A DISSERTATION ON

# "Evaluation of Serum Prolactin Levels in Acute Myocardial Infarction and the Role of Pharmacotherapy"

Submitted to

**THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY**
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In partial fulfillment of the Regulations for the Award of the Degree of

**M.D. BRANCH - I**

**GENERAL MEDICINE**


**DEPARTMENT OF GENERAL MEDICINE**
**STANLEY MEDICAL COLLEGE**
**CHENNAI – 600 001**
**MAY 2018**

## CERTIFICATE BY THE INSTITUTION

This is to certify that **Dr.SANTHI .C,** Post - Graduate Student (May 2015 TO April 2018) in the Department of General Medicine STANLEY MEDICAL COLLEGE, Chennai- 600 001, has done this dissertation on "**Evaluation Of Serum Prolactin Levels In Acute Myocardial Infarction: The Role Of Pharmacotherapy**" under my guidance and supervision in partial fulfillment of the regulations laid down by the Tamil Nadu Dr. M. G. R. Medical University, Chennai, for M.D. (General Medicine), Degree Examination to be held in April 2018.

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## CERTIFICATE BY THE GUIDE

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## DECLARATION

I, **Dr. SANTHI .C,** declare that I carried out this work on **"Evaluation of Serum Prolactin Levels In Acute Myocardial Infarction: The Role Of Pharmacotherapy"** at the outpatient department and Medical wards of Government Stanley Hospital. I also declare that this bonafide work or a part of this work was not submitted by me or any other for any award, degree, or diploma to any other university, board either in India or abroad.

This is submitted to The Tamil Nadu DR. M. G. R. Medical University, Chennai in partial fulfillment of the rules and regulation for the M. D. Degree Examination in General Medicine.

**Dr. SANTHI C.**

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**Dr.SANTHI C.**

## TABLE OF CONTENTS

# INTRODUCTION

Acute myocardial infarction is a life threatening condition. Sudden coronary artery occlusion leads to abrupt cessation of blood and oxygen flow to the heart muscle which in turn causes necrosis of the particular part of myocardium. The necrotic areas of heart muscles stops it contractile function.

Lactotrophic cells of anterior pituitary synthesizes prolactin hormone. During acute coronary syndrome excess prolactin secreted via neuroendocrine stress pathway. Excess prolactin may aggravate arteriosclerosis, augmentation of arterial stiffness and hypertension.

Excess prolactin level increases adhesion of the immune cells to endothelium through integrin-mediated effects that may lead on to proliferation of vascular smooth muscle cells, which may produces atherosclerotic expansion and elevation of cardiac risk profile.

Excess prolactin secreted via neuroendocrine stress pathway during acute coronary syndromes, induces acute endothelial dysfunction, insulin resistance, and induction of vascular immune reactions, thus, prolonged hyperprolactinemia plays a potential role in the development of ischemic cardiac diseases.

## REVIEW OF LITERATURE

## ATHEROSCLEROSIS – An Introduction

Atherosclerosis is a chronic pathological process which damages coronary blood vessel and producing acute myocardial infarction. The patient may present with either ST elevation or Non ST elevation MI. Atherosclerotic plaques are susceptible to following pathologic changes with clinical significance:[13]

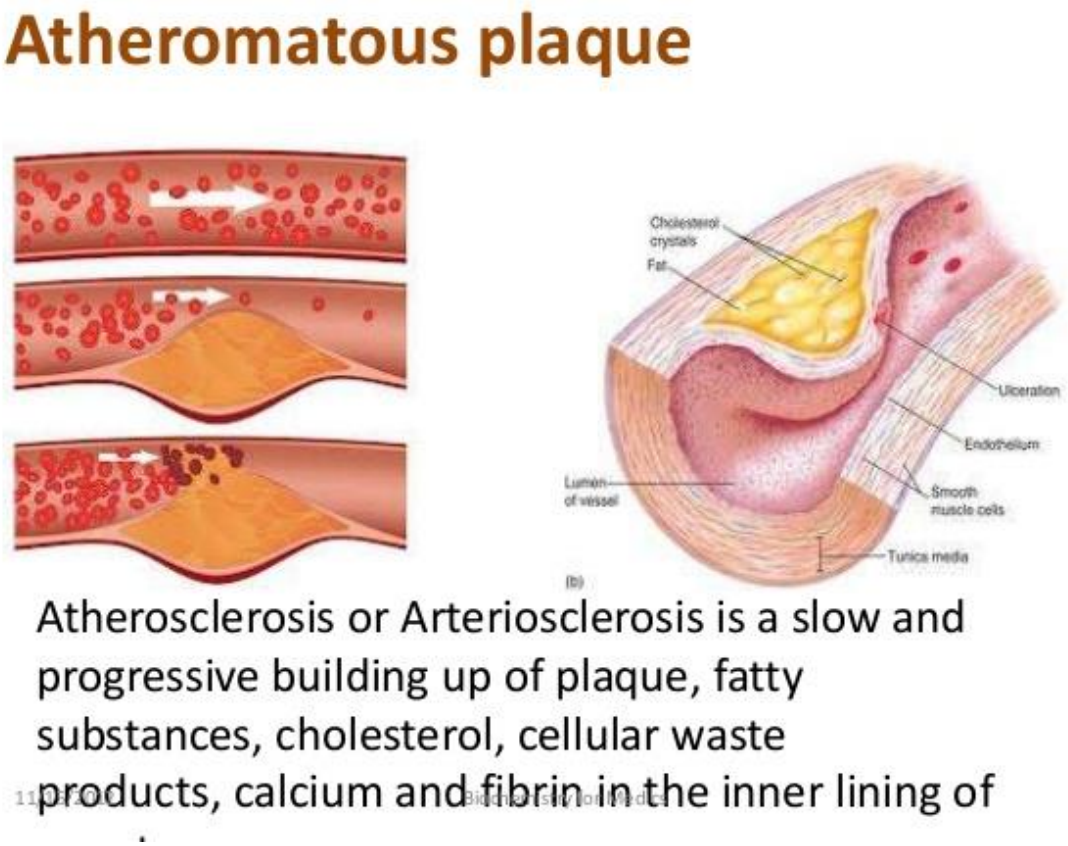
- Rupture, Ulceration, or Erosion
- Hemorrhage
- Atheroembolism
- Aneurysm formation

## PATHOGENESIS:

Numerous pathogenic factors play potential role in the development of atherosclerosis[11]. Atherosclerosis is a disease of large and medium-sized muscular arteries and is characterized by[2] –

- Endothelial Dysfunction
- Vascular Inflammation
- Monocyte Adhesion to the endothelium
- SMC Proliferations and ECM Production
- Factor Release
- Platelet Adhesion

- Deposition  of lipids, cholesterol, calcium, and cellular debris within the intima of the vessel wall
- An Atheromatous plaque consisting of raised lesion with a soft, yellow, grumous core of lipid (mainly cholesterol and cholesterol esters) covered by a firm, white fibrouscap[16].




- Besides obstructing blood flow, atherosclerotic plaques weaken the underlying media and can themselves rupture, causing acute thrombosis

## ENDOTHELIAL DYSFUNCTION

Endothelium acts as a protective barrier between blood products and surface of vessel lumen. Endothelial injury is the initial triggering event in the development of atherosclerotic lesions inside the blood vessel lumen and there is decreased in NO {Nitrous Oxide} secretion and an increased releases of serotonin, thromboxane A2 and thrombin causing vasoconstriction or abnormal vasodilatation under vasoactive substances, at the site of the plaque which damage the endothelium.

Other causes of endothelial injury including hemodynamic force, mechanical trauma, chemical and immunological mechanisms, metabolic agents like chronic hyperlipidemia, high level of homocystine, circulating toxins from systemic infections, certain viruses, and tobacco products[5].

Beyond this, Endothelial injury is caused by diabetes, hypercholestrilemia, cigarette smoking, hypertension and high LDL. This can be prevented and controlled by life style modification, diet and drugs like ACE inhibitors, Statin, Flavonoids and Vitamin C.

## INFLAMMATION

Inflammation plays potential role in genesis of atherosclerosis. During endothelial injury monocyte adheres to the endothelium, migrates and transform into macrophage. Then these macrophages engulf oxidized LDL cholesterol. Oxidized LDL produces modification in macrophage surface area which

release certain inflammatory substances like cytokines and growth factors. The important cytokines are intercellular adhesion molecule (ICAM-1), monocyte chemotactic protein (MCP-1), soluble CD4 ligand, macrophage and granulocyte-macrophage colony stimulating factors. Interleukin IL-1, IL-3, IL-6, IL-8, IL-18 and TNF-Alpha[5]. They are all stimulate atherogenesis.

## DYSLIPIDEMIA IN ATHEROSCLEROSIS

Lipid abnormalities play an important role in pathogenesis of atherosclerosis. The atherosclerosis is accelerated by high cholesterol diet intake. The risk is increased if serum cholesterol is more than 150 mg/dl. It accelerates cholesterol deposition over blood vessels[2].

## ROLE OF LIPOPROTEINS IN ATHEROSCLEROSIS

- Important risk factor for atherosclerosis development is high LDL cholesterol and low levels of high density lipoprotein (HDL) .
- LDL cholesterol engulfed by Macrophages. Inside the macrophages LDL undergoes oxidative modification. Because of these changes LDL-induced endothelial injury prevented. Accumulation of excess cholesterol in foam cells damage mitochondrium and induces apoptosis which releases chemokines, cytokines and prothrombotic molecules.
- Endothelial cell surfaces are disrupted by oxidized LDL cholesterol. It releases cytokines and inflammatory substances from LDL engulfed

macrophages which accelerate accumulation of platelets. This unstabilised plaque and oxidized LDL levels are raised in acute coronary syndrome patients and directly correlate with the severity of symptoms[2].

- HDL cholesterol reverses atherogenesis by reverse cholesterol transport mechanism. It maintains the endothelial cell function and protect from thrombus formation. The longevity increased when serum HDL cholesterol more than 75mg/dl. The Framingham Risk Assessment score gives negative risk factor for serum HDL more than 60 mg/dl. But there is no proven evidence to show increasing HDL cholesterol has reduces cardiovascular disease.
- The apolipoprotein C3 belongs to triglyceride- rich lipoproteins which is more atherogenic in nature.

**SMC PROLIFERATIONS AND ECM PRODUCTION.**

Inflamed artery increases cholesterol plaque deposition which lead on to smooth muscle cells enlargement and form a hard cover over the affected area. Because of hard cover the artery becomes narrow and it reduces the blood flow and rises the blood pressure[52]

**HYPERTENSION**

Among many risk factor hypertension is one of the leading cause of atherosclerosis development. The coronary and cerebral circulatory vessels are

commonly affected. The important mechanism of hypertension is rising of arterial wall tension which damages the endothelium and produces development of fatty streaks[2].

**SMOKING**:

In Genesis of atherosclerosis cigarette smoking is an important risk factor for endothelial damage which lead on to development of arterial thrombosis[4].

Following event happens while smoking

- Cigarette smoke inhibits nitric oxide production. So, endothelium mediated vasodilator function is affected.
- Smoking rises interleukin-6, CRP, and TNF- alpha in both sexes.
- Smoking reduces the accessibility of NO to platelets, so sensitivity of exogenous NO is reduced in platelets. This leads to increased platelet activation and adhesion, associated with raised serum fibrinogen and decreased fibrinolysis[4].
- Smoking augments the LDL oxidation, which lead on to atherosclerosis.

**DIABETES**:

Diabetes produce derangement of lipid profile lead on to dyslipidemia, excess insulin levels in serum predisposes to arterial diseases. Excess insulin acts on the macrophages and decreases ABCA – 1 and enhances the expression of CD 36, which lead on to cholesterol accumulation in the macrophages and monocyte surface

area. In general Cytokines like interleukin-6 (IL-6), MCP-1 and Oxidized LDL are raised in both Atherosclerosis and T2DM.[34] Low grade inflammation is present in both. T2DM enhances atherosclerosis resulting in end organ damage.

**Lp-PLA2:**

Macrophages secrete the enzyme called Lipoprotein-associated phospholipase $A_2$ (Lp-$PLA_2$) which precipitates the plaque inflammatory surface. Its high level predict a 40 to 400 percent higher risk of myocardial infarction (MI).

**CYTOKINES:**

Most commonly encountered Cytokines in atherosclerosis are interleukin-1 or Tumour Necrosis Factor-alpha. It increases the expression of many cell surface adhesion molecules such as, VCAM-1, ICAM-1, CD40L, CD40, and selectins.[18] These changes take place in smooth muscle cells, endothelial cells and macrophages. Pro-inflammatory cytokines promote cell proliferation, release oxygen free radicals, stimulate MMP - 9, which induces the tissue factor expression. The antiatherogenic cytokines are IL-4 and IL-10.[16] Interferon-gamma enhances the development of atherogenesis.

**LEUKOCYTE ACTIVATION:**

In early stage of atherosclerosis inflammatory cells like Leukocyte (Monocytes and T lymphocytes) recruitment occurs in atherosclerosis site. which proving some evidence systemic inflammatory reaction takes place in atherogenesis.

**PREGNANCY-ASSOCIATED PLASMA PROTEIN-A (PAPP-A):**

It is a zinc binding metalloproteinase enzyme. Atherosclerotic plaques surrounded by fibrous cap which prevent plaque rupture. PAPP-A degrades this fibrous cap and promotes plaque rupture. PAPP-A is secreted by fibroblasts, osteoblast, syncytiotrophoblast, endothelial, Macrophages/Monocyte and blood vessel smooth muscle cells.[33] PAPP-A is seen in ruptured atherosclerotic plaque not in stable plaque.

**DYSLIPIDEMIA:**

The Important pathogenic hallmark of atherosclerosis is lipid abnormalities. High intake of cholesterol containing food accelerates atherosclerosis[3]. If serum cholesterol is > 150 mg/dl, the rate of atherosclerosis development is high .[28]

**TISSUE FACTOR:**

Tissue factor is found in the atheromatous plaque along with other factors. Tissue factor initiates coagulation which leads on to thrombosis development. Tissue factor augments atherosclerosis via both coagulation-dependent and coagulation independent pathways.

**ANGIOTENSIN II:**

High level of Angiotensin II plays major role in atherogenesis. The level of Angiotensin II directly proportional to the severity of atherosclerosis. Tone of smooth

muscles in blood vessel are modulated by Angiotensin II. It interferes with extracellular matrix proliferation and synthesis.

**ENDOTHELIN-1:**

Endothelin-1 plays potential role in vasoconstriction as well as chemokine (Mitogen) of vascular smooth muscle cells. Endothelin 1is strongly associated with atherosclerosis formation. Oxidized LDL stimulates endothelin 1 synthesis and augments its vasoconstriction properties.

**ADHESION MOLECULES:**

Expression of ICAM-1 and VCAM-1 adhesion molecules are enhanced by Inflammation of endothelial injury. They bind with WBC and augment atherogenesis. In atherosclerosis VCAM-1 is more specific than ICAM.[27]

P-Selectin, is a receptor of platelet and endothelial cells. It adheres with vascular endothelial cells. It also a sign which shows that inflow of inflammatory cells into early as well as advanced atherosclerotic lesions.[25]

L-Arginin is the precursor of nitric oxide which inhibits adhesion of monocytes to endothelial cells and alpha tocopherol (vitamin E). Adhesion is increased by androgen because it increases the expression of VCAM-1. Antibodies against this will reduce the adhesion.

