate in a normal recipient. The level of glycosylated haemoglobin appears to be an index of the levels of the blood sugar for a period of several weeks prior to the time of sampling. It has therefore been suggested that the measurement of haemoglobin glycosylation would be a more reliable indicator of the adequacy of control of diabetic state than occasional measurement of blood and urine glucose.[55]

Structure of HbA1c [56,57,58.59]

The main obstacle in analyzing HbA1c which contributes the major portion of the total glycosylated haemoglobins was that the other minor haemoglobins were present in fairly small amounts. The earlier work of Holquist and Schroeder was the key in determining the structural difference between HbA and HbA1c. Large amounts of HbA1c were purified from large (10x100cm) Bio – Rex Columns. Up to 2g of HbA1c could be isolated from 1 pint of blood. β1C chains were separated from HbA1c and β0 chains from HbA after removal of the heme. Tryptic peptides were prepared and separated on

cation exchange or anion exchange columns; βT-1, β1CT-1 and sodium borohydride (NaBH4) reduced β1CT1 were prepared and further treated with papain. Thus Val–His, R-Val–His and reduced R-Val–His peptides were prepared.[56]

The aminoacid comparison of each peptide was determined by amino acid analysis, the sequence by the Edman degradation and the N terminal analysis by the Sanger's procedure. It was concluded from these studies that HbA1c is the condensation product (a Schiff base) of 1 molecule of HbA and 1 molecule of a ketone or an aldehyde R=O (the present concept is 2 molecules of ketone or an aldehyde for one molecule of HbA). The point linkage of R=O to the haemoglobin was the N terminus of the β chains. Strong evidence for the presence of a Schiff base adduct was also found. The pKa of the Schiff base was 6.64. Other than this, no difference has been found between the primary structure of the α and β chains of the HbA and HbA1c.

The keto or aldehyde group had a molecular weight of approximately 280. Carbohydrate was excluded as a possible identity for the R=O group, but long chain aromatic aldehyde or ketone was strongly suggested. In HbA1c, only one of the β chain was originally thought to have undergone Schiff base formation. Later studies by Bookchin and Gallop established that a hexose is linked to the amino terminus of both β chains of HbA1c. They examined the structure of the blocking group by mass spectrometry.[57]

Tritiated N-alkylated valine was prepared by acid hydrolysis of HbA1c after reducing the linkage with NaB3H4. Mass spectral analysis was possible after reacting the tritiated product with acetic anhydride. The mass spectrum of the acetylated derivative was consistent with N-1-(1-deoxyhexitol) or N-1-(1-galactitol) valine. Thus it was

established that a simple sugar rather than a long chain aldehyde or a ketone is attached to each of the β chains in HbA1c.

It is rather puzzling that although glucose is considered to be the most logical substrate in the glycosylation reaction, the N terminus is a n-1(deoxy-galactitol) valine. Thus it is possible that a rearrangement has taken place after the initial reaction, namely, Schiff base formation. When HbA1c was subjected to mild acid hydrolysis, reducing sugars were formed. In fact, glucose and mannose present in a 3:1 ratio accounted for nearly all the reducing sugars. The appearance of mannose in the hydrolysate cannot be explained, since red cells contain little or no mannose. Just as in maillard browining reaction, in red cells glucose reacts initially with the amino terminal group of the β chain to form an aldimine linkage, which subsequently undergoes Amadori rearrangement to form a more stable ketoamine linkage.

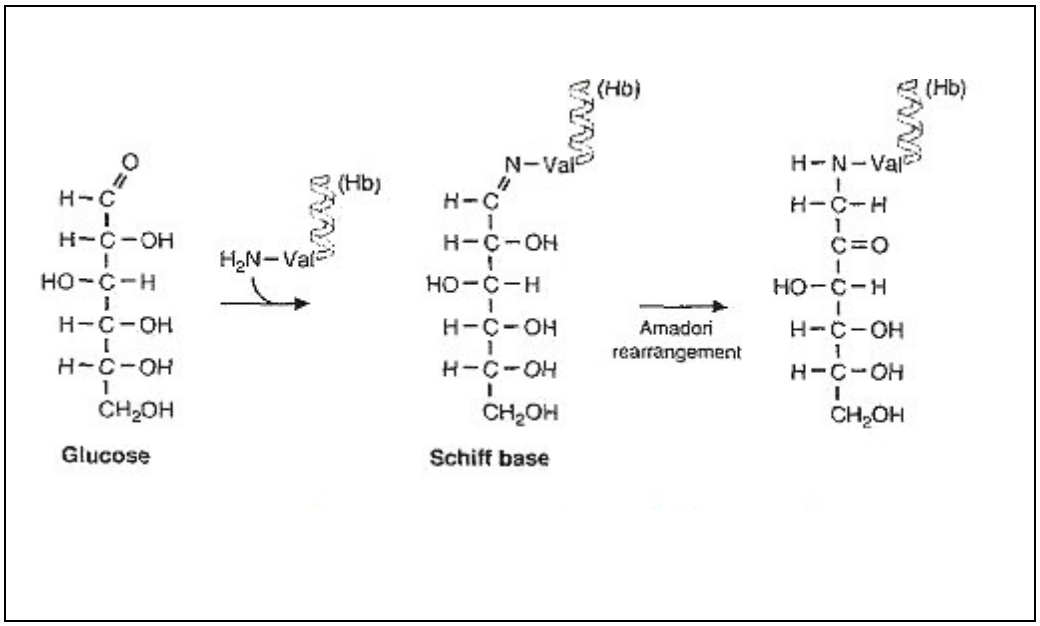
The evidence for this was obtained as follows: when HbA1c was treated with NaBH4 and then with sodium periodate, nearly all the radioactivity was recovered as formaldehyde. This observation suggested that the second carbon atom rather than the first was reduced. Additional evidence was gathered to support Amadori rearrangement as an integral step even in invivo glycosylation reactions. Such evidence come from the proton magnetic resonance spectroscopic and thin layer chromatographic analyzer of β chain N terminal peptides, Val-His and R-Val-His and synthetic model reactions showed that glucose and mannose reacted with valine of synthetic Val-His under mild conditions to form an adduct that upon NaBH4 reduction, yielded glucitol- and mannitol-valines in both cases. The simple fact that 5- hydroxymethyl furfural (5-HMF) can be formed by heating HbA1c with mild oxalic acid is consistent with the ketoamine linkage.[58]

Nonenzymatic Glycosylation:

Glucose chemically attaches to proteins and nucleic acids without the aid of enzymes. Initially, chemical reversible Schiff base and Amadori product adducts form in proportion to glucose concentration. Equilibrium is reached after several weeks, however, the further accumulation of these early nonenzymatic glycosylation products doesn't continue beyond the time. Subsequent reactions of the Amadori product slowly give rise to nonequilibrium advanced glycosylation and products which continue to accumulate indefinitely on longer lived molecules. Excessive formation of both types of nonenzymatic glycosylation product appears to be the common biochemical link between chronic hyperglycemia and a number of pathophysiologic processes potentially involved in the development of long term diabetic complications.[59]

Formation of Glycosylated Haemoglobin: [60, 61]

Glucose reacts nonenzymatically with the NH2 terminal amino acid of the beta chain of the human haemoglobin by way of keto amine linkage, resulting in the formation of glycosylated haemoglobin. The enhanced electrophoretic mobility of this fast moving minor haemoglobin component is due to the nonenzymatic glycosylation of the amino acid valine and lysine. The reaction is as follows



HbA **PreA1C** **HbA1C**

RAPID SLOW

Fig 3: NONENZYMATIC GLYCOSYLATION

In this figure beta NH2 stands for the terminal valine of the beta chain of haemoglobin. Aldimine formation is reversible so that pre A1c is liable while ketoamine formation is irreversible and thus stable. Pre A1c levels depend on the ambient glucose concentrations and do not reflect long term control although they are measured in chromatographic methods for determining HbA1c. Pre A1c must thus be removed to assess true HbA1c values accurately. Many laboratories employ High Performance Liquid Chromatography (HPLC) to make the measurement. A colorimetric method utilizing thiobarbituric acid also doesn't measure the labile pre A1c fraction. When properly assayed, the percent of glycosylated haemoglobin gives an estimate of diabetic control for the preceding 3 month period.[60] Glucose is also linked to either sites on the haemoglobin molecule such as N terminal of alpha chain lysine residues but these

modified components cannot be separated by conventional chromatographic or electrophoretic technique. Glycosylated haemoglobin indicates the integrated, time averaged blood glucose level as shown by Koening, Peterson, and Jones et al. In this study, before control of diabetes the mean fasting blood sugar for all patients was 343mg/dl (range 280 to 450) and haemoglobin A1c concentration 9.8% (range 6.8 to 12.1). During optimal diabetic control the blood sugar concentration was 84mg/dl (range 70 to 100mg) and HbA1c concentration 5.8% (range 4.2 to 7.6%). The periodic monitoring of HbA1c levels provide a useful way of documenting the degree of control of glucose metabolism in diabetic patients and provides a means whereby the relation of carbohydrate control to the development of sequel can be assessed. Thus HbA1c estimation is now providing unique information that was not previously available and has helped not only in patient management but also in research.[61]

Alterations in Glycosylated Haemoglobin in various pathologic states:

- The disadvantage of glycosylated haemoglobin is that its level is low whenever there is rapid turnover of red cells with influx of young RBC's. Hence its level is low in patients with hemolytic anemia.
- In acute and chronic blood loss due to conditions like iron deficiency anemia, recent history of haematemesis or malaena, and the HbA1c level may be lowered.
- In beta thalassaemia where levels of HbF are increased, this may give rise to misleadingly high result in both diabetic and non diabetic subjects.[60]
- Uraemia may itself cause glucose intolerance tending to rise HbA1c levels.

- Chronic renal failure may be associated with increased haemolysis, gastrointestinal blood loss and decreased erythropoiesis and HbA1c level may be low.
- HbA1c value didn't alter in normal pregnancy. But in pregnant diabetic patients it was raised in the first trimester, falling as pregnancy progresses presumably because of better diabetic control.[62]

The major drawback as was shown by Guenther and Boder et al in 1980 was that HbA1c probably reflected disproportionately in the recent episodes of poor control in comparison to recent improvement in diabetes.

The specific activity of the major component haemoglobin increased to a maximum by day 15 and remained nearly constant during next 80 days. This pattern is entirely consistent with normal erythropoiesis. The specific activity of HbA1c increased gradually over the life span of red cells reaching that of adult haemoglobin approximately by day 60, thereafter the specific activation of minor components exceeded that of haemoglobin. These results indicate that these minor components form slowly, continuously and nearly irreversibly during the 120 day life span of the red cells. Patients with a shortened life span of red cells (haemolytic anemia) have much less glycosylated haemoglobin compared to normal haemoglobin.

Conditions leading to falsely abnormal values for the HbA1c: 62,63,64

I. Conditions leading to false elevation of HbA1c

A. Chromatographic abnormalities

1. Hyperlipidemia (due to lactescence)
2. Elevated temperature and or buffer pH.
3. Negatively charged Hb variants, such as HbF
4. Acute hyperglycemia ("Fast Glycosylation")

B. Other post transnational modification of Hb

1. Aspirin (acetylation)
2. Antibiotics (Penicilloylation)
3. Alcohol (5-deoxy-xylulose-1-PO)
4. Uremia (Carbamylation)

II. Conditions leading to falsely low HbA1c Values

A. Chromatographic abnormalities

1. Low temperature and/or buffer pH.
2. Positively charged Hb variants, such as HbS or HbC.

B. Altered RBC dynamics

1. Increased destruction of RBCs – Hemolytic Anaemia.
2. Active erythropoiesis as in pregnancy
3. Recent blood transfusion.[62]

Glycosylated Haemoglobin in Diabetes Mellitus:

Glycosylated haemoglobin specifically measures the number of glucose molecules attached to haemoglobin, a substance in red blood cells. People who do not have diabetes generally have an HbA1c level of less than 6 %. This means that < 6 % of their hemoglobin molecules have glucose permanently attached.

