Serum Homocysteine Level As A Risk Factor For Acute Coronary Syndrome In Middle Aged

by

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LIST OF ABBREVIATIONS USED

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

ABSTRACT

Introduction: Abnormal Homocysteine (HCY) level appear to contribute to atherosclerosis by direct toxic effect that damages the arterial linings, interfering with the clotting factors and oxidation of LDL. Some 10% to 20% of cases of Coronary heart disease have been linked to elevated level of serum Homocysteine

Objective: This is an observational study designed to study the Homocysteine levels in middle age group patients with acute coronary syndrome & to carry out statistical analysis to evaluate Homocysteine as an independent risk factor for MI.

Methods: The mean serum Homocysteine in patients of MI and control was calculated and its association with fasting lipid profile, 2decho and ECG was done .

Results: The mean serum Homocysteine in case and control was 29.77 µmol / L with a significant p value of 0.001. The difference in Homocysteine levels observed between patients with LDL-C ≥ 100 mg% and those with LDL-C < 100 mg% was not significant. The difference in Homocysteine levels observed between patients very low ejection fraction with 20% EF and with high EF 50% has significant correlation with mortality more with low EF. Alsoin our study more common presentation was anterolateral wall MI but there was no significant correlation.

Conclusion: From the above findings, in this study the low levels of LDL-C and high levels of HDL-C did not protect the patients against the Homocysteine induced coronary artery disease. Also increased levels of homocystiene are directly proportional to the complications of acute coronary syndrome Henceforth, plasma total homocystiene plays a vital role and an independent risk factor for middle aged patients with acute coronary syndrome even without any conventional risk factors

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INTRODUCTION

Acute myocardial infarction (ACS) refers to a group of health conditions due to reduced blood flow in the artery, and therefore cannot function properly or dies. The most common symptoms are chest pain, which usually radiates to the left or right corner of the jaw and is associated with nausea and sweating[(1).]

Acute coronary syndrome usually occurs as a result of one of three problems:

--ST elevation myocardial infarction (30%)

--Non ST elevation myocardial infarction (25%)

--Unstable angina (38%)

Acute myocardial infarction is a significant form of IHD. AMI has quickly came as the main provider to raising morbidity and mortality.

Many asymptomatic individuals are at risk for MI due to genetic predisposition, smoking behavior and sedentary lifestyle. About one-third of patients with advanced myocardial infarction die without being admitted to the hospital for effective treatment. Thus, myocardial infarction is an important health problem and deserves constant attention from key and clinical scientists, epidemiologists and practicing physicians.

Cardiovascular diseases (CVDs) have now become the leading cause of mortality in India. A quarter of all mortality is attributable to CVD. Ischemic heart disease and stroke are the predominant causes and are responsible for >80% of CVD deaths. The Global Burden of Disease study estimate of age-standardized CVD death rate of 272 per 100 000 population in India is higher than the global average of 235 per 100000 population

Hyperhomocysteinemia, described as an raised plasma total homocysteine levels (>13 µM), is one such factor[2].

Some studies have shown that elevated serum homocysteine is a major risk factor for Acute coronary syndrome in middle aged patients

Hyperhomocysteinemia is involved in the etiology of stroke, vascular dementia and alzhimers disease.

Hyperhomocysteineis a major prothrombotic factor associated with acute coronary syndrome in middle-aged patients. Hyperhomocystinemia is a major risk factor for arterial malfunction in mature, wellbeing individuals.

Hyperhomocysteinemia leads to an increase in blood pressure, raising the complication of acute coronary syndrome. High plasma homocysteine will show to cause oxidative damage to endothelial some of the mechanisms involve platelet aggregation attachment to endothelial cells, promoting smooth muscle cell growth of vascular endothelium, and raised homocysteine binding to major factors of thrombosis such as β- thromboglobulin, factor VIIc and tissue plasminogen activator

One of the amino acid in blood is homocystiene. It wont come from the diet and is synthesized from methionine through a multiple process.

Through diet and genetic factors, plasma homocystiene levels are strongly influenced. The most effective food ingredients were folic acid and vitamins B6 n B12. B vitamins and folic acid helps in synthesizing homocystiene in our body. Many researches shown raised serum levels of B vitamins are at average partially associated with lesser homocysteine levels. Few past findings indicates lesser folic acid serum levels are associated with raised risk of dangerous heart disease.

Many other research trials are underway to study whether reducing homocysteinereduces the complication of cardiovascular disease. Newer information shows that fortification of eatables with folic acid lowered the medium ranged homocysteine level in the US population.

Newer results shows laboratory tests for homocysteine levels in plasma may help the risk evaluation. It might be mainly get in use in subjects having a history of family history or personal history of cardiac problem, however they wont have the risk factors (cholesterol, high blood pressure ,smoking).

However there is no proof for the benefits of reducing homocysteine levels, high-risk subjects will be warned that their diet contains sufficient vitamins B6 and B12, folic acid . significant- folate eatables include green leafy vegetables and folic acid-enriched cereal products. However, hence is one of the risk factors. A physician using any nutritional approach to reduce the complication will take the general risk factor profile of a person and adjust their diet likewise[(2).]

Main cause to the decrease in the incidence of severe MI in newer years is not clear, possibly because of the treatment of risk factors like high blood pressure and cholesterol levels being high.

AIMS AND OBJECTIVES

‘‘To evaluate levels of homocystiene in Acute coronary syndrome as a risk factor in middle aged patients’’.

REVIEW OF LITERATURE

The first study to support the cooperation between advanced CAD and elevated concentrations of Hcy was published in 1976. Since then, multicatalytic and case management studies have been carried out, most of them supporting the association. In 1992, the first prospective case control study was published

In 2006 Wood Ward et al., studied 364 MI patients and concluded that homocysteine has an effect on cardiovascular risk over and above that of inflammatory, markers and the major cardiovascular risk factors

In 2005 Banu and Mollah FH, Alam, M. K., Rahman, M. A., Hamid, M. A., Wahab, M. F., Arsion, M. I. studied 70 subjects and concluded that serum homocysteine concentration was increased in patients with acute MI([3])

In 2003 Woodward M. Rumley, A. G., Rumley, A., Love G. studied 90 cases of MI and they concluded one of the risk factor for MI is homocystiene, indivisualistic of classical bad factors and markers of inflammation[(4)]

In 2002 Thomas J Wang et al., observed that the most informative biomarkers for predicting death in cardiovascular disease were blood levels of HSCRP, homocysteine and fibrinogen, B type natriuretic peptide, renin, urinary albumin to creatinine ratio([5])

In Obaidi et al study, it was seen that the increase of cardiac troponin-I become specifically at homocysteine levels> 16.5 umol / L in AMI patients[(6)]

In Sadeghian S and Dey, here the researcher discovered that serum homocysteine levels were particularly raised in subjects of smoking, dyslipidemia with family history of ischemic disease of heart[(7)].

Gregory m. gauthier a conducted a study, where thy conducted study on 100 patients, Studies have suggested that elevated Hcy accumulation is associated with an increase in stroke, coronary artery disease (CAD), circulatory disorders, and deep blood vessel thrombosis[8].

Knekt P et al, did short-term study among females. In total, 74 and 75 important events of coronary vessels (coronary death either non-fatal heart attack) seen in females with and without coronary heart disease, in reference to above, meanwhile a 13-year observation followed by 2 controls singularly matched on a case-by-case basis[9].

Among females with initial coronary problem, the relative risk (95% CI) of these incidents, calculated for age, smoking, hypertension, diabetes, serum cholesterol and body mass index, used to be 3.32 (1.05 ± 10 , 5) which is more among homocysteine quintile relative to the lesser quintile. Among females not having heart disease in the start of the study, the corresponding relative probability price used to be 0.77 (0.24 ± 2.45). This potential learns about support for speculation, homocysteine will be a casual element for coronary events more contrary being females with disease of heart.

In a study done with the help of Coen D.A. Stehouwer et al. Investigated whether high serum homocysteine had a dangerous visual effect on disease of vessels in 878 very old men (average age at onset, 71.5 years; range, sixty-four-four years) in a representative population group observed after 10 years in Zutphen, Netherlands . 21% had nonfasting homocysteine in the 17 mmol / L range. later correction for different significant risk factors, raised baseline homocysteine values (1/3 as opposed

to the first tertile) were associated with increased baseline myocardial infarction and coronary loss of life[10]

Refsum, MD; et al conducted studies ontotal of 750 patients of atherosclerotic disease of vessels (cardiac, cerebral, and peripheral) and 800 control subjects of both sexes very younger than 60 years.

Plasma total homocysteine then asessed where subjects did fasting, and they concluded.That serum homocysteine levels were steadily raised in patients with acute coronary syndrome[11]

Ottarnygard, M.D., studied 587 subjects with angiographic proof of disease of coronary artery. complicating factors for disease of coronary vessels, includes homocysteine values, were considered during angiography in 1991 or 1992. Sixty-four patients (10.9 percent) were dead after an average follow-up of 4.6 years. We found a strong, differentiated relationship between plasma homocysteine degrees and typical mortality

They finally concluded that Plasma total homocysteine levels being a powerful predictor of death in subjects with angiographically seen coronary artery disease[12].

TorbjørnOmland, MD, PhD, MPH; Anita Samuelsson; Marianne Hartford, MD, PhD; et al, tested the hypothesis which circulating homocysteine values, got during the initial 24 hours getting hospital admission in subjects with acute coronary syndromes ,which are indicative of prolong-term deaths.

They conducted a possible start-up cohort to study at an educational institution in Gothenburg, Sweden. A total of 579 patients (179 girls and 400 men; median age, sixty-seven years) were considered (Q-wave myocardial infarction in 163 patients,

non-Q-wave myocardial infarction in 210 patients, unstable angina pectoris in 206 patients).

They concluded that serum homocysteine levels is an objective predictor of long-term survival in patients with acute coronary syndrome[13]

TorbjørnOmland et al did a prospective inception cohort study in a teaching hospital in Gothenburg, Sweden. Among 579 subjects (179 females and 400 males; median age, 67 years)got involved (Q-wave myocardial infarction in 163 subjects, non– Q-wave myocardial infarction among 210 patients, unstable angina pectoris among 206 subjects) and concluded that The serum homocysteine level on hospital admission is an independent predictor of long-term survival in patients with acute coronary syndromes[13].

ShlomiMatetzky, MD; DovFreimark, MD; Sela Ben-Ami, PhD; et al determined Homocysteine levels within 24 hours of presentation in 157 consecutive patients with acute myocardial infarction and concluded that elevated homocysteine levels are associated with a higher risk of recurrent coronary events and death, independent of other risk factors and the extent of coronary artery disease[14]

FranciscoMartín-HerreroJavierMartín-MoreirasPedroPabónPedro et al studied Homocysteine levels were determined within 24 h after admission in 244 consecutive patients aged less than 56 years who presented with an acute coronary syndrome and concluded that High homocysteine levels at admission strongly predict late cardiac events in young patients with acute coronary syndromes[15].

Mabrouka EL Oudi, MD et al, studied in total of 122 subjects with ACS and 80 case control people were joined from the cardiac intensive care unit of the Military

Hospital of Tunis, Tunisia then concluded that elevated values of tHcy, IL-6, TNFα and HsCRP seen to be with a higher number of diseased arteries and subsequently, the high risk of coronary artery disease[16]

Ramachandran S. Vasan, MD did follow-up study on 156 patients (88 women) got CHF and did multivariable analysing controlling for already containing risk factors for CHF involving the presence of myocardial infarction and gave opinion that an raised plasma homocysteine level in particular finds out risk of the developing of CHF in adults not having previous myocardial infarction[17].

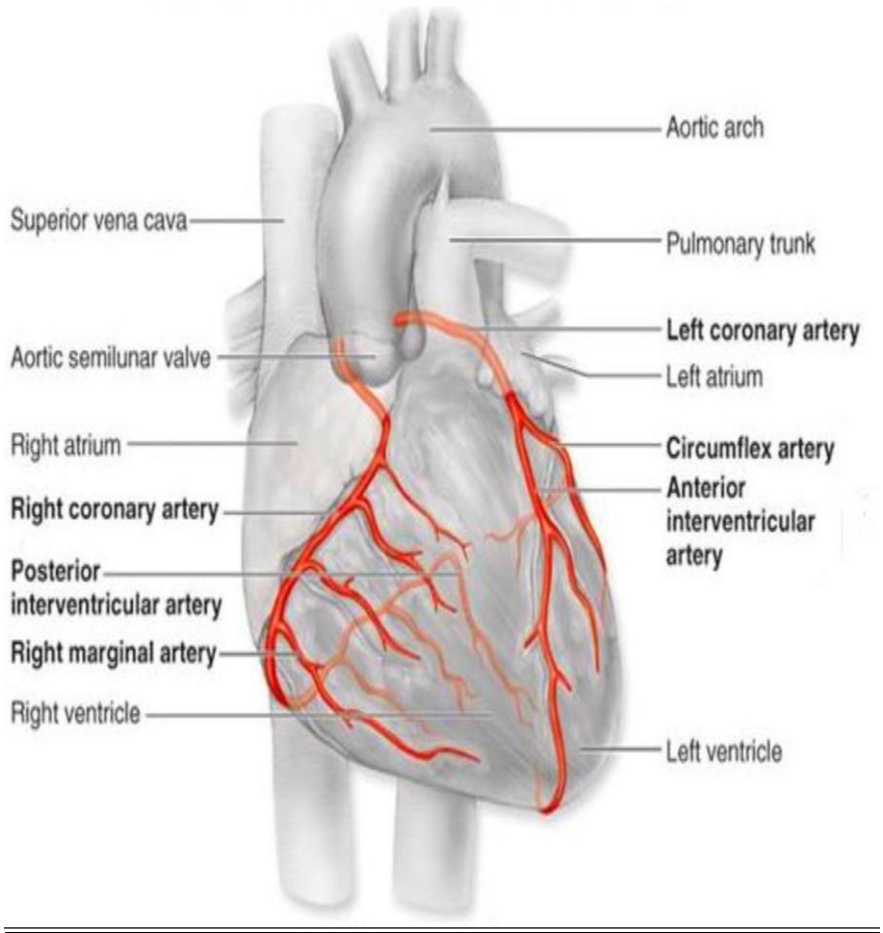
‘‘Ching-Yu Julius Chen, Tzu-Ching Yang et al studied STEMI patients who were consecutively admitted to an intensive care unit following coronary intervention in a single medical center in Taiwan. Control subjects were individuals who presented to the outpatient or emergency department with acute chest pain but subsequently revealed patent coronary arteries by coronary arteriography and concluded that Homocysteine was not elevated in STEMI patients regardless of Killip severity, suggesting that homocysteine is a bystander instead of a causative factor of STEMI [18]

Yan Ma, Duanliang Peng, et al studied Serum Hcy, folic acid and vitaminB_{12} (19) from 292 CAD patients and concluded that raised levels of Hcy and low values of folic acid and vitamin B_{12} are highly linked with CAD subgroups[20].

CORONARY CIRCULATION

Anatomy of Coronary Arteries

The heart derives its blood supply from the right and left coronary arteries, which arise from anterior aortic and left posterior aortic sinus respectively .Right coronary artery after arising from the anterior sinus passes between the right auricular appendage and the infundibulum of the right ventricle. Passing now vertically downwards in the atrioventricular groove the artery turns backwards at the inferior border of the heart and runs posteriorly. It distributes branches to both atria and ventricles as it passes vertically downwards. At the inferior border, the marginal branch passes to the left along the right ventricle. On the diaphragmatic surface, the inferior interventricular branch is given off. This large artery passes along the interventricular groove to the apex of the heart.



The terminal part anastomoses with the terminal arterioles of the coronary artery at the lower part of the left atrium.

The left coronary artery immediately after its origin divides into anterior descending artery and left circumflex artery. The anterior descending artery runs in the interventricular groove to anastomose at the apex along the end branches of the inferior interventricular artery.

The left circumflex gives off branches to the posterior wall of the left ventricle and runs on to anastomose with the termination of the right coronary artery, below the coronary sinus. Here in 40% of the individuals it gives off a sizable branch which running up over the posterior surface of the left atrium ends in the auricular appendage of the right atrium at the sino-atrial node[21].

Anastomoses of Coronary Arteries

Anastomoses were located between the distal end of the right and left ventricles of the atrrioventricular groove and floor anastomoses were not significant.

There are intercoronary anastomoses freely at arteriolar level, between the inter-ventricular arteries. If the intraventricular arteries meet at the apex, this provides maximum anastomoes. If the meeting place of the intraventricular arteries falls short of the apex above or below, this diminishes the potential anastomotic area. In 10% of the individuals the inferior as well as the anterior interventricular artery is a branch of the left coronary, in these cases there is no anastomoses between the coronaries Potential anastomoses exists between the coronary arteries and pericardial arteries which are derived from the pericardiophrenic, the bronchial and the internal thoracic arteries. In very rare instances one of these may open to replace a coronary artery

Distribution of theCoronaries

Right ventricle is supplied by the right coronary artery except at the upper margin of its anterior surface, where it is supplied by branches of anterior interventricular arteries.

Left ventricle is supplied by the left coronary artery except for a narrow strip of the diaphragmatic surface where it is supplied by the inferior interventricular artery. The two interventricular arteries share the supply of the interventricular septum, usually about equally.

The anterior surface of the right atrium is supplied by right coronary artery. The posterior surface and the auricular appendage of the left atrium are supplied from left coronary artery.

SA Node:

It is supplied by a branch of right coronary artery in 60% of cases and from left coronary artery in 40%. AV node and bundle of His are supplied by the inferior interventricular artery, which arises in 90% of cases from the right coronary and in only 10% from the left coronary.

Dominant Arteries:

In 67% of the cases right coronary is dominant, 15% of cases left coronary and in 18% of cases there is a balanced coronary arterial pattern

Physiology of Coronary Circulation

Functionally, the right and left coronary arteries behave as end arteries, although anatomically there are numerous intercoronary anastomoses in most of the normal hearts in the order of 40% microns in diameter.

Only the inner 75-100 microns of the endocardium can obtain significant amount of nutrition directly from the blood in the cardiac chamber.

Normal Coronary Blood Flow

Resting coronary blood flow in human beings averages about 225 ml/ min or 0.7-0.8 ml/G of heart muscle or 4.5 percent of the total cardiac output. Four to five fold increase can occur during exercise.

Phasic Changes in Coronary Blood Flow

As a result of cardiac muscle compression blood flow decreases during systole and increases during diastole, in which left ventricle is more affected than the right because of its thickness.