**FLOW CHARACTERISTICS:**

Atheroma formation is often increased in bends, branches and bifurcations of blood vessel. Because of the low shear stress it produces atherosclerosis. Altered blood flow disturbs the endothelial cell function and impair the protective functions. It is mainly due to the release of NO from the endothelial cells.[16]

**ANTI-OXIDIZED LDL ANTIBODIES**

Hydroperoxides produced by oxidation of fatty acid..

Hydroperoxide

⇩

convert to active aldehydes like malondialdehyde. Malondialdehyde

⇩

lipoprotein become more antigenic to the scavenger receptor on macrophage

⇩

This oxidized LDL, becomes antigenic.[31]

⇩

Antibodies are produced against the oxidized LDL.

⇩

But these antibodies accumulate in the atheromatous plaques.

⇩

When compared to chronic coronary condition the titre of these antibodies significantly rises within a month after an acute coronary syndrome.

**MITOCHONDRIAL DNA DAMAGE**:

Mitochondrial DNA damage produces development of atheroma which is proven experimentally in aortas of mice. Lesions in mDNA produces thin cap fibroma formation which is high risk in cardiovascular events.

**GENETIC ASSOCIATIONS**:

Atherosclerosis is polygenic. Environmental factors are important for the diseases progression and manifestation. In atherosclerosis Polymorphisms of many genes play potential role in development of inflammation, thrombogenesis and derangements in lipid metabolism.

**INFECTION:**

Long standing chronic infection has been found to increase the risk of atherosclerosis. Commonly encountered pathogens are herpes simplex virus (HSV) type 1 and type 2, Chlamydia Pneumoniae, Enterovirus (primarily Coxsackie B virus), hepatitis A virus (HAV), H .Pylori and Cytomegalovirus (CMV). [17]

Many mechanisms are involved in atherosclerosis genesis via chronic infectious state including

1. Direct Endothelium Injury

2. Inducing a Systemic Inflammatory State.

Not only infections, excess pathogenic burden itself a risk factor for atherosclerosis. Many studies showed that more than one pathogenic involvement directly correlated with the presence and severity of coronary disease .

## IMPORTANCE OF PLAQUE RUPTURE:

For symptomatic Atherosclerosis the lumen diameter should be reduced to at least 70%, until the patient will be asymptomatic. This happens when plaque is ruptured. When plaque ruptures lumen diameter gets narrowed and leads to symptoms pertaining to the end organ damage.

ACS (myocardial infarction, unstable angina, stroke, and sudden death) are mainly due to plaque rupture and the silent plaque rupture and recurrent plaque ruptures followed by thrombosis formation shows advancement of atherosclerosis, associated with an increase in plaque size and an increase blood vessel lumen and a reduced arterial remodelling.

## ACUTE MYOCARDIAL INFACRTION – AN OVERVIEW

### INTRODUCTION:

### DEFINITION

Myocardial infarction (MI) is the irreversible necrosis and death of cardiac muscle due to diminished blood supply to the heart which leads to myocardial cell damage and ischemia supplied by that artery. It happens mainly due to prolonged ischemia[23]. The atheromatous plaque rupture followed by thrombus formation is the hallmark event to develop MI.

## EPIDEMIOLOGY AND GLOBAL BURDEN

Acute MI is one of the single largest killer of male and female . An American suffers a Ischemic heart disease [IHD] event every 29 seconds, and dies of one every minute. 47% of people having a IHD event will die from it that year. More than 4,50,000 people die each year from a IHD event without being hospitalized, most from cardiac arrest, 84% of IHD deaths are among people aged ≥65 years and greater than 7 million have sustained a myocardial infarction. IHD is likely to become leading cause of death worldwide by 2020. Half of the death rate are reduced due to prompt diagnosis, treatment and life style modification. Global burden of diseases analysis showing there is shift from communicable diseases to non communicable diseases[23].

## ETIOLOGY

The following causes are important etiology for IHD development[7]

1. Atherosclerotic plaque rupture with superimposed thrombus formation is the most common [95%] cause for MI [27]
2. Vasculitic syndromes
3. Increased blood viscosity (e.g., Polycythemia Vera, Thrombocytosis)
4. Coronary embolism (e.g., from Endocarditis, Artificial heart valves)
5. Congenital anomalies of the coronary arteries
6. Severe coronary artery spasm (primary or cocaine-induced)
7. Coronary trauma or aneurysm

8. Spontaneous coronary artery dissection
9. Markedly increased myocardial oxygen demand (e.g., severe aortic stenosis)

The above said are most common causes of acute myocardial infarction development.

## RISK FACTOR

The presence of following any risk factor is associated with doubling the risk of an MI[7,52].

| **Major independent risk factors** | **Predisposing risk factors** | **Possible risk factors** |
|---|---|---|
| Hypertension<br>Diabetes mellitus<br>Cigarette smoking<br>Elevated total and LDL cholesterol<br>Low HDL cholesterol<br>Older Age | Obesity<br>Physical inactivity<br>Family history of premature Coronary diseases<br>Psychosocial factors<br>Ethnicity | C-reactive protein<br>Fibrinogen<br>Elevated Lp(a)<br>Homocysteine |

European Society of Cardiology table of lifestyles and characteristics associated with an increased risk of a future coronary heart disease event.Resource: "Cardiology explained"

**AGE**

Cardiovascular risk rises with advancing age. More than half of all heart attacks occur in persons over the age of 65, and 80 % of those who die of heart disease are in this age bracket. You can't turn back or stop the clock, but lifestyle factors—such as diet, exercise, and stress management—certainly minimize the adverse effects of advancing age[7].

**GENDER**

Heart disease is by far the most common cause of death in both men and women, but there are important gender differences in risk, diagnosis, and treatment. This is mainly due to anatomy and hormones undoubtedly play important roles. For example, women have smaller coronary arteries than men—a consideration when treating coronary artery disease. After menopause, women face an increasing risk of heart attack due to lack of estrogen production[7].

**FAMILY HISTORY**

We've known for many decades that people with a strong family history of heart attacks, stroke, and other cardiovascular disorders face an increased risk of suffering similar fates. This has been amply demonstrated by the Framingham Heart Study and other large population studies. The risk is highest among those whose close relatives (sibling, parent, or grandparent) suffered a heart attack before

age fifty. There are some genes that increase cardiovascular risk. For example, some people inherit a gene that results in very high levels of LDL cholesterol, the bad form of this blood lipid, leading to early coronary artery disease[11].

**RACE AND ETHNIC BACKGROUND**

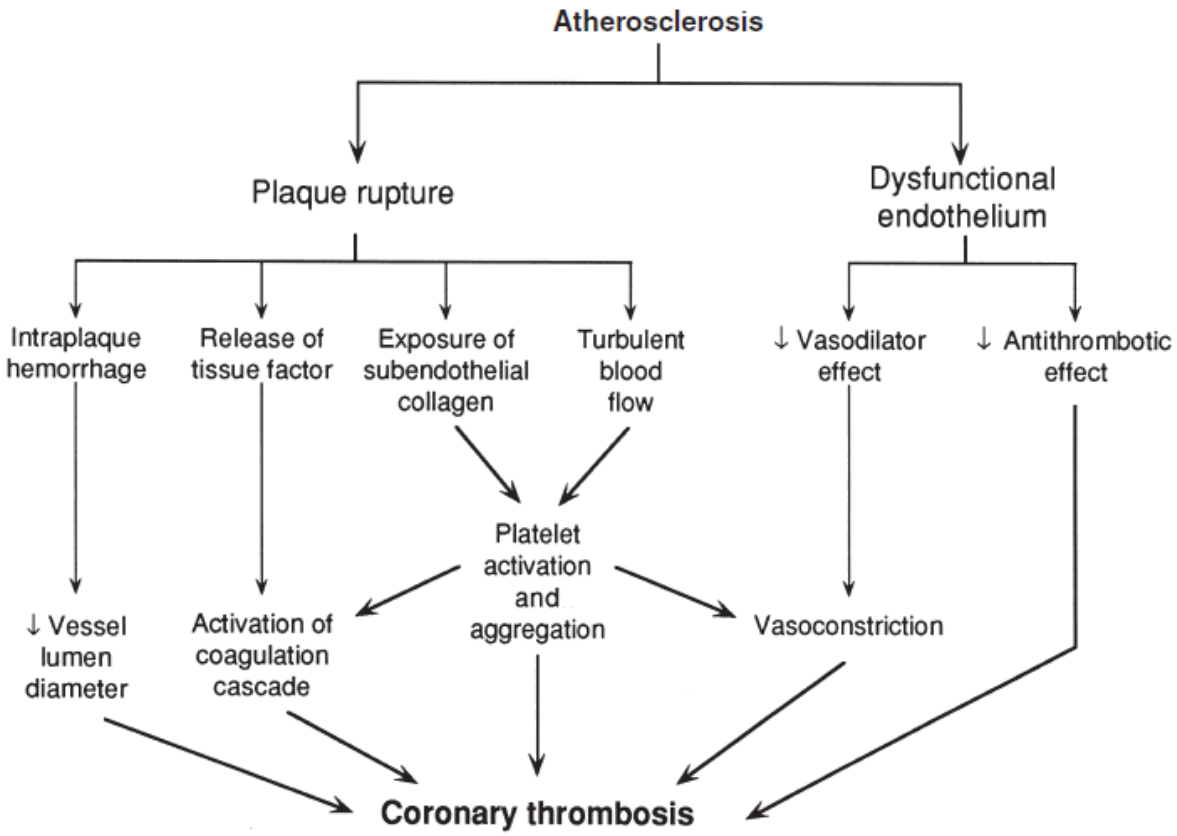
Certain Racial or Ethnic groups have an especially high risk of heart disease. The highest risk groups are African Americans, Mexican Americans, Native Americans, native Hawaiians, and people from the Indian subcontinent. For example, African Americans tend to be highly salt-sensitive, which increases the risk of high blood pressure. Other factors that may play a role include unidentified genetic differences, diet, stress, low income, and limited access to health care[7].

**ACQUIRED RISK FACTORS**

The list of acquired risk factors which can be modified or prevented are much larger than those that are beyond our control. Reducing or eliminating these risk factors is key role for achieving and maintaining heart healthy, so they deserve special attention. Elevated blood cholesterol and other lipids regardless of the underlying cause, can lead on to atherosclerosis, the buildup of fatty deposits (plaque) in the coronary arteries and the other blood vessels[7].

**ATHEROSCLEROSIS**

The following diagram clearly explain the relationship between atherosclerosis and arterial thrombus formation[2, 3, 5].




## HIGH BLOOD PRESSURE

Often called the silent killer, high blood pressure produces no obvious symptoms until it reaches the advanced stage and damages organs, especially the kidneys, heart, brain, and blood vessels. It is one of the most common risk factors for heart attack, stroke, kidney failure, peripheral vascular disease, atherosclerosis, and heart failure[11].

## METABOLIC SYNDROME

Metabolic syndrome is a major health issues to develop heart attack. It has been recently found as a major cardiovascular risk factor. Diagnosis is based on a patients having three or more of the following risk factors[27]:

- Abdominal Obesity (a waist circumference greater than 40 inches in a man and 35 inches in a woman),
- Elevated Triglycerides (>150 mg/dl ), low HDL cholesterol level
- High Blood Pressure (more than 130/90), and Insulin Resistance

## DIABETES AND INSULIN RESISTANCE

There is no doubt that persons with diabetes mellitus, both type I and type II, have an increased risk of heart attacks, stroke, and other cardiovascular diseases. Obesity Until recently, most people considered being overweight more a matter of aesthetics than a potentially deadly disease[21],the greater the weight, the higher the risk of developing cardiac problem, high BP, Diabetes, and other major health issues. Obesity is defined as a body mass index (BMI) of 30 or higher—is now accepted as a leading cause of premature death.

## CIGARETTE SMOKING

Cigarette use is now recognized as the single most common cause of premature death in the United States and many other countries. Although most people know that smoking increases the risk of many forms of cancer, many are unaware of its role in cardiovascular disease, including sudden cardiac death, heart attacks, and strokes. Smoking also increases the risk to develop heart failure and circulatory disorders[28].

## STRESS

There is a lot of contraversies regarding relationship between stress and development of heartattack[30].

## OTHER PSYCHOLOGICAL FACTORS

Several studies supports that the depression is one among the risk factor to develop heart attack. Early diagnosis and treatment prevent heart attack.

## SEDENTARY LIFESTYLE

Numerous studies have found that exercise is an important factor in preventing or treating heart disease[37], the People who exercise regularly escapes from their cardiovascular morbidity and mortality. Not only live longer, but they also feel and look better. They are less likely to gain overweight, They also less likely to develop diabetes, high blood pressure, and elevated blood cholesterol.

## NEWLY IDENTIFIED RISK FACTORS

## FIBRINOGEN

Fibrinogen is a component of blood that promotes the formation of blood clots, although it is essential for stopping bleeding from cuts and other wounds, high levels raise the risk of a heart attack—or a stroke if a clot were to block the essential flow of blood to the heart or brain[10]. Fibrinogen levels tend to rise with advancing age; smoking also promotes increased fibrinogen production, many experts believe this is one reason why smoking greatly increases cardiovascular risk[7].

**LIPOPROTEIN** ( Lp(a))

It Increase the risk of coronary artery disease and heart attacks[31]. Lp (a) is the component of LDL (the carrier of the harmful type of cholesterol) that prevents blood clots from dissolving normally[16]. The Studies have shown that high levels of Lp (a) are perhaps more important risk factor to determine the heart attack than is high total cholesterol or low HDL cholesterol[31].

**INFLAMMATION AND C-REACTIVE PROTEIN**

The high levels of C-reactive protein, or CRP, may be a risk factor even when a patient's cholesterol is normal, because CRP is a protein in the blood that indicates inflammation somewhere in the body, and because chronic inflammatory disorders such as rheumatoid arthritis have been associated with major risk of cardiac problems[18.19]. The precise mechanism is unknown, but some have theorized that an underlying bacterial or viral infection may contribute to, or even cause, the buildup of fatty plaque along arterial walls[52].

Inflammation in the arteries appears to promote the development of atherosclerosis and instability of the atherosclerotic plaque that can lead to formation of blood clots.

**HOMOCYSTEINE**

Homocysteine is an amino acid that is a natural product of protein metabolism. Some people inherit a genetic defect that causes them to produce very high levels of homocysteine, putting them at a major risk to develop atherosclerosis

and suffering an early heart attack. It is easily reduced with large doses of folic acid in some instances, other B vitamins are added to the regimen[44].

**COCAINE USE**

Cocaine use has led to an increase in high blood pressure, abnormal heart rhythms, angina, cardiomyopathy, and heart attacks among young people. During pregnancy, cocaine consumption increases the risk of congenital heart defects. Even the first use of cocaine can lead to a cardiac crisis, heart attack, and even death. It reduces blood flow to the heart muscle by constricting the coronary arteries, which can result in a coronary artery spasm. At the same time, it speeds up the heart rate and increases blood pressure. As a result, the amount of oxygen reaching the heart muscle itself is reduced just when the heart muscle is demanding more oxygen[7].