Based on the results of studies such as the Diabetes Control and Complications Trial (DCCT), which showed that tight blood glucose control could reduce the risk of diabetic eye, kidney and nerve disease, the American Diabetes Association (ADA) recommends that people with diabetes should try to keep their HbA1c level below 7%.

Underlying Principle:

In the normal 120-day life span of the red blood cell glucose molecules join hemoglobin, forming glycosylated haemoglobin. In individuals with poorly controlled diabetes, increases in the quantities of this glycosylated haemoglobin are noted. Once a haemoglobin molecule is glycosylated, it remains that way. A build up of glycosylated haemoglobin within the red cell reflects the average level of glucose to which the cell has been exposed during its life cycle. Measuring glycosylated haemoglobin assesses the effectiveness of therapy by monitoring long-term serum glucose regulation.

The HbA1c level is proportional to average blood glucose concentration over the previous three months .HbA1c levels depend on the blood glucose concentration. That is, the higher the glucose concentration in blood, the higher the level of HbA1c; and not influenced by daily fluctuations in the blood glucose concentration but reflect the average glucose levels over the prior six to eight weeks. Therefore, HbA1c is a useful indicator of

how well the blood glucose level has been controlled in the recent past and may be used to monitor the effects of diet, exercise and drug therapy on blood glucose in diabetic patients.

Importance:

Patient's daily blood glucose tests provide only a snapshot of glycaemic control at the moment of testing. The HbA1c test, on the other hand, gives the big picture by showing how patient blood glucose control has been over the previous couple of months. HbA1c tests are helpful to physician because they give an immediate indication of patient blood glucose control.

Over a longer period of time, consecutive HbA1c tests may provide an overall trend in diabetes control. If HbA1c is progressively raising each time patient visit the clinic then it may suggest that the treatment plan needs modification. Finally, HbA1c tests are often used in setting and achieving treatment goals.[63]

A major study, the UKPDS Study published in 2000, managed to quantify many of the benefits of reducing a high HbA1c level by just 1%.

- A 16% decrease in risk of heart failure
- A 14% decrease in risk of fatal or nonfatal myocardial infarction (heart attack)
- A 12% decrease in risk of fatal or nonfatal stroke
- A 21% decrease in risk of diabetes-related death
- A 14% decrease in risk of death from all causes
- A 43% decrease in risk of amputation

A 37% decrease in risk of small blood vessel disease (e.g. retinal blood vessel disease causing vision loss).[64]

Assay methods 65,66

The various methods that have been used to determine glycosylated haemoglobin are:

- Cation exchange chromatography.
- Batch chromatography.
- Affinity chromatography.
- High performance liquid chromatography.
- Colorimetry.
- Isoelectric focusing.
- Radio immuno assay.
- Spectrophotometric assay.
- Electrophoresis/Electroendosmosis. [65]

Among these, chromatographic method has been widely used to estimate HbA1c. It is a simple and rapid method (microchromatography). It has better resolution and more precision. It requires small amount of sample and no special equipment. Its cost and use of cyanide as buffer are the main disadvantages.

METHODOLOGY

METHODOLOGY

MATERIALS AND METHODS

1. SOURCE OF DATA:

- The material for the present study is collected from patients who are admitted in ICU in BLDEU'S Shri B.M.Patil's medical college hospital and research centre, Bijapur .
- Period of study is from OCTOBER 2011 to JULY 2013

2. METHOD OF COLLECTION OF DATA:

By detail history

- By detail clinical examination.
- By relevant investigations like ECG , lipid profile and CPK-MB or troponin-T enzyme levels .
- The patient are followed uptill discharge and all complications like arrhythmias , cardiac failure and outcome are noted .

3. INCLUSION CRITERIA :

- Patients of any age who are admitted in ICU in BLDEU`s Shri B.M.Patil medical college hospital Bijapur between October 2011 to July 2013.
- *The whole spectrum of acute cardiac state include unstable angina, non-ST segment elevation MI, ST segment elevation MI , accelerated hypertension and

cardiomyopathies are selected on basis of history like chest pain, clinical examination and relevant investigation which will include ECG changes, lipid profile and CPKMB or troponin levels.

3. EXCLUSION CRITERIA:

1) Sepsis

2) Hemoglobinopathies

3) Hypothyroidism

4) Patients with history of non cardiac chest pain with no ecg changes suggestive of acute cardiac state.

5. SAMPLE SIZE

Time period of study from October 2011 to July 2013 . Incidence of acute cardiac state is 7 percent

(A P I Text Book of Medicine) . Margin of error is 4 percent at 95 percent of level of confidence,

the calculated sample size is 156 using the below statistical formula

$$n = \frac{(1.96)^2 (9) (1- P)}{d^2}$$

6. STATISTICAL ANALYSIS

1) Data will be presented with

MEAN $\pm$ SD

2) Results will be compared by X^2 test

3) Correlation will be found by logistic regression (if necessary)

INVESTIGATIONS

1)Blood- Hb, Total count ,Differential count , ESR .

2)Urine – Protein , Sugar , Microscopy .

3)Lipid Profile

4)Blood sugar

5)Blood Urea

6)Serum Creatinine

7)Chest X ray

8)ECG

9)CPK-MB or TROPONIN-T

10)HBA1C

Ion exchange chromatographic method has been used in this study. The principle and the procedures of the method are dealt below.

Principle

Whole blood is mixed with a lysing reagent to prepare a hemolysate. This is then mixed with a weakly binding cation exchange resin. The non-glycosylated hemoglobin binds to resin leaving Glycosylated Hemoglobin (HbA1c) free in the supernatant. The HbA1c % is determined by measuring the absorbance of the HbA1c fraction and of the total Hb.

Reagents and apparatus

1. Ion exchange Resin (Bio-Rex 70)

2. Hemolysing Reagent

- 0.3 g white saponin
- 0.5 g potassium cyanide

Dissolved in a Buffer pH 6.7 to make 1 litre

3. Control (lyophilized).

4. Apparatus – Plastic Tubes and Resin Separators.

Specimen

Whole blood is collected in EDTA bulb. Heparin may also be used. HbA1c in blood is found to be stable for one week at 2-8OC.

Equipment Required

1. Spectrophotometer/photocolorimeter

2. Cuvettes

3. Test tubes

4. Vortex Mixer

5. Pipettes and Micropipette

Reagent Preparation

Reagents 1 and 2 are ready to use. HbA1c control (3) is dissolved in 1 ml. of deionized water by inverting / swirling. Reconstituted control is stable for 30 mins only at Room temp or 15 days at -200C.

Procedure

Assay Temperature : 23 ± 20C

Wave length : 415 nm (Hg 405 nm)

Step 1: Hemolysate preparation

1. 0.5ml of lysing reagent (2) is pipetted into a test tube.

2. To it 0.1ml of well mixed whole blood sample is to be added.

3. Mixed and allowed to stand at room temperature for 5 minutes

Step 2: Hb A1C Separation and Assay.

1. 3.0 ml of Ion Exchange Resin (1) is pipetted into the plastic tube which was mixed well before use.

2. 1.0ml of the hemolysate is added (from step 1)

3. The resin separator is positioned in the plastic tube so that the rubber sleeve is approximately 2 cms above the liquid level.

4. Plastic tube is placed on cortex mixer and is mixed for 5 minutes.

5.The resin separator is pushed down in the plastic tube until the resin is firmly packed.

6. The supernatant is poured directly into a cuvette and absorbance is measured against deionized water within 60 minutes.

Step: 3 Total Hemoglobin (THB) Assay

1. 5.0ml of deionized water is pipetted into test tube.
2. 0.02ml of hemolysate (from step 1) is pipetted into it.
3. Mixed and absorbance is read against deionized water within 60 minutes.

Calculations

Absorbance of HbA1c

HbA1c % = ---------- X 10 X Temp. factor (Ff)

Absorbance of THb

Tf for Assay at 23 ± 20C = 1.0

Tf for Assay at 300C = 0.7

Finally, the pooled information is analyzed using appropriate statistical methods. The interpretation of HbA1c test in this study is as follows:

Normal - 4 - 6%

Good Control - 6.1 - 7%

Fair Control - 7.1 - 8%

Poor Control-> 8%.

RESULTS

1)Age Distribution:

Maximum incidence of acute cardiac state was observed in age group between 61 to 70 years, accounting for 49 (31%) patients. Youngest was 30 years old male and suffered UA. Oldest was 102 years male, who had NSTEMI.

2)Sex Distribution:

In this study of the 156 patients we observed, 111(71%) patients were males and 45(29%) female patients. Maximum incidence of acute cardiac state both in male and female was in the age group of 61-70 years .

Distribution of acute cardiac state among different age group & sex

Table 1

Age groups in years	Males	Females	Total	Percentage
30-40	14	3	17	10.89
41-50	22	3	25	16.02
51-60	29	11	40	25.64
61-70	32	17	49	31.41
71-80	12	11	23	14.74
81-90	2	0	2	1.28
Total	111	45	156	100 %
Percentage	71.15%	28.85%	100%	

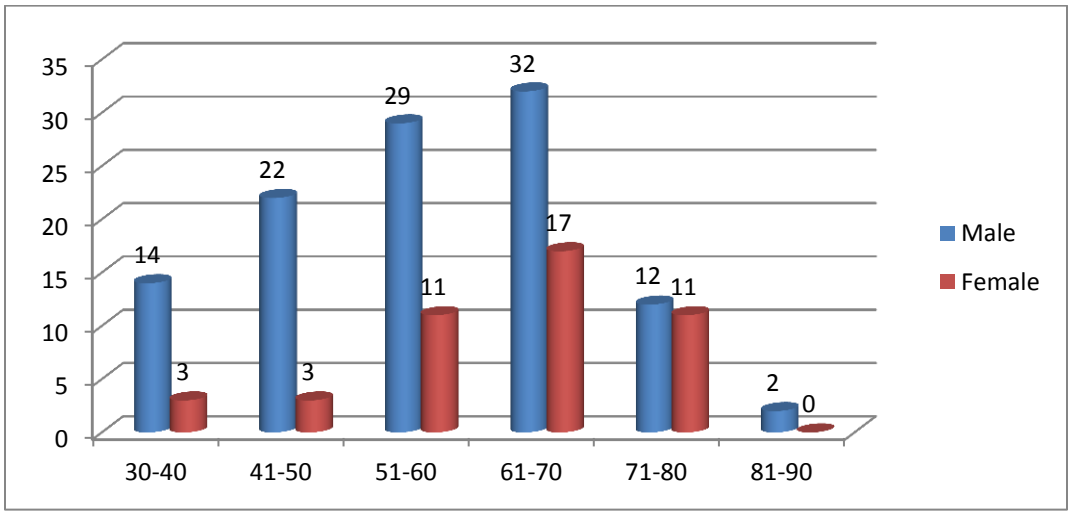


Figure 1. Number of patients in each age group

3)Religion:

Table 2: Religion wise distribution

Religion	No of patients	Percentages
Hindu	132	84.6
Muslim	24	15.4
Total	156	

Out of 50 patients studied, 132 (84.6%) were Hindus and 24(15.4%) were Muslims.