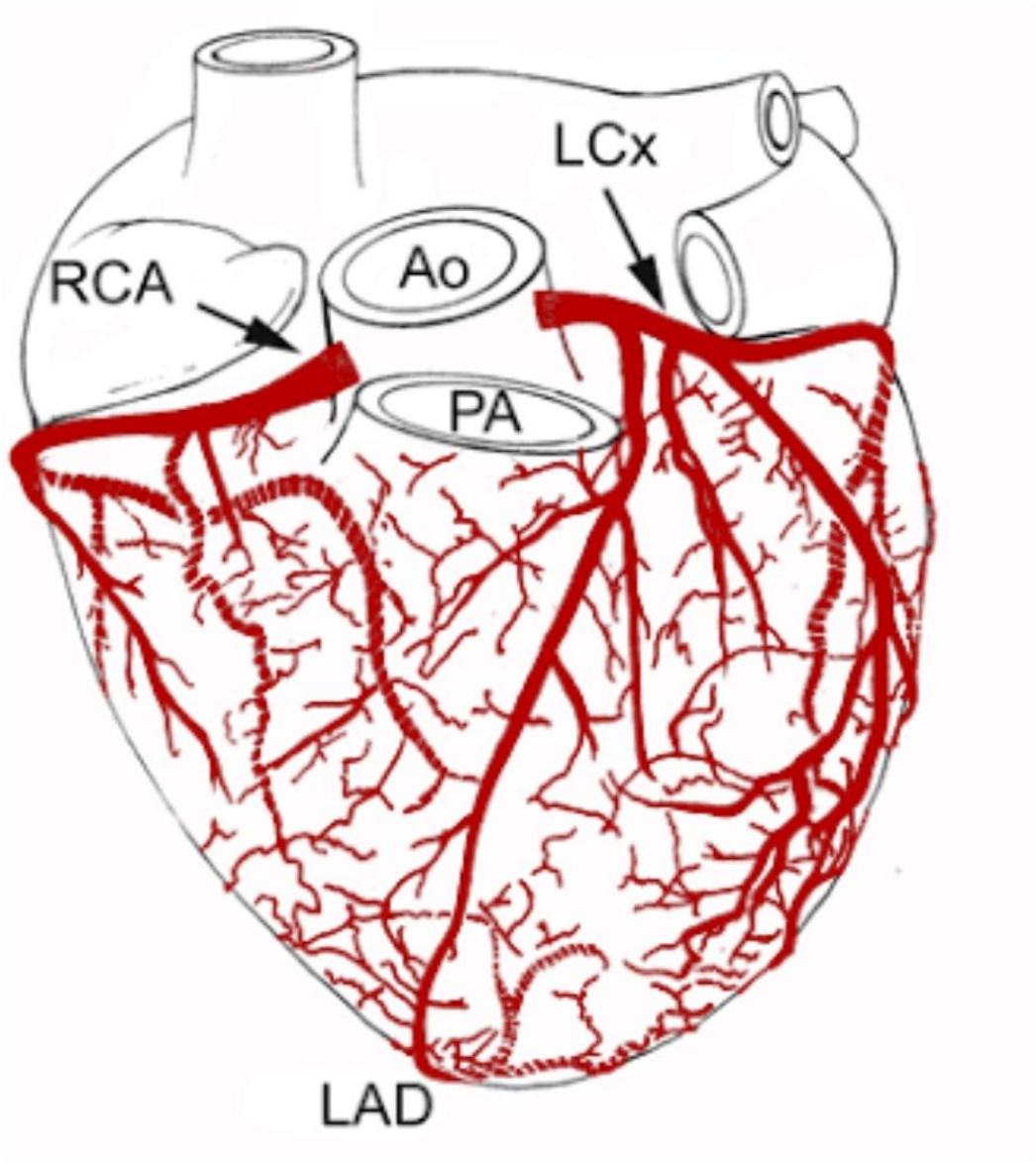
The intramyocardial pressures compress the subendocardial blood vessels more than the outer vessels, which throttle its blood supply and to compensate for this one, the subendocardial vessel are much larger than the nutrient arteries in the middle and outer layers of the heart, which increases the blood flow during diastole proportionately.

Control of Coronary Blood Flow:

1. Local metabolism of myocardium – A prime controller
2. Nervous control

i) Local metabolism of myocardium: The rate of flow increases with the vigor of contraction and decreases with decrease in activity. The factors responsible are:

a) **Oxygen Demand**:



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

1. **Vasodilator Theory**: Anoxia will liberate many vasodilator materials from myocardial cells which increase the blood flow:
    i) Adenosine from the ATP
    ii) Potassium ion
    iii) Hydrogen ion
    iv) Carbon dioxide
    v) Bradykinin and possibly
    vi) Prostaglandins
2. **Arterial Smooth Muscle Relaxation Theory**: Decrease in oxygen supply leads to anoxia of coronary arterial smooth muscle cells, which loses their tone thus getting the artery dilated. Factors that determine the oxygen consumption are:
    a) Greater the work, the greater the oxygen consumption, within the physiological limitations.
    b) Oxygen consumption is proportionate to peak myocardial muscle tension.
        i) Increased arterial pressure, increases the work load and hence tension.
        ii) Dilatation of the heart increases the tension development in myocardium to pump the blood according to Laplace law, which states that tension required to generate a given pressure increases in proportion to the diameter of the heart.
    c) Other factors which increases the oxygen consumption like stimulation of the heart by epinephrine and norepinephrine, thyroxine, digitalis, calcium ions ,increased temperature of heart, will increase the oxygen consumption.

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

iii) Nervous Control

a) **Indirect**: Sympathetics increases the heart rate and contractility, through the local metabolic mechanisms, and hence increases the coronary flow.

Parasympathetics decrease the heart rate and depresses the myocardium and hence brings about coronary constriction.

b) Direct Effect:

Parasympathetics: As the vagal supply to ventricles is negligible, except for slight dilatation which may occur, there is no effect of its stimulation.

Sympathetics: Epinephrine and norepinephrine through their receptors in coronary vessels usually bring about vasoconstriction or no change. When alpha effect dominates, severe constriction occurs which may bring about anginal attack.

EPIDEMIOLOGY OF CORONARY HEART DISEASE

Major cause of morbidity and mortality is coronary artery disease in individual aged 45 years or more throughout the world including India. Wide variations have been reported in the prevalence rate of CAD in different geographical regions. Finland and US lead all other countries in death rates from CAD.

In the US it is estimated that for those over 30 years of age 213 per 100,000 individual have ischemic heart disease.

Accurate data regarding the prevalence of CAD in India are not available. Surveys carried out in recent years, in different geographical locations and in small population groups using different protocols, estimate a prevalence rate of about 5% in urban population and a much lower prevalence in the rural setting.

The pattern of CAD in India has been reported to be as follows:

a) Males are affected more than females.

b) Hypertension and diabetes accounts 40% of all cases.

c) Heavy smoking is responsible etiology in a good number of cases.

d) Other factor includes high fat & energy rich diet, sedentary life style.

Many Indians internists believe that the prevalence of CAD in India has increased over the last three decades and many more younger persons are prone to the disease since 1970, there has been approximately 30% decline in mortality due to CAD.

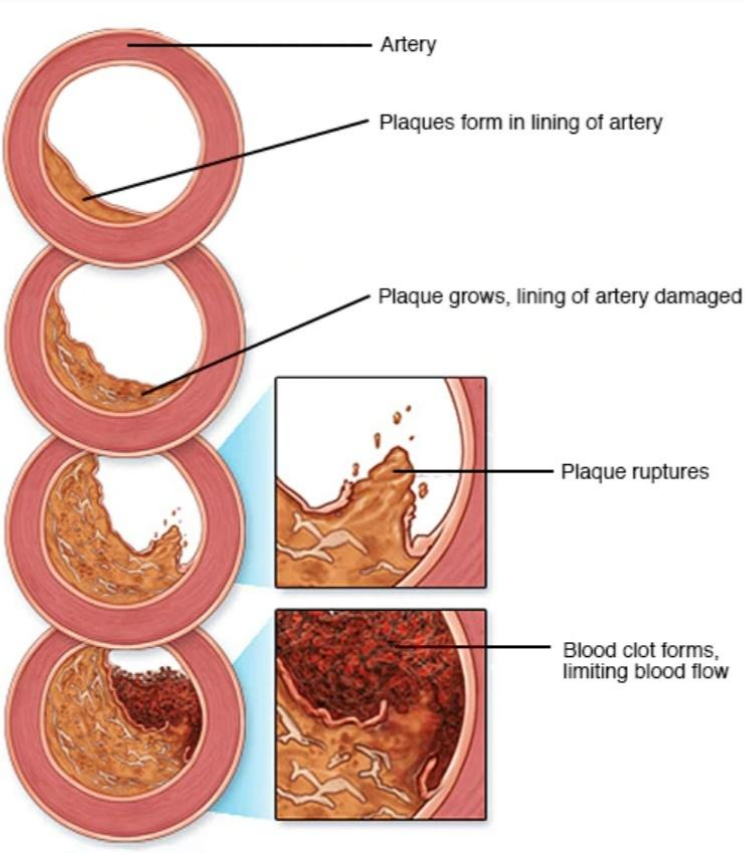
PATHOPHYSIOLOGY OF ACUTE MYOCARDIAL INFARCTION

‘‘Myocardial infarction usually occurs when there is a sudden decrease in coronary blood flow with flow after obstruction of coronary arterial thrombosis, previously narrowed by atherosclerotic fissures, rupture or ulcer, and when thrombosis is needed. plaque position break and leads to occlusion of coronary artery. After a temporary

formation of a platelet monolayer at the site of plaque rupture, different agonists (collagen, ADP, After agonist staining, release and production of thromboxane A2, as well as thrombotic activation and sustained thrombolysis resistance, are observed.''

Similarly to thromboxane A2, platelet activation by agonists promotes conformational changes in glycoprotein IIb, IIIa expression. When introduced into practice, this receptor promotes an increased ability to block arginine - glycine - aspartic acid on the alpha chain of fibrinogen as well as the dodecapeptide chain on the gamma chain of fibrinogen. Because fibrinogen is a multicellular molecule, it can bind to two unique thrombi simultaneously, binding the thrombin cross-linker and the interruption epinephrine, serotonin) promote platelet activation.

The cascade of coagulation is stimulated by contacting a tissue element in place of a damaged plaque in endothelial cells. Activated factor7 and factor 10, eventually helps in prothrombin to thrombin conversion, which then converts fibrinogen to fibrin. The artery of coronary to be injured will sooner or later be closed with a thrombus having platelet aggregates and fibrin strands



‘‘Finally, the extent of myocardial damage caused by coronary occlusion depends on the area affected by the vessel, whether or not the vessel becomes completely obstructed, from the natural elements that can cause early occlusion thrombus spontaneous lysis, the amount of blood passing through the vessel is supplied to affected tissues, and demand for myocardial oxygen, whose blood supply is sharply restricted’’.

CLINICAL FEATURES OF ACUTE MYOCARDIAL INFARCTION

Acute myocardial infarction presents itself as a sudden catastrophic incident and its definite clinical picture may be established without warning. The clinical pictures can be classified as follows:

1) Cases dominated by chest pain
2) Cases dominated by shock
3) Cases dominated by pulmonary edema or other evidence of LV failure.

4) Cases characterized by the gradual development of CCF
5) Cases dominated by complication
6) Some cases may present with combination of any of the above.

1. Pain in theChest:

In 80-85% of cases this is a presenting complaint. It is a deep visceral pain, involving the central portion of the chest and epigastrium, described as tightness, heaviness or constriction in the chest. In 25% of cases, it radiates to the arms and commonly it will be associated with weakness, sweating, nausea, giddiness and anxiety. It may occurs during exertion and emotional outbursts, not relieved with rest and makes the patient to mobilise in an attempt to find a convenient position.

2. Breathlessness

Second most important symptom, breathlessness may be sudden in onset and intense or it may be exertional. It is common in those who had'painless myocardial infarction' particularly diabetics and aged individuals, and those having complications like cardiogenic shock and pulmonary edema.

1. Sudden loss of conscious level, a confusional state, a sense of profound weakness or unexplained fall in blood pressure with giddiness, syncope and/ or convulsions may be a presenting complaint.
2. Choking sensation in the neck may be the only presenting symptom.
3. Some patients present with gradual onset of breathlessness, paroxysmal nocturnal dyspnea and pain in abdomen with oliguria and swelling of lower limbs, a picture that of CCF.
4. In rare cases the infarct may go unrecognized until endocardial thrombosis resulting from its leads to systemic embolism.

Physical Signs.Patient may come with the hand on their pericardium indicating the site of maximum intensity of pain (Levine sign).

Always associated with sweating and cold at the peripheries, cyanosis may be there when the patient is having severe pulmonary edema or shock.

Pulse

May show bradycardia, normal sinus rythm, tachycardia with or without irregularities, depending upon the presence or absence of arrhythmias and the type of arrhythmia.

Blood Pressure

Usually shows an initial rise because of pain, anxiety or the unfamiliarity of the environment, which will become normal within 3 or 4 days. Fall in the blood pressure may be due to cardiogenic shock or due to 'Bezold -Jarisch reflex', which is due to increased vagal tone that occurs in inferior wall infarction.

Neck veins:

Collapse of neck veins occurs when patient is in shock, cannon waves can be made out in complete heart block in which they are irregular.

Precordium

Apical impulse can be a challenge to palpate. About one quarter of patients with anterior wall infarction have an abnormal systolic pulse , develops in the periapical area within the first few days of illness, which may resolve later, which represents a transient, palpable systolic bulging of the infarcted ventricle. Other physical symptoms of ventricular dysfunction that may be present are the paradoxical split between silent heart sounds, atrial (S4) and ventricular (S3) sounds, and second sounds. Transient apical systolic murmur may occur during acute infarction due to mitral regurgitation secondary to papillary muscle dysfunction. If the heart attack is

transmural in most cases, pericardial friction is heard.

Temperature elevations in the range of 37 to 38ºC are common during the first 3 to 4 days due to myocardial necrosis(22)

Respiratory System: Tachypnea is common and crepitations are heard at the base or all over the lung fields depending upon the amount of pulmonary congestion.

Gastrointestinal System: enlarged tender liver will be present when patient is in CCF.

Central Nervous System: Anxiety, restlessness, stupor, coma, focal neurological deficit may occur when the patient is having fall in blood pressure and/ or thromboembolic phenomenon.

Renal System: Oliguria may be present if the patient is having fall in blood pressure

HOMOCYSTEINE AND ITS ROLE IN ACUTEMYOCARDIAL INFARCTION

Homocysteine is an amino acid, which is not proteinogenic in nature and contains Sulfur. It is biosynthesized from methionine, and place an important role in the activated methyl cycles and folate whereby it consists of 3 metabolic fates, and undergoes remethylation to methionine entering the biosynthetic pathway of cystiene and can be given into extracellular medium. The third fate of release into extracellular medium, is the direct cause of high homocysteine levels in plasma and urine. Another metabolic pathway of homocysteine metabolism involves deamination and is of less significance.

Homocysteine Structure:

Homocysteine exists as an zwitter ion at neutral PH

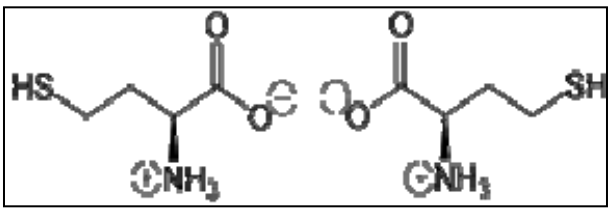


Figure – 1: Structure of homocysteine

Hyperhomocystienemia has association with deficiencies of folate and cobalamin, pregnanacy related complications, neural tube defects, intellectual disorders, psoriasis, few tumors, geriatric dementia.

However, relatively higher levels of total homocysteine has higher risk of cardiovascular disease, that includes atherosclerosis and thrombosis

To study the pathogenicity of hyperhomocystienemia its metabolic roles are to be understood. In view of novel metabolic roles of homocysteine being discovered, the interaction with intermediate molecules, modification of enzyme activity and protein modifications are to be studied.

The important purpose of this study is to emphasise the importance of metabolism and the biochemical properties of homocysteine and to understand the pathophysiology of increased intracellular and extracellular levels of homocysteine.

L- Homocysteine has two main metabolic pathways:

1. Conversion into methionine via formation of tetrahydrofolate.
2. Conversion to cystathionine.

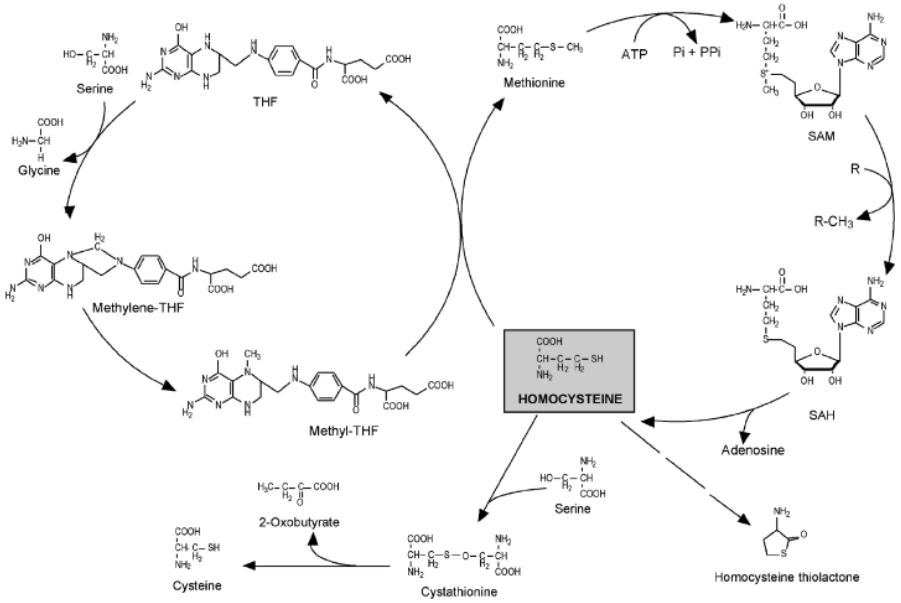


Figure – 2: metabolic pathway of Homocysteine

Homocystiene acts as an intermediate in the formation of S-adenosyl methionine by transfer of activated methyl group from tetrahydrofolate. It is also an intermediate in the transsulfuration pathway of synthesis of methionine cystiene. It also helps in the formation of highly reactive thiolactonederivative due to activation of homocystienyl-t RNA.

The remethylation pathway (activated methyl cycle)

A Switch of methyl groups is necessary for biosynthetic reaction. Tetrahydrofolate is adonor of methyl groups, but is inefficient in giving potential biosynthetic methylation. s – adenosyl methionine is formed by way of shift of adenosyl group from ATP to methionine sulfur atom. The transfer of methyl group to an acceptar leads to s -adenosyl methionine to s – adenosyl homocysteine which on activating of hydrolase is converted to adenosine and homocystiene.