**PATHOGENESIS**

Ischemia can develop whenever the blood flow stopped within 10 seconds to longer than 20 minutes, which produce irreversible cell death. The death of myocardial cell starts from the Endocardium[22], the area most distal to the arterial blood supply. Occlusion is typically seen in the proximal 2 cm of the LAD and left circumflex arteries and in the proximal and distal thirds of the RAD.

- When the duration of blood flow occlusion prolonged, the cell death extending from the inner part of myocardium to outer part of Epicardium[11].
- Three important factors determine the severity of MI[12]

– Site of vessel wall occlusion

– Duration of vessel wall occlusion

– Presence or absence of collateral circulation.

– Depending upon the duration of vessel wall occlusion, the following changes happen in the myocardial cell. ATP depletion is the first changes noted in cell injury[44].

| **FEATURES** | **DURATION** |
|---|---|
| Onset of ATP depletion | Seconds |
| Loss of contractility | <2 Minutes |
| ATP reduced<br>to 50% of normal | 10 minutes |
| to 10% of normal | 40 minutes |
| Irreversible cell injury | 20-40 minutes |
| Microvascular injury | > 1 hour |

ATP-Adenosine Triphosphate

## MECHANISM OF BLOOD VESSEL OCCLUSION

- Rupture of the lipid-rich atheromatous plaque, intraluminal thrombus, and intraplaque hemorrhage, are three pathological hallmarks most commonly recognized in the infarct-related coronary artery at the site of acuteMI[15].
- Platelet aggregation promoted by the platelet-derived mediators like TXA2, serotonin, ADP, & PDGF that augment thrombosis and vasoconstriction. This is mainly due to diminished availability of naturally occurring endogenous substances that inhibit platelet aggregation, such as EDRF, tissue plasminogen activator, and PGI2[11, 12].
- Platelets releases certain mediators which produce vasospasm of coronary blood vessels .
- The coagulation pathway activated by tissue factor.
- Thrombus occludes the lumen of vessel.
- Ischemia without detection of coronary thrombosis due to vasculitis

| VASOSPASM | EMBOLI | OTHERS |
|---|---|---|
| • Intravascular Platelet aggregation<br>• Drug ingestion (e.g., cocaine or ephedrine) | • Vegetations of infective endocarditis,<br>• Intracardiac prosthetic material | • Vasculitis,<br>• Hematologic abnormalities (e.g., sickle cell disease),<br>• Amyloid deposition,<br>• Vascular dissection,<br>• Aortic stenosis,<br>Lowered systemic blood pressure (e.g., shock) |

## CLASSIFICATION OF MI

Anatomically MI sub classified into two types[9]

- Transmural and Subendocardial infarction

According to ECG finding it divided into two types

- ST elevation (STEMI) and Non ST elevation MI (NSTEMI)

- **TRANSMURAL INFARCTION-**This infarction mainly due to complete occlusion of coronary artery which produce infarction of whole thickness of myocardial muscle supplied by that particular artery, otherwise called ST elevation MI (STEMI) [15].

- **SUBENDOCARDIAL INFARCTION**–This infarction mainly involves small portion of the subendocardial region like a part of left ventricular wall, septum, or papillary muscles.

## SIGNS AND SYMPTOMS

According to a person signs and symptoms varies. A person may experience no symptoms to sudden death due to cardiac arrest[41]. Chest pain is the most common manifestation of MI. Patient may experience chest tightness, compression or squeezing type of pain which was not subsided by rest. Often pain radiate to left arm, back, shoulder and epigastric region.

- **LEVINE'S SIGN:** Localization of chest pain by clenching the fists over the sternum. 20-30% of patients are asymptomatic. They won't experience chest pain, especially elderly patients, diabetes mellitus and hypertension.
- Sudden onset of ischemia produces vasovagal reflex.

- BREATHLESSNESS
    - During acute MI, left ventricular failure occurs. So patient may develop acute pulmonary edema.
- Diaphoresis
- Dizziness
- Loss of consciousness (cerebral hypoperfusion and cardiogenic shock)
- palpitation
- Sudden cardiac arrest (due to ventricular fibrillation)

**KILLIP CLASSIFICATION**

The patient prognosis is best assessed by killip classification. It classifies the heart failure in acute MI patient[27].

| CLASS | DEFINITION | 30 DAY MORTALITY |
|---|---|---|
| 1 | No S3 and Clear lung | 5% |
| 11 | S3 or crackles <50% of lung | 14% |
| 111 | Crackles > 50% of lungs | 32% |
| 1V | Shock | 57% |

**DIAGNOSIS**

**PHYSICAL EXAMINATION**

- Patients usually presents with restless and in distress state[41].
- The periphery feel cold.
- Dysnoea with abnormal auscultatory lung field like fine crackles, coarse crackles or rhonchi.
- Hypertension related to anxiety or hypotension caused by cardiogenic shock.
- The heart rate may vary from bradycardia to tachycardia.

- On auscultation, s1 muffled due to reduced cardiac contractility.
- Almost s4 heard in all mi patients. Whereas s3 detected only 10 to 20 percentage of patients.
- Transient systolic murmurs and pericardial friction rub may be heard
- Whereas in right ventricular infarcts, patient may develop distended jvp , peripheral edema and high central venous pressure.

**DIAGNOSIS OF ACUTE MYOCARDIAL INFARCTION BASED ON THREE PARAMETERS**

1. Clinical Symptoms
2. ECG Findings
3. Myocardial Enzymes and Protein Elevation (CPK-MB and Troponin I and T**)**

**ECG FINDINGS:**

1. ST segment elevation (Transmural infarct) or ST depression (subendocardial infarct)[25, 26].
2. T wave inversion and Q waves formation

- ECG help us to identify location, size, time of infarction.

**PLASMA MARKERS OF MYOCARDIAL NECROSIS**

Myocardial dead cells releases the following enzymes and protein[17,47].

| MARKER | RISE TIME | PEAK TIME | RETURN TO BASELINE |
|---|---|---|---|
| Myoglobin | 1 to 4 hours | 6 to 7 hours | 24 hours |
| Troponin I | 3 to 12 hours | 24 hours | 5 to 10 days |
| Troponin T | 3 to 12 hours | 12 to 48 hours | 3 to 4 days |
| Creatin kinase | 4 to 8 hours | 12 to 24 hours | 3 to 4 days |
| CK-MB | 4 to 8 hours | 18 to 36 hours | 2 to 3 days |
| AST | 8 to 12 hours | 18 to 36 hours | 3 to 4 hours |
| LDH | 8 to 12 hours | 3 to 6 days | 8 to 14 days |

CK, Creatine kinase; AST, Aspartate Transaminase; LDH, Lactate Dehydragenase

**ADDITIONAL INVESTIGATIONS**:

- Echocardiogram
- Radionuclide Imaging
- Stress Test
- Coronary Angiography

## TREATMENT

The patient's complaints, history and ECG are the first line of investigations to diagnose acute myocardial infarction[27].

- Once the diagnosis confirmed patient should be treated with following procedure.
- Serial ECG and cardiac monitoring is important.
- Should give adequate bed rest with nasal oxygen supplementation.
- Administer loading dose of T.Aspirin 325 mg chewed. T.Clopidogrel 300mg. T.Atorvastatin 80mg. Give sublingual T. Nitroglycerin 5 -10 mg (if SBP >90)
- Chest pain may be relieved with morphine sulfate.

## PRIMARY CORONARY INTERVENTION (PCI):

- Stenting PCI and angioplasty is the gold standard treatment of choice to restore coronary blood flow to ischemic myocardium[46].
- In this invasive procedure blocked coronary artery dilated.
- The duration of symptoms to procedure must be within 2 hours to get excellent reperfusion.

Before the PCI procedure, we have to administer T.Clopidogrel loading dose (300-600 mg) or T.Ticagrelor 180 mg.

Following one year after PCI procedure advise the patient to take dual antiplatelet drugs with aspirin and clopidogrel or ticagrelor

- Thrombolytic therapy
- Thrombolytic drugs dissolve coronary blood clot by converting plasminogen to plasmin.
- The maximal benefit of thrombolysis is achieved when a person gets thrombolytic therapy within 3 hours of symptoms onset**.**

## CONTRAINDICATION TO THROMBOLYTIC THERAPY

The Americans College of Cardiology/ American Heart Association (Acc/Aha) And By The European Society Of Cardiology (Esc)[14]

| ACC/AHA | ESC |
|---|---|
| **Absolute Contraindications:**<br>■ Any prior intracranial hemorrhage (ICH)<br>■ Known structural cerebral vascular lesion (e.g., arteriovenous malformation)<br>■ Known malignant intracranial neoplasm (primary or metastatic)<br>■ Ischemic stroke within 3 months (except acute ischemic stroke within 4.5 hours)<br>■ Suspected aortic dissection<br>■ Active bleeding (excluding menses) or bleeding diathesis<br>■ Significant closed-head or facial trauma within 3 months | **Absolute Contraindications:**<br>■ Hemorrhagic stroke or stroke of unknown origin at any time<br>■ Ischemic stroke in preceding 6 months<br>■ Central nervous system (CNS) damage or neoplasms<br>■ Recent major trauma/ surgery/head injury (within preceding 3 weeks)<br>■ Gastrointestinal bleeding within the last month<br>■ Known bleeding disorder<br>■ Aortic dissection |
| **Cautions/Relative Contraindications:**<br>■ History of chronic, severe, poorly controlled hypertension<br>■ Severe uncontrolled hypertension of presentation (systolic blood pressure [SBP] > 180 mm Hg or diastolic blood pressure [DBP] > 110 mm Hg)<br>■ Traumatic or prolonged (>10 minutes) cardiopulmonary resuscitation (CPR) or major surgery within 3 weeks<br>■ Recent (within 2-4 weeks) internal bleeding<br>■ Noncompressible vascular punctures<br>■ Pregnancy<br>■ Active peptic ulcer<br>■ Current use of anticoagulants with high international normalized ratio (INR); the higher the INR, the higher the risk of bleeding<br>■ For streptokinase or anistreplase: prior exposure (more than 5 days ago) or prior allergic reaction to these agents | **Relative Contraindications:**<br>■ Transient ischemic attack in preceding 6 months<br>■ Oral anticoagulant therapy<br>■ Pregnancy or within 1 week post-partum<br>■ Non-compressible punctures<br>■ Traumatic resuscitation<br>■ Refractory hypertension (SBP > 180 mm Hg)<br>■ Advanced liver disease<br>■ Infective endocarditis<br>■ Active peptic ulcer |

## TREATMENT

| | COR | LOE |
|---|---|---|
| **Antiplatelet therapy** | | |
| ***Aspirin*** | | |
| ■ 162- to 325-mg loading dose | I | A |
| ■ 81- to 325-mg daily maintenance dose (indefinite) | I | A |
| ■ 81 mg daily is the preferred maintenance dose | IIa | B |
| ***$P2Y_{12}$ receptor inhibitors*** | | |
| ■ Clopidogrel: | I | A |
| ○ Age ≤75 y: 300-mg loading dose | | |
| Followed by 75 mg daily for at least 14 d and up to 1 y in absence of bleeding | I | A (14 d)<br>C (up to 1 y) |
| ○ Age >75 y: no loading dose, give 75 mg | I | A |
| Followed by 75 mg daily for at least 14 d and up to 1 y in absence of bleeding | I | A (14 d)<br>C (up to 1 y) |

*COR*- Class of Recommendation;*LOE*, LOE-Level of Evidence;

## ACE INHIBITOR

- Angiotensin-Converting Enzyme (ACE) inhibitors are given to patients who have an MI with cardiac failure in the absence of hypotension[49].

- It also help us to prevent from ventricular remodelling and preserve systolic ejection fraction.

## ANTICOAGULATION THERAPY

- During percutaneous or surgical revascularization procedure, heparin is used as a thrombolytic therapy with alteplase[49].

Patients presenting with non–Q-wave MI, Low molecular weight heparin is the anticoagulant of choice.

| Anticoagulant therapy | | |
|---|---|---|
| ■ UFH:<br>○ Weight-based IV bolus and infusion adjusted to obtain aPTT of 1.5 to 2.0 times control for 48 h or until revascularization. IV bolus of 60 U/kg (maximum 4000 U) followed by an infusion of 12 U/kg/h (maximum 1000 U) initially, adjusted to maintain aPTT at 1.5 to 2.0 times control (approximately 50 to 70 s) for 48 h or until revascularization | I | C |
| ■ Enoxaparin:<br>○ If age <75 y: 30-mg IV bolus, followed in 15 min by 1 mg/kg subcutaneously every 12 h (maximum 100 mg for the first 2 doses)<br>○ If age ≥75 y: no bolus, 0.75 mg/kg subcutaneously every 12 h (maximum 75 mg for the first 2 doses)<br>○ Regardless of ages, if CrCl < 30 mL/min: 1 mg/kg subcutaneously every 24 h<br>○ Duration: For the index hospitalization, up to 8 d or until revascularization | I | A |
| ■ Fondaparinux:<br>○ Initial dose 2.5 mg IV, then 2.5 mg subcutaneously daily starting the following day, for the index hospitalization up to 8 d or until revascularization<br>○ Contraindicated if CrCl < 30 mL/min | I | B |

ACC-American College of Cardiolog,,AHA-American Heart Association, aPPT-activated partial thromboplastin time *COR*- Class of Recommendation. *CrCl*-creatinine clearance. *IV*- intravenous.LOE- Level of Evidence, *N/A*- not available,STEMI- ST segment elevation myocardial infarction, UFH- unfractionated heparin.

## COMPLICATIONS

## VASCULAR COMPLICATIONS

- Recurrent ischemia and infarction

## MECHANICAL COMPLICATIONS

- Mitral Regurgitation
- Cardiac Rupture (Papillary muscle, left ventricular free wall andventricular septum)

## MYOCARDIAL COMPLICATIONS

- Cardiac Failure
- Dilatation Of Ventricular Cavity
- Systolic And Diastolic Dysfunction
- Cardiogenic Shock
- Right Ventricular Infarction
- True Or False Aneurysm Formation

## PERICARDIAL COMPLICATIONS

- Pericarditis And Pericardial Effusion
- Dressler's Syndrome

## THROMBOEMBOLIC COMPLICATIONS

- Left ventricular Mural thrombosis
- Systemic and peripheral thromboembolism (Example- Stroke, DVT, pulmonary embolism etc)

## ELECTRICAL COMPLICATIONS

- Ventricular tachycardia or ventricular fibrillation
- Tachyarrythmia (ex-SVT) or bradyarrythmia (ex-Heart block)

## LIFE STYLE MODIFICATIONS

Life style modification is one of the most important primordial prevention from the myocardial infarction. It helps us to control the risk factors of high blood cholesterol, diabetes mellitus and obesity, it also maintain normal blood pressure[27]. Cessation of smoking and alcohol consumption: the risk of AMI 50% reduced, after 2 year cessation of smoking.

- Regular Physical activity
- Daily Exercise 30 minutes.
- Regular Exercise helps us to reduce blood cholesterol, diabetes mellitus, obesity and blood pressure.

## DIET MODIFICATION

- An Ideal Diet should be rich in vegetables, whole grains, fruits, and soluble fiber and low level of cholesterol and saturated fatty acids .