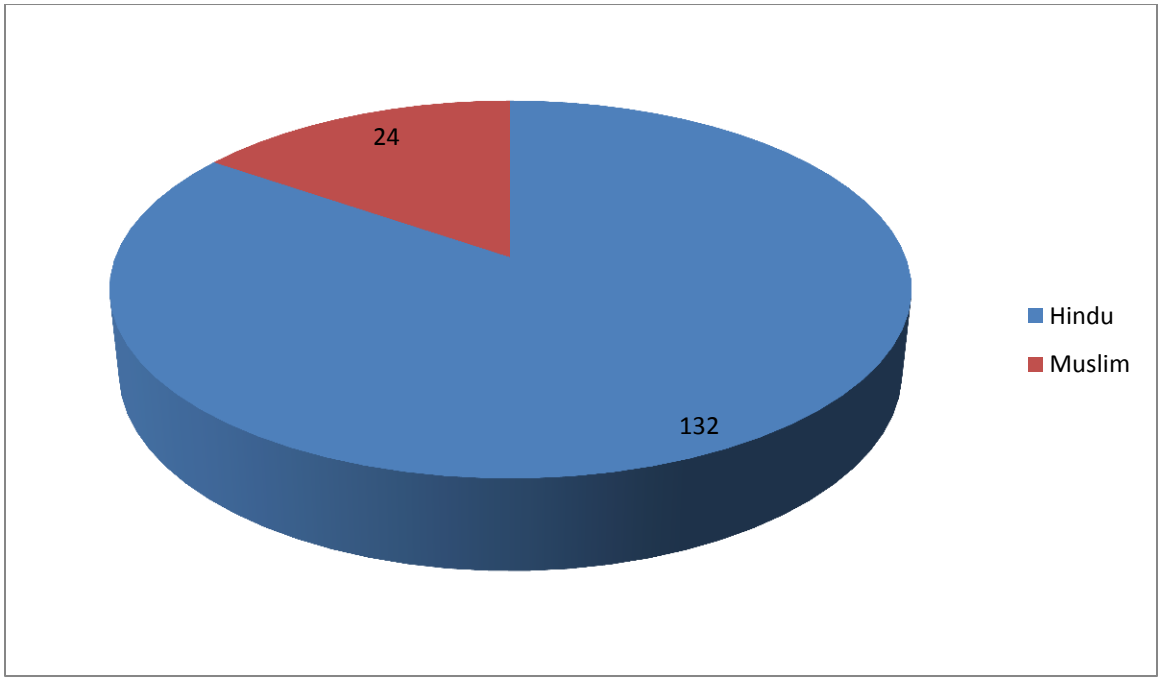


Fig 2: Religion wise distribution

4) Symptoms:

The presenting feature are shown below.

Table 3: Distribution of symptoms

Symptoms	No Patients	Percentage
Chest pain	128	82.05
Breathlessness	46	29.48
Sweating	74	47.43
Palpitation	4	2.56
Others- Giddines, Vomiting	8	5.12

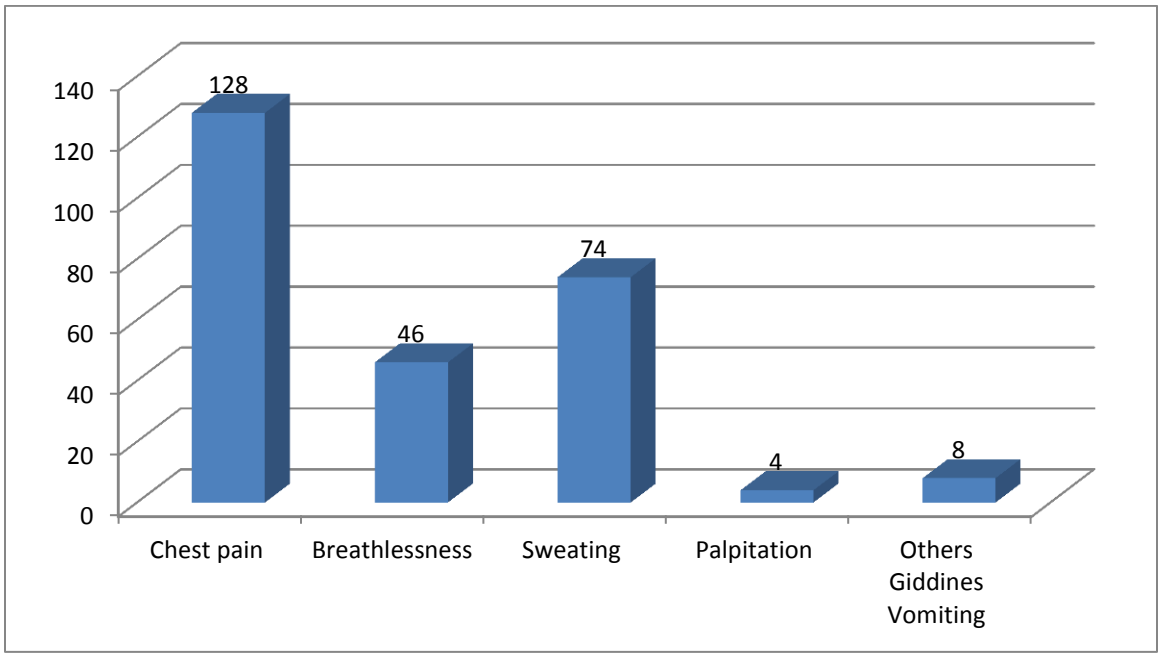


Fig 3: Symptom analysis

Chest pain was the most common symptom accounting for 128(82%) patients, followed by sweating in 74(47%), Breathlessness in 46(29%) Giddiness in 8(5%) patients. palpitations in 5(3%).

5)Risk Factors:

Table 4: Analysis of Risk Factors

Risk factors	No of Patients	Percentage
Smoking	99	63.46
Diabetes Mellitus	35	22.43
Hypertension	47	30.12
Dyslipidemia	40	25.64
Family History	26	16.66
Age > 60	95	60.89
Male gender	111	71.15

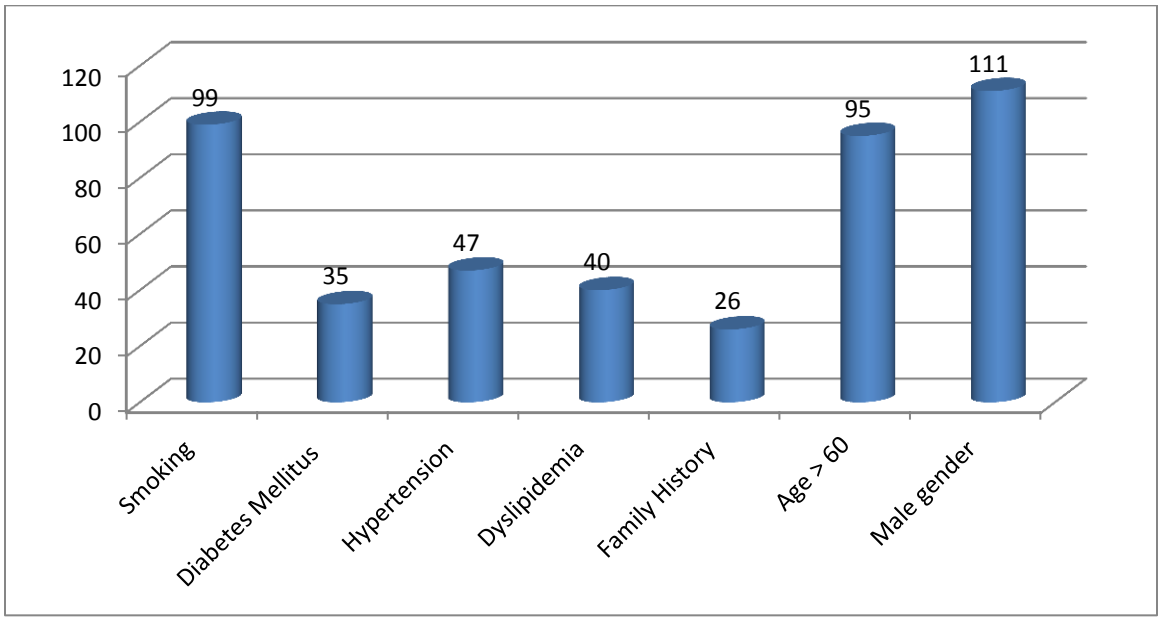


Figure 4. Analysis of Risk Factors

In this study the most common non modifiable risk factor was male gender 111(71%), followed by age factor i.e age (>60 years) accounting for 95(61%) patients and family history of cardiac diseases was noted in 26(17%). The most common modifiable risk factor was smoking accounting for 99(64%) patients followed by , hypertension 47(30%), dyslipidemias 40(27%) and known case of diabetics 35(22%) .

6) DISTRIBUTION OF ACUTE CARDIAC STATES

TABLE 5: ANALYSIS OF ACUTE CARDIAC CONDITIONS

Condition Analysed	Number of Patients	Percentage
Unstable Angina	23	14.74
NSTEMI	45	28.84
STEMI	73	46.79
Accelerated HTN	13	8.33
Cardiomyopathies	2	1.12

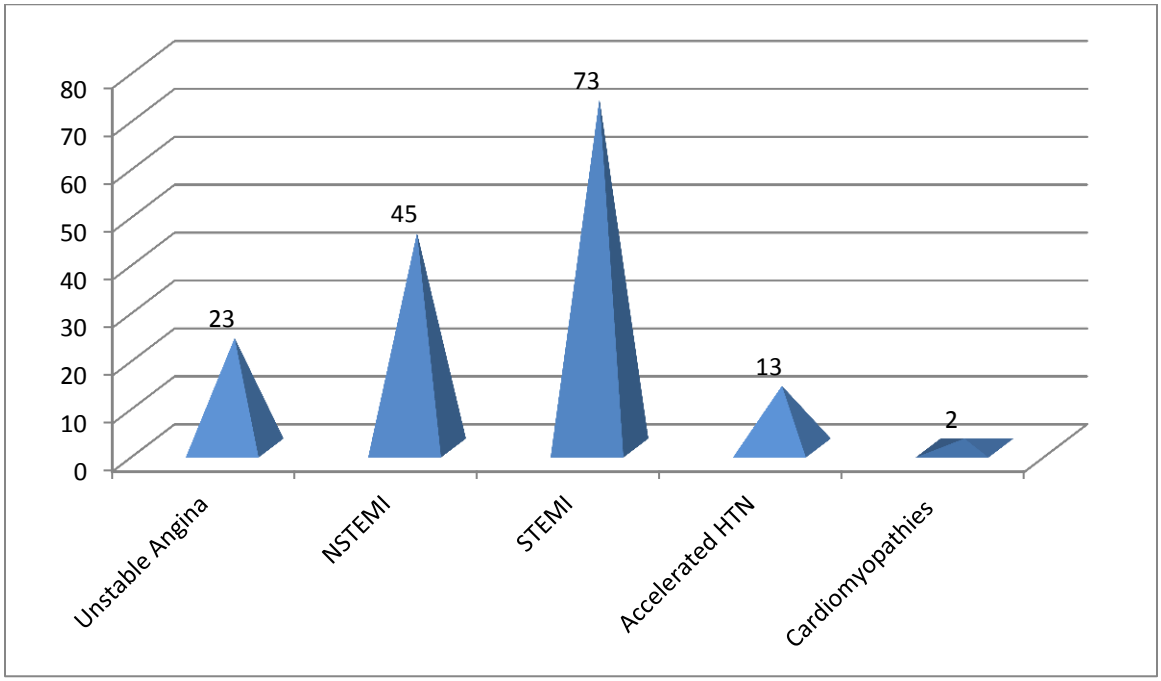


Figure 5: Graph Showing Analysis Of Acute Cardiac States

Out of 156 patients of acute cardiac state studied 73(46.79%) were STEMI , 45(28.84%) patients had NSTEMI , 23(14.74%) patients had unstable angina , 13(8.33%) patients had accelerated hypertension and 2(1.12%) patients had cardiomyopathies .