In the reactivated methylation pathway, methionine is remethylated by homocystiene by transferring of N-5 tetrahydrofolate to methyl group reaction being , processed by using methionine synthase or an enzyme N-5 methyl tetrahydrofolate-homocysteine methyl transferase, requiring vitamin B12 as a cofactor. This is the last point of the remethyl pathway and the factor which is shared by the folate

cycle .Tetrahydrofolate will receive singlr carbon groups nitrogen atoms of both N-5 and N-10. For example , the exchange of single carbon group from serine produces glycine and methylene tetrahydrofolateat N-5, N10.This folate cycle is completed with the reaction catalyzed by using methylene tetrahydrofolate reductase, to produce N5-methyltetrahydrofolate.

In the liver and kidney of rats, a vast portion of homocysteine is remethylated with the aid of an additional route such that betaine acts as a donor of methyl group for the reaction processed by means of betaine-homocysteine methyltransferase.In humanbeings ,proof shows that a large quantity of dietary choline will be used for betaine-dependency methyl switch.

Recently, additional path for the conversion of methionine from homocystiene had been studied. This path necessitates homocysteine thiolactone end product. It looks like homocysteine thiolactone formation will be a signa of improper methylation of homocysteine-tRNA to methionine-tRNA. Since in several instancesN-terminal methionine is launched from the polypeptide just later chain maturation, homocysteine will be converted by using this path can enter the cellular pool of methionine.

The trans-sulfuration pathway

Cysteine is usually synthesized from methionine by using trans-sulfuration pathway. The first most important steps of this pathway are divided by the activated methyl ring and methionine is formed into homocysteine. By trans-sulfuration the substrate of homocysteine for vit B6 dependent enzyme that is cysthathione-betasynthase, which processes through condensation with serine to form cysthathione.This is a critical step on the road, because under physiological conditions it is irreversible; from now on, the homocyst is determined to follow this path. In the

last stage of pathway of transsulfuration, gamma cysthathionase which is cleaved from cystatin and another vitamin B6 dependant enzyme which will finally form cysteine and 2 oxoglutarate. The more cysteine will be oxidized to taurine and lastly into inorganic sulphates. Hence, along with cysteine synthesis this pathway will effectively catabolise the excess toxicity of homocysteine which is not required for transfer of methyl group.

Impairment of homocysteine metabolism

Determinants of homocysteine metabolism impairment:

The metabolism of homocysteine is strictly regulated, based on heterogenous affinities for cystathionine beta synthase and methionine synthase for homocysteine. the initial enzyme as less homocysteine values of km compared to the next second which has more homocysteine km values (above 1mm). Thus, low concentrations of homocysteine are preferable to the preservation of methionine; and at high homocysteine concentrations, the first and sustained outflow of homozysteineis provided by the transsulfuration pathway.

As mentioned before, abnormal elevations in plasma and urine concentration of homocystiene are due to increased homocysteine export, reflecting the imbalance between homocysteine formation and metabolism. This condition can be caused by several hereditary disorders, renal failure and also in nutritional disorders.

Congenital disorders include polymorphisms in genes encoding methylene tetrahydrofolate reductase, methionine synthase and cystathionine β-synthase. The most common genetic defect associated with mild hyperhomocysteinemia is a point mutation, namely the replacement of C to T by nucleotide 677 (C677 → T) in the open reading frame of the methylene tetrahydrofolate reductase gene. Mutation at this point results in the substitution of valine for alanine in a functional enzyme, resulting

in a fermobilized variant with reduced total activity . It is an autosomal recessive mutation, and the incidence of C677 → T polymorphism varies between races and ethnicities: 10-13% T / T is homozygous and 50% C / T heterozygous among Caucasian and Asian populations, and very low prevalence between Caucasian and Asian populations. Asian populations.African Americans.

A well documented increase in total plasma homocysteine levels associated with the homozygous T / T genotype could result in a higher predicted incidence of cardiovascular disease in the T / T population. However, very little evidence has yet been found to associate the T / T genotype with an increased incidence of cardiovascular disease, although in some reports the T / T genotype appears to be associated with an increased incidence of certain disease vessel forms in selected populations . In such scenario, it is advised that raised plasma levels of homocysteine may not be harmful but could contribute to vascular blockade in conditions predisposed to vascular disease.

Nutritional deficiencies such as vit b12, folate and niacin can lead to abnormal homocystiene metabolism, since the methionine methyl group synthesis de novo requires both vitamin B12 cofactors and folate, while cystathionine synthesis requires pyridoxal 5'-phosphate. . Although vitamin B12 and folate deficiency has been shown to be associated with elevated plasma levels of homocysteine , the relationship between homocysteine levels and vitamin B6 is relatively unclear.

In a rat study, the kidneys were found to be the important site of clearance and metabolism of homocysteine. Metabolic control appears to result in the metabolism of this homocysteine, which is excreted by the kidneys mainly by transsulfurization. Humans have conflicting results: some data seem to support this hypothesis but van Guldener et al, show data that contradict the hypothesis. Impaired renal function

typically leads to hyperhomocysteinemia, reflecting the major role of the kidney in plasma clearance of homocysteine, this may be attributed to a higher incidence of cardiovascular complications in the setting of chronic renal failure.

Role of *S*-adenosylmethionine in homocysteine metabolism

Selhub and Miller suggested a vital role for S-adenosylmethionine in conduction and control of homocysteine metabolism. S-adenosine methionine an inhibitor of methelynetetrahidrofolatereductase , in vitro betaine-homocysteine methtransferase inhibitor[19] cistationin β-synthase activator. S- adenosyl methionine also contributes in the remethylation and transsulfuration pathways . If the concentration of s adenosyl methionine in cells is low, the synthesis of 5-metiltetrahydrofolate will proceed uninhibited, while the synthesis of cystathionine will be suppressed, resulting in the maintenance of homocysteine for mehionine synthesis. Conversely, when the concentration of S-adenosylmethionine is high, homocysteine is diverted through the transsulfuration pathway to inhibit the synthesis of 5-metiltetrahydrofolate and stimulate cystathionine synthesis. Although the initial effect of this control which is co-ordinated in the regulation of s adenosyl methionine of cellular concentration, which also contributes to maintaning homocysteine concentration which is easily syncs with the need of methyl groups.

Hypomethylation:

S adenosine methinine which is the important contributor of methyl group. Methylation cell which involves the phspholipid synthesis, nucleic acid synthesis, amine synthesis and other neurotrnsmitter synthesis, regulates expression of genes and modifies protein function, with the exception of main function of methyl transferases. In view of adenosine, homocysteine is effectively transferred to s adenosyl homocysteine, which is a strong suppressor of reactions of methyl

transferase. Infact, s adenosly homocysteine which is an end product of reactions of methyl transferase using s adenosyl methionine substrate. Many of the methyl transferases attaches to s adenosyl homocysteine with more affinity than s adenosylmethinine and are therefore prone to strong product inhibition. Hence one of the primary biochemical mechanisms of hyperhomocystenemia toxicity by hypomethylation by storage of Sadenosyl homocysteine.

The S-adenosylmethionine / S-adenosylhomocysteinefraction is a better and important indicator of the state of cell methylation . Recently, physiologically comparable concentration of homocysteine (not other thiols) in view of adeosine have been reported to inhibit vascular endothelium cell growth by a process which involves reduced carboxymethylation of p21r. This effect of homocysteine will not be absorbed in cells of smooth muscle, a difference explained by the capability of homocysteine to statistically increase S-adenosyl homocysteine levels in cells of vascular endothelium but not in cells of vascular smooth muscle.

Red blood cells are mature and well differentiated cells that have lost there functions of biosynthetic proteins. During the aging of circulating cells, spontaneous post-translational modifications occur in erythrocyte proteins, which are thought to exacerbate protein fatigue. These are usually restored by enzymes, via transmethylation reaction.Membrane protein methylation inerythrocytes is considerably reduced in chronic renal failure and patients on hemodialysis in compared to healthy subjects.in novel studies, patients with peripheral arterial occlusion have been shown to have impaired plasma erythrocyte / S-adenosylmethionine / S-adenosylhomocysteineratio, suggesting that these patients may have faulty methylation.

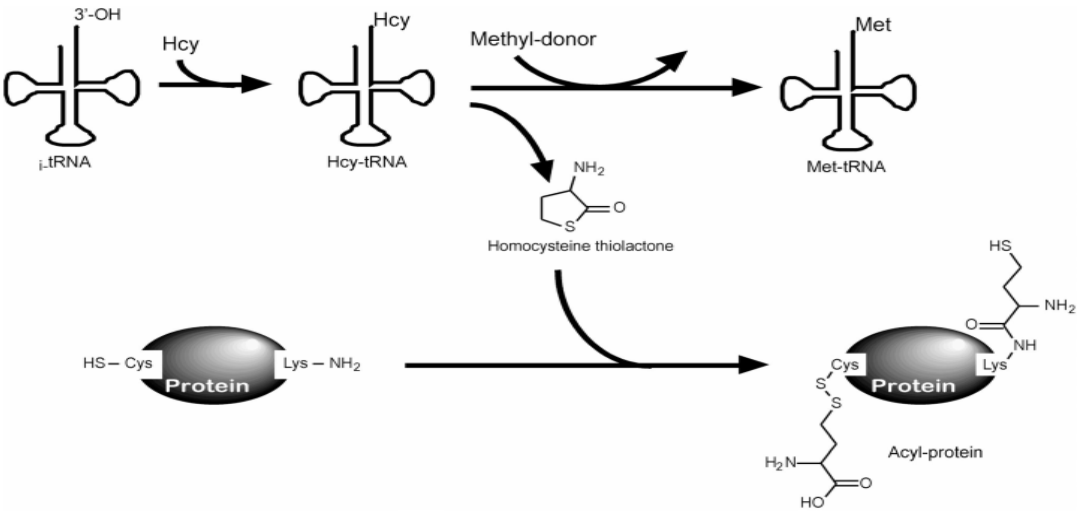
Effective removal of S-adenosylhomocysteineis required where the efficacy of methyltransferase reactions is to be maintained. This is effectively achieved by S-adenosylhomocysteinehydrolase, an enzyme that appears to act at least in the immediate vicinity of methyltransferases, at least in the nucleus. Surprisingly, the composition of folding of polypeptides in the domain catalytic of S adenocylhomocystein hydrolase which is almost similar to that reported for DNA methyltransferases, suggesting S adenosylhomocysteine will readily move in-between pockets of catalism of 2 enzymes. This binding similarity will further confirms the significant role of S adenosyl homocysteine more in the regulation of reactions of methylation. Recently a small increase in total plasma homocysteine concentration has been shown for the first time to be associated with a parallel increase in S-adenosyl concentration in plasma and hypomethylation of lymphocyte DNA. This information will support and indirect mechanism of pathogenicity of homocysteine following suppression of DNA methyltransferase, alteration of congenital DNA methylation patterns which can lead to chromatin structure changes and expression of gene changes which may support diseases of chronicity.

Protein homocysteinylation

Homocystiene t-rna is an activated product of homocystiene. For amino acylation of initiating t-rna in eukaryocytes, homocystiene is preferred amino acid. Both regulation of acylated initiator t-rna and acylation of mammalian initiator t- rna is done by homocystiene activated enzymes as it resembles with bacterial methionine t-RNA synthetase it is infact that homocystiene t-RNA is rapidly methylated to methionine t-RNA, it is similar to conversion of bacterial methionine t-RNA to formyl methionine t-RNA and therefore activated homocystiene is not detected in protiens.

Malignant cells lack methionine metabolism, therefore methionine t-RNA is not effective in them. Thus homocystienethiolactone production is a lack of methylation of homocystienethiolactone production is a lack of methylation of homocysteien t-RNA on the methionine protiens that are susceptible to acylation rather than homocystiene inactivation. Homocystiene has structural similarities with methionine, leucine, isoleucine, therefore can be activated by invivo synthesis of methionyl, isoleucyl and leucyl t-RNA.

High energy thioester bond is present in homocysteine thiolactoneacylate, asparagine, glutamine, arginine and lysine as it is chemically reactive. Therefore, human vascular diseases can involve homocysteine. As it leads protein homocysteinylation. Side chain amino group of lysine and cysteine residue can be efficiently homocystinylated. Model enzymes such as trypsin, completely loose their enzymatic activities after homocystenylation. Novel example of protein damage is protein homocystinylation. Fibrillin is the main component of extracellular connective tissue.



Scheme of the formation of initiator homocysteinyl-tRNA, and its transformation to initiator methionyl-tRNA or the alternative generation of reactive homocysteine thiolactone, which could induce damage in proteins

PATHOGENESIS OF VASCULAR DISEASE IN HYPERHOMOCYSTEINEMIA

Homocystinuria was invented first in 1962 in children who have disabilities in learning. Since then, associations were made between congenital disease with few other pathologies, particularly pathologies in vessels, have been noted. Before thirty years, high levels of homocysteine were shown to be very dangerous to cells. Maccaulley gave a suggestion that homocysteine will have a direct lethal effect on cells of endothelium. Keeping basis on these data, the knowledge of homocysteine atherosclerogenesis had been conceptualised in 1975. The primary study suggesting that slightly raised homocysteinemia may be a new risk factor for cardiac and vascular disease was publicated in 1976. but, over the next 15 years, this field of research has solely produced a few important individual data. In 1991,raised plasma levels of homocysteine were identified as an single important risk factor for cardiac disease.

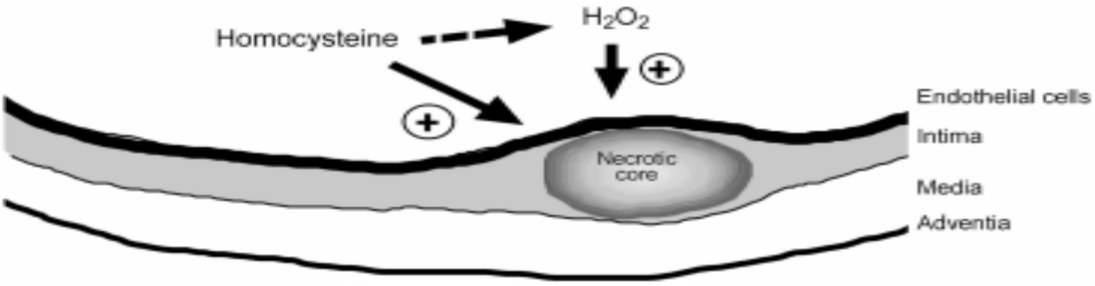
Many recent meta-analyzes and studied in many patients suggest that low level hyperhomocysteinemia is actually a risk factor for cardiac disease, not in all but in few people. However recent analysis called metaanalysis concluded that homocysteine will not be as dangerous to the cardiac as it looks, inspite of contrary studies to it ; as said to this study, homocysteine can be sign of a bad lifestyle and, as such, could be an very useful indicator for cardiologists to consider while evaluating patients after cardiac disease. But there is ongoing discussion to either raised plasma homocysteine levels are the cause of the pathology of cardiac disease or just an

indicator of this continuos process. The current state of this discussion is made clear in the editorial and two different aspects from the opposite perspective recently been publicated.

Randomized trials had investigated the outcomes of complete homocysteine depletion on severe clinical cardiac parameters are underway and will be undertaken in 50 to 60,000 people over the next 5 years, including those who are asymptomatic and not at high risk.

But there is currently no information available on randomized and controlled pathways indicating reduction in cardiac events in the treating hyperhomocysteinemia. Few days ago, homocysteine therapy along folic acid and vitamin B6 in siblings who are maintaining good health in patients who have atherothrombotic phenomenon prematurely, disease has been involved with a reduced incidence of subnormal exercise electrocardiography examination, persistent with a lower risk of atherosclerotic events of coronary vessel.

Pathogenesis of hyperhomocysteinemia: vascular wall damage;



In research of atherogenesis, raised plasma total homocysteine levels are accompanied by dietary lipids, which cause intimate damage. An alternative hypothesis for the straight forward effect of decreased homocysteine on cells of endothelium damage is the thing that homocysteine acts inversly by oxidizing it along simultaneously generating species of reactive oxygen. On the other side, since solid

proof suggests that atherosclerosis progression is involved with increased pro-oxidative activity, vascular disease of prematuration associated with elevated plasma homocysteine levels may get associated with raised pro-oxidative activity but not raised homocysteinemia.

High levels of homocysteine have been shown to induce permanent damage to endothelial cells of artery, accelerating the thrombosis development with atherosclerosis. When lab animals have been injected with homocystiene of 0.1-0.3 mM, their blood vessels exhibited stronger intima, smooth muscle cell proliferation, increased luminescence (cell separation in the arterial or vein area), and high cellular foam levels . The proliferative action of this homocysteine on smooth muscle cells of artery is an important atherosclerosis feature. In fact, this amino acid had showed us DNA increase synthesis in smooth muscle cells of vessels, during preventing damaged endothelial cell renewal by inhibiting endothelial cell growth. Although homocysteine itself induces smooth muscle cells to return to the cycle of cells and proliferate, interaction of homocystiene synergistically with serum to provide the cells proliferation. Thus, it is possible that interaction of homocystiene with different growth factors and cytokines which are there in pathology of atherosclerosis to provide smooth muscle cell growth while processing of atherosclerosis.

As given above, Wang et al. showed the lesser concentration addition of homocysteine (10–50 μmol·L - 1) not but cysteine is inhibited vascular endothelial cell multiplication by a process including reduced p21ras carboxymethylation not affecting different cell types. It shall be emphasized that few reports in which concentrations which are physilologically relevant had been used and in which specificity of thiol has been showed.

‘‘Homocysteine shown to regulate glutathione peroxidase enzyme expression and nitric oxide bioavailability .if we start comparing to control cells, homocysteine-treated aortic endothelial cells of bovine has showing a major decrease in glutathione peroxidase expressing levels and its working levels. Based on the authors, these information shows a new activity by that homocysteine, along with increasing hydrogen peroxide formation, can particularly alter the ability of cells of endothelium to detoxify it, making nitric oxide very much sensitive to oxidative deactivation. This effects would work gatherly with largely trusted capacity of homocysteine to modify the cells having surface properties of endothelium by modifying anticoagulant to procoagulant phenotype. But, physiological levels of homocysteine can raise attaching of lipoprotein to the component fibrin . On the alternative side, raised values of homocysteine decrease activation of protein C, thereby decreasing the anticoagulant work making decreasing of higher than 75% antithrombin III inhibition of anticoagulant heparan sulfate synthesis induced by a change in redox potential reducing thrombomodulin and inactivating activity of its cofactor and restricting the binding of tissue plasminogen activator to cells of endothelium. Hencemore, homocysteine expresses to induce protease activity that stimulates factor V, thereby initiating coagulation in the mispresence of thrombin. Homocysteine reacts hastily with nitric oxide to produce S-nitroso-homocysteine, which usually behaves as an powerful antiplatelet agent; production of this adduct may alter the formation of peroxides from homocysteine and herebyby acts against the properties of atherogenicityof homocysteine. Vascular damage can be affected by an altered balance between nitric oxide production from endothelial cells which are non functional and homocysteine levels’’

In a few days old research data provided by Nappo et al. show that acute hyperhomocysteinemia alter function of endothelium, activates coagulation, then alters endothelial adhesion and vessel response for l-arginine. Since before treatment with antioxidant vitamin E along with ascorbic acid restricts this effect, so appears that an oxidation activity may be involved. manymore research efforts are needed to examine this hypothetical theory.