## LIPID MANAGEMENT

- Consumption of <200 mg/day of cholesterol and trans fatty acids should advice ,along with saturated fatty acids less than 7% of total calories.
- Per day 10 gram of viscous fiber, fish born omega -3 fatty acids and 2 gram of plant sterols advisable limit[50].
- Instead of saturated fat, It should be replaced with rapeseed oil, olive oil to prevent excess cholesterol.

Even 10% of our current weight loss, greatly decrease cardiac risk.

## CONTROL AND MANAGEMENT OF COMORBID DISEASES

## CONTROL OF HYPERTENSION AND DIABETES MELLITUS

Patients with CAD should achieve the following goal to maintain their Blood pressure and glycaemic control.

- The blood pressure should be maintained at < 130/80 mm Hg and the HbA1c in diabetic should be < 7%
- Multimodal approach needs to attain our goal, this include Lifestyle changes, Diet plan ,Physical activity and Medications.

**PATIENT EDUCATION:**

Proper education of Entire community regarding heart attack signs and symptoms especially how to handle the situation of acute phase is important to avoid MI related morbidity and mortality[49].

The following health tips are useful to prevent heart attack in future

- Regular Exercise
- Healthy Food Habits
- Quit Smoking
- Avoid Drinking

**PROLACTIN HORMONE**

- **INTRODUCTION**

In 1928 sticker discovered prolactin hormone. It is a polypeptide hormone secreted by lactotrophic cells of Anterior pituitary gland. It containing 198 AA (amino acid) and molecular weight of 22 kDa (kilodalton).

It located on Chromosome 6 and half life of 20 to 30 minutes .The milk secretion is important function of Prolactin[33].

Lactotrophs, desidual cells are main source of prolactin hormone. It mainly acts on breast, gonad and sex hormone. It excreted by liver and kidney. D2 receptor present in lactotrophs, dopamine act via this receptor and inhibit prolactin secretion[33] .

According to size, it circulates three different forms:

- Small molecular size ( 22kDa)
- Big molecular size (50kDa)
- Larger molecular size(100kDa)
- 80% of the hormones are biologically active, small molecular forms.

**FUNCTIONS OF PROLACTIN HORMONE**

- The Importance of Prolactin is initiation of lactation[34].
- During pregnancy ,along with Estrogen it stimulate breast development.
- During pregnancy ,it suppress the secretion of FSH and LH which turn on to inhibit Ovulation.
- Immune System regulated by T cell stimulation.

- t involve Osmoregulation which is transportation of fluid,Ca,Na and Cl, across intestinal epithelial membrane and helps to retain Na,K and Water in the kidney.
- It involve the metabolism of fat cell synthesis,differentiation and regulation.
- Excess prolactin lead on to dyslipidemia,increased platelete aggregation that promote on vascular thromosis which lead on to acute coronary syndrome.

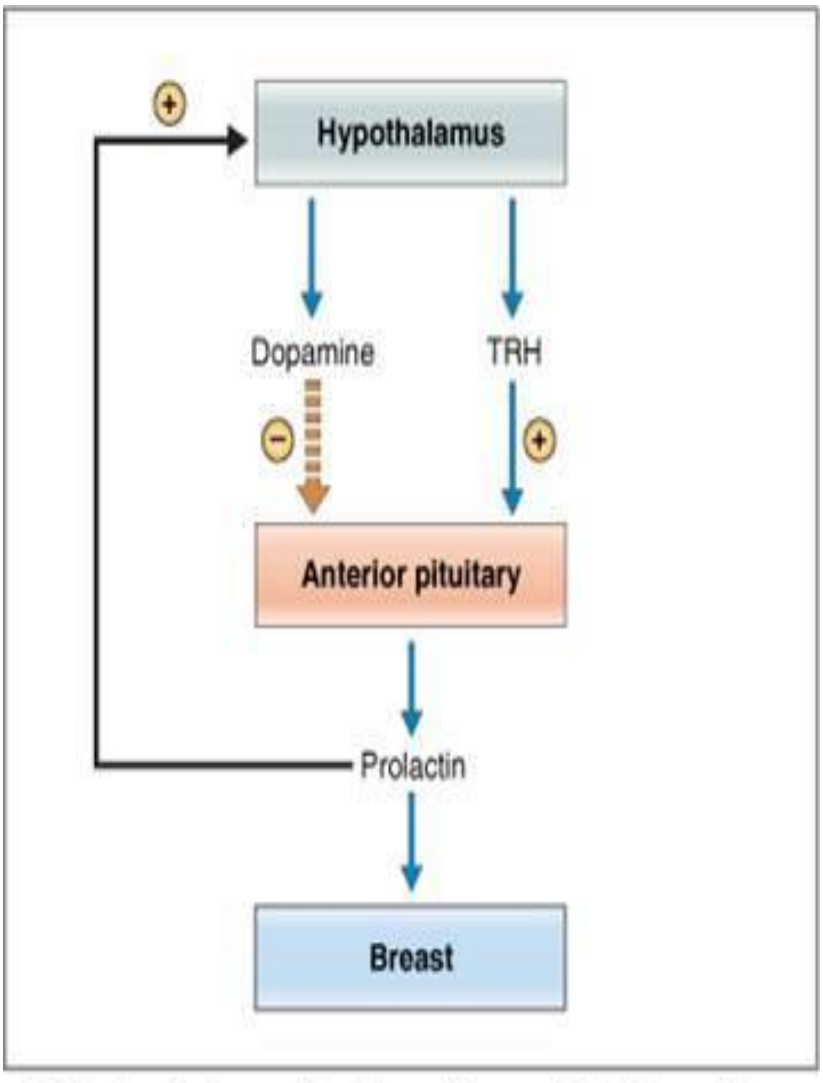
**FACTORS AFFECTING SECRETION**

| **Factors Increasing Prolactin Secretion** | **Factors Decreasing Prolactin Secretion** |
|---|---|
| • PRH-Prolactin releasing hormone<br>• Oxytocin - causes muscle contractions to expel milk.<br>• Estrogen -during pregnancy ,it stimulates lactotropes to secrete prolactin.<br>• TRH-Thyrotropin-releasing hormone | • Excess Dopamine<br>• Dopamine agonist like Bromocryptine<br>• Head injury<br>• Autoimmune disease<br>• Growth hormone deficiency<br>• Sheehan's syndrome |

| | |
|---|---|
| • VIP-Vasoactive intestinal peptide<br>• Stress and Breast feeding<br>• Sleep and chest wall trauma<br>• Dopamine antagonist drugs like antipsychatric drugs | • Infection(e.g.histoplasmosis,Tuberculosis) |

Anterior pituitary dysfunction causes decreased prolactin secretion.most of the anterior pituitary hormones increases prolactin secreting hormones[35].

**REGULATION OF SECRETION**

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- Stimulation of Prolactin secretion mainly comes under Breast feeding action. Which is Triggered by PRH(prolactin releasing hormone) ,inhibited by Dopamine a prolactin inhibitory hormone(PIH)[33].

- PIH level predominates in male.
- In females, according to blood estrogen , prolctin level varies.;

-PIH secretion , increased in low level of blood estrogen.

-PRH secretion, increased in high level of blood estrogen.

**SYMPTOMS OF HYPOPROLACTINEMIA AND HYPERPROLACTINEMIA**

| HYPOPROLACTINEMIA | HYPERPROLACTINEMIA |
|---|---|
| • Ovarian Diseases<br>• Impotence<br>• Delayed Puberty<br>• Abnormal Spermatogenesis.<br>• Infertility | **Women**:<br>Amenorrhoea And Oligomenorrhoea<br>GalactorrhoeaAnd Infertility<br>HirsutimAnd Osteoporosis<br>**Men**(Late Onset):<br>Gynaecomastia And Impotence.<br>Osteoporosis |

**DIAGNOSIS:**

- Detailed History including medications, menstrual cycle[35]
- Local Examination ( galactorrhoea)

**LABORATORY**

- Measurement of serum Prolactin level
- Thyroid function test
- LH and FSH assay
- Pregnancy teST

**IMAGING MODALITY**

- MRI scan is the best image of choice.it detect very minimal lesion even 3 to 5mm size
- High speed helical- CT scan also very useful.

**TREATMENT:**

**MEDICAL AND SURGICAL MANAGEMENT**

**HYPERPROLACTINOMA MANAGEMENT GUIDE**

- **Dopamine agonist :**Bromocriptine,Lisuride,Quinagolide,Cabergoline[35].
- Large pituitary tumour treated with surgical removal or radiation therapy

If needed, replacement of thyroid hormone or other hormonal replacement therapy like estrogen and progestins in ovarian insufficiency is adviced.

## AIM AND OBJECTIVES

- Aim of the present study was evaluation of the serum prolactin level in the acute myocardial infarction (MI) regarding the current
- Pharmacotherapy in management of MI.
- To compare the levels of serum prolactin in patients with acute myocardial infarction and normal population, to know the role of current pharmacotherapy.
- To compare Serum Prolactin with Serum Troponin I .

## MATERIALS AND METHODS

Method of collection of clinical sample and data-Patients admitted in the CCU, dept.of cardiology,Govt Stanley Hospital with Acute myocardial infarction shall be studied.

## STUDY DESIGN:

CASE CONTROL STUDY.

## STUDY PERIOD:

March 2017 to October 2017 [ 8 month ]

**CASE DEFINITION:**

Myocardial infarction (MI) is the irreversible necrosis and death of cardiac muscle due to diminished blood supply to the heart which leads to myocardial cell damage and ischemia supplied by that artery. The diagnosis of acute myocardial infarction based clinically ,electro and Echocardiographically.

**INCLUSION CRITERIA:**

Patients with acute ST elevation changes in ECG and hypokinesia of reginal wall motion abnormality in Echocardiographically.

**EXCLUSION CRITERIA:**

1. Hypothyroidism Patients.
2. Chronic dopamine agonist drug intaker
3. 3.Smoker

**SAMPLE SIZE :**

- 50

**METHODOLOGY:**

- The Acute MI patients are subjected to a detailed history and clinical examination with the help of ECG and ECHO.
- Detailed Past history of drug intake like T.Metformin, T.Aspirin, T.Clopidogrel, T.Metoprolol, T,Atorvastatin and T,Isosorbidedinitrate.

- The Acute MI patients are divided into 50 subjects in one group, with healthy controls as second group.
- The subjects of each group are appropriately matched for age and sex.
- Basic investigations with serum prolactin and serum troponin are taken within 24 hours onset of symptoms.
- The serum prolactin levels of the two groups are then compared.
- The serum prolcatin levels are compared with serum troponin among the acute MI patients.
- T.Metformin.T.Aspirin, combined T.aspirin and T.Clopidogrel and other drugs like T.Atorvasatin,T.Metoprolol,T.ISDN compared with paitents and control group
- **TABLE :**

**PATIENTS GROUP and CONTROL GROUP**

| **Age** | **Sex** | **Serum Prolactin** | **Serum Troponin I** | **T. Aspirin** | **T.Aspirin and T.Clopidogrel** | **T.Metformin** | **Other Drugs** |
|---|---|---|---|---|---|---|---|
| | | | | | | | |

**REFERENCE VALUE**

- Serum Prolactin Normal Range - Male less than 15ng/dl.

  Female less than 20ng/dl.

- Serum Troponin I Normal Range-Both Sex Less than 50ng/L.

The **Normal Population** Is Selected From Patients Attending Master Health Check Up.