7)ANALYSIS OF COMPLICATIONS

Table 6: Complications

Complication	No of Patients	Percentage`
Left ventricular failure	49	31.4
Cardiogenic Shock	14	8.97
Bundle branch block	7	4.48
Mitral Regurgitation	12	7.69
VT/VF	7	4.48
Death	8	5.12

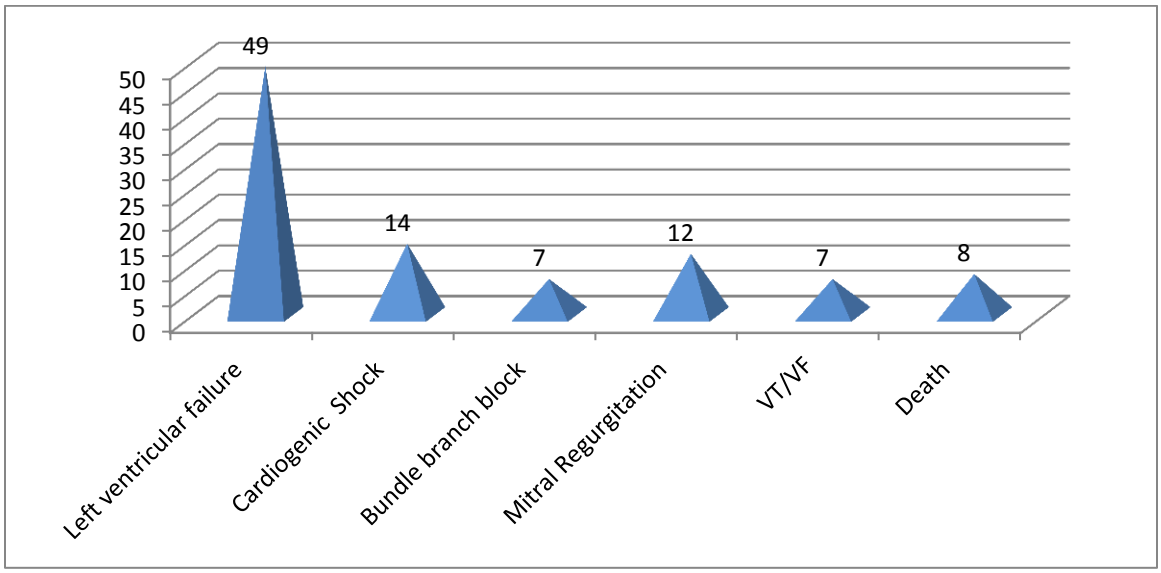


Figure 6: Complications

Left ventricular failure was the most common complication seen in 49(31.4%) patients, followed by Cardiogenic shock in 14 (8.97%) patients, bundle branch block was seen in 7(4.48%) patients , mitral regurgitation was seen in 12(7.79%) patients , ventricular tachycardia and ventricular fibrillation were seen in 7(4.48%) patients and death occurred in 8(5.12%) patients .

HBA1C LEVELS AT ADMISSION

According to chromatographic method of HBA1c estimation, a level equal to or more than 7% is taken as higher value and a level below 7% is taken as normal value . In our study 87(55.76%) patients values less than 7% and 69(44.23% patients had values more than 7%. The following table shows HBA1c levels and their relation to complications.

Table 7: HBA1c in patients with and without complications

HbA1C levels	Acute cardiac state with complications	Acute cardiac state without complication	Total	Percentage
< 7 %	24	63	87	55.76
≥ 7 %	55	14	69	44.23
Total	79	77		
Percentage	50.6 %	49.4 %		

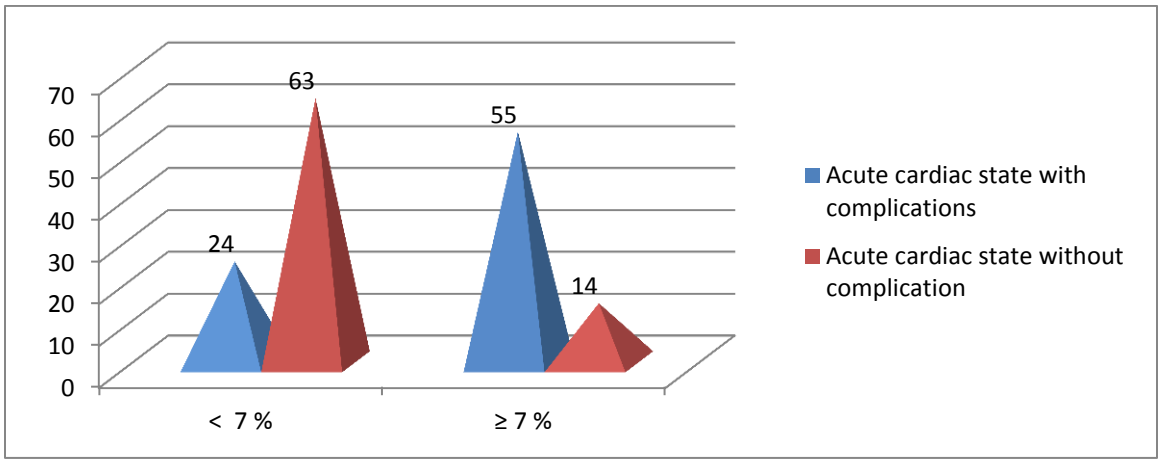


Figure 7:HBA1c in patients with or without complications

Chi Square value found out by Z test (proportions) = 7.65 . At one degree of freedom p value is highly significant ($p<0.01$). This indicates that, the patients with HBA1c values more than 7% during admission are prone for going in to complications . And levels were low in patients who did not undergo complications.

Other Investigations:

Erythrocyte Sedimentation Rate:

As ESR is also a marker of inflammation it may also be raised in acute cardiac state . In this study, ESR was raised in 78(50%) patients, (normal values: Males= 0-17mm after 1 hr; Females= 1-25mm after 1 hr).

Total Leukocyte Counts:

Leukocytosis is seen in the setting of acute coronary syndrome, but we observed raised leukocyte counts only in 63(40.38%) patients.

TABLE 8 :ESR AND TLC VALUES IN ACUTE CARDIAC STATES

Test	Normal	Raised	Percentage
ESR	78	78	50
TLC	93	63	40.38

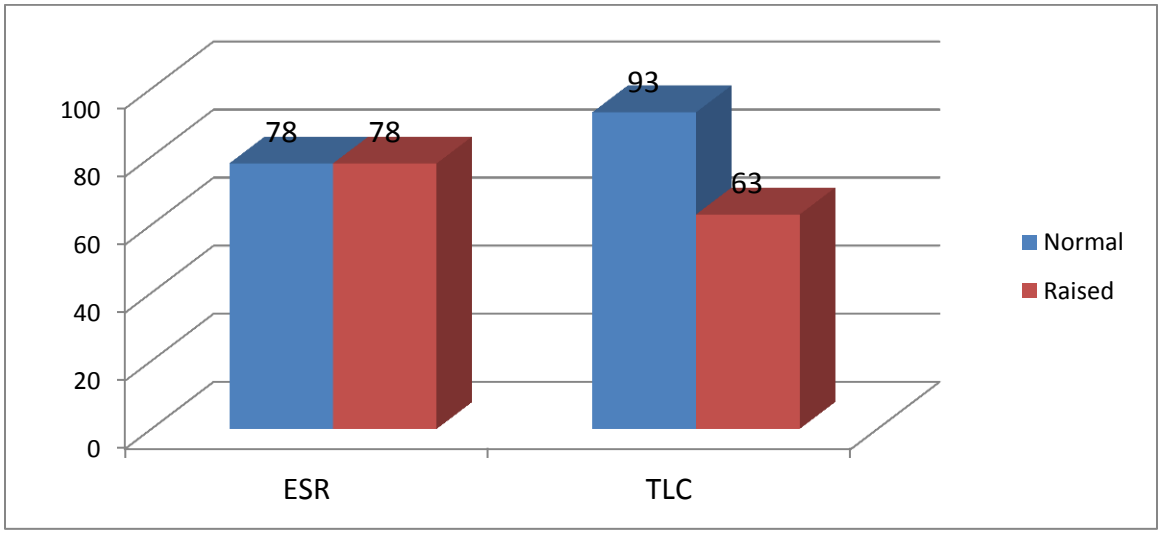


Figure 8 : ESR And TLC Values In Acute Cardiac States

DISCUSSION

Acute cardiac state is now a major cause of morbidity and mortality in our country . The present study consisted of 156 patients admitted with acute cardiac state .The study included both diabetic and non-diabetic patients. The subjects taken into study were admitted in ICCU in our hospital and had fulfilled the exclusion and inclusion criteria .

Heart disease in patients with diabetes mellitus is different from that in non-diabetics . Established diabetics develop coronary artery disease earlier , and more extensive atherosclerosis. Hemoglobin A1c significantly predicted all cause morbidity and mortality in cardiovascular events , even below the threshold commonly accepted for diagnosis of diabetes and is independent of age and classic risk factors [67] .

The present study results show significant differences in the risk factors , clinical presentation and complications of cardiovascular diseases in between patients with HBA1c greater than 7 % and less than 7%. A significant differences was noted in additional risk factors like hypertension dyslipidemia and previous history of coronary heart disease between the two groups. Prospective studies done earlier indicate that all these cardiovascular risk factors continue to act as independent predictors of cardiovascular disease in patients with diabetics [68] .

Fifty three patients in this study were detected to have diabetes for the first time when they presented with an acute cardiac event. Majority of these patients (38/53) had HBA1c levels >7% indicating that these patients had long time pre-existing undiagnosed diabetes . There is some evidence that people with known diabetes were better treated for established cardiovascular risk factors, such as hypertension , dyslipidemia and smoking .

In the rest the hyperglycemia could represent stress hyperglycemia which is a common occurrence in patients admitted to the intensive care units with acute cardiac event. Stress hyperglycemia is defined as a transient elevation of blood glucose due to the stress of the illness . There is no consensus regarding the cut off value to define stress hyperglycemia as various studies have used different values ranging from an admission RBS >125mg/dl to >200mg/dl . The blood sugar levels in stress hyperglycemia are usually between 140mg/dl to 300mg/dl. Forty one non-diabetic patients in our study had blood sugar values above 140mg/dl.[69,70,71]

A important observation made in this study is a highly significant correlation between poorly controlled diabetes as indicated by HBA1c >7% and the acute cardiac states(79% Vs 28%) . A significant higher proportion of patients with Unstable angina , NSTEMI, STEMI , cardiomyopathies and accelerated hypertension had HBA1c levels more than 7% (69%) . Complications like left ventricular failure (71% Vs 29%) , cardiogenic shock (70% Vs 30%) and others were more common in diabetics with HBA1c more than 7%.