The appearance of atherosclerosis increases gradually as ages. Uptill date, no other mechanical connection between aging and vessel disease has been established. Hernancs et al. have shown increased aging-related homocysteine synthesis, which in turn should have increased endothelial oxidative activity and altered intracellular antioxidant potentiality, causing to increased lipid peroxidation with a decrease in complete intracellular glutathione quantity. At the cell level, aging will be usually described as re-aging. Cell entering inside the sensory pool is poorly understood, furthermore it appears to be gene products capable of regulating the in side cellular redox state, like as ras n p53. This also usually assumed that when the telomeres got a minimum integral length, a messenger is triggered to initiate senescence program.This has led to the hypothesis that telomeres behaves like a mitotic clock for regulating life expectancy . More recently, homocysteine therapy has been shown to increase the speed of endothelial aging .more curiously, the speed of telomere getting shorten in human umbilical vein cells of endothelium treated with homocysteine was maximally improved relatively to control cells. According to these results, the magnitude of telomere disappearance will never appear to be strongly dependent on the several of cell divisions, but may be regulated by multiple intercellular activities. The findings that characterises partially inverses this outcome suggests that the intracellular redox state should be one among these intercellular variants(20).

Clinical outcome ofhyperhomocysteinemia:

Hyperhomocysteinemia is well to affect the following problems: ischemic heart disease, hypertension,central retinal vein occlusion, venous thromboembolism, cerebrovascular disease, peripheral arterial disease, acute mesenteric arterial thrombosis and neural tube defects.

Hyperhomocysteinemia is associated with the some of few clinical conditions: spontaneous abortion, abortus of placenta, low birth weight, neuropsychiatric disease and osteoporosis.

Treatment of hyperhomocysteinemia:

Moreover particular treatment to hyperhomocysteinemia is the most appropriate underlying cause, more than 90% of patients respond to multivitamin therapy within 2-6 weeks, regardless of the cause. Folic acid therapy in combination with vitamins B12 and B6 reduces homocysteine levels in patients who are deficient in vitamin 85. Folic acid is the single most effective therapy for hyperhomocysteinemia.

Folate intake of 300-400 µg / day provides low plasma levels or normal homocysteine. For most patients, multiple tests had shown that 0.65 to 10 mg daily folic acid, singly and in combination with vitamin B12 and / or vitamin B6, decreases homocysteine levels to 25-50% in either healthy subjects and in whom who have vascular disease. No significance was found 2.5 mg and 10 mg / day folic acid in a subject with infarction of myocardium or 0.5 mg and 5 mg / day in well to do subjects.

An analysis called meta analyses of the Homocystein Collaboration, which minimizes collaboration between different randomized controlled studies, found it to be proportional and absolute folic acid-produced homocysteine was higher at higher

homocysteine levels before treatment and lower at folate levels before treatment. Folate singly reduced the amount of homocysteine by 25% with the adding of vitamin B12, but it did not significantly reduce it with the addition of vitamin B6.

Folic acid-produced homocysteine was higher at higher homocysteine levels before treatment and lower at folate levels before treatment. Folate singly reduced homocysteine levels by 25% with the adding of vitamin B12, but it did not significantly reduce it with the addition of vitamin B6. An expected side effect of therapy of folic acid is subacute combined spinal cord degeneration in subjects who have subclinical mecobalamin deficiency48. hence unusual problems will be prevented either by eliminating vitamin B12 deficiency prior to folic acid supplementation or by substituting folic acid therapy with vitamin B12 at doses between 400 and 1000 µgm

The recommended daily consumption of vitamin B12 is problematic for vegetarians. Full milk is around 200-300 ml / day. Only 1-3% of mecobalamin is taken up by our body through simple diffusion. A dose of 1500 µg mecobalamin will therefore be proposed. Since 10-30% of the elderly cannot fully absorb the food-related vitamin B12, it is recommended that those over 50 years of age take a higher dose or supplement of vitamin B12.

The dose of vitamin B6 needed to cure mild to moderate hyperhomocysteinemia is lesser, ie 10 mg / day. subjects with cystathione beta synthase deficiency may require large doses of pyridoxine up to 500 mg daily. High doses of pyridoxine can cause peripheral sensory neuropathy.

In the Indian population, the requirement of riboflavin, vitamin B6 then vitamin B12, with the exception of low folate intake, is low comparatively with western people.

Pulses, green leafy vegetables ,eggs and fruits will be entertained to raise the vitamin B input[23].

ROLE OF OTHER ELEMENTS:

Other supplements play a minor role in lowering homocysteine levels. The following supplement has been shown to be effective in lowering homocysteine levels: betaine, choline, zinc, S-adenosylmethionine, inositol, alpha lipoic acid and other antioxidants

MATERIALS AND METHODS

This is an observational study among the patients admitted with acute coronary syndrome in the dept. of medicine in _____, from December 2017 to April 2019.

SOURCE OF DATA:

- The study is among the patients with acute coronary syndrome admitted in

- The patients will be informed about study in all respects and informed consent will be obtained.
- Period of study will be from DECEMBER 2017 TO APRIL 2019

SAMPLE COLLECTION

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

INCLUSION CRITERIA:

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

EXCLUSION CRITERIA:

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

LIST OF INVESTIGATIONS

Complete haemogram,

Random blood sugar

serum homocysteine levels.

Ecg

2d echo/echo doppler

Trop t, cpkmb

Chest xray

Lipid profile

Serum homocysteime level will be done by chemiluminiscense method in laboratory and considered high if it is > 13 mg/dl.

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

Investigations or interventions required in this study are routine standardized procedures. There is no animal experiment involved in this study.

Sample size calculation

With 95% confidence level and margin of error of ±10%, a sample size of 65 subjects will allow the study to assess the serum homocysteine level among ACS patients with finite population correction.

By using the formula:

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

where

Z= z statistic at 5% level of significance

d is margin of error

p is anticipated prevalence rate

Statistical analysis used

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

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

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

RESULTS

The study of Serum Homocysteine Level As A Risk Factor For Acute Coronary Syndrome In Middle Aged Patients admitted to ICCU of ----------Centre from December 2017 to April 2019. Total of 65 patients were admitted with acute coronary syndrome, who fulfilled the inclusion criteria.

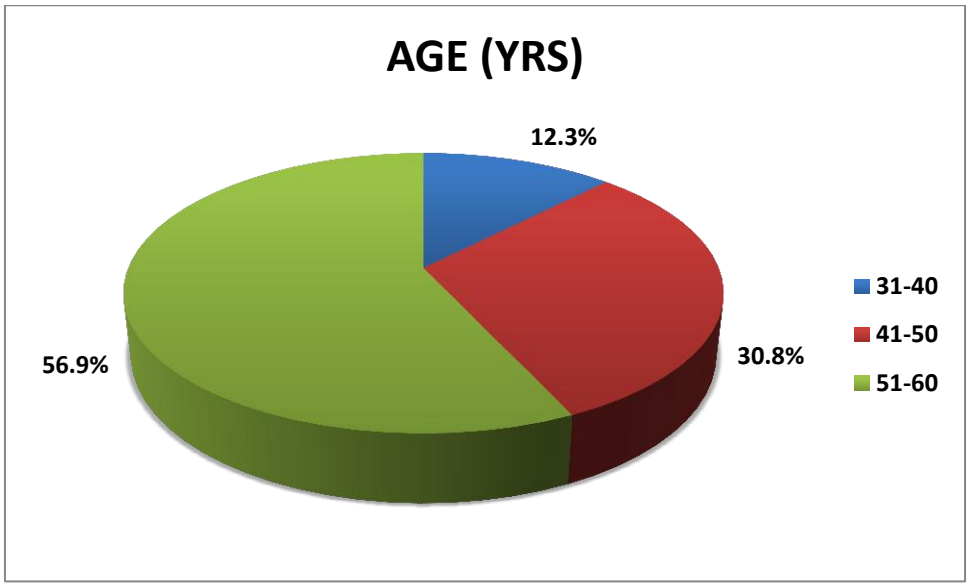
TABLE: DISTRIBUTION OF CASES ACCORDING TO AGE

AGE (YRS)	**N**	**%**
31-40	8	12.3
41-50	20	30.8
51-60	37	56.9
Total	65	100

	RANGE	**Mean**	**SD**
AGE (YRS)	32-60	52.1	7.8

In this study of 65 patients presenting with acute coronary syndrome between 30-60 years , age group of 50-60 years are affected more compared to other age groups with mean range of 52.1 and SD OF 7.8 observed respectively.

FIGURE: DISTRIBUTION OF CASES ACCORDING TO AGE



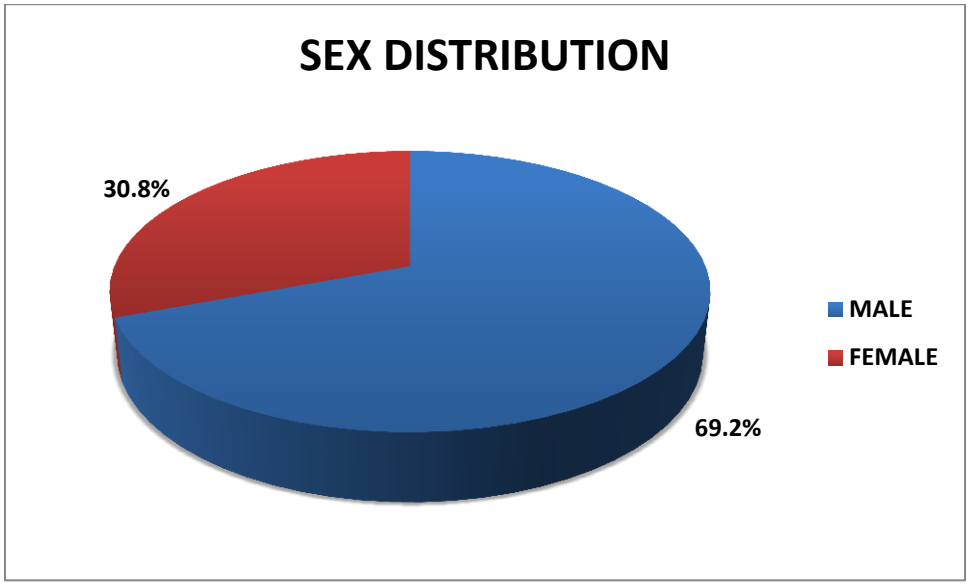
This graph depicts that most common age group involved in our study were between 51 to 60 yrs

TABLE: DISTRIBUTION OF CASES ACCORDING TO SEX

SEX	N	%
MALE	45	69.2
FEMALE	20	30.8
Total	65	100

In this study of 65 patients, males were 45 patients and females were 20 patients

FIGURE: DISTRIBUTION OF CASES ACCORDING TO SEX



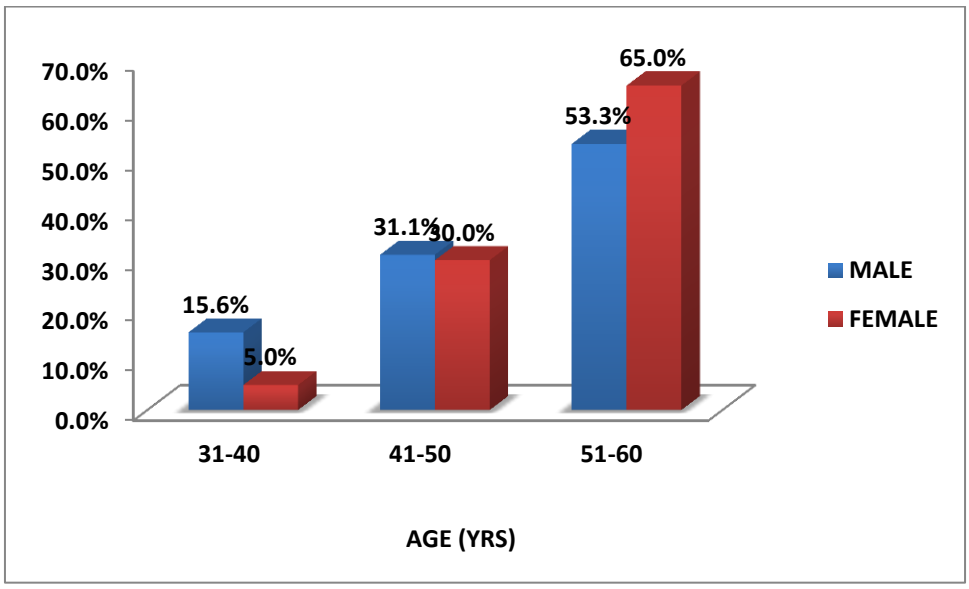
This graph depicts that male patients were studied more compared to female patients

TABLE: ASSOCIATION OF AGE AND SEX

AGE (YRS)	MALE		FEMALE		p value
	N	%	N	%	
31-40	7	15.6%	1	5.0%	0.452
41-50	14	31.1%	6	30.0%	
51-60	24	53.3%	13	65.0%	
Total	45	100.0%	20	100.0%	

In this study, out of 65 patients, there were7 male patients with age group between 31 to 40yrs , 14 male patients with age group between 41 to 50 yrs and 24 male patients with age group between 51 to 60yrs and 1 female with age group between 31 to 40 yrs , 6 females with age group between 41 to 50 yrs and 13 female patients with age group between 51 to 60 yrs , out of which 51 to 60 yrs age group were most commonly affected age group between male and female patients, however the difference is not statistically significant with p value 0.452

FIGURE: ASSOCIATION OF AGE AND SEX



This graph depicts the association of age and sex correlation in acute coronary syndrome

TABLE: OVERALL MEAN LEVEL OF SERUM HOMOCYSTEINE

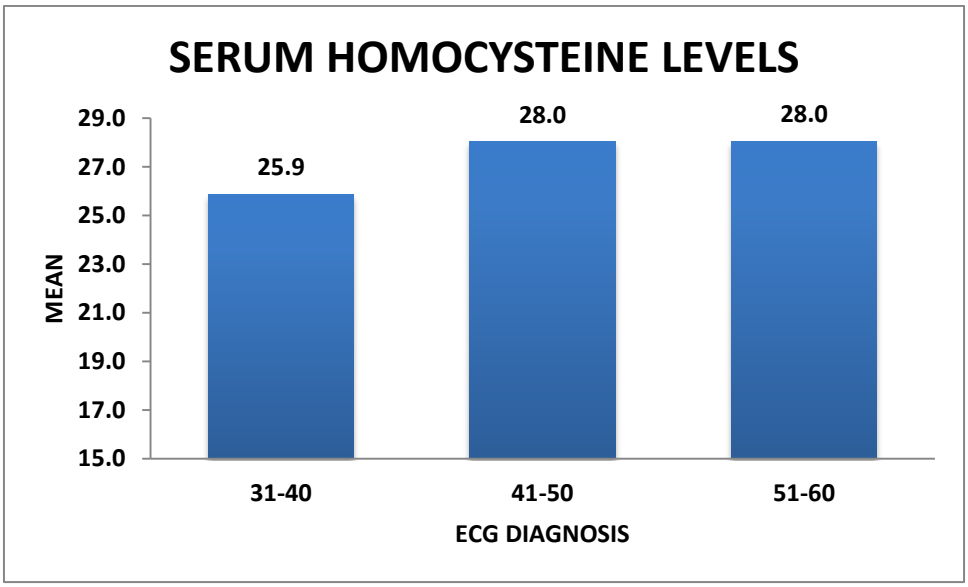
	RANGE	Mean	SD
SERUM HOMOCYSTEINE LEVELS	15-42	27.8	6.1

TABLE: MEAN LEVEL OF SERUM HOMOCYSTEINE ACCORDING TO AGE

AGE (YRS)	SERUM HOMOCYSTEINE LEVELS		p value
	Mean	SD	
31-40	25.9	8.2	0.649
41-50	28.0	5.4	
51-60	28.0	6.0	
Total	27.8	6.1	

In our study, mean level of serum homocysteine is higher in age group between 51-60 years than younger patients below 50 years respectively with Satistically significant **p value** 0.649

FIGURE: MEAN LEVEL OF SERUM HOMOCYSTEINE ACCORDING TO AGE



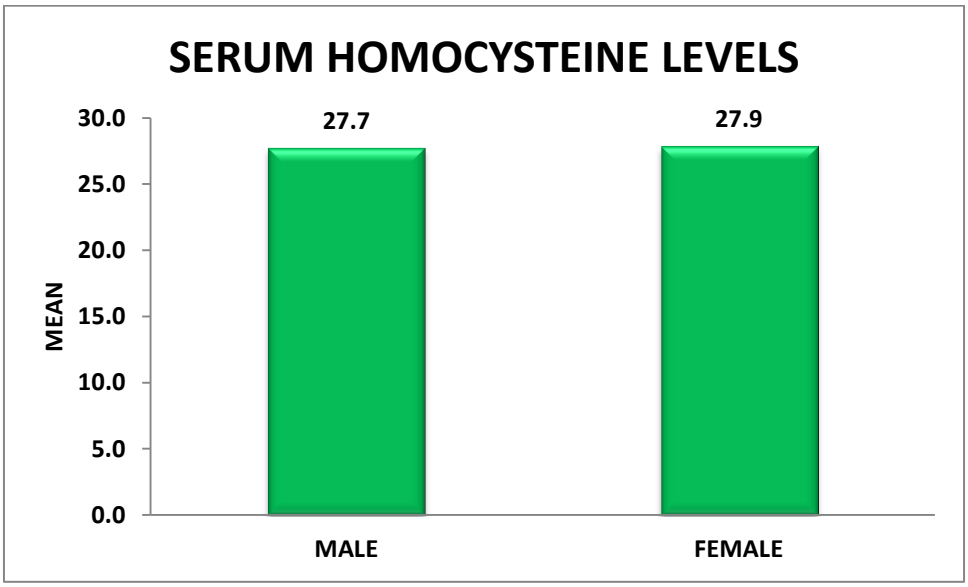
This is the graph depicting the mean homocystiene levels which are higher among age group between 51 to 60 yrs who are more prone for acute coronary syndrome.