**METHOD USED FOR ESTIMATION OF SERUM PROLACTIN :**

ELISA kit method

**METHOD USED FOR ESTIMATION OF SERUM TROPONIN I:**

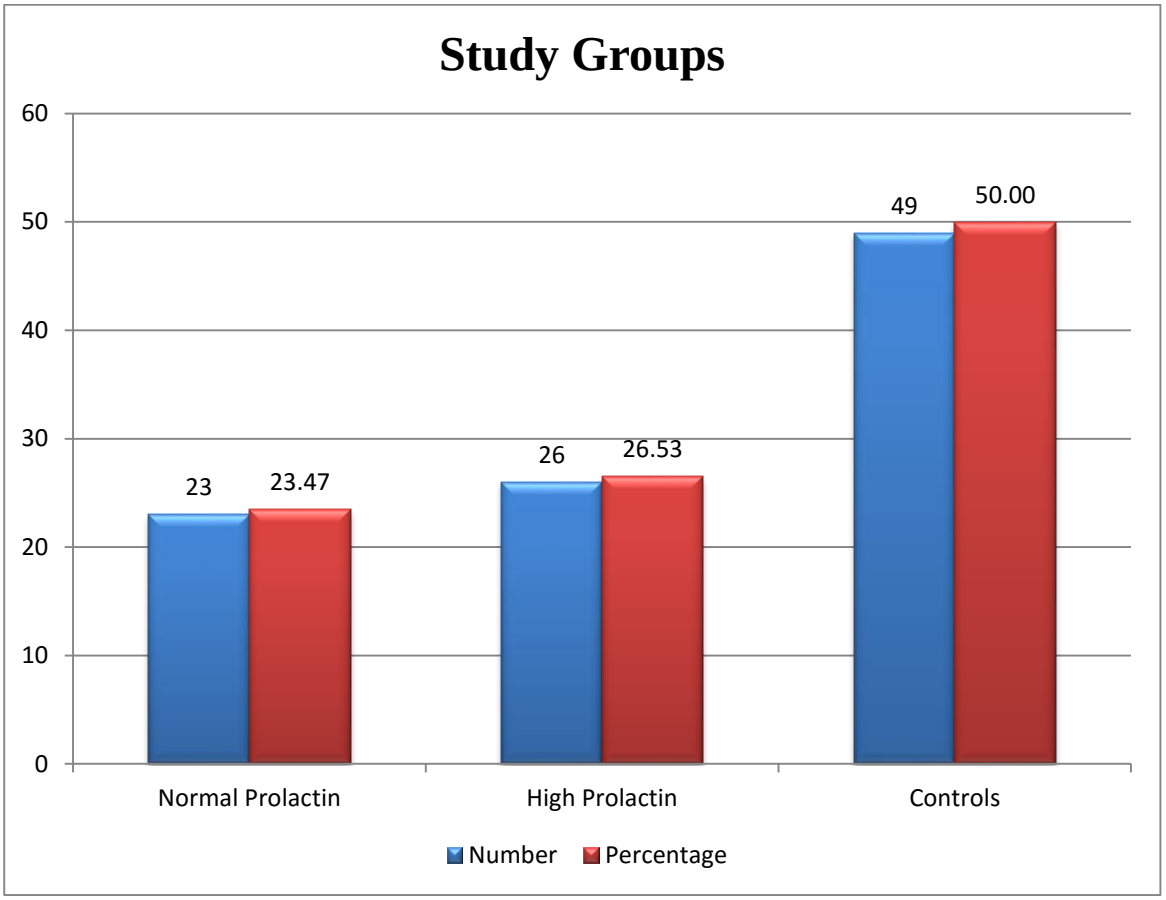
ELISA kit method

**RESULTS AND DISCUSSION**

**STATISTICALANALYSIS**

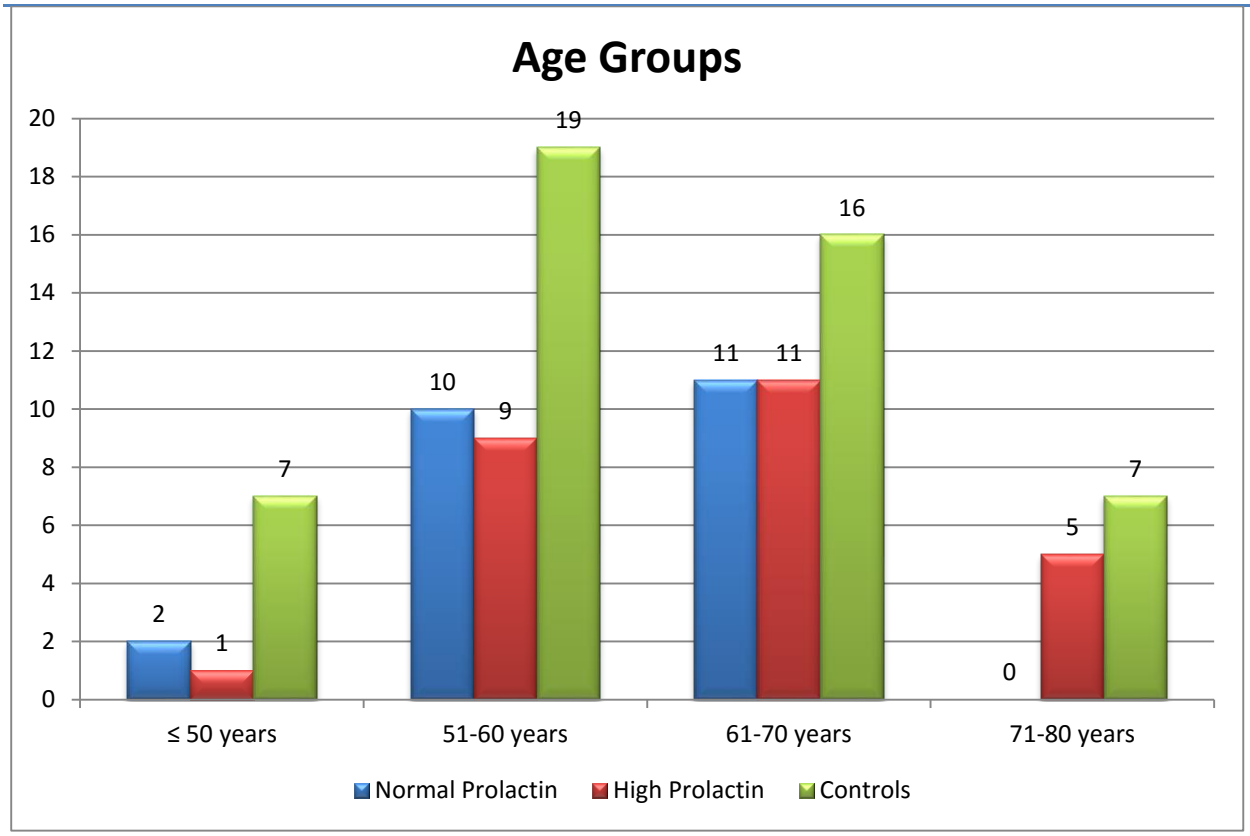
Descriptive statistics was done for all data and suitable statistical tests of comparison were done. Continuous variables were analyzed with the Unpaired t test and Single factor ANOVA and categorical variables were analyzed with Fisher Exact Test. correlation analysis was done using persons r. Statistical significance was taken as $P < 0.05$. The data was analyzed using SPSS Version 16. Microsoft Excel 2010.was used to generate charts

## Study Groups




| Study Groups | Normal Prolactin | High Prolactin | Controls |
|---|---|---|---|
| **Number** | 23 | 26 | 49 |
| **Percentage** | 23.47 | 26.53 | 50.00 |

## Age



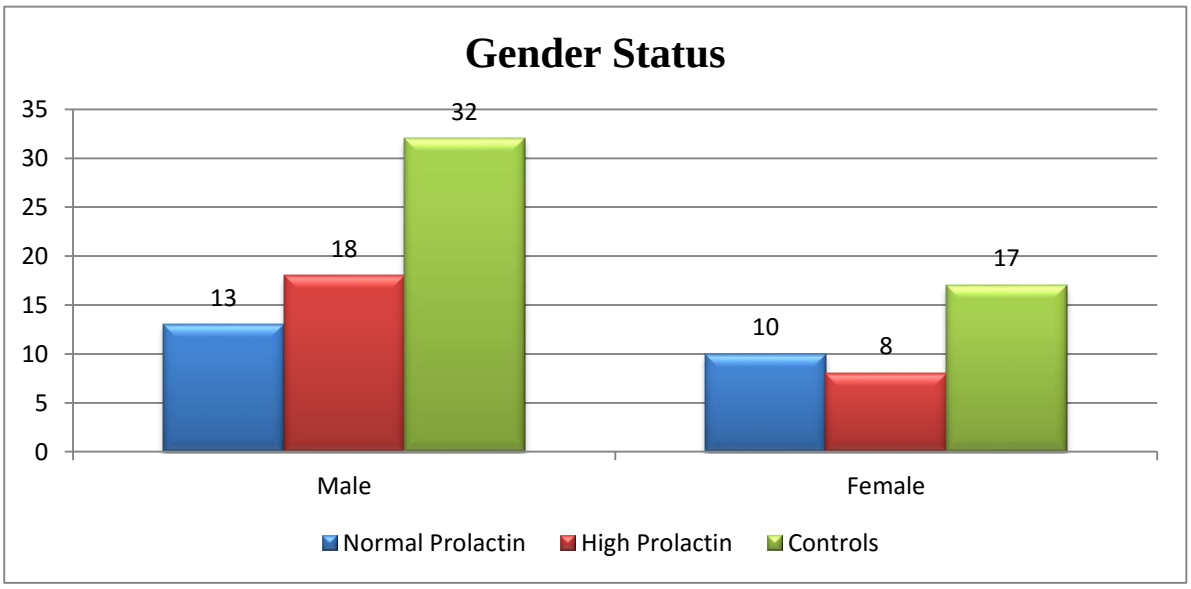

| Age Groups | Normal Prolactin | % | High Prolactin | % | Controls | % |
|---|---|---|---|---|---|---|
| **≤ 50 years** | 2 | 8.70 | 1 | 3.85 | 7 | 14.29 |
| **51-60 years** | 10 | 43.48 | 9 | 34.62 | 19 | 38.78 |
| **61-70 years** | 11 | 47.83 | 11 | 42.31 | 16 | 32.65 |
| **71-80 years** | 0 | 0.00 | 5 | 19.23 | 7 | 14.29 |
| **Total** | 23 | 100.00 | 26 | 100.00 | 49 | 100.00 |

| Age Distribution | Normal Prolactin | High Prolactin | Controls |
|---|---|---|---|
| **Mean** | 58.61 | 61.65 | 59.86 |
| **SD** | 6.18 | 7.39 | 8.35 |
| **P value**<br>**Single Factor ANOVA Test** | | | 0.3732 |

Majority of the normal prolactin group patients belonged to 61-70 years age class interval (n=11, 47.83%) with a mean age of 58.61 years. In the high prolactin group patients, majority belonged to 61-70 years age class interval (n=11, 42.31%) with a mean age of 61.65 years. In the control group patients, majority belonged to 51-60 years class interval (n=19, 38.78%) with a mean age of 59.86 years.

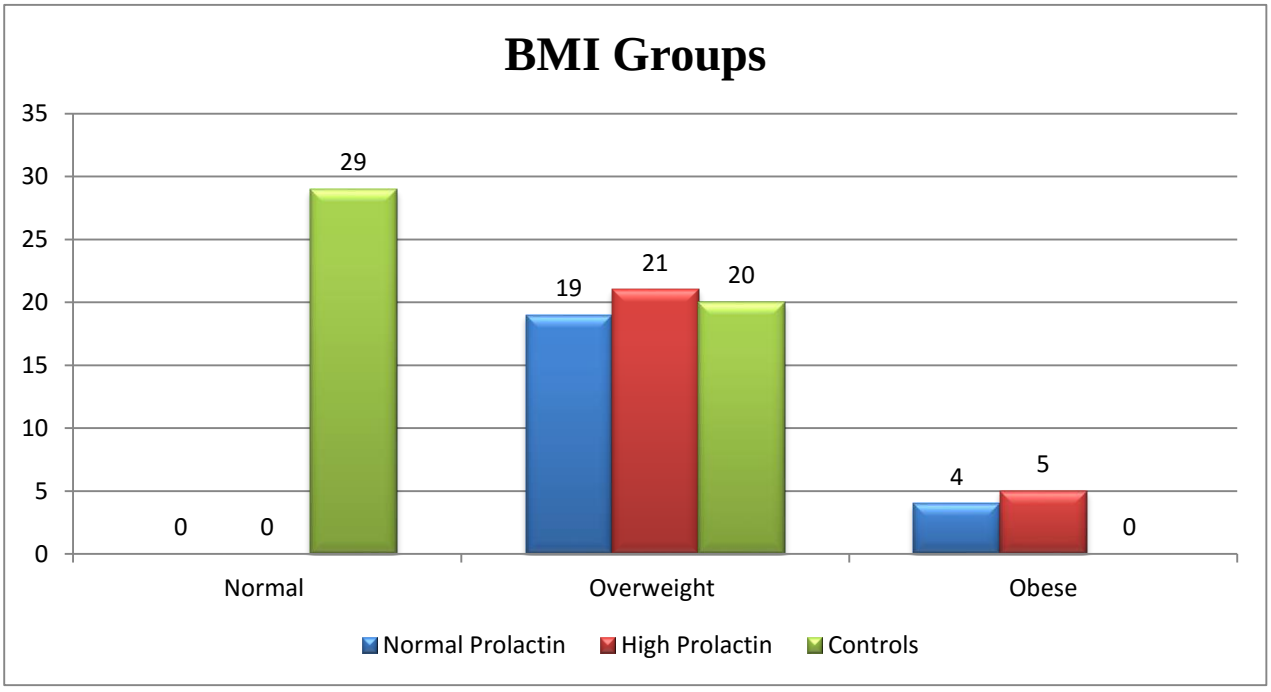
The association between the study groups and age distribution is considered to be not statistically significant since $p > 0.05$ as per single factor ANOVA test.

## Gender



| Gender Status | Normal Prolactin | % | High Prolactin | % | Controls | % |
|---|---|---|---|---|---|---|
| **Male** | 13 | 56.52 | 18 | 69.23 | 32 | 65.31 |
| **Female** | 10 | 43.48 | 8 | 30.77 | 17 | 34.69 |
| **Total** | 23 | 100.00 | 26 | 100.00 | 49 | 100.00 |
| **P value**<br>**Chi Squared Test** | | | | | 0.6373 | |

Majority of the study subjects were males in normal prolactin group patients (n=13, 56,52%), high prolactin group patients (n=18, 69.23%) and control group patients (n=32, 65.31%), The association between the study groups and gender status is considered to be not statistically significant since p > 0.05 as per chi squared **test.BMI**



| BMI Groups | Normal Prolactin | % | High Prolactin | % | Controls | % |
|---|---|---|---|---|---|---|
| **Normal** | 0 | 0.00 | 0 | 0.00 | 29 | 59.18 |
| **Overweight** | 19 | 82.61 | 21 | 80.77 | 20 | 40.82 |
| **Obese** | 4 | 17.39 | 5 | 19.23 | 0 | 0.00 |
| **Total** | 23 | 100.00 | 26 | 100.00 | 49 | 100.00 |

| BMI Distribution | Normal Prolactin | High Prolactin | Controls |
|---|---|---|---|
| **Mean** | 26.40 | 28.43 | 24.25 |
| **SD** | 1.91 | 1.66 | 1.68 |
| **P value Single Factor ANOVA Test** | | | <0.0001 |

Majority of the normal prolactin group patients belonged to overweight BMI class interval (n=19, 82.61%) with a mean BMI of 28.40. In the high prolactin group patients, majority belonged to overweight BMI class interval (n=21, 80.77%) with a mean BMI of 28.43. In the control group patients, majority belonged to normal BMI class interval (n=29, 59.18%) with a mean BMI of 24.25.

The association between the study groups and BMI distribution is considered to be statistically significant since $p < 0.05$ as per single factor ANOVA test.

## DISCUSSION

The mean BMI levels were significantly elevated in high prolactin group compared to control group by a mean difference of 4.19(15% higher).

The mean BMI levels were significantly elevated in normal prolactin group compared to control group by a mean difference of 2.15(8% higher)

The mean BMI levels were significantly elevated in high prolactin group compared to normal prolactin group by a mean difference of 2.03(7% higher)

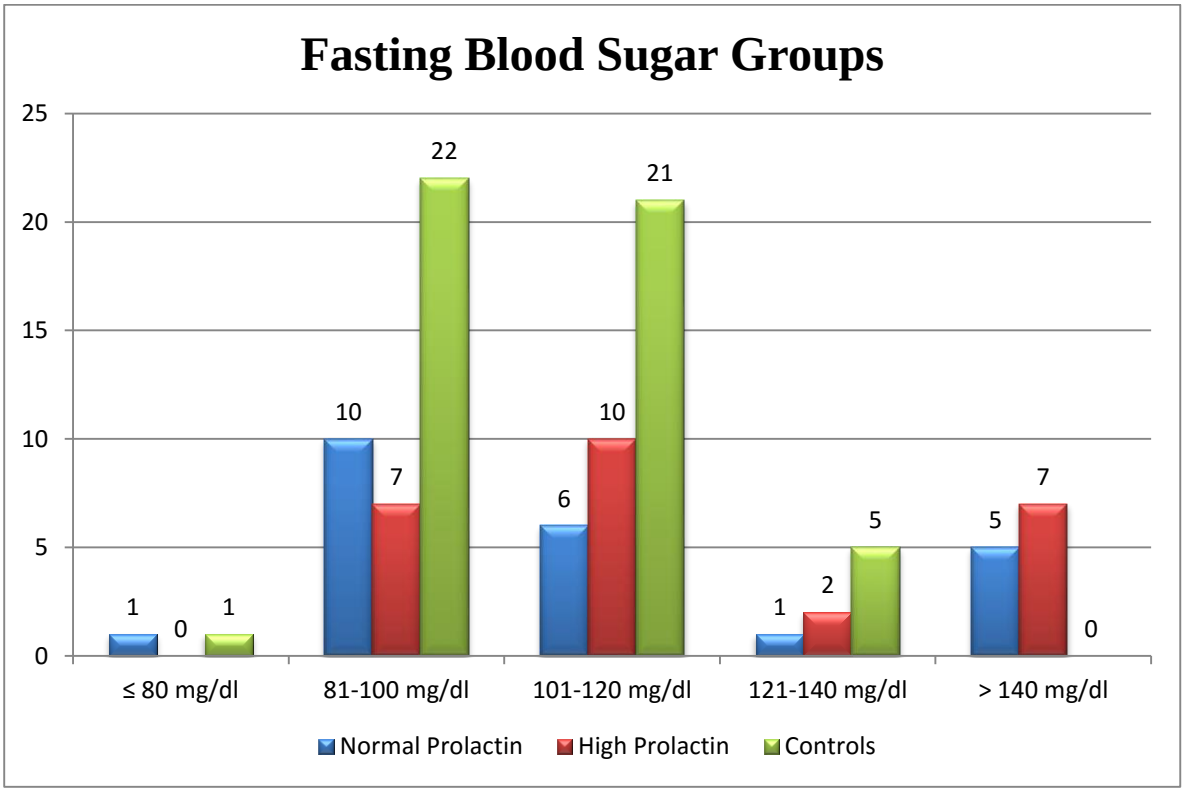
This difference is significant with a p-value <0.0001 as per single factor ANOVA test.