This was similar to studies by Bertoni et al [72] , Lu et al [73] and other studies . 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 with (HBA1c <7%), 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]

Khaw and colleagues [75] carefully analyzed the relationship of HBA1c measurement to incident of morbidity and mortality in acute cardiac events in a 6 year cohort study in both diabetic and non-diabetic patients . They observed that there was a 21% increase in acute coronary event for every one percentage point increase in HBA1c and a similar relationships were observed for total mortality (22% for men and 28% for women) per one percentage point increase in HBA1c .

Some early studies reported variable results for the relationship between blood glucose levels and acute cardiovascular events [76-78] . Few prospective studies with all three measures of glucose metabolism are large enough to compare their relative abilities to predict cardiovascular events. In Rancho Bernardo study [79] , HBA1c concentration , but not fasting blood glucose or post-challenge blood glucose level, was significantly related to morbidity and mortality in acute cardiovascular events , independent of other risk factors .

The Hoorn population study [80] reported that post challenge blood glucose and HBA1c were associated with an increase risk of cardiovascular disease . The Framingham Offspring study[81] reported that fasting blood glucose , 2-hour post challenge blood glucose and HBA1c tests were individually significant predictors of cardiovascular events . Nevertheless, HBA1c is a more feasible measure of glucose metabolism in terms of individual predictive value for cardiovascular disease and total mortality .

The correlation between HBA1c and cardiovascular disease among the non diabetics was not statistically significant in our study . Majority of our non diabetic patients i.e 27/66 (40%) had HBA1c less than 5.5% , 26/66(39%) had HBA1c more than or equal to 5.5% but less than 6.0%. and 13/66(21%) had HBA1c more than 6.0% . Khaw et al [75] reported that macrovascular complications start taking place at lower blood sugar levels than the diagnostic cut off values for diabetics. Selvin et al[82] found no risk of cardiovascular events in patients with HBA1c <4.6%. However for every one percentage increase in HBA1c over 4.6%, there was a 2.5 times risk of cardiovascular disease.

Comparison to Other Studies:

Elizabeth Mani et al conducted a prospective study in 2006 in which 166 patients admitted to ICU with acute cardiac state (unstable angina ,NSTEMI, STEMI ,accelerated hypertension, cardiomyopathy)were studied. They concluded that there was a significant direct correlation between HbA1c and severity and complications of heart disease .A large number of patients presenting with acute cardiac states i.e 97.2% had HbA1C values >=5.[13]

Chi Yuen chan et al conducted a retrospective study in 317 patients admitted with acute cardiac state They concluded that majority of these patients had higher value of HbA1c and higher values of HbA1c are associated with increased short term complications .[14]

Stamler J Vaccaro et al conducted a study between 1973 to 1975, they concluded that individuals with acute cardiac conditions had higher value of HbA1c and had increased rates of complications of acute cardiac state .[14]

Kelly J hunt et al conducted a study in 4996 peoples and concluded that increased levels of HbA1c in acute cardiac state were associated with increased rates of complication in acute cardiac state.[15]

Garcia MJ et al conducted a study in patients with acute cardiac states and concluded that cardiovascular mortality is twice in men with HBA1C >7% and four times in women with HBA1c >7 % compared to their counterparts with HBA1C <7 %.[83]

Haffner SM et al conducted a study in 1998 in patients admitted with acute cardiac states and concluded that HBA1C more than 7% are associated with significant increase in the risk of cardiac events and cardiac deaths .[84]

Gerstein HC et al conducted a study in 2004 in patients with increased HBA1C and concluded that the correlation between higher HBA1C levels and increased cardiovascular morbidity occurs even before the diagnosis of clinical diabetes .[85]

Dilley J et al conducted a study in Asian Indians in 2007 and concluded that increased values of HBA1C are found in patients with metabolic syndrome and coronary artery diseases and increased HBA1c levels have a increased rate of morbidity and mortality in patients with cardiac diseases.[86]

Khaw KT et al in 2004 found a continuous and significant relationship between HBA1C , cardiovascular events and all cause mortality whereby persons with lower values of HBA1C had lowest rates of cardiovascular disease and mortality . They found

a one percentage point increase in the HBA1C to be associated with a relative risk of death of 1.24 in men and 1.28 in women . [75]

Selvin E et al conducted a study in 2004 in patients with acute cardiac states and found no risk of coronary artery diseases in patients with HBA1c less than 4.6%. However for every one percentage increase in HBA1c over 4.6%, there was a 2.5 times risk of cardiovascular diseases and increased levels of HBA1c are associated with increased rates of complications and death . [82]

CONCLUSION

1) HBA1c levels on admission serves to identify high risk patients in the setting of acute cardiac states . The effective risk stratification provided may be of specific value for early therapeutic decision making and patient treatment in the heterogeneous population of patients presenting with acute cardiac states.
2) Raised HBA1c levels are independent markers of adverse outcomes.

SUMMARY

1. In this study, 111(71%) patients were males and 45(29%) female patients.
2. Maximum incidence of acute coronary syndrome was observed in age group between 61 to 70 years, accounting for 49 (31%%) patients.
3. Out of 50 patients studied, 132 (84.6%) were Hindus and 24(15.4%) Muslims.
4. Chest pain was the most common symptom accounting for 128(82%) of patients
5. In this study the most common modifiable risk factor was Smoking, accounting for 99(63.46%) patients followed by hypertension and dyslipidemias.
6. Out of 156 patients with acute cardiac states , 73(46.79%) patients had STEMI.
7. Out of 156 patients with acute cardiac states , 79(50.6) had developed complications .
8. Left ventricular failure was the most common complication seen in 49(31.4%) patients.
9. ESR was raised in 50% patients and TLC were raised in 40.38%
10. The HBA1c levels more than 7 were seen in 69(44.23%) patients of acute cardiac states and 55 patients developed complications. This was statistically significant.

BIBLOGRAPHY

1. WHO. WHO Statis.Rep., 1972: 25:430
2. Gupta R. Burden of coronary heart disease in India. Indian Heart J 2005; *57:632-38.*
3. Pahlajani DB. Myocardial infarction. In: Shah SN. API textbook of medicine.7th revised ed: The association of physicians of India, Mumbai; 2006:441-446.
4. Selwyn AP, Braunwald E: Ischemic Heart Disease. In: Harrison's Principles of Internal Medicine, 16th eds, Kasper et al (eds).McGraw-Hil; 2005**:**1434-43
5. Keith A,Website.Stress hyperglycemia and enhanced sensitivity to myocardial infarction .Current Hypertension Reports 2008;10:78-84.
6. Braunwald E. The Simon Dack lecture. Cardiology: The past, the present, and the future. *J Am Coll Cardiol* 2003; 42:2031-41.
7. Stanek V, Progress in the therapy of ischemic heart disease, *Kapitoly z kardiologie* 2002; 4:3-11.
8. 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.
9. Paul Durrington: Hyperlipidemias-Diagnosis and Management 2000:232-236
10. Burton ES**:** ST-elevation Myocardial Infarction. . In; Cecil's textbook Of Medicine 22nd eds Philadelphia, WB Saunders; 2004.410-17.
11. Pearl R.Tobacco smoking and longevity. Science 1938; 87:216.
12. Luce BR, Schweitzer SO. Smoking and Alcohol Abuse: A Comparison of their economic consequences. N Engl J Med 1978; 298:569-71.

13. Elizebeth Mani,Mary John , Rajneesh Calton .Impact of HbA1c on acute cardiac states .Japi , June 2011, vol-59 ;356-59.
14. Chi yun chan , Rujije li , Joseph Yat Sun ,Qing Zhang , Chin Pang chan , Ming Dong et al ; The value of admission HbA1c level in patients with acute coronary syndrome ;June 2011. Clin –Cardiol, 34,8,507,-2.
15. Haffner SM , Stern MP , Hazuda HP .Jama 1990; vol 263 ;2893-98.
16. Kelly J Hunt , Ken Williams , Helen P Hazuda , Michael P Sten , Steve m Haffner, www.huntke@musc.edu , 2006.
17. K.K.Sethi, Ischaemic Heart Disease .In A P I Text Book of Medicine Vol , 8th edition ,2008.509.
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; p-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-Hil, New York 2005.1243-1263
25. Chumny S. "Blood supply of heart"; Lasts anatomy- regional and applied; 10th Edn; 2000; p-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 eds, Elseviner 2005.1014-1018.
27. Kumar V, Abbas AK, Fausto N, Pathologic basis of diseases; 7th Edn; Philadelphia: Elsevier; 2004; p 572-581
28. Barkhoff D, Weisfeldt ML. Cardiac Function and its Circulatory Control. In; Cecil's textbook Of Medicine 22nd eds 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 Edn; Delhi; Oxford university press; 1990; p131-155
35. Peter J. Zimetbaum et al; "Use of electrocardiogram in acute MI"; *NEJM* 2003; 348; p 933-940
36. Tierney LM Jr, Mc Phee SJ, Papadakis MA; CMDT 2005; 44th Edn; New York; Mc Graw Hill; 2005; p- 346-355
37. R. Wayne Alexander , "Diagnosis and management of patients with acute myocardial infarction"; Hurst's The Heart; 9th Edn; Chap-47; p-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; p- 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; p- 1455-1459
42. Dittrich H, Elizabeth G, Nicod P, Cali G, Henning H, Ross J. Acute myocardial infarction in women: influence of gender on mortality and prognostic variables. Am J Cardiol 1988;62:1-7.

43. Huisman TH, Martis EA, Dozy A (1958). "Chromatography of hemoglobin types on carboxymethylcellulose". J. Lab. Clin. Med. 52 (2): 312–27.
44. Bookchin RM, Gallop PM (1968). "Structure of hemoglobin A1c: nature of the N-terminal beta chain blocking group". Biochem. Biophys. Res Commun. 32 (1): 86–93.
45. Rahbar S, Blumenfeld O, Ranney HM (1969). "Studies of an unusual hemoglobin in patients with diabetes mellitus". Biochem. Biophys. Res. Commun. 36 (5): 838–43.
46. Bunn HF, Haney DN, Gabbay KH, Gallop PM (1975). "Further identification of the nature and linkage of the carbohydrate in hemoglobin A1c". Biochem. Biophys. Res. Commun. 67 (1): 103–9.
47. Koenig RJ, Peterson CM, Jones RL, Saudek C, Lehrman M, Cerami A (1976). "Correlation of glucose regulation and hemoglobin A1c in diabetes mellitus". N. Engl. J. Med. 295 (8): 417–20.
48. Bunn HF, Kenneth H, Gabbay, Gallop M. The glycosylation of haemoglobin: Relevance to diabetes mellitus. Science 1978; 200:21-5.
49. Trivelli LA, Ranney HM, Lai HT. Haemoglobin components in patients with diabetes mellitus. N Engl J Med 1971; 284: 353-7.
50. Perutz MF. Structure of haemoglobin. Brookhaven symposia in biology 1960; 13:165-83.
51. Guyton, Arthur C, Hall JE. Textbook of medical physiology. 11th edn. Phiadelphia: Elsevier Saunders; 2006: 511.
52. Ganong WF. Review of medical physiology. 22nd edn. Lange; 2005: 534.