TABLE: MEAN LEVEL OF SERUM HOMOCYSTEINE ACCORDING TO SEX

SEX	MALE		FEMALE		p value
	Mean	SD	Mean	SD	
SERUM HOMOCYSTEINE LEVELS	27.7	6.0	27.9	6.4	0.932

In our study, mean value of serum homocysteine level is higher in female patients than male patients with statisticallynon significant**p value** 0.932 with not much association of risk of acute coronary syndrome between the gender of patients.

FIGURE: MEAN LEVEL OF SERUM HOMOCYSTEINE ACCORDING TO SEX



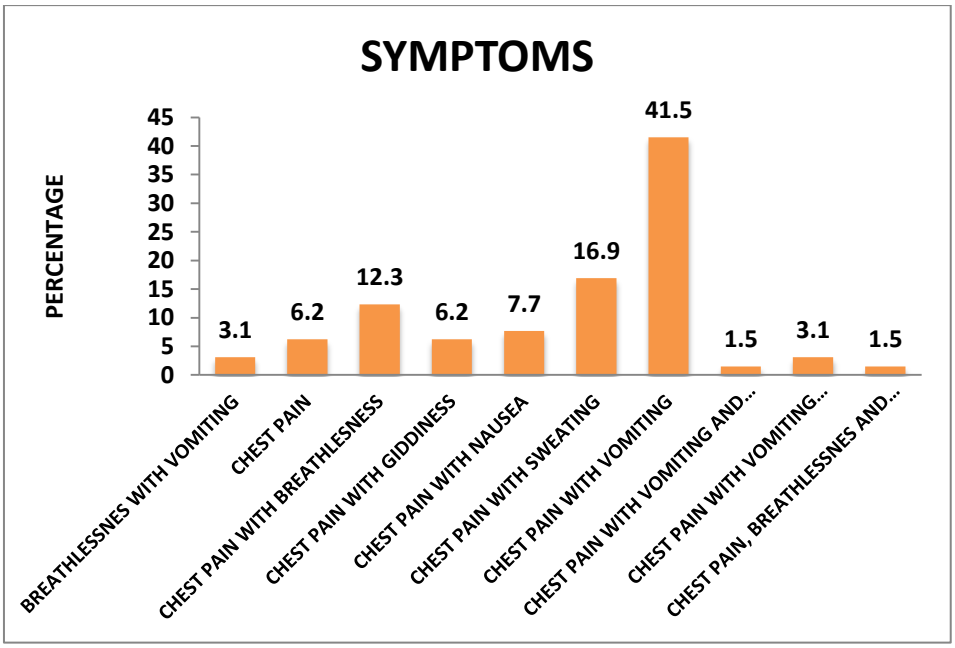
This is the graph depicting mean serum homocystiene levels between male and female patients which does not show any correlation between association of risk of acute coronary syndrome.

TABLE: DISTRIBUTION OF CASES ACCORDING TO SYMPTOMS

SYMPTOMS	N	%
BREATHLESSNES WITH VOMITING	2	3.1
CHEST PAIN	4	6.2
CHEST PAIN WITH BREATHLESNESS	8	12.3
CHEST PAIN WITH GIDDINESS	4	6.2
CHEST PAIN WITH NAUSEA	5	7.7
CHEST PAIN WITH SWEATING	11	16.9
CHEST PAIN WITH VOMITING	27	41.5
CHEST PAIN WITH VOMITING AND NAUSEA	1	1.5
CHEST PAIN WITH VOMITING WITH SWEATING	2	3.1
CHEST PAIN, BREATHLESSNES AND VOMITING	1	1.5
Total	65	100

` In our study of 65 patients, most of the patients came with complaints of chest pain with vomiting that is 27 patients(41.5%) ,with next most common presenting complaints with chest pain with sweating ,11 patients(16.9%).

FIGURE: DISTRIBUTION OF CASES ACCORDING TO SYMPTOMS



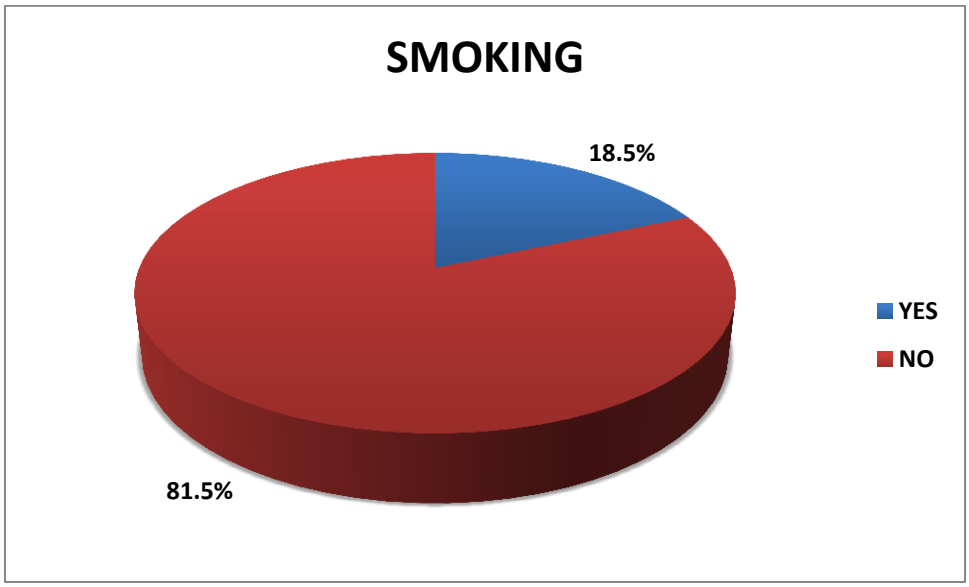
This is the graph depicting the patients of acute coronary syndrome , most commonly they presented with complaints of chest pain with vomiting with mean percentage of 41.5% patients are presented to our hospital

TABLE: DISTRIBUTION OF CASES ACCORDING TO SMOKING

SMOKING	N	%
YES	12	18.5
NO	53	81.5
Total	65	100

In our study of 65 patients only 12(18.5%) patients were smokers and remaining 53(81.5%) patients were non smokers with no significant association of hyperhomocystienemia in these patients .

FIGURE: DISTRIBUTION OF CASES ACCORDING TO SMOKING



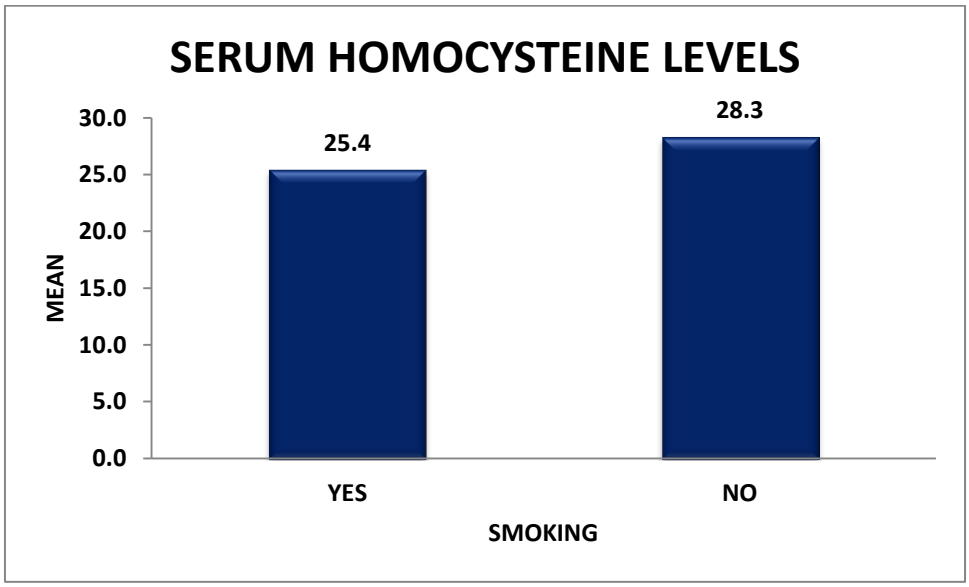
This graph depicts that non smokers were involved more compared to smokers

TABLE: MEAN LEVEL OF SERUM HOMOCYSTEINE ACCORDING TO SMOKING

SMOKING	YES		NO		p value
	Mean	SD	Mean	SD	
SERUM HOMOCYSTEINE LEVELS	25.4	5.7	28.3	6.1	0.144

Mean value of serum homocysteine level is higher among non smokers(28.3) compared to smokers(25.4) with statistically non significant**p value** 0.144 ,as smoking is one of the important risk factor for acute coronary syndrome.

FIGURE: MEAN LEVEL OF SERUM HOMOCYSTEINE ACCORDING TO SMOKING



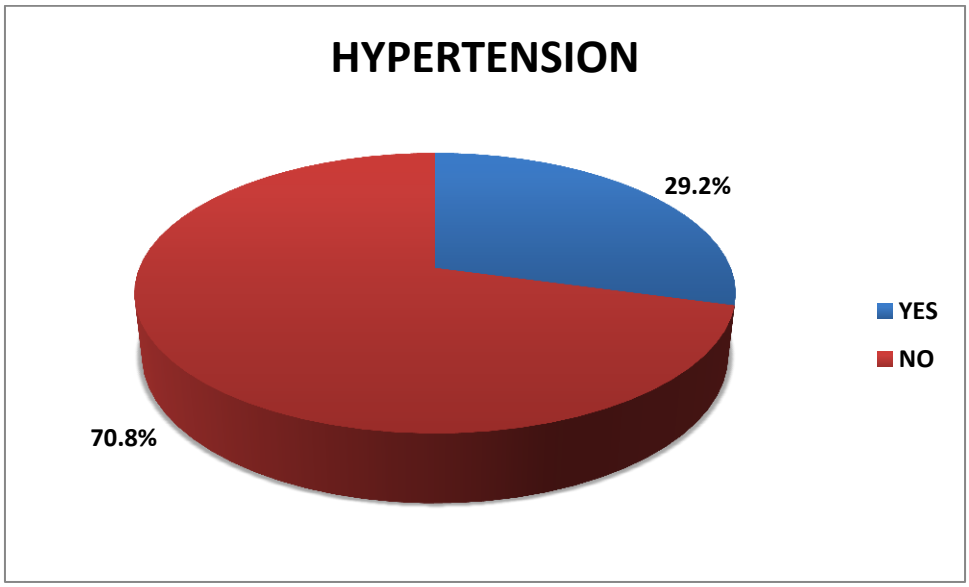
This is the graph depicting homocysteiene levels in smokers and non smokers with no significant association of hyperhomocysteinemia in non smokers , as smokers are more prone for acute coronary syndrome

TABLE: DISTRIBUTION OF CASES ACCORDING TO HYPERTENSION

HYPERTENSION	N	%
YES	19	29.2
NO	46	70.8
Total	65	100

In our patients with acute coronary syndrome normotensive patients are 46(70.8%)and hypertensivesare 19(29.2%) respectively.

FIGURE: DISTRIBUTION OF CASES ACCORDING TO HYPERTENSION



This is the graph depicting the hypertensives and non hypertensives in our study group

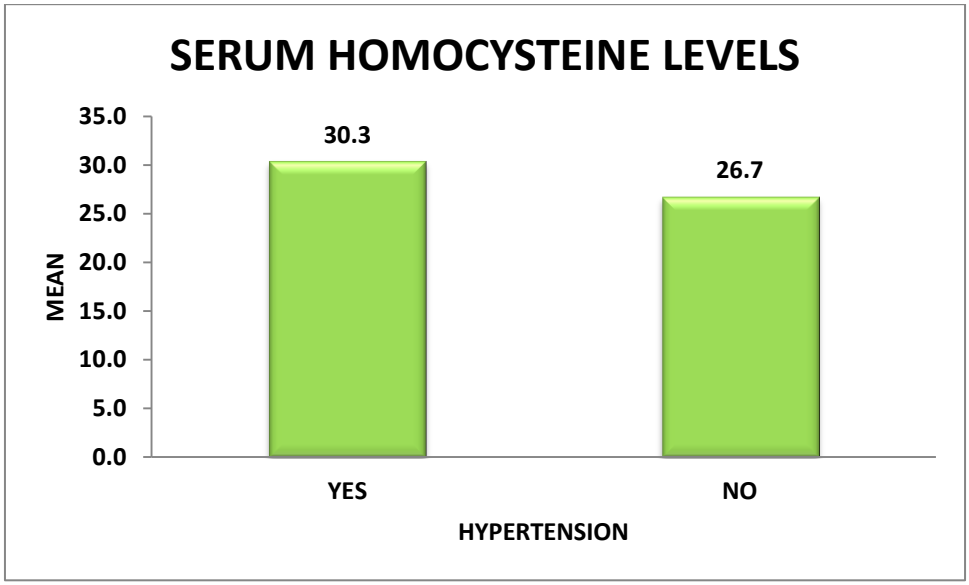
TABLE: MEAN LEVEL OF SERUM HOMOCYSTEINE ACCORDING TO HYPERTENSION

HYPERTENSION	YES		NO		p value
	Mean	SD	Mean	SD	
SERUM HOMOCYSTEINE LEVELS	30.3	7.2	26.7	5.3	0.027*

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

In our study of 65 patients , mean value of serum homocysteine level is higher in Hypertensives, with a mean of30.3 with SD 7.2 compared tonormotensive patients with a mean of 26.7 with SD 5.3, with statistically significant correlation with p value 0.027.

FIGURE: MEAN LEVEL OF SERUM HOMOCYSTEINE ACCORDING TO HYPERTENSION



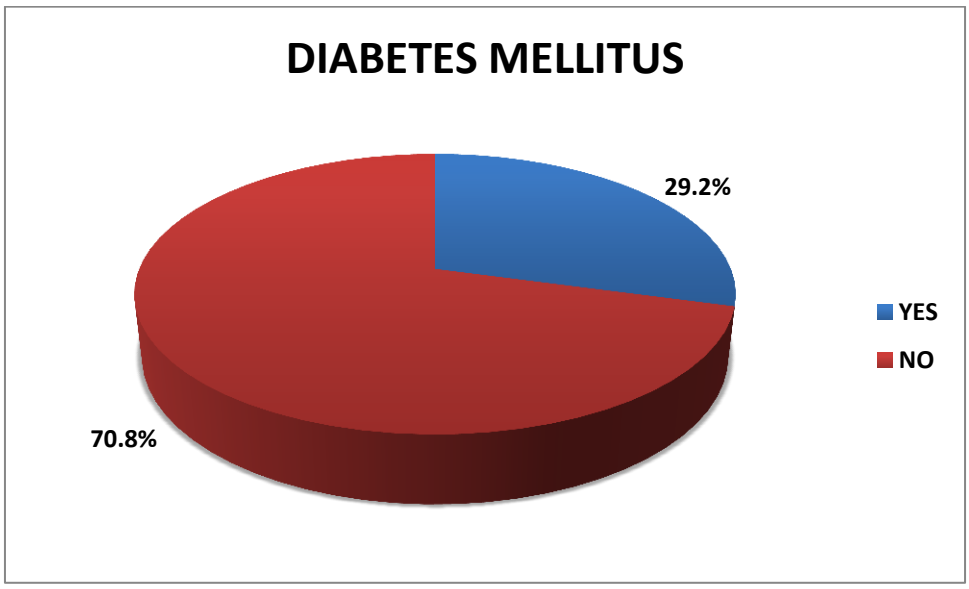
This is the graph depicting mean homocysteiene level higher among hypertensives compared to normotensives

TABLE: DISTRIBUTION OF CASES ACCORDING TO DIABETES MELLITUS

DIABETES MELLITUS	N	%
YES	19	29.2
NO	46	70.8
Total	65	100

Out of 65 patients in our study,19(29.2%) patients were diabetic and rest ofthe patients were non diabetic 46(70.8%).

FIGURE: DISTRIBUTION OF CASES ACCORDING TO DIABETES MELLITUS



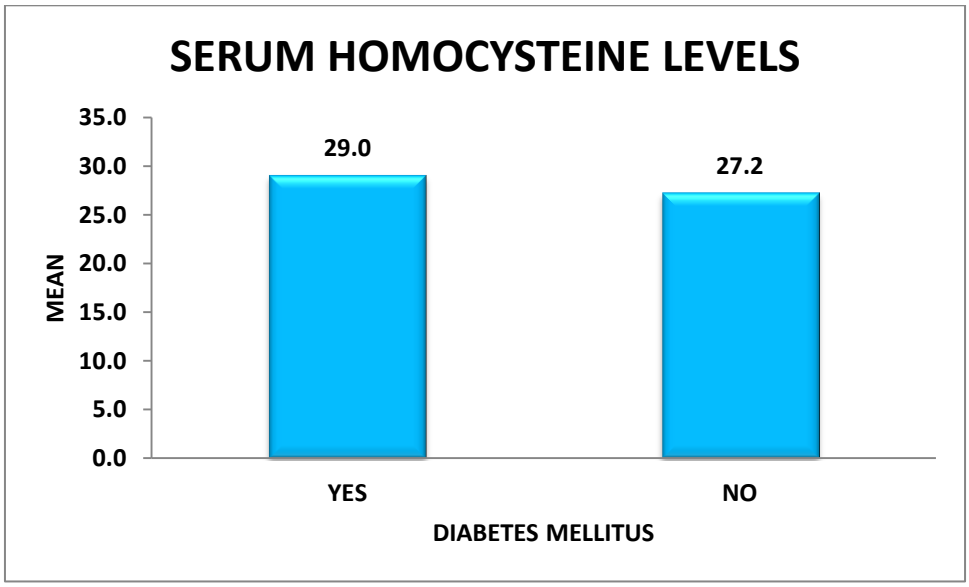
This graph depicts 29.2% were diabetic and 70.8% were non diabetic

TABLE: MEAN LEVEL OF SERUM HOMOCYSTEINE ACCORDING TO DIABETES MELLITUS

DIABETES MELLITUS	YES		NO		p value
	Mean	SD	Mean	SD	
SERUM HOMOCYSTEINE LEVELS	29.0	6.6	27.2	5.8	0.281

Out of 65 patients, mean value of serum homocysteine level is higher in diabetics (29.0) with SD 6.6 than non diabetic patients (27.2) with SD 5.8, with statistically significant p value 0.281.thereby there is strong association of high risk of acute coronary syndrome.