## CONCLUSION

In this study we can safely conclude that high and normal prolactin group had significantly higher levels of BMI compared to control group and high prolactin group had significantly higher levels of BMI compared to normal prolactin group among acute MI patients.

In conclusion, we observed that higher serum prolactin concentrations is associated acute MI patients with elevated BMI

FBS




| Fasting Blood Sugar Groups | Normal Prolactin | % | High Prolactin | % | Controls | % |
|---|---|---|---|---|---|---|
| **≤ 80 mg/dl** | 1 | 4.35 | 0 | 0.00 | 1 | 2.04 |
| **81-100 mg/dl** | 10 | 43.48 | 7 | 26.92 | 22 | 44.90 |
| **101-120 mg/dl** | 6 | 26.09 | 10 | 38.46 | 21 | 42.86 |
| **121-140 mg/dl** | 1 | 4.35 | 2 | 7.69 | 5 | 10.20 |
| **>140 mg/dl** | 5 | 21.74 | 7 | 26.92 | 0 | 0.00 |
| **Total** | 23 | 100.00 | 26 | 100.00 | 49 | 100.00 |

| Age Distribution | Normal Prolactin | High Prolactin | Controls |
|---|---|---|---|
| **Mean** | 118.30 | 121.27 | 102.80 |
| **SD** | 40.95 | 31.99 | 12.48 |
| **P value** **Single Factor ANOVA Test** | | | 0.0092 |

Majority of the normal prolactin group patients belonged to 81-100 mg/dl FBS class interval (n=10, 43.48%) with a mean FBS of 118.30 mg/dl. In the high prolactin group patients, majority belonged to 101-120 mg/dl FBS class interval (n=10, 38.46%) with a mean FBS of 121.27 mg/dl. In the control group patients, majority belonged to 81-100 mg/dlFBS class interval (n=22, 44.90%) with a mean FBS of 102.80 mg/dl.

The association between the study groups and FBS distribution is considered to be statistically significant since $p < 0.05$ as per single factor ANOVA test.

## DISCUSSION

The mean FBS levels were significantly elevated in high prolactin group compared to control group by a mean difference of 18.47(15% higher).

The mean FBS levels were significantly elevated in normal prolactin group compared to control group by a mean difference of 15.51(13% higher)

The mean FBS levels were significantly elevated in high prolactin group compared to normal prolactin group by a mean difference of 2.96(2% higher)

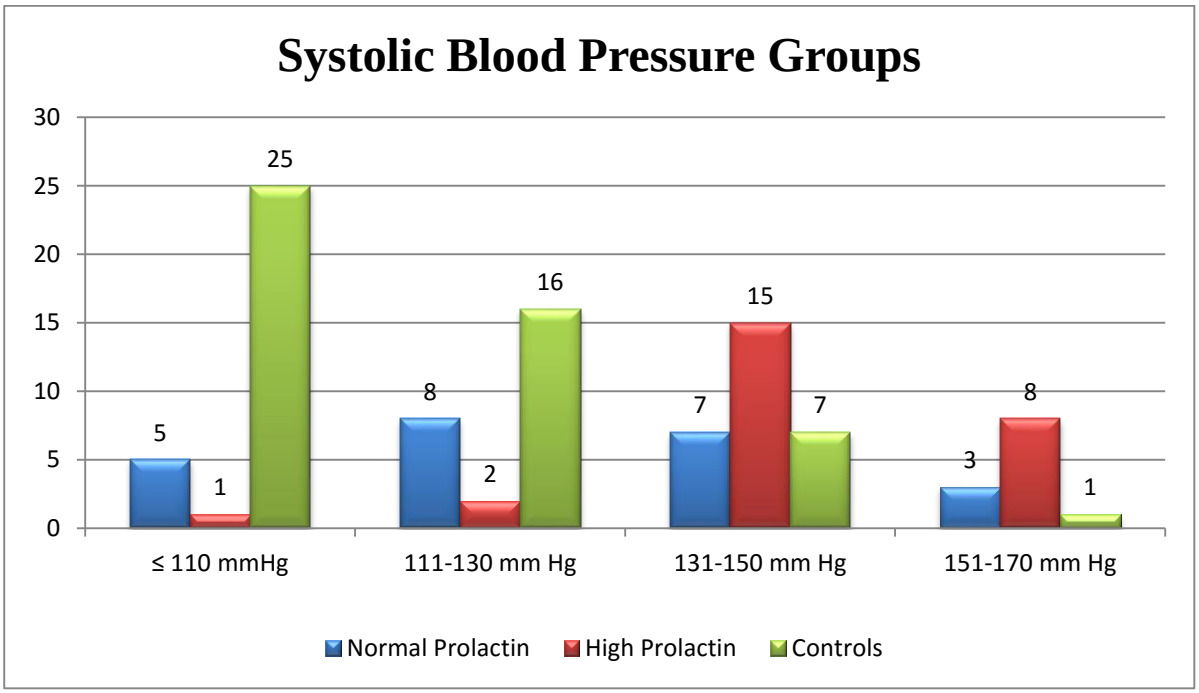
This difference is significant with a p-value 0.0092 as per single factor ANOVA test.

## CONCLUSION

In this study we can safely conclude that high and normal prolactin group had significantly elevated levels of FBS compared to control group and high prolactin group had significantly elevated levels of FBS compared to normal prolactin group among acute MI patients.

In conclusion, we observed that higher serum prolactin concentrations is associated acute MI patients with elevated FBS

### SBP



| Systolic Blood Pressure Groups | Normal Prolactin | % | High Prolactin | % | Controls | % |
|---|---|---|---|---|---|---|
| **≤ 110 mm Hg** | 5 | 21.74 | 1 | 3.85 | 25 | 51.02 |
| **111-130 mm Hg** | 8 | 34.78 | 2 | 7.69 | 16 | 32.65 |
| **131-150 mm Hg** | 7 | 30.43 | 15 | 57.69 | 7 | 14.29 |
| **151-170 mm Hg** | 3 | 13.04 | 8 | 30.77 | 1 | 2.04 |
| **Total** | 23 | 100.00 | 26 | 100.00 | 49 | 100.00 |

| Systolic Blood Pressure Distribution | Normal Prolactin | High Prolactin | Controls |
|---|---|---|---|
| **Mean** | 132.61 | 147.69 | 118.35 |
| **SD** | 16.57 | 14.51 | 15.16 |
| **P value Single Factor ANOVA Test** | | | <0.0001 |

Majority of the normal prolactin group patients belonged to 111-130 mm Hg SBP class interval (n=8, 34.78%) with a mean SBP of 132.61.mm Hg. In the high prolactin group patients, majority belonged to 131-150 mm Hg SBP class interval (n=15, 57.69%) with a mean SBP of 147.69 mm Hg. In the control group patients, majority belonged to ≤ 110 mmHg SBP class interval (n=25, 51.02%) with a mean SBP of 118.35 mm Hg.

The association between the study groups and SBP distribution is considered to be statistically significant since $p < 0.05$ as per single factor ANOVA test.

## DISCUSSION

The mean SBP levels were significantly elevated in high prolactin group compared to control group by a mean difference of 29.35(20% higher).

The mean SBP levels were significantly elevated in normal prolactin group compared to control group by a mean difference of 14.26(11% higher)

The mean SBP levels were significantly elevated in high prolactin group compared to normal prolactin group by a mean difference of 15.08(10% higher)

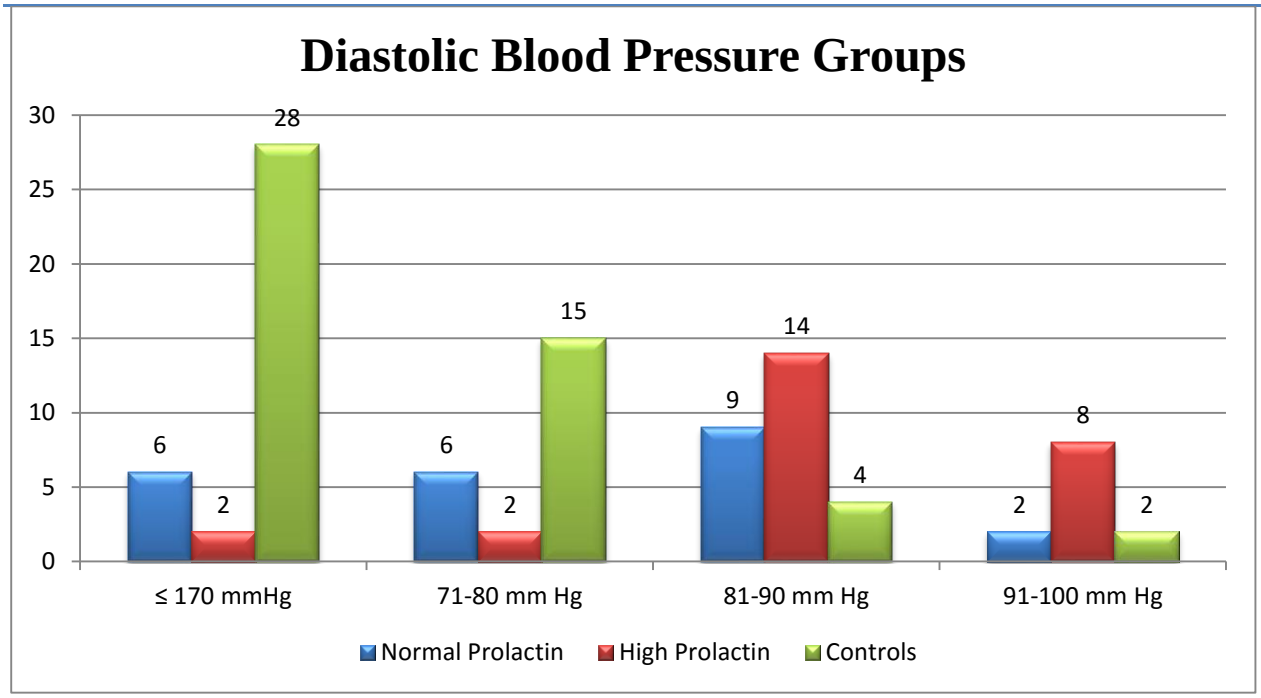
This difference is significant with a p-value <0.0001 as per single factor ANOVA test.

## CONCLUSION

In this study we can safely conclude that high and normal prolactin group had significantly elevated levels of SBP compared to control group and high prolactin group had significantly elevated levels of SBP compared to normal prolactin group among acute MI patients.

In conclusion, we observed that higher serum prolactin concentrations is associated acute MI patients with elevated SBP

DBP




| Diastolic Blood Pressure Groups | Normal Prolactin | % | High Prolactin | % | Controls | % |
|---|---|---|---|---|---|---|
| **≤ 170 mmHg** | 6 | 26.09 | 2 | 7.69 | 28 | 57.14 |
| **71-80 mm Hg** | 6 | 26.09 | 2 | 7.69 | 15 | 30.61 |
| **81-90 mm Hg** | 9 | 39.13 | 14 | 53.85 | 4 | 8.16 |
| **91-100 mm Hg** | 2 | 8.70 | 8 | 30.77 | 2 | 4.08 |
| **Total** | 23 | 100.00 | 26 | 100.00 | 49 | 100.00 |

| Diastolic Blood Pressure Distribution | Normal Prolactin | High Prolactin | Controls |
|---|---|---|---|
| **Mean** | 83.04 | 90.77 | 73.67 |
| **SD** | 9.74 | 8.45 | 10.55 |
| **P value** **Single Factor ANOVA Test** | | | <0.0001 |

Majority of the normal prolactin group patients belonged to 81-90 mm Hg DBP class interval (n=9, 39.13%) with a mean DBP of 83.04.mm Hg. In the high prolactin group patients, majority belonged to 81-90 mm Hg DBP class interval (n=14, 53.85%) with a mean DBP of 90.77 mm Hg. In the control group patients, majority belonged to ≤ 170 mmHg DBP class interval (n=28, 57.14%) with a mean DBP of 74.67 mm Hg.

The association between the study groups and DBP distribution is considered to be statistically significant since $p < 0.05$ as per single factor ANOVA test.

## DISCUSSION

The mean DBP levels were significantly elevated in high prolactin group compared to control group by a mean difference of 17.10(19% higher).

The mean DBP levels were significantly elevated in normal prolactin group compared to control group by a mean difference of 9.37(11% higher)

The mean DBP levels were significantly elevated in high prolactin group compared to normal prolactin group by a mean difference of 7.73(9% higher)

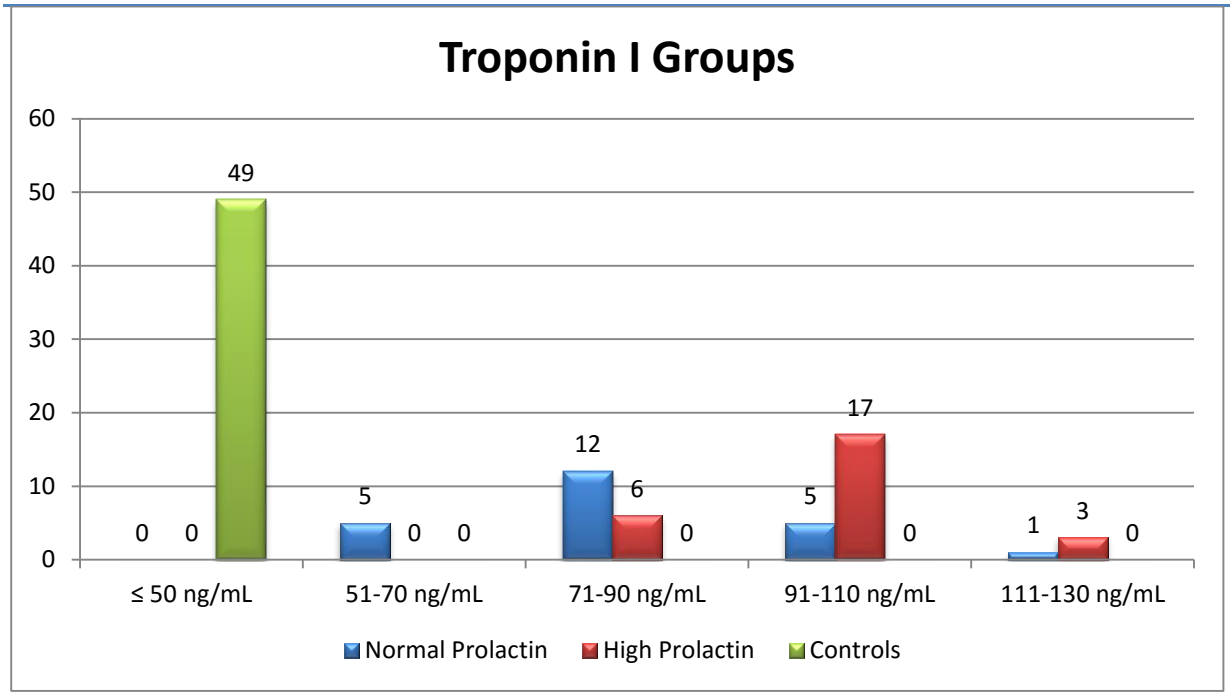
This difference is significant with a p-value <0.0001 as per single factor ANOVA test.