53. Leow MKS. Configuration of the haemoglobin oxygen dissociation curvedemystified: a basic mathematical proof for medical and biological sciencesundergraduates. Adv Physiol Edu 2007; 31: 198-01.
54. Bunn HF, Kenneth H, Gabbay, Gallop M. The glycosylation of haemoglobin:Relevance to diabetes mellitus. Science 1978; 200:21-5.
55. Trivelli LA, Ranney HM, Lai HT. Haemoglobin components in patients withdiabetes mellitus. N Engl J Med 1971; 284: 353-7.
56. Proenca MC, Martinsesilva J. Glycosylated haemoglobin – structure, importanceand methods of determination. Acta med Port 1981; 3(3): 233-7.
57. Svendsen PA, Christiansen JS, Welinder B, Nerup J. Fast glycosylation ofhaemoglobin. Lancet 1979; 1: 603-7.
58. Ditzel J, Forsham PH, Lorenzim. Rapid fluctuations in glycosylated haemoglobinconcentration as related to acute changes in blood glucose. Diabetologia 1980; 19: 403-4.
59. Weykamp CW, Penders TJ, Muskiet FAJ, Vanderslik W. Influence ofhaemoglobin variants and derivatives on glycohaemoglobin determinations asinvestigated by 102 laboratories using 16 methods. Clin Chem 1993; 39: 1717-23.
60. Nathan DM, Singer DE, Hurxthal K, Goodson JD. The clinical information value of the Glycosylated haemoglobin assay. NEJM 1984; 310: 341-6.
61. Fluckiger R, Mortensen HB. Review: Glycated haemoglobins. J of Chromatography 1988; 429:

62. Sosensko, J.M. et al. “Glycosylation of various haemoglobin in normal and diabetic subject”, diabetes care 1980; 3: 590-3.
63. Fluckinger. R; et al. “Haemoglobin carbomylation in uremia”. N.Engl. J. Med.1981; 304: 8237
64. Verillo A: et al. Nunziata. V: Diabetologia 1983; 24: 291
65. Peacock I. Glycosylated haemoglobin: measurement and clinical use. J Clin Pathol 1984; 37: 841-51.
66. Bunn HF, Haney DN, Kamin S, Gabbay KH, Gallop PM. The biosynthesis of human haemoglobin A1c, slow glycosylation of haemoglobin in vivo. J Clin Invest 1976; 57: 1652-9.
67. Goraya TY,Leibson CL,PalumboPJ et al .Coronary atherosclerosis in diabetis mellitus. A population based study. J Am Coll Cardio 2002;40:946-53.
68. Brezinka V, Padmos I.Coronary heart disease risk factors in women.Eur Heart J 1994;15:1571-84.
69. Claresa L,Meeta S,Case study, The recipe for diabetes success in the hospital .Diabetes Spectrum 2002;15:40-43.
70. Keith A,Website.Stress hyperglycemia and enhanced sensitivity to myocardial infarction .Current Hypertension Reports 2008;10:78-84.
71. Umpreizz GE, Issac SD,Bazargan N,et al.Hyperglycemia:An independent marker of in-hospital mortality in patients with undiagnosed diabetes.J Clin Endocrinol Metab 2002;87:978-982.
72. Bertoni Ag, Hundly Wg,Massing MW,et al. Heart failure prevalence , incidence and mortality in the elderly with diabetes . Diabetes Care 2004;27:699-703.

73. Lu WQ,Resnick HE,Jablonski KA,et al .Effects of glycemic control on cardiovascular disease in diabetic American Indians. The strong Heart study. Diabet Med 2004;21:311-7.
74. Cai L, Li,W, Wang G et al. Hyperglycemia induced apoptosis in mouse myocardium. Mitochondrial cytochrome C mediated caspase-3 activation pathway.Diabetes 2002;51:1938-48.
75. Khaw KT,Wareham N,Bingham S,et al. Association of hemoglobin A1c with cardiovascular disease and mortality in adults.The European prospective Investigations into cancer in Norfolk. Ann Intern Med 2004;141:413-20.
76. Pylora K,Savolainen E, Lehtovirta E, Punsar S et al . Glucose tolerance and coronary heart disease : Helseinki policeman study .J chronic Dis.1979;32;729-45.
77. Balkau B, Shipley M, Pylora k et al . High blood glucose concentration is a risk factor for mortality in middle aged nondiatic men.20 year follow up in the Whitehall study , the Paris Prospective study and the Helsinki Policeman study . Diabetis care 1998;21:360-7.
78. Scheidt Nave C, Barrett Connor E, Wingard Dl et al . Sex differences in fasting glycemia as a risk factor for IHD death. Am J Epidemiol.1991;133:565-76.
79. Park S, Barrett Connor E, Wingard Dl et al .GHb is a better predictor of cardiovascular disease than fasting or post cahallenge plasma glucose in women without diabetes. The Rancho Bernardo Study. Diabetes care.1996;19:450-6.

80. de Vegt F, Dekker JM, Ruhe HG et al .Hyperglycemia is associated with all cause and cardiovascular mortality in the Hoorn population. The Hoorn Studt.Diabetologia.1999;42:26-31.
81. Meigs Jb, Nathan Dm, D'AgastinoRb et al . Fasting and post challenge glycemia and cardiovascular disease risk:the Framingham Offspring study.Diabetes Care.2002;25:1845-53.
82. Selvin E,Marinopoulos S,Berkinbit G et al .Meta analysis Glycolated hemoglobin and cardiovascular disease in diabetes mellitus. Ann Intern Med 2004;141:421-31.
83. Garcia MJ,McNamara PM,Gordon T,Kannel WB.Morbidity and mortality in diabetics in the Framingham population. Diabetics 1974;23:105-116.
84. Haffner SM,Lehto S,Ronnemaa T,Pyorala K,Laakso M. Mortality from coronary artery disease in subjects with type 2 diabetis and in non diabetic subjects with or without prior myocardial infarction.N Engl J Med 1998;339:229-34.
85. Gerstin Hc,Glycosylated Hemoglobin.Finally ready for prime time as a cardiovascular risk factor. ANN Intern Med 2004;141:475-6.
86. Dilley J,Ganesan A,Deepa R et al, Association of A1c with cardiovascular disease and metabolic syndrome in Asian Indians with normal glucose tolerance.Diabetes Care 2007;30:1527-32.

ANNEXURE I

Ethical Committee
BIJAPUR-586103
OUT WARD
No 27/2011
Date 21-10-11
B.L.D.E. UNIVERSITY'S 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 20-10-2011 *at* 10-30am *to scrutinize the Synopsis/Research projects of postgraduate/undergraduate student/Faculty members of this college from Ethical Clearance point of view. After scrutiny the following original/corrected & revised version synopsis of the Thesis/Research project has been accorded Ethical Clearance.*

Title "Impact of HBA1C on acute cardiac state"

Name of P.G./U.G. student/Faculty member Dr. Gous. M. Farash
Dept of Medicine

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

DR.M.S.BIRADAR,
CHAIRMAN
INSTITUTIONAL ETHICAL COMMITTEE
BLDEU'S, SHRI.B.M.PATIL
MEDICAL COLLEGE, BIJAPUR.
Chairman
Ethical Committee
BLDEA'S Shri. B.M. Patil
Medical College
Bijapur-586103

Following documents were placed before E.C. for Scrutinization
1) Copy of Synopsis/Research project.
2) Copy of informed consent form
3) Any other relevant documents.

o/c

ANNEXURE II

CONSENT FORM

TITLE OF RESEARCH: "Impact of HBA1c on acute cardiac states both in diabetic and non-diabetic patients."

GUIDE : DR. SHASIDHAR S DEVARMANI

P.G. STUDENT : DR. GOUS MOHIDDIN FARASH

PURPOSE OF RESEARCH:

I have been informed that the purpose of this research is to study the impact of HBA1c in acute cardiac states.

PROCEDURE:

I understand that a detailed medical history of mine will be taken & that I shall have to undergo a complete physical examination and be subjected to investigations.

RISKS AND DISCOMFORTS:

I understand that there is no risk involved and I may experience mild pain during the above-mentioned procedures.

BENEFITS:

I understand that my participation in this study will help in determining the relationship between increased HBA1c and complications in acute cardiac states.

CONFIDENTIALITY:

I understand that the medical information produced by the study will become a part of hospital record and will be subjected to confidentiality and privacy regulations of hospital. If the data is used for publications, the identity of the patient will not be revealed.

REQUEST FOR MORE INFORMATION:

I understand that I may be asked for more information if required, for inclusion into study at any time.

REFUSAL OR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and I may refuse to participate or withdraw from the study at any time.

INJURY STATEMENT:

I understand that, in the unlikely event of injury to me anytime during the study, I shall get medical treatment for the same but no further compensations.

CONSENT STATEMENT

I, _____ unreservedly and in my full sense give my complete consent to take part in this study. The risk and benefits as mentioned above have been read by me/explained to me in my vernacular language.

Signature of Patient

ANNEXURE III

BLDE'S SHRI B.M.PATIL MEDICAL COLLEGE

HOSPITAL AND RESEARCH CENTRE, BIJAPUR

SCHEME OF CASE TAKING

Name: CASE NO:

Age: IP NO:

Sex: DOA:

Religion: DOD:

Occupation:

Residence:

Presenting complaints with duration:

Chest pain

-Duration

-Site

-Radiation

-Type

-Aggravating factors

-Relieving factors

Palpitation

-Duration

-Site

-Radiation

-Type

-Aggravating factors

-Relieving factors

Breathlessness

-Duration

-Grade

-Orthopnea

-PND attack

Other symptoms

-Sweating

-Haemoptysis

-Cough

History of presenting complaints:

Past History:

History of hypertension

History of diabetes mellitus

Past history of IHD

Personal History:

Diet

Appetite

Sleep

Bladder and bowel habits :

Smoking/Tobacco chewing/Snuff Inhalation

Duration

Number of cigarettes/beedis pack year smoked

Amount of tobacco chewed/snuff inhaled

Alcohol

Duration

Quantity/Frequency

Type

Family History:

History of suggestive of Ischemic Heart Disease/hypertension/ diabetis mellitus

Treatment History :

General Physical Examination

Pallor:	present/absent
Icterus:	present/absent
Clubbing:	present/absent
Generalized Lymphadenopathy:	present/absent
Built:	Poor/Middle /Well
Nourishment:	Poor / Middle / Well

Vitals

PR:

BP:

RR:

Temp:

SYSTEMIC EXAMINATION.