FIGURE: MEAN LEVEL OF SERUM HOMOCYSTEINE ACCORDING TO DIABETES MELLITUS



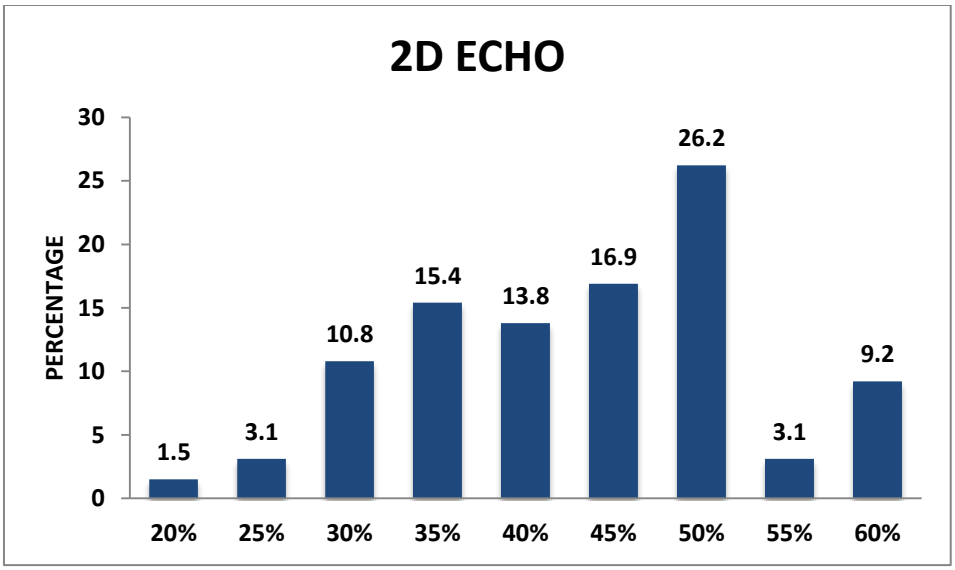
This graph depicts serum homocystiene levels are higher in diabetic patients than non diabetics

TABLE: DISTRIBUTION OF CASES ACCORDING TO 2D ECHO

2D ECHO	N	%
20%	1	1.5
25%	2	3.1
30%	7	10.8
35%	10	15.4
40%	9	13.8
45%	11	16.9
50%	17	26.2
55%	2	3.1
60%	6	9.2
Total	65	100

In our study of 65 patients mean value of serum homocysteine level is higher in17 patients(26.2%) with ejection fraction of 50% respectively and mean value of serum homocysteine least in 1 patient with ejection fraction 20%. However the death rate is more significant in patients with ejection fraction 20%

FIGURE: DISTRIBUTION OF CASES ACCORDING TO 2D ECHO



This is the graph depicting patients with ejection fraction 50%(26.2) are most commonly having the moderate level of homocystiene with moderate risk of acute coronary syndrome in these patients but compared patient with ejection fraction 20% , homocystiene is higher in these patients with high mortality among these patients

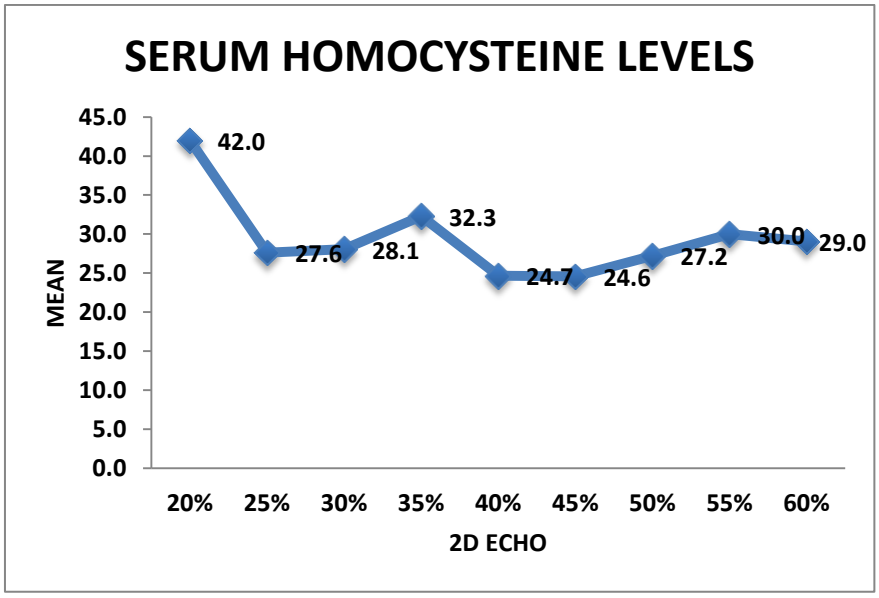
TABLE: MEAN LEVEL OF SERUM HOMOCYSTEINE ACCORDING TO 2D ECHO

2D ECHO	SERUM HOMOCYSTEINE LEVELS		p value
	Mean	SD	
20%	42.0	0.0	0.019*
25%	27.6	6.2	
30%	28.1	2.6	
35%	32.3	6.9	
40%	24.7	6.5	
45%	24.6	6.3	
50%	27.2	4.1	
55%	30.0	2.8	
60%	29.0	6.7	
Total	27.8	6.1	

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

Mean value of serum homocysteine level is higher in patients 20% ejection fraction with a mean of 42.0 with SD 0.0, than others with statistically significant p value 0.019 respectively.

FIGURE: MEAN LEVEL OF SERUM HOMOCYSTEINE ACCORDING TO 2D ECHO



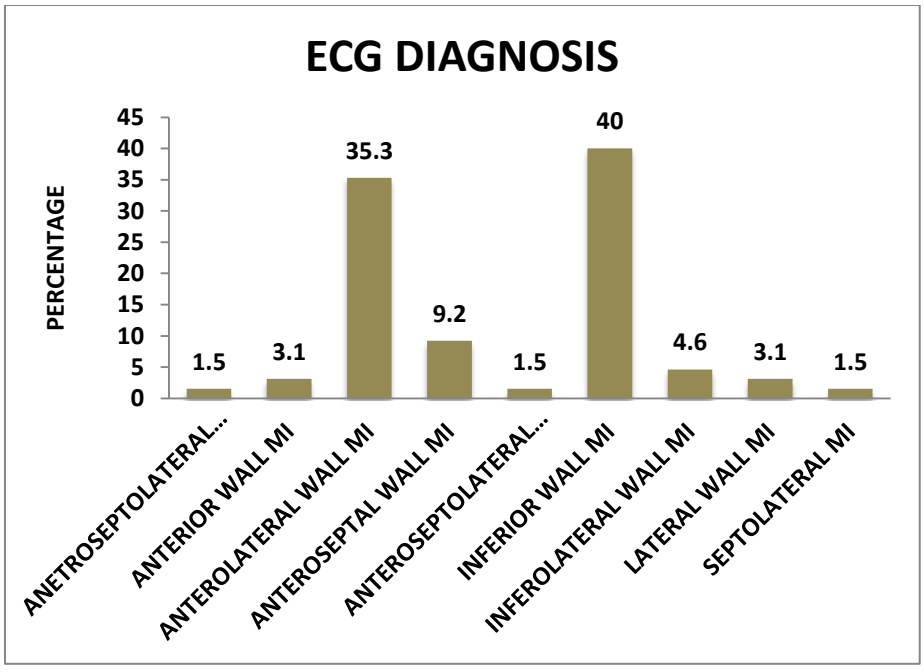
This graph depicts that serum homocysteine levels with low ejection fraction has higher risk of acute coronary syndrome

TABLE: DISTRIBUTION OF CASES ACCORDING TO ECG DIAGNOSIS

ECG DIAGNOSIS	N	%
ANETROSEPTOLATERAL WALL MI	1	1.5
ANTERIOR WALL MI	2	3.1
ANTEROLATERAL WALL MI	23	35.3
ANTEROSEPTAL WALL MI	6	9.2
ANTEROSEPTOLATERAL WALL MI	1	1.5
INFERIOR WALL MI	26	40
INFEROLATERAL WALL MI	3	4.6
LATERAL WALL MI	2	3.1
SEPTOLATERAL MI	1	1.5
Total	65	100

In our study of 65 patients, majority of patients are presented with inferior wall mi that is around 26 patients (40%), and also presented with anterolateral wall mi that is around 23 patients (35%).

FIGURE: DISTRIBUTION OF CASES ACCORDING TO ECG DIAGNOSIS



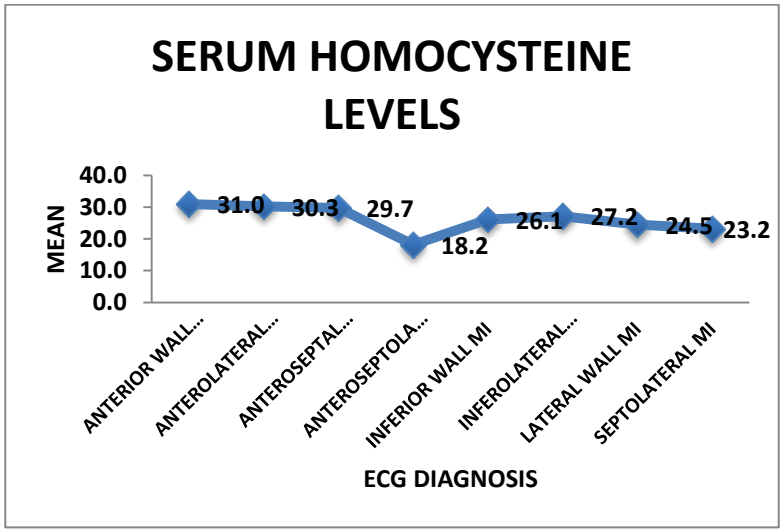
This graph depicts that majority of patients presented in our study are inferior wall mi , next most common are anterolateral wall mi with least being anteroseptolateral wall mi.

TABLE: MEAN LEVEL OF SERUM HOMOCYSTEINE ACCORDING TO ECG DIAGNOSIS

ECG DIAGNOSIS	SERUM HOMOCYSTEINE LEVELS		p value
	Mean	SD	
ANTERIOR WALL MI	31.0	11.3	0.059
ANTEROLATERAL WALL MI	30.3	5.8	
ANTEROSEPTAL WALL MI	29.7	7.7	
ANTEROSEPTOLATERAL WALL MI	18.2	4.0	
INFERIOR WALL MI	26.1	4.7	
INFEROLATERAL WALL MI	27.2	7.3	
LATERAL WALL MI	24.5	7.8	
SEPTOLATERAL MI	23.2	0.0	
Total	27.8	6.1	

Mean value of serum homocysteine level in our patients is higher in patients with Anterior wall MI with mean value of 31.0 and SD of 11.3 with statisticallysignificant p value 0.059 suggestive of high risk of death among these patient groups

FIGURE: MEAN LEVEL OF SERUM HOMOCYSTEINE ACCORDING TO ECG DIAGNOSIS



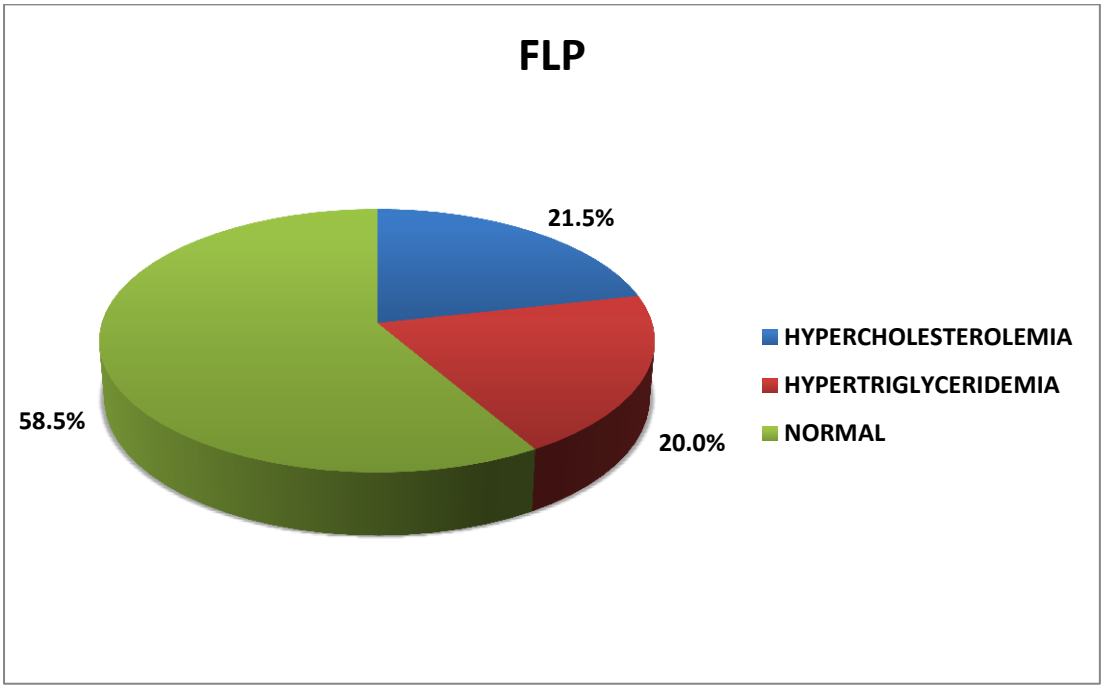
This above graph depicts that patients with anterior wall mi have higher values of serum homocystiene levels with high risk of death among these patient groups

TABLE: DISTRIBUTION OF CASES ACCORDING TO FLP

F. L. P	N	%
HYPERCHOLESTEROLEMIA	14	21.5
HYPERTRIGLYCERIDEMIA	13	20
NORMAL	38	58.5
Total	65	100

In our study of 65 patients, hypercholesterolemia is seen in 14 patients(21.5%) and hypertriglyceridemia patients were 13 (20%) and 38(58.5%) patients were having normal lipid profile.

FIGURE: DISTRIBUTION OF CASES ACCORDING TO FLP



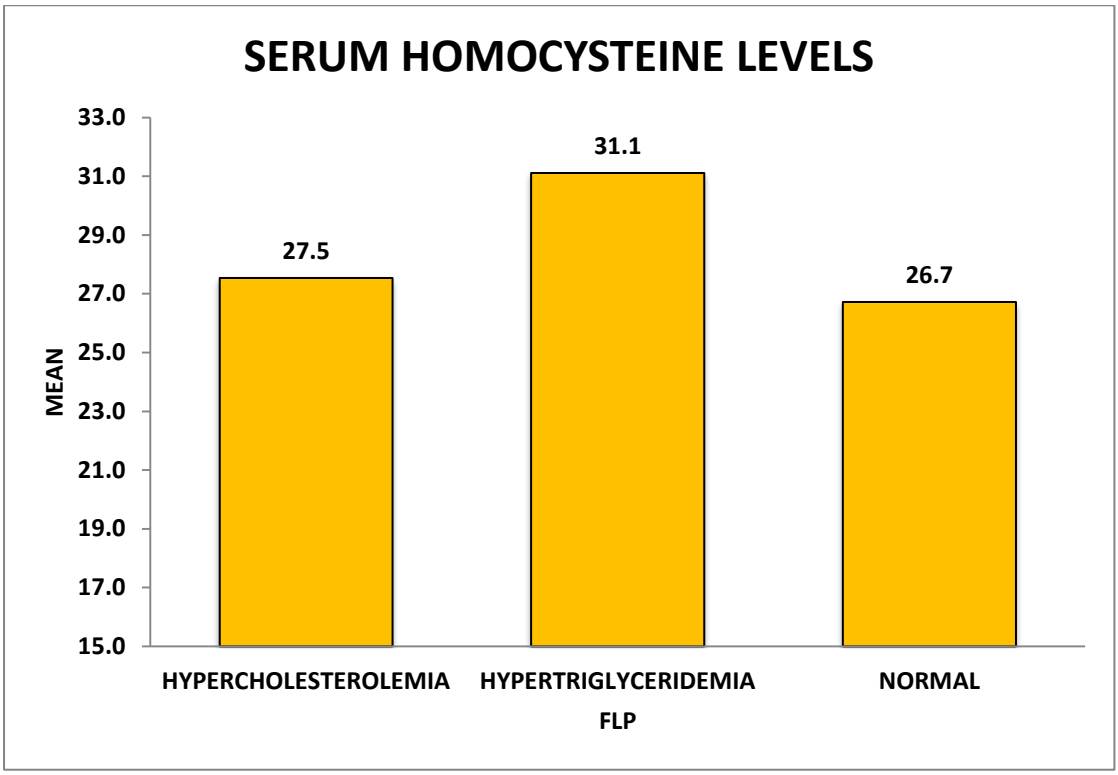
This graph depicts that hypertriglyceridemia patients were more in our study group compared to hypercholesterolemia and normal patients

TABLE: MEAN LEVEL OF SERUM HOMOCYSTEINE ACCORDING TO FLP

FLP(FASTING LIPID PROFILE)	SERUM HOMOCYSTEINE LEVELS		p value
	Mean	SD	
HYPERCHOLESTEROLEMIA	27.5	6.5	0.077
HYPERTRIGLYCERIDEMIA	31.1	7.4	
NORMAL	26.7	5.1	
Total	27.8	6.1	

In our study group , mean value of serum homocysteine level is higher in hypertriglyceridemia patients with mean of 31.1 with SD of 7.4% than hypercholesterolemia patients with mean of 27.5 with SD of 6.5%, however the association is statistically non significant with p value 0.077 and hence in patients with low serum cholesterol levels have no significant correlation with hyperhomocystienemia and hence in patients with normal cholesterol levels , homocystiene acts as a triggering factor for acute coronary syndrome.

FIGURE: MEAN LEVEL OF SERUM HOMOCYSTEINE ACCORDING TO FLP



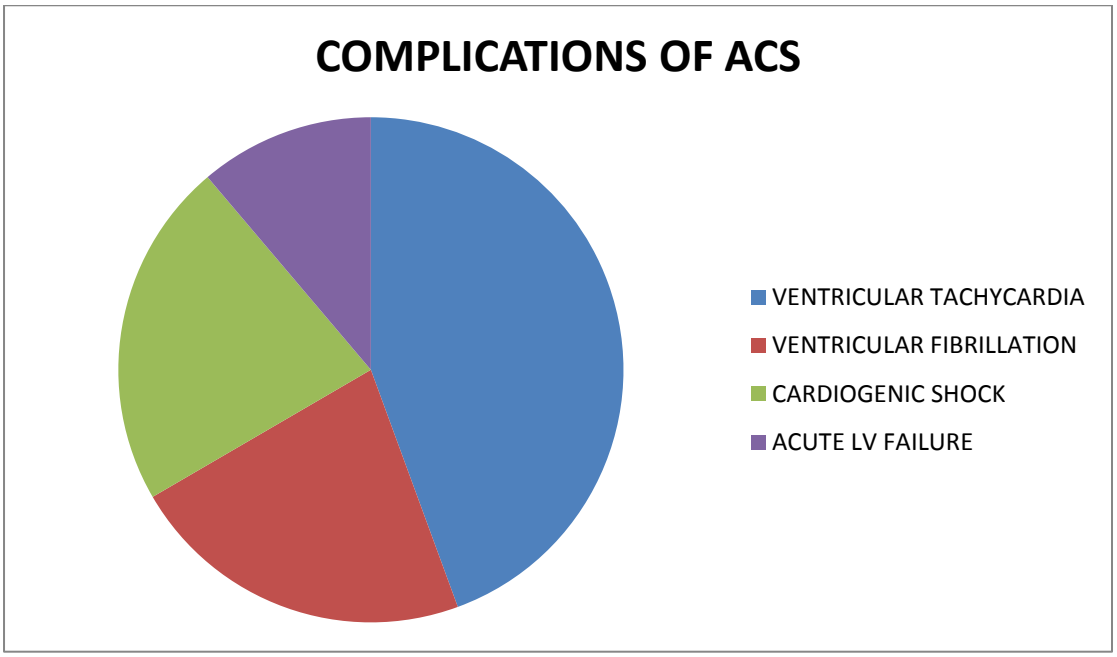
This graph depicts serum homocystiene values are higher in hypertriglyceridemia patients compared to normal patients.