## CONCLUSION

In this study we can safely conclude that high and normal prolactin group had significantly elevated levels of DBP compared to control group and high prolactin group had significantly elevated levels of DBP compared to normal prolactin group among acute MI patients.

In conclusion, we observed that higher serum prolactin concentrations is associated acute MI patients with elevated DBP

## TROPONIN I



| Troponin I Groups | Normal Prolactin | % | High Prolactin | % | Controls | % |
|---|---|---|---|---|---|---|
| **≤ 50 ng/mL** | 0 | 0.00 | 0 | 0.00 | 49 | 100.00 |
| **51-70 ng/mL** | 5 | 21.74 | 0 | 0.00 | 0 | 0.00 |
| **71-90 ng/mL** | 12 | 52.17 | 6 | 23.08 | 0 | 0.00 |
| **91-110 ng/mL** | 5 | 21.74 | 17 | 65.38 | 0 | 0.00 |
| **111-130 ng/Ml** | 1 | 4.35 | 3 | 11.54 | 0 | 0.00 |
| **Total** | 23 | 100.00 | 26 | 100.00 | 49 | 100.00 |

| Troponin I Distribution | Normal Prolactin | High Prolactin | Controls |
|---|---|---|---|
| **Mean** | 81.96 | 95.65 | 17.16 |
| **SD** | 14.77 | 9.27 | 5.95 |
| **P value Single Factor ANOVA Test** | | | <0.0001 |

Majority of the normal prolactin group patients belonged to 71-90 ng/mL troponin I class interval (n=12, 52.17%) with a mean troponin I of 83.04. ng/mL. In the high prolactin group patients, majority belonged to 91-110 ng/mL troponin I class interval (n=17, 65.38%) with a mean troponin I of 90.77 ng/mL. In the control group patients,

majority belonged to ≤ 50 ng/mL troponin I class interval (n=49, 100%) with a mean troponin I of 74.67 ng/mL.

The association between the study groups and troponin I distribution is considered to be statistically significant since $p < 0.05$ as per single factor ANOVA test.

## DISCUSSION

The mean troponin Ilevels were significantly elevated in high prolactin group compared to control group by a mean difference of 78.49(82% higher).

The mean troponin Ilevels were significantly elevated in normal prolactin group compared to control group by a mean difference of 64.79(79% higher)

The mean troponin Ilevels were significantly elevated in high prolactin group compared to normal prolactin group by a mean difference of 13.70(14% higher)

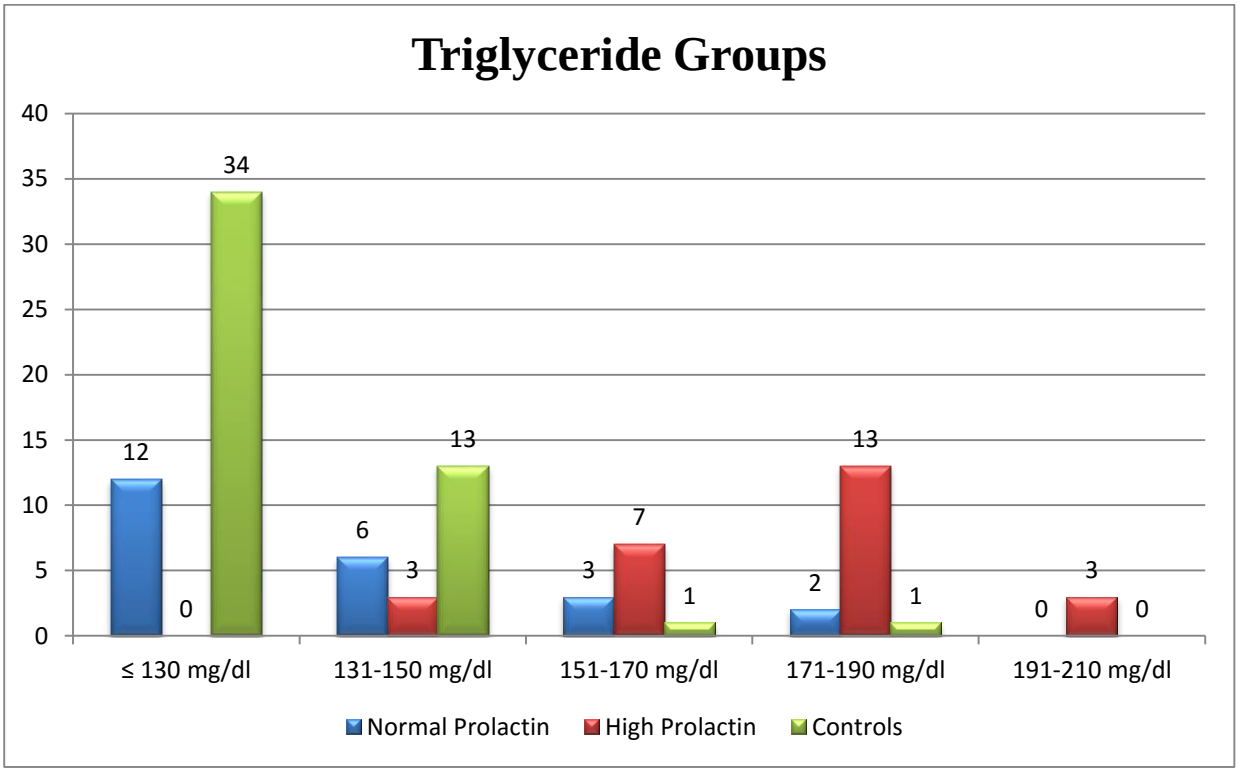
This difference is significant with a p-value<0.0001 as per single factor ANOVA test.

## CONCLUSION

In this study we can safely conclude that high and normal prolactin group had significantly elevated levels of troponin I compared to control group and high prolactin group had significantly elevated levels of troponin I compared to normal prolactin group among acute MI patients.

In conclusion, we observed that higher serum prolactin concentrations is associated acute MI patients with elevated troponin I.

## TGL




| Triglyceride Groups | Normal Prolactin | % | High Prolactin | % | Controls | % |
|---|---|---|---|---|---|---|
| **≤ 130 mg/dl** | 12 | 52.17 | 0 | 0.00 | 34 | 69.39 |
| **131-150 mg/dl** | 6 | 26.09 | 3 | 11.54 | 13 | 26.53 |
| **151-170 mg/dl** | 3 | 13.04 | 7 | 26.92 | 1 | 2.04 |
| **171-190 mg/dl** | 2 | 8.70 | 13 | 50.00 | 1 | 2.04 |
| **191-210 mg/dl** | 0 | 0.00 | 3 | 11.54 | 0 | 0.00 |
| **Total** | 23 | 100.00 | 26 | 100.00 | 49 | 100.00 |

| Triglyceride Distribution | Normal Prolactin | High Prolactin | Controls |
|---|---|---|---|
| **Mean** | 134.96 | 172.65 | 121.94 |
| **SD** | 20.79 | 17.80 | 18.06 |
| **P value** **Single Factor ANOVA Test** | | | <0.0001 |

Majority of the normal prolactin group patients belonged to ≤ 130 mg/dl triglyceride class interval (n=12, 52.17%) with a mean triglyceride of 134.96. mg/dl. In the high prolactin group patients, majority belonged to 171-190 mg/dl triglyceride class interval (n=13, 50%) with a mean triglyceride of 172.65 mg/dl. In the control group patients, majority belonged to ≤ 130 mg/dl triglyceride class interval (n=34, 69.39%) with a mean triglyceride of 121.94 mg/dl.

The association between the study groups and triglyceride distribution is considered to be statistically significant since $p < 0.05$ as per single factor ANOVA test.

## DISCUSSION

The mean triglyceride levels were significantly elevated in high prolactin group compared to control group by a mean difference of 50.72(29% higher).

The mean triglyceride levels were significantly elevated in normal prolactin group compared to control group by a mean difference of 13.02(10% higher)

The mean triglyceride levels were significantly elevated in high prolactin group compared to normal prolactin group by a mean difference of 37.70(22% higher)

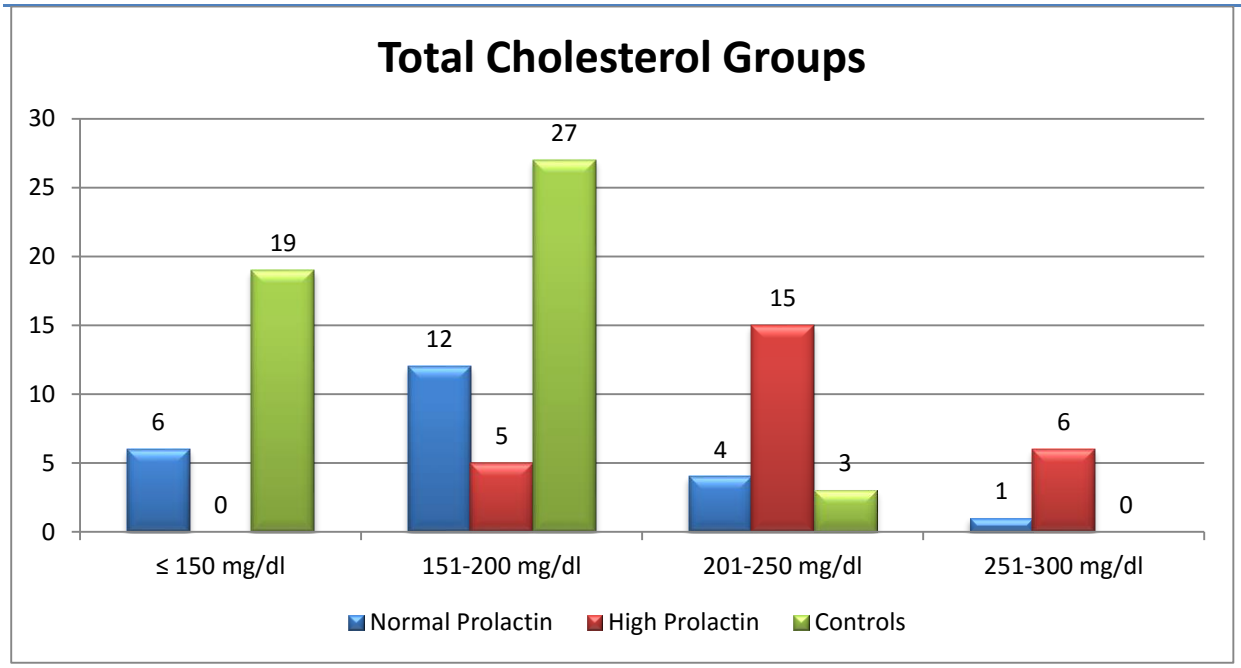
This difference is significant with a p-value < 0.0001 as per single factor ANOVA test.

## CONCLUSION

In this study we can safely conclude that high and normal prolactin group had significantly elevated levels of triglyceride compared to control group and high prolactin group had significantly elevated levels of triglyceride compared to normal prolactin group among acute MI patients.

In conclusion, we observed that higher serum prolactin concentrations is associated acute MI patients with elevated triglyceride

## CHOLESTEROL



| Total Cholesterol Groups | Normal Prolactin | % | High Prolactin | % | Controls | % |
|---|---|---|---|---|---|---|
| **≤ 150 mg/dl** | 6 | 26.09 | 0 | 0.00 | 19 | 38.78 |
| **151-200 mg/dl** | 12 | 52.17 | 5 | 19.23 | 27 | 55.10 |
| **201-250 mg/dl** | 4 | 17.39 | 15 | 57.69 | 3 | 6.12 |
| **251-300 mg/dl** | 1 | 4.35 | 6 | 23.08 | 0 | 0.00 |
| **Total** | 23 | 100.00 | 26 | 100.00 | 49 | 100.00 |

| Total Cholesterol Distribution | Normal Prolactin | High Prolactin | Controls |
|---|---|---|---|
| **Mean** | 174.13 | 217.96 | 161.22 |
| **SD** | 34.33 | 29.56 | 21.24 |
| **P value** **Single Factor ANOVA Test** | | | <0.0001 |

Majority of the normal prolactin group patients belonged to 151-200 mg/dl cholesterol class interval (n=12, 52.17%) with a mean cholesterol of 174.13. mg/dl. In the high prolactin group patients, majority belonged to 201-250 mg/dl cholesterol class interval (n=15, 57.59%) with a mean cholesterol of 217.96 mg/dl. In the control

group patients, majority belonged to ≤ 150 mg/dl cholesterol class interval (n=19, 38.78%) with a mean cholesterol of 161.22 mg/dl.

The association between the study groups and cholesterol distribution is considered to be statistically significant since $p < 0.05$ as per single factor ANOVA test.

## DISCUSSION

The mean cholesterol levels were significantly elevated in high prolactin group compared to control group by a mean difference of 56.74(26% higher).

The mean cholesterol levels were significantly elevated in normal prolactin group compared to control group by a mean difference of 12.91(7% higher)

The mean cholesterol levels were significantly elevated in high prolactin group compared to normal prolactin group by a mean difference of 43.83(20% higher)

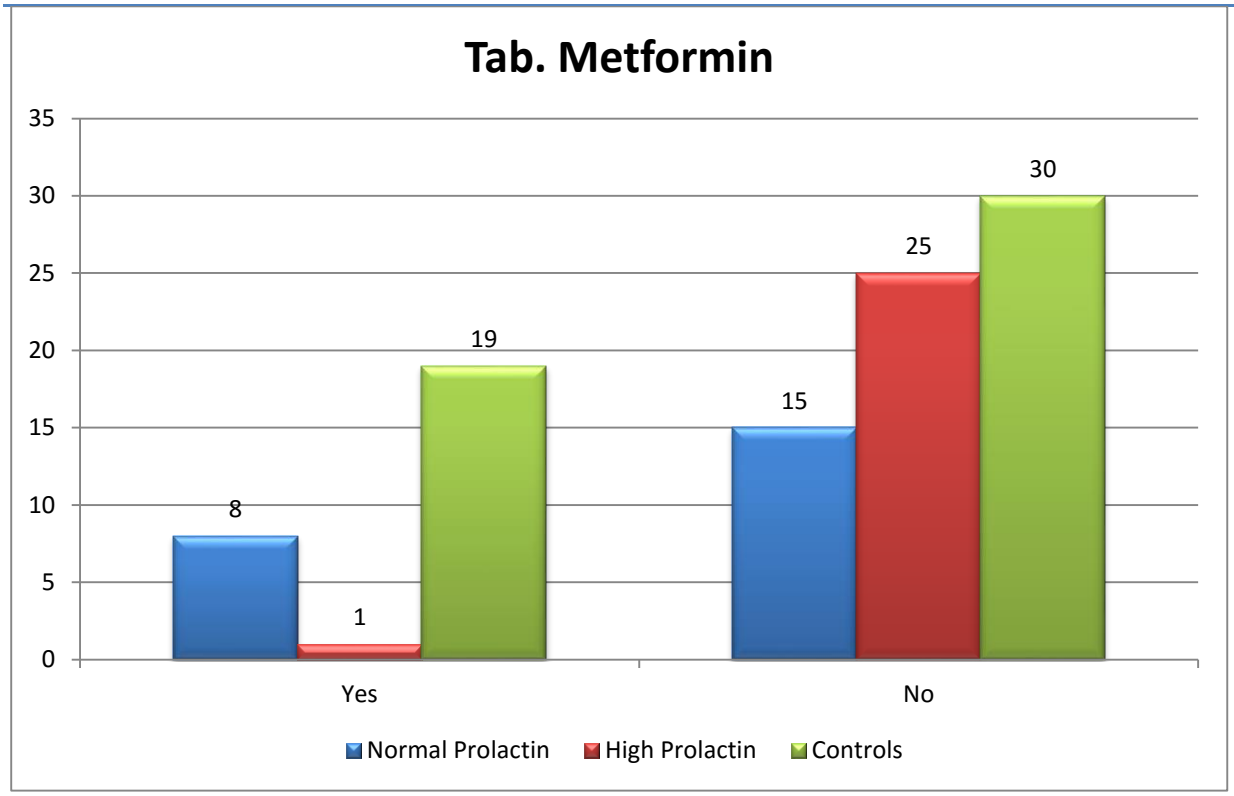
This difference is significant with a p-value <0.0001as per single factor ANOVA test.