- Cardiovascular system

  Arterial system

  BP

  Pulse

  -PR

  -Rate

  -Rhythm

  -Volume

  -condition of the arterial wall

  -Comparision of the arterial wall

  -Radio femoral delay

  -Any special character

  -Other peripheral pulses

  Ulnar artery

  Brachial artery

  Subclavian artery

  Carotid artery

  Femoral artery

Popliteal artery

Posterior tibial artery

Dorsalis pedis artery

Venous System

Engorged veins in neck

JVP

Inspection

-Precordial bulge

-Parasternal bulge

-Epigastric pulsation

-Visible apical impulse

-Any engorged veins

Palpation

Apical impulse

Site

Character

Thrill

Palpable P2

Percussion

Auscultation

Mitral area

Heart sounds

Murmurs

Tricuspid area

Heart sounds

Murmurs

Aortic area

Heart sounds

Murmurs

Pulmonary area

Heart sounds

Murmurs

- Respiratory System

Position of treachea

Chest symmetry

Liver dullness

Breath sounds

Any added sounds

Per Abdomen

Organomegaly

Any evidence of free fluid

Central Nervous System

Consciousness

Orientation

Any focal neurological defect

INVESTIGATIONS

HAEMATOLOGY –

Haemoglobin	gm %
Total WBC counts	Cells/mm^3
Differential counts -	
Neutrophils	%
Lymphocytes	%
Eosinophils	%
Monocytes	%
Basophils	%
ESR	mm after 1 hour

BIOCHEMISTRY–

Random blood sugar	
Blood Urea	
Serum creatinine	
HBA1c	

URINE EXAMINATION -

Protein	
Sugar	
Microscopy	

Lipid Profile

Chest X Ray

ECG

CPK-MB

<u>FINAL DIAGONOSIS</u> :

ANNEXURE IV

KEY TO MASTERCHART

M	MALE
F	FEMALE
h	HINDU
m	MUSLIM
DM	DIABETIS MELLITUS
H	HYPERTENSION
D	DYSLIPIDEMIA
S	SMOKING
FY	FAMILY HISTORY
B	BREATHLESSNESS
C	CHEST PAIN
S	SWEATING
P	PALPITATION
N	NORMAL
E	ELEVATED
LVF	LEFT VENTRICULAR FAILURE
CS	CARDIOGENIC SHOCK
MR	MITRAL REGURGITATION
LBBB	LEFT BUNDLE BRANCH BLOCK
RBBB	RIGHT BUNDLE BRANCH BLOCK
VT	VENTRICULAR TACHYCARDIA
SVT	SUPRAVENTRICULAR TACHYCARDIA
VPC	VENTRICULAR PREMATURE COMPLEXES
DCM	DILATED CARDIOMYOPATHY
RLGN	RELIGION
R/F	RISK FACTORS
HSTRY	HISTORY
DURT	DURATION
BP	BLOOD PRESSURE
DGNS	DIAGNOSIS
RBS	RANDOM BLOOD SUGAR
ESR	ERYTHROCYTE SEDIMENTATION RATE
TLC	TOTAL LEUCOCYTE COUNT
CPTN	COMPLICATION

ANNEXURE-V

MASTERCHART

Sl No	IP NO	NAME	AGE	SEX	RLGN	R/F	HSTRY	DURT	BP	DGNS	Hba1c	RBS	ESR	TLC	CPTN
1	18280	VIJENDRA.K	60	M	h	DM,H,S	C,B	6 HRS	170/100	NSTEMI	9.2	447	E	E	LVF
2	19348	GANGAPPA.G	34	M	h	H,S	C	2 D	138/80	NSTEMI	6	137	E	N	-
3	19482	BABUSAB.K	32	M	h	H	S	1 D	210/140	ACC HTN	7.2	240	N	N	LVF
4	24385	SAVITRI.B	35	F	h	H,F	C,B	1 D	220/130	ACC HTN	5.7	180	N	N	-
5	25111	BAYAMMA.B	75	F	h	DM	C,B	1 D	130/80	UA	11.4	420	N	N	-
6	25175	JANABAI.C	61	F	h	H,D	C,B	2 D	130/80	STEMI	5.4	102	N	E	LVF
7	25382	ARAVIND.C	49	M	h	S,F	C	1 D	120/80	UA	6.6	180	E	E	-
8	26186	GURAPPA.K	56	M	h	H,S	C.B	2 HRS	116/80	STEMI	7.3	148	N	E	RBBB,LVF
9	26297	HANAMANTH.P	37	M	h	S,F	C,S	3 HRS	146/80	STEMI	6.8	208	N	N	-
10	25662	SHANTA.H	73	F	h	D	B	1 D	SBP-60	STEMI	9	318	E	E	CS,LVF
11	26020	DR MALLAPPA	60	M	h	S,	C	4 HRS	156/90	NSTEMI	8.5	360	N	E	-
12	26867	UMAKANTH.S	40	M	h	S,F	C	30 MTS	140/90	NSTEMI	8.6	218	N	N	VPC
13	22768	YAMAJI	59	M	h	S,H,DM	C,B	1 D	130/76	UA	9.8	250	E	N	LVF
14	26631	GOPAL.K	55	M	h	S,F	C	2HRS	166/90	STEMI	8.8	237	N	N	-
					h										
15	27214	SHAKIL.K	44	M	m	S,F	C	2 D	160/100	STEMI	5.7	90	N	N	-
16	27240	MAMTAZ.I	63	F	m	DM,H	B	4 HRS	170/100	STEMI	10	398	E	E	LVF.MR
17	27091	SUSALABAI	65	F	h	H,D	C	1 D	218/100	ACC HTN	5.6	218	N	N	-
18	119	KASTURI.S	48	F	h	H,DM	C,B	2 D	104/80	STEMI	8.4	130	N	E	LBBB,DEAD
19	27360	KAREKEPPA.K	55	M	h	S	C	2 D	150/90	NSTEMI	6.7	246	N	N	-
20	858	ABDUL.R	80	M	m	H,S,D	C	2D	140/80	STEMI	5.8	151	N	E	LVF

21	2737	RUDRAGOUDA.B	65	M	h	S	C	2 HRS	110/80	STEMI	4.8	198	N	N	-
22	3532	MALLAPPA.A	48	M	h	S,F	C,S	2 HRS	170/80	STEMI	6.7	229	N	E	LVF
23	7074	ADIVEWWA.S	70	F	h	-	C	3 HRS	140/90	STEMI	5.1	195	E	N	-
24	17015	DONGRISAB	70	M	h	S	C,S	2 HRS	170/90	STEMI	5.3	197	N	N	LVF
25	16448	PARVATI.A	60	F	h	F,D	B	4 HRS	150/80	UA	7.5	160	E	E	-
26	18793	HAFIZABI.B	65	F	m	H	C,S	4 HRS	70/50	STEMI	7.8	170	E	E	CS,VT, DEAD
27	8137	GURRAPPA.T	65	M	h	-	B,S	2 D	120/90	NSTEMI	6.7	106	E	E	-
28	8289	ALISAB.D	60	M	m	D,S	C,B	15 D	156/80	NSTEMI	5.5	122	N	E	RBBB
29	7210	ISHRAWWA	75	F	h	H	C,S	5 D	146/90	STEMI	7.6	135	E	E	LVF
30	7317	SAROJINI.K	72	F	h	H	C.B	3 D	208/100	ACC HTN	7.1	275	N	N	LVF
31	6083	RAMAPPA.H	75	M	h	S	C	3 D	104/70	NSTEMI	5.8	210	N	N	-
32	6545	NINGAPPA.H	48	M	h	S	C,S	4 HRS	120/70	STEMI	6.8	110	N	N	-
33	17031	SHABANA.M	60	F	m	H,DM	B,S	1 D	120/80	STEMI	7.4	178	E	N	LVF
34	17083	TIPANNA.T	65	M	h	S	C	1 D	146/100	STEMI	6.5	162	E	E	MR
35	15905	MOHIUDDIN .I	83	M	m	H	C,S	1 D	160/80	NSTEMI	6.9	132	E	E	-
36	16466	SIDDAPPA.B	55	M	h	S	B,S	7 D	74/50	NSTEMI	5	109	E	E	VT,DEAD
37	3602	KALLAPA.D	65	M	h	S	C	15 D	80/60	NSTEMI	6.4	168	E	N	CS
38	10321	YAMANAWWA.K	65	F	h	DM,H	C,B,P	1 D	210/120	ACC HTN	10.8	228	N	N	-
39	10009	BASALINGAYA.G	65	M	h	S,H	B,P	3 D	216/120	ACC HTN	7.2	178	E	N	LVF
40	10206	SHIVARAYA.K	51	M	h	DM,S	C,S	3 HRS	122/76	UA	7.	251	N	N	-
41	8905	AAMIR H	72	M	m	S	C,S	1 D	108/60	STEMI	7.2	180	E	E	LVF
42	9180	NASIR PATEL	50	M	m	S	C,S	1 D	142/90	STEMI	6.6	80	N	N	-
43	13866	MOINUDDIN.I	60	M	m	DM,S	C	3 HRS	140/80	STEMI	6.5	175	N	E	LVF
44	11057	SHANKREPPA	50	M	h	S,F,D	C,S	4 HRS	150/90	NSTEMI	9.6	326	E	N	
45	13214	PUSHPA.R	60	F	h	H	B	4 HRS	100/70	UA	6.4	212	N	N	-
46	12819	SANJEVAPPA.G	75	M	h	DM,S	C,S	2 D	130/70	NSTEMI	7.4	251	E	E	
47	13630	GOKUL.M	62	M	h	S	C,S	1 HR	140/90	UA	5.2	138	N	N	-
48	13637	BANDAGIRSAB	65	M	m	S	C,S	6 HRS	150/90	UA	6.5	85	N	N	-

49	13743	SHIKANDAR.C	36	M	m	D	C	1 D	110/70	NSTEMI	5.9	91	N	N	LVF
50	13814	SHARADA.R	32	F	h		C,S	1 HRS	104/70	NSTEMI	6.0	214	N	N	-
51	13876	SHIVAJI.G	67	M	h	S	C	1 D	130/180	NSTEMI	6.6	190	N	N	-
52	11629	IMAM.M	61	M	m	DM,H,S	C,S	3 HR	128/80	STEMI	7.0	180	E	E	LVF MR
53	11162	RAMANNA.M	102	M	h		B	1 D	80/50	NSTEMI	7.6	208	N	N	
54	10594	BABU.K	61	M	h	S	S,G	3 HR	110/70	STEMI	8.2	300	E	E	LVF
55	11057	SHANKRAPPA.K	50	M	h	S	C	4 HR	150/90	NSTEMI	9.6	310	E	N	-
56	10637	ANNASAHEB.B	32	M	h	S	G,S	4 HR	122/80	UA	5.4	103	N	N	-
57	10818	BASAMMA.B	45	F	h	DM,H	C	2 HR	110/70	NSTEMI	6.8	199	E	E	-
58	9644	ISHWAR.B	44	M	h	DM,S	S,G	1 HR	150/80	STEMI	7.8	208	N	N	LVF
59	11553	MALLAPPA.B	65	M	h	,H,DMS	S,C	4 D	180/90	NSTEMI	5.5	69	E	E	-
60	10949	RANIBAI.M	65	F	h	H	B,S	1 D	204/106	ACC HTN	7.3	218	E	E	-
61	11092	ARUNKUMAR.M	46	M	h	.H,DM,S	C,S	4 HR	140/90	NSTEMI	5.9	148	N	N	-
62	8850	KASHIBAI.P	65	F	h		C	4 D	120/76	NSTEMI	6	290	E	N	-
63	12422	SAHEBGOUDA	41	M	h	D	C	1 D	156/90	NSTEMI	7.8	131	N	N	-
64	12008	SURYAKANT.H	60	M	h	S	C	4 HR	140/90	NSTEMI	6.7	220	N	N	-
65	12776	RAMESH.N	40	M	h	H,S	C,S	3 D	110/60	STEMI	6.8	168	N	N	MR
66	15662	SHANKRAPPA.D	65	M	h	S,D	P,B	1 D	100/60	DCM	7.6	188	E	E	-LVF
67	12795	MALLIKRJUN.D	59	M	h	H,S	C,S	1 D	120/70	UA	6.9	210	E	N	-
68	12794	UMARSAB.S	62	M	m		C,S	6 HR	160/90	NSTEMI	66	140	N	N	-
69	12672	IMAMSAB.B	40	M	m	S	C	3 D	160/90	NSTEMI	6.1	108	N	N	-
70	12808	KHAIRUNNISSA.H	60	F	m	H,F	G,S	6 HR	160/84	UA	6.4	127	N	N	-
71	14891	SHANTEPPA.B	45	M	h	S,F	C	6 HR	110/80	UA	4.5	240	E	N	-
72	14976	CHANAPPA.M	30	M	h	S	C,S	2 D	116/80	UA	5.9	130	E	N	-
73	14947	BASAVANTAPPA.P	60	M	h	S,D	C,S	30 MIN	200/110	ACC HTN	7.2	238	N	E	LVF
74	14803	ROSHANBEE.P	75	F	m	F	C,S	4 HR	130/80	STEMI	5.2	180	E	N	LVF
75	14234	YALLAWWA.G	65	F	h	H	C,B	2 HR	210/106	ACC HTN	6.8	380	N	E	LVF
76	13734	RAMANGOUDA.C	45	M	h	M	C,S	4 D	160/70	NSTEMI	5	968	N	N	-
77	14141	MAHADEVAPPA.B	58	M	h	H,DM,S	B	2 D	150/80	NSTEMI	5.6	109	N	N	-
78	13970	DHARMU.R	50	M	h	S	C,S	3 D	160/110	STEMI	6.8	120	N	N	LVF