Distribution Of Cases According To Complications

COMPLICATIONS OF ACUTE CORONARY SYNDROME	NUMBER OF DEATHS DUE TO COMPLICATIONS WITH HIGH HOMOCYSTIENE LEVELS(N)	SERUM HOMOCYSTIENE LEVELS RANGE	%
VENTRICULAR FIBRILLATION	**2**	**32 -34**	**22.2**
VENTRICULAR TACHYCARDIA	**4**	**35 -40**	**44.4**
CARDIOGENIC SHOCK	**2**	**30-33**	**22.2**
ACUTE LV FAILURE	**1**	**30-34**	**11.2**
TOTAL DEATHS	**9**	**30-40**	**100**

In our study out of 65 patients, 9 deaths happened secondary to complications of acute coronary syndrome with very high homocystiene levels have more complications leading to death. Out of 9 patients with high homocystiene levels, ventricular tachycardia patients(4) have very high mortality rate(44.4%)

FIGURE: DISTRIBUTION OF CASES ACCORDING TO COMPLICATIONS WITH HIGH HOMOCYSTIENE LEVELS



This graph depicts that deaths due to complications with very high homocystiene levels is more commonly with ventricular tachycardia

TABLE: MEAN LEVEL OF HOMOCYSTIENE ACCORDING TO COMPLICATIONS

COMPLICATIONS OF HIGH HOMOCYSTIENE LEVELS	MEAN	STANDARD DEVIATION(SD)	P value
VENTRICULAR FIBRILLATION	**28.1**	**6.2**	
VENTRICULAR TACHYCARDIA	**33.2**	**2.1**	
CARDIOGENIC SHOCK	**27.4**	**4.6**	
ACUTE LV FAILURE	**22.2**	**5.2**	
TOTAL	**27.1**	**3.6**	0.012

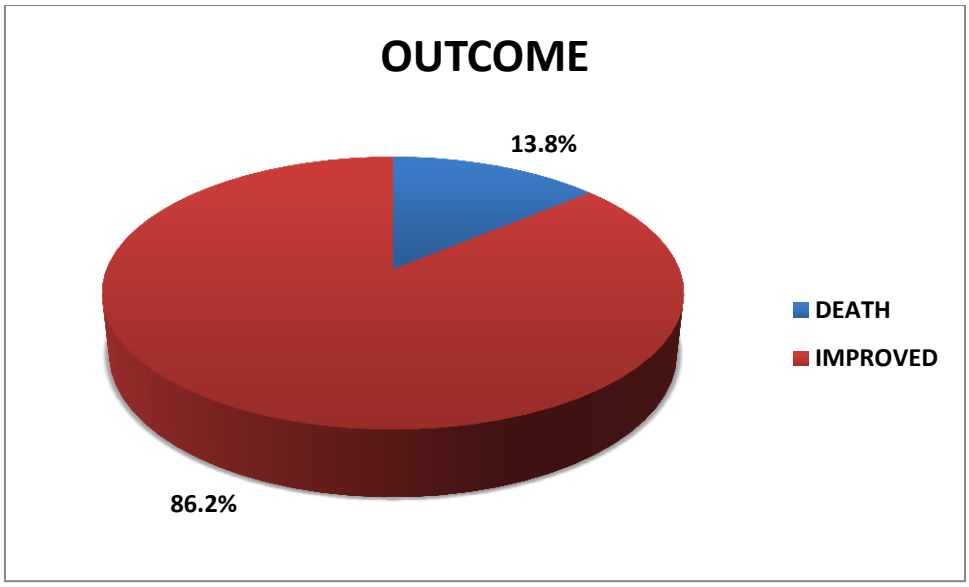
Out of 9 patients who died because of complications, ventricular tachycardia is the most common complication with a mean of 33.2 with SD OF 2.1 leading to death in patients with very high homocystiene levels**.**

TABLE: DISTRIBUTION OF CASES ACCORDING TO OUTCOME

OUTCOME	N	%
DEATH	9	13.8
IMPROVED	56	86.2
Total	65	100

In our study of 65 patients with acute coronary syndrome , 9 patients(13.8%) had very high serum homocysteine levels and died and 56 patients(86.2%) of who are having moderately high serum homocysteiene levels have been improved with medical therapy

FIGURE: DISTRIBUTION OF CASES ACCORDING TO OUTCOME



This graph depicting the number of deaths in acute coronary syndrome patients with comparing to improved patients with medical therapy

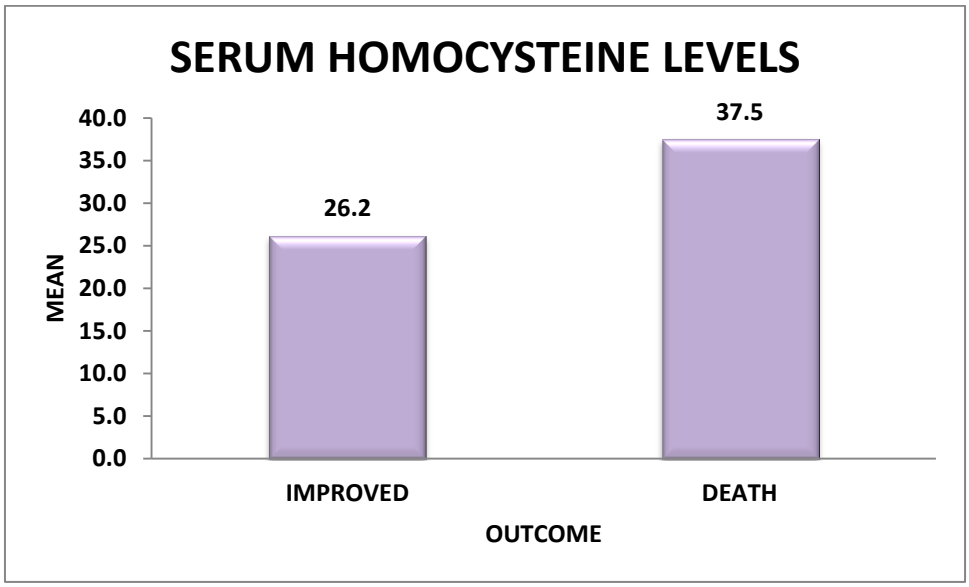
TABLE: MEAN LEVEL OF SERUM HOMOCYSTEINE ACCORDING TO OUTCOME

OUTCOME	IMPROVED		DEATH		p value
	Mean	SD	Mean	SD	
SERUM HOMOCYSTEINE LEVELS	26.2	4.8	37.5	3.6	<0.001*

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

In our study mean value of serum homocystienelevels is significantly correlating to the outcome of the patients in acute coronary syndrome patients with a mean death of 37.5 with SD 3.6 who are having higher homocysteine levels compared to patients who have improved with a mean improval rate of 26.2 with SD of 4.8, which proves a statistically very significant correlation with a p value of <0.001.

FIGURE: MEAN LEVEL OF SERUM HOMOCYSTEINE ACCORDING TO OUTCOME



This graph depicts among 65patients with acute coronary syndrome mean value of homocystiene level is higher among death patients with significant p-value of <0.001 with compared to patients who got improved after acute coronary syndrome.

DISCUSSION

This study is an observational studyconducted over a period of one and half years from December 2017 to April 2019 to analyze serum homocystiene as a risk factor in acute coronary syndrome of middle age group . A total of 65 patients included in this study and were analyzed to study homocystiene levels in acute coronary syndrome patients

Hyperhomocysteinemia is currently regarded as an independent and modifiable risk factor for ischemic vascular diseases and thrombosis. We measured fasting plasma total homocysteine levels by HPLC with fluorescence detection in 65 patients presenting with acute coronary syndromes. Demographic data, classical risk factors (systolic blood pressure, diabetes mellitus, smoking, ethanol intake, family history of ischaemic heart disease) and life-style habits were recorded. Lipid fractions including total cholesterol, triglycerides, HDL-cholesterol, total cholesterol/HDL-cholesterol ratio, serum creatinine, LDL-cholesterol and vitamins involved in the metabolism of homocysteine, folic acid and vitamin B12 were also assessed[(24).]

.In our study, the most common age group affected is 50-60 years more compared to other age groups with mean range of 52.1 and SD OF 7.8 observed respectively.

Another study done by Mesas C et al [(25)] in 50 patients hospitalized with acute coronary syndrome in Southern Brazil, they observed that, mean age group was 59 years (standard deviation SD = 10.5 years) which was significantly similar as in this study. In a study done by Ajay VS et al [(26)] it was found than mean age group has changed in last 50 years. In a study done by Kristensen B[1], Malm J, et althey found out that increase in Hcy levels in middle aged adults had thrombogenic risk mediated in part by interactions with the fibrinolytic system in acute coronary syndrome

patients[27].

In this study there was male predominance i.e, 69.2% of patients and female patients were 30.8%, which was similar to study done by Scholz K et al [28] where male patients were 74% and female patients were 26%. In a study done by Cenko E et al [29] out of 8834 subjects studied, male patients were 69.9% and female were 30.1%, and they all found that gender association was not there with hyperhomocysteinemia in acute coronary syndrome patients.

In our study of 65 patients , 63 patients (96.9%) had chest pain with vomiting and nausea, 2 patients(3.1%) had breathlessness with vomiting. The common presenting symptom was chest pain (63 patients). Similarly in a study done by Goel PK et al [30] in 609 patients admitted with ACS for 1 year in 2008, they found that the most common symptom in patients with acute coronary syndrome was chest pain (84%), followed by breathlessness (8.7%) and vomiting(2.6%)[31].

In other study done by Conto J G et al[32] in 434877 patients admitted with acute myocardial infarction, they found that chest pain was present in 67% of patients[33] which is same as that observed in this study and they all find out that most common presenting symptom is chest pain in acute coronary syndrome. In all these middle aged patients homocystiene levels were found to be persistently high[34]

In this study of out of 65 patients, anterolateral wall MI in 23 patients (35.3%), inferior wall MI in 26 patients(40%). Out of 65 patients with ST segment elevation in anterior leads (such as anterior, anteroseptal and anterolateral leads ST elevation) was seen in 36 patients, inferior leads ST elevation was seen in 29 patients. The most common ST segment elevation was seen in anterior leads. In a study done by Alashetty AS et al [35]in 2014, only 48.2% of patients had ST segment elevation which was significantly lower than this study. In another study done by Saczynski J et al [36]

out of 7215 patients with acute myocardial infarction, STEMI was found in 61.56% and 38.04% were NSTEMI which is significantly lower than this study[37]. The most common ST segment elevation was seen in anterior leads. In a study done by Reddy C S T et al [38]in 2013, they concluded that electrocardiogram identification of culprit artery helps in not only localization of proximal or distal occlusion but also to predict severity of myocardial infarction and plan emergency management. In a study done by VijethaShenoy, VeenaMehendale et al[39] found out that homocysteine was an independent risk factor for cardiovascular disease and it estimated that 10 % of population's CVD risk is attributed to the elevated levels of homocysteine. In this study they had shown that homocysteine suppresses the vasodilator nitric oxide by increasing the levels of asymmetric dimethylarginine (ADMA), a strong inhibitor of nitric oxide synthase (eNOS). If this mechanism is true, this could certainly account for dramatic changes in vascular endothelial compliance and platelet coagulation changes that promote cardiovascular disease, in our study most common mortality is associated with anterior wall MI

In this study of 65 patients, echocardiographic parameters like regional wall motion abnormality, ejection fraction had been studied. Out of 65 patients, 10 patients had ejection fraction of 35%, 11 patients had EF(ejection fraction) of 45% , 17 patients had EF of 50%, 6 patients had EF of 60%, 2 patients had EF of 25% and 1 patient had EF of 20%. In our study patients with anterior wall MI with EF of less than 40% had higher mortality.

In our study moderately raised plasma homocystiene concentration measured on admission to our hospital is a strong predictor of adverse cardiac events in acute coronary syndrome. The multiple risk factors trial of intervention suggested that homocystiene may be a stronger risk factor for cardiovascular event. In a study done

by nygardet al[40] who examined the prognostic significance for cardiac death of homocystiene concentrations in a selected group of patients referred for coronary angiogram.

Different geographic locations and different ethnic backgrounds have different genetic responses and to evaluate hyper-homocysteinemia effect in our population we compared our results to similar studies from Asian populations. Mahalle et al. [40]conducted a similar study in Asia having 216 patients with coronary artery disease, among whom 95.3% had hyper-homocysteinemia

The main pathological phenomenon here is toxic effects on vascular endothelium, impaired endothelium dependant relaxation , a hypercoagulable state due to downregulation of thrombomodulin expression , activation of factor V , inhibition of protein C , increased platelet aggregation , henceforth all of these explain that hyperhomocystienemia will leads to adverse cardiac events in acute coronary syndrome by indirectly affecting the coagulation cascade[41].

In a study done by peter J. stubbs et al[42], concluded that elevated levels of homocystiene strongly predicts late cardiac events in acute coronary syndromes.

Similarly in a study done by torbjornomland,et al. conducted study on 65 patients over median follow up of 628days , the relative risk of mortality for patients with homocystiene with upper quartile is more compared to patients with lower quartile (RR-1.69, 95% CI) Henceforth homocystiene levels are strongest predictor for acute coronary syndrome.

SUMMARY

Sixty five patients with acute coronary syndrome were studied in ----------

----------between December 2017 to april 2019.

This study was conducted to know serum homocystiene level as a risk factor for in acute coronary syndrome in middle aged patients.

1. The common age group was 30 to 60 years. Age more than 30 years with vegetarian diet has increased risk of hyperhomocystienemia leading to high risk of hypercoaguable state leading to high risk of acute coronary syndrome.
2. In the present study male patients (69.2%) were more common than female (30.8%).
3. Out of 65 patients, the common wall motion abnormality was anteriolateral wall occurring in 23 patients. There was no significant association between hyperhomocystienemia and wall motion abnormality as p value was ≥0.059. Also the mean ejection fraction with high mortality is with 20% in these patients which was significant with p value <0.019.
4. Increased levels of homocystiene are directly proportional to the complications of acute coronary syndrome .
5. Serum homocystiene levels more than 30 was associated with occurrence of in-hospital major adverse cardiac events like death with significant p value<0.001.
6. Serum homocystiene levels should be routinely measured in patients with acute coronary syndrome for assessment of risk factors especially

who do not have traditional risk factors such as hypertension , smoking, and diabetes mellitus.

CONCLUSION

We can conclude from our study that hyperhomocystinemia is a strong risk factor for developing atherosclerosis and thrombus formation & thus leads to ischemic heart disease in middle aged patients .

Also increased levels of homocystiene are directly proportional to the complications of acute coronary syndrome. So hyperhomocysteinemia should be considered in the work-up of acute Myocardial infarction in middle aged people and those without conventional risk factors.

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ANNEXURE I

ETHICAL COMMITTEE CERTIFICATE

ANNEXURE II

INFORMED CONSENT FORM

TITLE OF THE PROJECT "SERUM HOMOCYSTEINE LEVEL AS A RISK FACTOR FOR ACUTE CORONARY SYNDROME IN MIDDLE AGED PERSONS."

PRINCIPAL INVESTIGATOR -

P.G.GUIDE NAME -

CHAIRMAN ETHICAL COMMITTEE

.

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

I) **INFORMED PART**

1) PURPOSE OF RESEARCH:

I have been informed about this study. I have also been given a free choice of participation in this study.

2) PROCEDURE:

I am aware that in addition to routine care received I will be asked series of questions by the investigator. I have been asked to undergo the necessary investigations and treatment, which will help the investigator in this study.

3) RISK AND DISCOMFORTS:

I understand that I may experience some pain and discomfort during the examination or during my treatment. This is mainly the result of my condition and the procedure of this study is not expected to exaggerate these feelings that are associated with the usual course of treatment.

4)BENEFITS:

I understand that my participation in this study will help to patients survival and better outcome.

5) CONFIDENTIALITY:

I understand that the medical information produced by this study will become a part of Hospital records and will be subject to the confidentiality and privacy regulation. Information of a sensitive personal nature will not be a part of the medical records, but will be stored in the investigator's research file and identified only by a code number. The code-key connecting name to numbers will be kept in a separate location.

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

6) REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study at any time.

----------is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of the study, which might influence my continued participation.

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

7) REFUSAL OR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and that I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice to my present or future care at this hospital. I also understand that ----------

----------may terminate my participation in the study after he has explained the reasons for doing so and has helped arrange for my continued care by my own physician or physical therapist, if this is appropriate.