79	15083	GUNDU.R	50	M	h	S,D	C,S	3 HR	130/80	STEMI	5.8	140	E	N	-
80	13103	DEVEDRA.K	70	M	h	H,DM,S	C,S	3 HR	80/40	NSTEMI	10	230	N	E	CS,DEAD
81	13365	SURESH.K	65	M	h	S,D	C	2 D	140/90	STEMI	4.1	102	N	N	LVF
82	15280	BHIMANNA.M	60	M	h	S,DM	C	2 D	80/64	NSTEMI	7.1	160	N	N	LBBB,CS
83	15443	MALLAPPA.M	55	M	h	H,S	C,S	2 D	140/80	NSTEMI	5	128	E	E	LVF
84	15442	POLARAM.P	36	M	h	S,F	C	1 HR	138/80	STEMI	5.2	110	E	E	-
85	13193	VIJAYA.B	48	F	h	DM	C	1 D	150/90	UA	7.4	227	E	N	-
86	14806	ALLAHBAKSHA.M	55	M	m	S,H	C,B,S	6 HR	250/120	ACC HTN	4.8	148	E	E	-
87	15543	MALLAPPA.D	48	M	h	S,D	C	5 HR	110/80	STEM I	5.8	194	N	N	-
88	16004	SIDDALING.K	67	M	h	S	C,S,B	5 HR	150/90	STEMI	7.3	127	E	E	MR,LVF
89	16078	SHIVAJI.A	37	M	h	S	C,S	1 D	126/70	UA	4.9	97	E	N	-
90	15968	GURUPADAPPA	37	F	h	F	C,S	6 D	120/80	NSTEMI	5	172	N	N	-
91	15557	SATTEWWA.N	70	F	h	F	C,S	4 HR	120/80	UA	5.3	103	N	N	-
92	16102	KASTURBAI.P	80	F	h	D	C	6 HR	90/70	STEMI	7.2	240	E	E	LVF
93	15798	HOUSABAI.G	75	F	h		CS	1 D	130/80	NSTEMI	7	182	E	E	-
94	18198	VEERESH U	48	M	h	S,D	C,P	3 HR	230/120	ACC HTN	7.9	261	E	N	LVF
95	18740	MOHAMMED.K	60	M	m	S,F,DM	C	4 HR	550/70	STEMI	7.3	222	E	N	CS,MR
96	19176	ALISAB.N	75	M	m	S,F,D	C,B	1 D	82/56	NSTEMI	8	258	N	E	LBBB
97	7317	SAROJINI.K	72	F	h	H	C	3 D	170/80	UA	7.1	108	N	N	LVF
98	18237	ADVAYYA.M	65	M	h	S	C	6 HR	120/80	STEMI	7.5	205	N	N	LVF,DEAD
99	19053	PARVATI.A	70	F	h	H,DM	C,S	3 HR	170/90	STEMI	7.9	218	E	E	LVF
100	18322	PRAKASH.S	46	M	h	H,S,D	C,S	2 D	146/90	NSTEMI	6.2	238	N	H	-
101	18662	LAKEWWA.S	70	F	h	D	C,S	4 D	110/60	NSTEMI	5.8	119	E	N	-
102	18003	SHIVAPPA.B	70	M	h	S	C,S	4 HRS	120/90	STEMI	7.3	180	N	N	VT,DEAD
103	18863	LALESAB.J	47	M	m	S,D	B	3 D	110/80	NSTEMI	6	186	N	E	-
104	1029	BALASAB G	68	M	h	DM,S	C	1 D	140/90	STEMI	7.2	194	E	N	MR

105	1429	BASAPPA.M	60	M	h	D,S	C	2 D	126/90	STEMI	7.5	169	N	N	LVF
106	3178	LAXMIBAI	60	F	h	DM,H	B,S	15 MIN	210/110	ACC HTN	7.2	278	E	E	LBBB.LVF
107	679	MOHAN	55	M	h	S	C,B	1 D	130/80	UA	5.7	166	E	E	-
108	1429	SHREESAIL	45	M	h	S	C	3 D	110/70	NSTEMI	5.4	212	E	N	-
109	1455	GANGAPPA	50	M	h	S,F	B	4 D	100/60	NSTEMI	6	82	N	N	-
110	1508	BHAGREWWA.S	60	F	h	F	B	2 D	110/80	STEMI	6.7	123	E	N	LVF
111	768	LAKSHAMAN	79	M	h	DM,S	B	3 D	116/80	UA	5.8	128	E	N	-
112	501	MALAMMA	60	F	h	DM,D	C	1 D	140/80	STEMI	5.6	100	N	E	-
113	2761	JUMANNA	60	M	h	DM,H,D,S	C,S	1 D	100/60	STEMI	11.2	260	E	E	SVT
114	1235	CHANDREWWA	65	F	h	-	C,S	1 D	SBP 76	STEMI	5.9	254	N	E	CS
115	1339	HIARABAI.J	72	F	h	D	B,S	1 D	116/70	STEMI	5.8	214	E	N	-
116	643	SHRIKANT	55	M	h	S	C	2 D	96.60	STEMI	5.8	132	N	N	-
117	3820	SAYED.H	65	M	m	DM	S,C	6 HRS	90/60	STEMI	7.8	253	E	N	VT
118	3913	DANDAMMA	55	F	h	D	C	2 D	130/80	STEMI	8.6	145	E	E	CS
119	4364	SHIVAPPA.R	80	M	h	H,S	B	1 D	116/80	UA	6.8	216	E	N	VPC
120	4252	ASAGAR ALI	52	M	m	DM,S	C	4 HRS	80/40	STEMI	7.6	96	N	N	CS
121	4452	RAMALING.A	64	M	h	H,D	C	6 HRS	90/70	STEMI	5.6	137	N	E	-
122	4284	SANGAPPA	77	M	h	S	C,S	15 D	128/70	STEMI	7	135	E	N	LVF
123	5799	VITTAL.S	70	M	h	H,S,F	C	2 HRS	110/70	UA	9.1	296	E	E	-
124	5942	BANDOPAT	76	M	h	DM,S	C	2 HRS	128/70	NSTEMI	6	211	E	N	-
125	5932	YALLAPPA.G	70	M	h	DM,S	C,B,S	2 HRS	140/90	NSTEMI	9.6	153	N	E	-
126	5797	CHANAMALAPPA	63	M	h	D.H.S	C,B,S	2 D	230/120	ACC HTN	7.7	159	N	E	LVF
127	4284	SANGAPPA	77	M	h	D,S	C	8 D	100/60	STEMI	7.2	135	E	N	VF,DEAD
128	11162	SIDRAMAPPA	75	M	h	H,S,D	C,B,	4 HRS	260/120	ACC HTN	8.8	370	E	N	VPC,LVF
129	11105	SHEKREPPA	68	M	h	-	B	15 D	130/80	STEMI	5.8	191	E	N	LVF
130	5110	HANAMANTA .G	70	M	h	S	C,S	15 D	100/60	STEMI	5.8	127	E	E	VT,DEAD

131	11401	SHIVAPUTRAPPA	75	M	h	H,S	C,S	2 D	110/80	NSTEMI	4.8	86	N	N	-
132	4933	BAGAMMA	62	F	h	DM,D.F	C,S	6 HRS	100/70	STEMI	7.4	440	N	E	VT,DEAD
133	16220	KRISHNAJI	62	M	h	S,F	C	6 HRS	126/80	STEMI	5.6	181	E	N	-
134	13076	MALLANAGOUDA	60	M	h	S	B,S	6 D	120/70	UA	6.3	203	N	E	-
135	13405	MADIVALEPPA	40	M	h	S	C,S	4 HRS	120/70	STEMI	5.4	212	N	N	LVF
136	17517	MOHAMMED.A	72	M	m	H.S	C,S	2 D	90/50	STEMI	6	122	E	N	-
137	17243	GANGABAI.B	60	F	h	-	C,S	6 HRS	150/90	STEMI	7.1	185	N	E	LVF,MR
138	17186	AMARSINGH.H	58	M	h	F,D	C,S	10 HRS	SBP80	NSTEMI	4.2	135	E	N	CS
139	16443	BABU.J	70	M	h	S	B	1 D	120/90	STEMI	7.6	212	E	N	LVF
140	16321	NAZEER.C	55	M	m	H,S,F,D	C,S,B	8 HRS	100/70	NSTEMI	5.6	182	N	N	-
141	15144	SAMABAI.M	75	F	h	D	C,S	4 HRS	130/80	STEMI	5.4	85	E	N	-
142	15159	GOPAL.G	60	M	h	DM,F,S	C	1 D	100/60	NSTEMI	10.3	209	E	E	LVF
143	15969	SHANKER.S	37	M	h	DM,H,S,F	C,S	2D	78/50	STEMI	5.4	113	E	E	CS
144	17289	DEVAKAWWE	60	F	h	D	C,S	1 D	70/50	STEMI	7.6	153	N	N	CS
145	17432	VASANTH.B	69	M	h	S	C,S	8 HRS	140/90	STEMI	5.2	156	E	E	-
146	13051	LATHA.G	40	F	h	D	C,S	6 HRS	116/80	UA	5.2	103	E	N	-
147	7902	SHIVAREMMA	80	F	h	H	C,S	1 D	130/80	NSTEMI	5.4	106	E	N	-
148	2499	MALLIKARJUN	69	M	h	-	P,B	1 D	100/60	DCM	7.3	148	E	E	LVF
149	4825	RAJESH	52	M	h	DM,S,D	C,S	8 HRS	100/70	STEMI	7.7	262	N	E	LVF,MR
150	3256	RAJU	45	M	h	S	C,B	6 HRS	116/70	STEMI	4.8	116	N	E	-
151	2250	CHIDAMBAR	62	M	h	F,S	C,B.S	1 D	1220/70	STEMI	8.4	151	E	E	LVF,MR
152	2068	SANGAMESH	65	M	h	D,S	C,S	4 HRS	116/70	STEMI	5.6	228	N	E	MR
153	1235	CHANDRAWWA	65	F	h	F	C,B	6 HRS	116/80	STEMI	7.2	154	E	E	LVF
154	1401	BABU.PATTAR	45	M	h	DM	C,S	7 HRS	70/50	STEMI	8.2	310	E	E	CS

155	680	SANGANNA	70	M	h	S,D	C,S	1 D	130/80	STEMI	7.1	128	E	N	MR
156	501	MALLAMMA	60	F	h	DM,D	C,B	12 HRS	136/70	STEMI	7.8	202	N	E	LVF