8) INJURY STATEMENT:

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

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

_____ _____

Date

(Investigator)

II) **STUDY SUBJECT CONSENT STATEMENT:**

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

Participant / Guardian Date:

Witness to signature Date:

ANNEXURE III

CASE PROFORMA

Name of the patient :

Age in years :

Sex :

Address:

Religion:

Occupation:

IP no/OP no:

Presenting Complaints :

Past history:

Personal history:

1. Tobacco chewing

2. Smoking

3. Alcoholism

4. Diet- Veg/Mixed

5. No habits

Family history:

GENERAL PHYSICAL EXAMINATION :

Built :

Nourishment :

Ht(Cm) :

Wt(Kg) :

BMI:

Pallor

Icterus

Clubbing

Cyanosis

Edema

6. Vital parameters a. Pulse :

b. BP :

c. Respiratory rate :

d. Temperature

SYSTEMIC EXAMINATION:

ABDOMEN EXAMINATION

CARDIOVASCULAR SYSTEM

RESPIRATORY SYSTEM

CENTRAL NERVOUS SYSTEM

BIOCHEMISTRY

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

PATHOLOGY 1)Urine Routine	
Urine albumin	
Urine sugar Urine bile salts Urine bile pigments	
Urine microscopy RBC's Pus cells Cast's Epithelial cells	
2)Complete blood count:	
Hb	gm/dl
Total count	Cells/cumm
Differential count Neutrophils	%
Lymphocytes	%
Eosinophils	%
Basophils	%
Monocytes	%
ESR	At end of 1st hour.
Platelet Count	Lakhs/cumm

2D-ECHOCARDIOGRAPHY

LVIVSd : cm LVIDd : cm RVIDd:

cm LVPWd : cm LVISd : cm Aorta:

cm RVIDd : cm EF% : % PA : cm

VALVES :

Mitral Valve :

Aortic Valve :

Tricuspid Valve :

Pulmonary Valve :

CHAMBERS :

Left Ventricle :

Right Ventricle :

Left Ventricle :

Right Ventricle :

SEPTAE : GREAT ARTERIES

Aorta : Pulmonary Artery :

DOPPLER STUDY

Mitral Valve :

Aortic Valve :

Tricuspid Valve :

Pulmonary Valve :

REGIONAL WALL MOTION ABNORMALITIES :

PERICARDIAL EFFUSION :

CLOT/VEGETATION :

CONCLUSION :

ECG:

IMPRESSION AND CONCLUSION:

SIGNATURE

DATE:

MASTER CHART

Sl. No	IP NO	D.O.A	NAME	AGE	SEX	SMOKING	HYPERTENSION	DIABETES MELLITUS	SYMPTOMS	2D ECHO	ECG DIAGNOSIS	F. L. P	SERUM HOMOCYSTEINE LEVELS	OUTCOME
1	3065	29-01-2019	SITARAM RAJPUT	60YRS	MALE	NO	NO	YES	CHEST PAIN WITH VOMITING	IHD WITH EF-55%	ANTEROLATERAL WALL MI	HYPERTRIGLYCERIDEMIA	32	IMPROVED
2	2219	20-01-2019	LAKKAPPA GUDIHAL	60YRS	MALE	NO	NO	NO	CHEST PAIN WITH SWEATING	IHD WITH EF-30%	INFERIOR WALL MI	NORMAL	33	IMPROVED
3	3057	29-01-2019	CHANDU TOPU	60YRS	MALE	NO	NO	NO	CHESTPAIN WITH VOMITING	IHD WITH EF-50%	INFERIOR WALL MI	HYPERTRIGLYCERIDEMIA	28	IMPROVED
4	9249	16-03-2018	SUNANDA	48YRS	FEMALE	NO	NO	NO	CHEST PAIN WITH VOMITING	IHD WITH EF-30%	ANTEROSEPTAL WALL MI	NORMAL	25	IMPROVED
5	6385	22-02-2018	SABEWWA YAMANAPPA	60YRS	FEMALE	NO	NO	YES	CHEST PAIN WITH GIDDINESS	IHD WITH 30%	ANTEROLATERAL WALL MI	HYPERCHOLESTEROLEMIA	29	IMPROVED
6	21575	26-06-2018	SHANKAR KALAL	59YRS	MALE	NO	NO	NO	BREATHLESSNESWITH VOMITING	IHD WITH EF-45%	ANTERIOR WALL MI	NORMAL	39	DEATH
7	17016	20-05-2018	MALLIKARJUN RAMAPPA PUJARI	53YRS	MALE	NO	NO	NO	CHEST PAIN WITH VOMITING	IHD WITH EF-40 TO 45%	LATERAL WALL MI	NORMAL	30	IMPROVED
8	23019	07-07-2018	ISMAIL MULLA	55YRS	MALE	NO	NO	NO	CHEST DISCOMFORT WITH BREATHLESSNESS	IHD WITH EF-50%	ANTEROLATERAL WALL MI	NORMAL	32	IMPROVED
9	24676	21-07-2018	TUKARAM BALAPPA SHINDE	60YRS	MALE	NO	YES	NO	CHEST PAIN WITH VOMITING	IHD WITH EF-45%	ANTEROSEPTAL WALL MI	NORMAL	25.1	IMPROVED
10	24481	20-07-2018	CHIDANAND PATIL	60 YRS	MALE	YES	NO	NO	BREATHLESSNESWITH VOMITING	IHD WITH EF-45%	ANTEROLATERAL WALL MI	NORMAL	23.7	IMPROVED

11	23519	12-07-2018	NAGARAJ TALALLI	32YRS	MALE	NO	NO	NO	CHEST PAIN, BREATHLESSNES AND VOMITING	IHD WITH EF-60%	ANTEROLATERAL WALL MI	NORMAL	35	IMPROVED
12	4747	07-02-2018	MAHADEV SHIVAPPA	48YRS	MALE	YES	NO	YES	CHEST PAIN WITH SWEATING	IHD WITH EF-50%	INFERIOR WALL MI	NORMAL	25.4	IMPROVED
13	42258	15-02-2018	SUBHADRA	54YRS	FEMALE	NO	YES	NO	CHEST PAIN	IHD WITH EF-25%	SEPTOLATERAL MI	HYPERCHOLESTEROLEMIA	23.2	IMPROVED
14	4642	08-02-2018	SHIVASANGAPPA	55YRS	MALE	YES	NO	NO	CHEST PAIN WITH NAUSEA	IHD WITH EF-45%	ANTEROSEPTOLATERAL WALL MI	HYPERTRIGLYCERIDEMIA	21	IMPROVED
15	6231	19-02-2018	MALLARAY BADIGER	60YRS	MALE	NO	NO	NO	CHEST PAIN WITH BREATHLESNESS	IHD WITH EF-45%	ANTERIOR WALL MI	HYPERTRIGLYCERIDEMIA	23	IMPROVED
16	13412	20-04-2018	SHANTAWWA MAKHANPUR	45YRS	FEMALE	NO	NO	NO	CHEST PAIN WITH VOMITING	IHD WITH EF-40%	INFERIOR WALL MI	HYPERCHOLESTEROLEMIA	25	IMPROVED
17	9185	15-03-2018	SAVALAGAYYA HIREMATH	55YRS	MALE	NO	NO	NO	CHEST PAIN WITH BREATHLESNESS	IHD WITH EF-45%	INFEROLATERAL WALL MI	NORMAL	20.5	IMPROVED
18	18776	03-06-2018	G M ROJARI	50YRS	MALE	YES	NO	YES	CHEST PAIN WITH VOMITING	IHD WITH EF-35%	INFERIOR WALL MI	NORMAL	32	DEATH
19	5131	10-02-2018	CHANNAMALLAPPA	35YRS	MALE	NO	YES	NO	CHEST PAIN WITH SWEATING	IHD WITH EF-50%	INFERIOR WALL MI	HYPERTRIGLYCERIDEMIA	22	IMPROVED
20	224	02-01-2018	GURURAJ TELAGON	40YRS	MALE	NO	NO	NO	CHEST PAIN	IHD WITH EF-50%	INFERIOR WALL MI	NORMAL	29	IMPROVED
21	44755	29-12-2017	SURESH	40YRS	MALE	NO	NO	NO	CHEST PAIN	IHD WITH EF-40%	INFERIOR WALL MI	HYPERCHOLESTEROLEMIA	16	IMPROVED
22	1811	15-01-2018	PREMA	43YRS	FEMALE	NO	YES	YES	CHEST PAIN WITH BREATHLESNESS	IHD WITH EF-60%	ANTEROLATERAL WALL MI	NORMAL	22	IMPROVED
23	42349	08-12-2017	SHAMRAYA	55YRS	MALE	YES	NO	NO	CHEST PAIN WITH SWEATING	IHD WITH EF-40%	ANETROSEPTOLATERAL WALL MI	HYPERCHOLESTEROLEMIA	15.3	IMPROVED
24	3013	25-01-2018	SHARADA	51YRS	FEMALE	NO	YES	NO	CHEST PAIN WITH SWEATING	IHD WITH EF-40%	LATERAL WALL MI	NORMAL	19	IMPROVED

25	43608	20-12-2017	SUBAS CHIKGALGALI	45YRS	MALE	NO	NO	YES	CHEST PAIN WITH VOMITING	IHD WITH EF-60%	INFERIOR WALL MI	NORMAL	23	IMPROVED
26	21669	27-06-2018	MAHADEVI BAGALI	60YRS	FEMALE	NO	YES	NO	CHEST PAIN WITH SWEATING	IHD WITH EF-35%	ANTEROLATERAL WALL MI	HYPERTRIGLYCERIDEMIA	40.5	DEATH
27	26565	06-08-2018	TULAJABAI KATTIMANI	60YRS	FEMALE	NO	NO	NO	CHEST PAIN WITH VOMITING	IHD WITH EF-35%	ANTEROSEPTAL WALL MI	NORMAL	33	IMPROVED
28	19845	12-06-2018	SAHEBGOUDA YAMANAPPA	60YRS	MALE	YES	YES	NO	CHEST PAIN , VOMITING AND SWEATING	IHD WITH EF 55%	INFERIOR WALL MI	NORMAL	28	IMPROVED
29	8947	13-03-2018	MOINSAB AJAGARALLI	55YRS	MALE	YES	NO	NO	CHEST PAIN WITH SWEATING	IHD WITH EF 35%	INFERIOR WALL MI	NORMAL	17	IMPROVED
30	1662	15-01-2019	SUBHASGOUDA BIRADAR	60YRS	MALE	NO	NO	NO	CHEST PAIN WITH VOMITING	IHD WITH EF-50%	INFERIOR WALL MI	NORMAL	23	IMPROVED
31	556	05-01-2019	CHANDRASHEKAR	46YRS	MALE	NO	YES	YES	RADIATING CHEST PAIN	IHD WITH EF-35%	ANTEROSEPTAL WALL MI	HYPERTRIGLYCERIDEMIA	40	DEATH
32	1452	13-01-2019	SONARAMJI TILOKRAMJI	57YRS	MALE	NO	NO	NO	CHEST PAIN WITH VOMITING	IHD WITH EF-50%	INFERIOR WALL MI	HYPERTRIGLYCERIDEMIA	28	IMPROVED
33	1578	14-01-2019	RATNABAI	60YRS	FEMALE	NO	NO	YES	CHEST PAIN WITH BREATHLESNESS	IHD WITH EF-30%	INFERIOR WALL MI	NORMAL	26	IMPROVED
34	1972	18-01-2019	KAMALABAI	54YRS	FEMALE	NO	NO	YES	CHEST PAIN WITH VOMITING	IHD WITH EF-50%	INFERIOR WALL MI	NORMAL	28	IMPROVED
35	4008	01-02-2018	SONABAI	55YRS	FEMALE	NO	NO	YES	CHEST PAIN WITH BREATHLESNESS	IHD WITH EF-45%	ANTEROLATERAL WALL MI	NORMAL	20	IMPROVED
36	5241	12-02-2018	RATNABAI	45YRS	FEMALE	NO	NO	YES	CHEST PAIN WITH BREATHLESNESS	IHD WITH EF-50%	ANTEROSEPTAL WALL MI	NORMAL	19.7	IMPROVED
37	13518	20-04-2018	GANGABAI PAIL	55YRS	FEMALE	NO	NO	NO	CHEST PAIN WITH VOMITING	IHD WITH EF-50%	ANTEROLATERAL WALL MI	HYPERCHOLESTEROLEMIA	28	IMPROVED

38	13772	23-04-2018	RAMACHANDRA	40YRS	MALE	NO	NO	NO	CHEST PAIN WITH VOMITING WITH SWEATING	IHD WITH EF-45%	INFERIOR WALL MI	NORMAL	15	IMPROVED
39	15169	06-05-2018	SHANTABAI CHIMALAGI	40YRS	FEMALE	NO	NO	NO	CHEST PAIN WITH VOMITING	IHD WITH EF-50%	ANTEROLATERAL WALL MI	HYPERCHOLESTEROLEMIA	25	IMPROVED
40	16000	12-05-2018	MALLAPPA	58YRS	MALE	NO	YES	YES	CHEST PAIN WITH GIDDINESS	IHD WITH EF-60%	ANTEROINFERIOR WALL MI	HYPERCHOLESTEROLEMIA	39	DEATH
41	17976	28-05-2018	YALLAPPA KAMBLE	50YRS	MALE	YES	NO	NO	CHEST PAIN WITH VOMITING	IHD WITH EF-30%	ANTEROLATERAL WALL MI	NORMAL	27.8	IMPROVED
42	23158	09-07-2018	MURTUJ MANTUR	42YRS	MALE	YES	NO	NO	CHEST PAIN WITH GIDDINESS	IHD WITH EF-60%	ANTEROLATERAL WALL MI	NORMAL	28.2	IMPROVED
43	27360	13-08-2018	ARAVIND TALAKERI	50YRS	MALE	NO	NO	NO	CHEST PAIN	IHD WITH EF-45%	INFEROLATERAL WALL MI	NORMAL	26	IMPROVED
44	28835	24-08-2018	RUDREGOWDA	47YRS	MALE	NO	NO	NO	CHEST PAIN WITH VOMITING	IHD WITH EF-50%	ANTEROLATERAL WALL MI	HYPERTRIGLYCERIDEMIA	26	IMPROVED
45	44093	13-08-2018	ARVIND JAKKALLI	50YRS	MALE	NO	NO	NO	CHEST PAIN WITH NAUSEA	IHD WITH EF-45%	INFERIOR WALL MI	NORMAL	27	IMPROVED
46	44093	01-01-2019	DAWALSAB	42YRS	MALE	YES	NO	NO	CHEST PAIN WITH VOMITING	IHD WITH EF-40%	INFERIOR WALL MI	NORMAL	24.59	IMPROVED
47	1132	10-01-2019	KISHORASING RAJPUT	56YRS	MALE	YES	NO	NO	CHEST PAIN WITH VOMITING	IHD WITH EF-35%	ANTEROSEPTAL WALL MI	HYPERTRIGLYCERIDEMIA	35.4	DEATH
48	1002	12-01-2019	IRAGONDAPPA	60YRS	MALE	NO	YES	YES	CHEST PAIN WITH SWEATING	IHD WITH EF-30%	ANTEROLATERAL WALL MI	HYPERTRIGLYCERIDEMIA	28.6	IMPROVED
49	1543	14-01-2019	NINGANAGOWDA	52YRS	MALE	NO	YES	YES	CHEST PAIN WITH VOMITING	IHD WITH EF-50%	INFERIOR WALL MI	NORMAL	25.2	IMPROVED
50	1562	14-01-2019	SARASWATHI	60YRS	FEMALE	NO	NO	YES	CHEST PAIN WITH VOMITING	IHD WITH EF-35%	ANTEROLATERAL WALL MI	HYPERCHOLESTEROLEMIA	28	IMPROVED
51	4599	11-02-2019	PARASAPPA HONAKERI	60YRS	MALE	NO	YES	YES	CHEST PAIN WITH VOMITING	IHD WITH EF-35%	ANTEROLATERAL WALL MI	NORMAL	27	IMPROVED
52	9432	15-02-2019	THIMMANNA	50YRS	MALE	NO	NO	NO	CHEST PAIN WITH SWEATING	IHD WITH EF-50%	INFERIOR WALL MI	NORMAL	30	IMPROVED

53	5341	17-02-2019	BOURAWWA BIRADAR	50YRS	FEMALE	NO	YES	YES	CHEST PAIN WITH VOMITING	IHD WITH EF-20%	ANTEROLATERAL WALL MI	HYPERTRIGLYCERIDEMIA	42	DEATH
54	9761	01-03-2019	BHIMANAGOWDA BIRADAR	40YRS	MALE	NO	YES	YES	CHEST PAIN WITH VOMITING AND NAUSEA	IHD WITH EF-50%	ANTEROLATERAL WALL MI	HYPERTRIGLYCERIDEMIA	38	DEATH
55	7081	05-03-2019	IRAYYA MALLIKARJUN	45YRS	MALE	NO	NO	NO	CHEST PAIN WITH VOMITING	IHD WITH EF-45%	INFERIOR WALL MI	HYPERCHOLESTEROLEMIA	30	IMPROVED
56	7166	06-03-2019	DRAKSHAYINI HIREMANI	60YRS	FEMALE	NO	YES	NO	CHEST PAIN WITH BREATHLESNESS	IHD WITH EF-35%	INFEROLATERAL WALL MI	HYPERCHOLESTEROLEMIA	35	IMPROVED
57	7495	10-03-2019	ASHOK LAXMAN	50YRS	MALE	NO	YES	NO	CHEST PAIN WITH NAUSEA	IHD WITH EF-50%	INFERIOR WALL MI	HYPERCHOLESTEROLEMIA	28	IMPROVED
58	7554	10-03-2019	BHIMANNA SHINDE	60YRS	MALE	NO	NO	NO	CHEST PAIN WITH NAUSEA	IHD WITH EF-40%	ANTEROLATERAL WALL MI	NORMAL	30	IMPROVED
59	8338	16-03-2019	SHANKREPPA SIDDAPPA	60YRS	MALE	NO	NO	NO	CHEST PAIN WITH VOMITING	IHD WITH EF-25%	ANTEROLATERAL WALL MI	HYPERCHOLESTEROLEMIA	32	DEATH
60	8408	18-03-2019	PARVATHI MALI	50YRS	FEMALE	NO	YES	NO	CHEST PAIN WITH NAUSEA	IHD WITH EF-30%	ANTEROLATERAL WALL MI	NORMAL	27	IMPROVED
61	8343	17-03-2019	VENKATESH HALAGIMANI	35YRS	MALE	YES	NO	NO	CHEST PAIN WITH SWEATING	IHD WITH EF-60%	INFERIOR WALL MI	NORMAL	27	IMPROVED
62	9099	20-03-2019	MAYAWWA JOLLI	60YRS	FEMALE	NO	NO	YES	CHEST PAIN WITH VOMITING	IHD WITH EF-50%	INFERIOR WALL MI	NORMAL	27	IMPROVED
63	9047	20-03-2019	NINGAPPA LONI	60YRS	MALE	NO	NO	NO	CHEST PAIN WITH GIDDINESS	IHD WITH EF-40%	INFERIOR WALL MI	NORMAL	30	IMPROVED
64	9842	31-03-2019	BANDUMA MULLA	60YRS	FEMALE	NO	YES	NO	CHEST PAIN WITH VOMITING	IHD WITH EF-35%	ANTEROLATERAL WALL MI	NORMAL	35	IMPROVED
65	9660	01-04-2019	S.CROSSWIN PAKKINATHAN	50YRS	MALE	NO	YES	NO	CHEST PAIN WITH SWEATING	IHD WITH EF-40%	INFERIOR WALL MI	HYPERCHOLESTEROLEMIA	32	IMPROVED