## CONCLUSION

In this study we can safely conclude that high and normal prolactin group had significantly elevated levels of cholesterol compared to control group and high prolactin group had significantly elevated levels of cholesterol compared to normal prolactin group among acute MI patients.

In conclusion, we observed that higher serum prolactin concentrations is associated acute MI patients with elevated cholesterol

**METFORMIN**




| Tab. Metformin | Normal Prolactin | % | High Prolactin | % | Controls | % |
|---|---|---|---|---|---|---|
| **Yes** | 8 | 34.78 | 1 | 3.85 | 19 | 38.78 |
| **No** | 15 | 65.22 | 25 | 96.15 | 30 | 61.22 |
| **Total** | 23 | 100.00 | 26 | 100.00 | 49 | 100.00 |
| **P value** **Chi Squared Test** | | | | | <0.0001 | |

The study subjects on treatment with metformin is 34.78%, 3,85% and 38.78% in normal prolactin group, high prolactin group and control group patients respectively.

The association between the study groups and metformin intake status is considered to be statistically significant since $p < 0.05$ as per chi squared test.

## DISCUSSION

The incidence of metformin intake is significantly decreased in high prolactin group compared to control group by a percentage difference of 34.93(90% lower).

The incidence of metformin intake is significantly decreased in normal prolactin group compared to control group by a percentage difference of 3.99(10% lower).

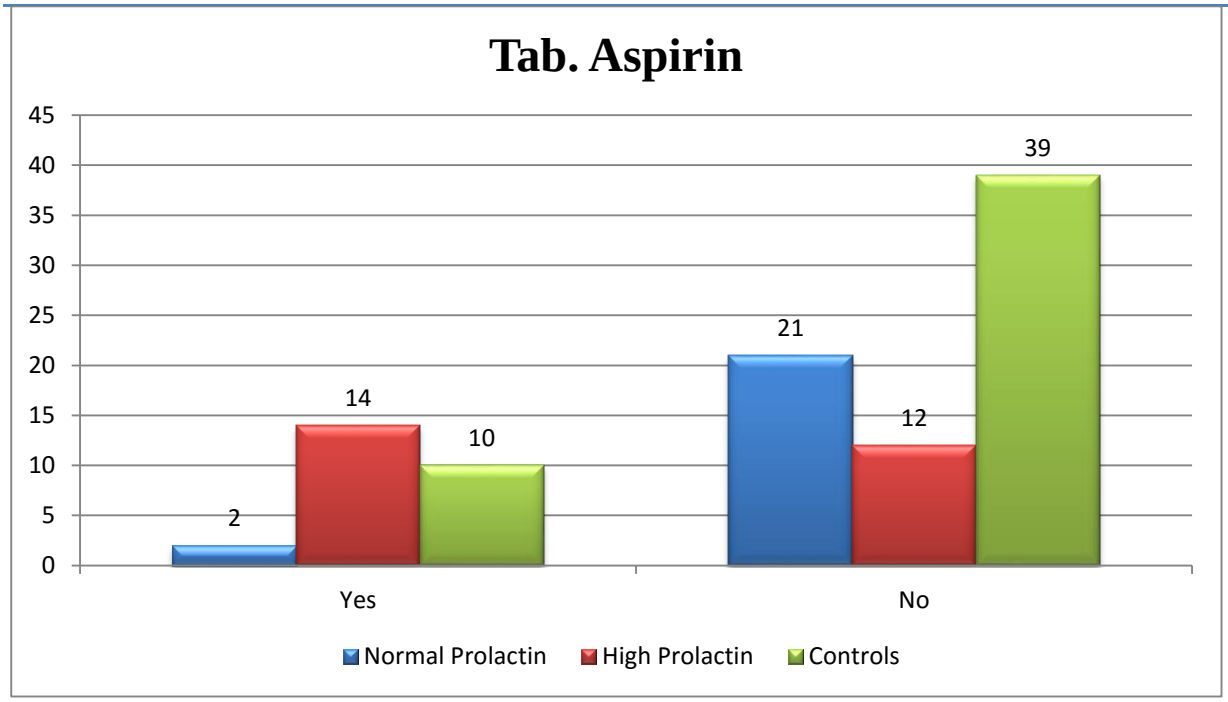
The incidence of metformin intake is significantly decreased in high prolactin group compared to normal prolactin l group by a percentage difference of 30.94(89% lower).

## CONCLUSION

In this study we can safely conclude that high and normal prolactin group had significantly decreased incidence of metformin intake compared to control group and high prolactin group had significantly decreased incidence of metformin intake compared to normal prolactin group among acute MI patients.

In conclusion, we observed that higher serum prolactin concentrations is associated acute MI patients with decreased incidence of metformin intake

**ASPIRIN**




| Tab. Aspirin | Normal Prolactin | % | High Prolactin | % | Controls | % |
|---|---|---|---|---|---|---|
| **Yes** | 7 | 30.43 | 14 | 53.85 | 10 | 20.41 |
| **No** | 16 | 69.57 | 12 | 46.15 | 39 | 79.59 |
| **Total** | 23 | 100.00 | 26 | 100.00 | 49 | 100.00 |
| **P value** **Chi Squared Test** | | | | | <0.0001 | |

The study subjects on treatment with asprin are 30.43%, 53.85% and 20.41% in normal prolactin group, high prolactin group and control group patients respectively.

The association between the study groups and asprin intake status is considered to be statistically significant since $p < 0.05$ as per chi squared test.

## DISCUSSION

The incidence of asprin intake is significantly decreased in high prolactin group compared to control group by a percentage difference of 33.44(62% higher).

The incidence of asprin intake is significantly decreased in normal prolactin group compared to control group by a percentage difference of 10.03(33% higher).

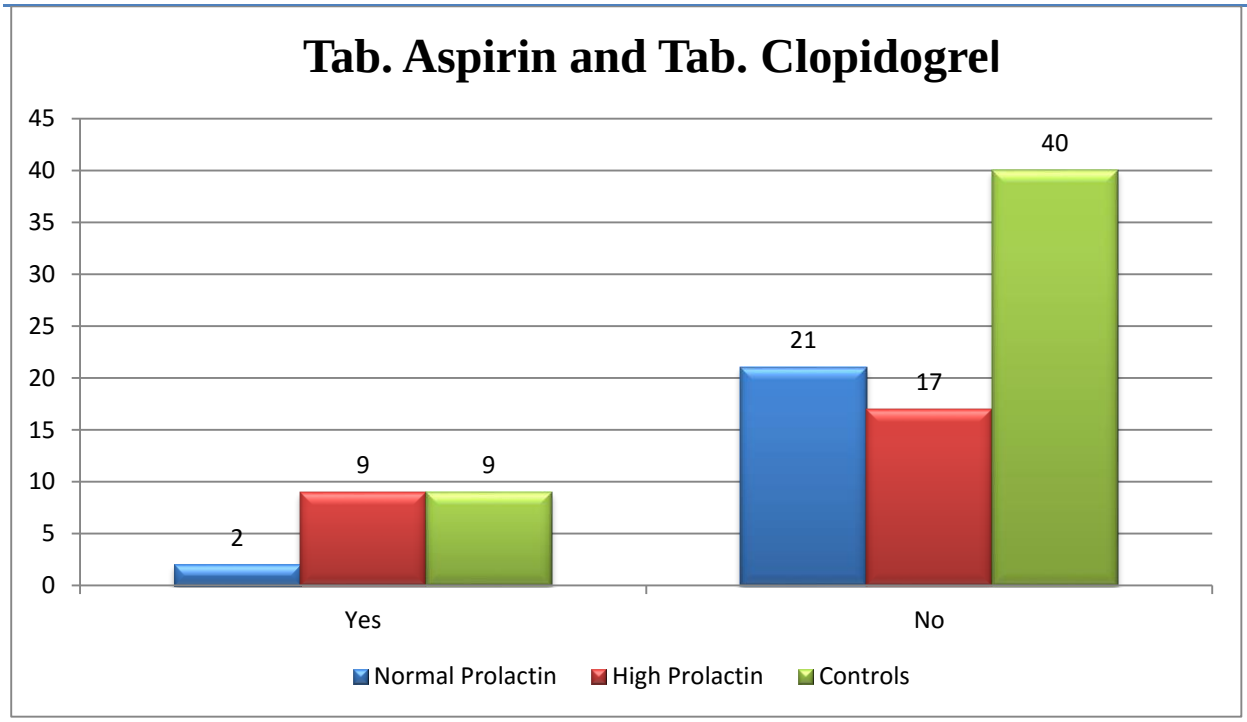
The incidence of asprin intake is significantly decreased in high prolactin group compared to normal prolactin l group by a percentage difference of 23.41(43% higher).

## CONCLUSION

In this study we can safely conclude that high and normal prolactin group had significantly increased incidence of asprin intakecompared to control group and high prolactin group had significantly increased incidence of asprin intakecompared to normal prolactin group among acute MI patients.

In conclusion, we observed that higher serum prolactin concentrations is associated acute MI patients with increased incidence of asprin intake

## ASPIRIN AND CLOPIDOGREL

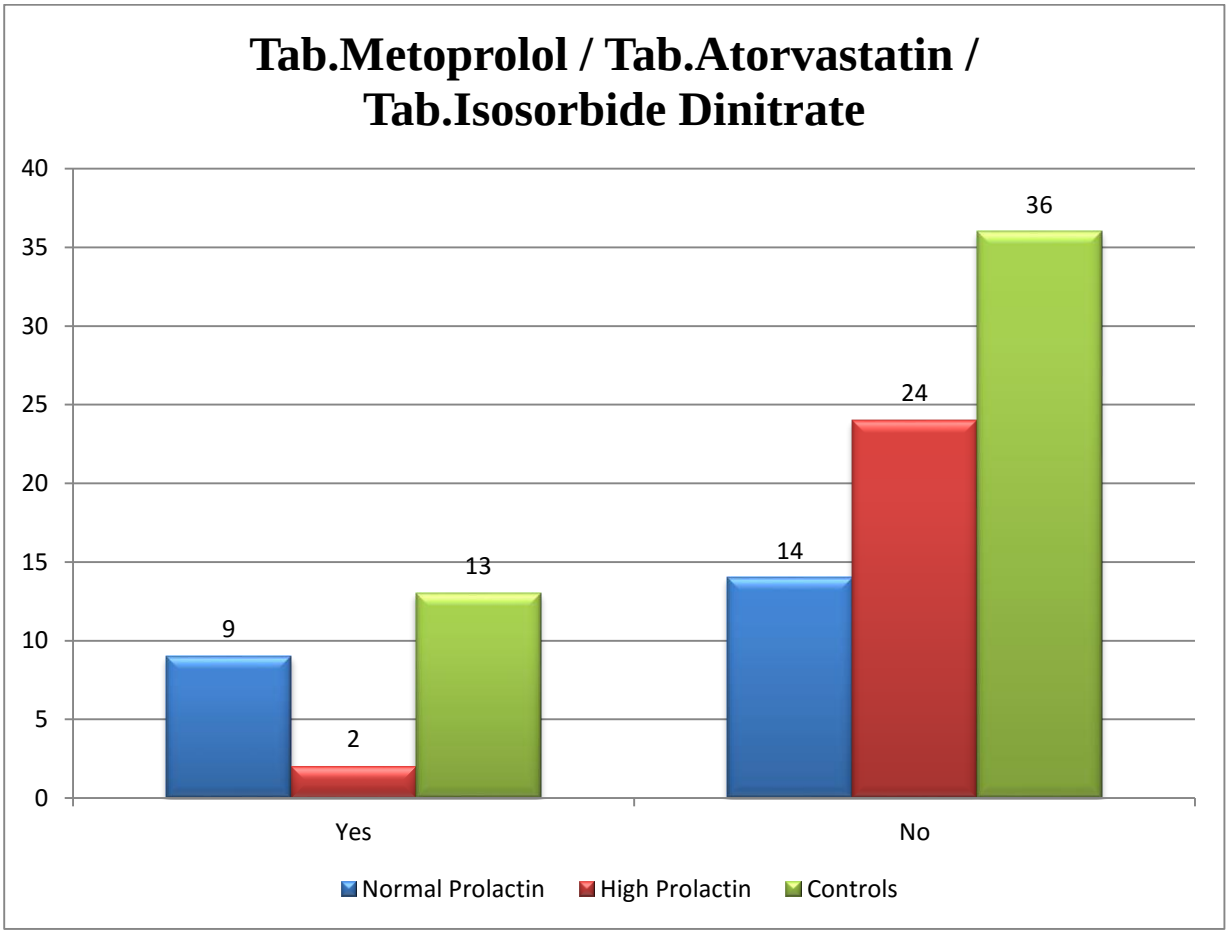



| Tab. Aspirin and Tab. Clopidogrel | Normal Prolactin | % | High Prolactin | % | Controls | % |
|---|---|---|---|---|---|---|
| **Yes** | 2 | 8.70 | 9 | 34.62 | 9 | 18.37 |
| **No** | 21 | 91.30 | 17 | 65.38 | 40 | 81.63 |
| **Total** | 23 | 100.00 | 26 | 100.00 | 49 | 100.00 |
| **P value Chi Squared Test** | | | | | 0.0711 | |

The study subjects on treatment with aspirin and clopidogrel are 8.70%, 32.46% and 18.37% in normal prolactin group, high prolactin group and control group patients respectively.

The association between the study groups and aspirin and clopidogrel intake status is considered to be not statistically significant since $p > 0.05$ as per chi squared test.

**METOPROLOL / ATORVASTATIN / ISOSORBIDE DINITRATE**



| Tab.Metoprolol / Tab.Atorvastatin / Tab.Isosorbide Dinitrate | Normal Prolactin | % | High Prolactin | % | Controls | % |
|---|---|---|---|---|---|---|
| **Yes** | 5 | 21.74 | 2 | 7.69 | 13 | 26.53 |
| **No** | 18 | 78.26 | 24 | 92.31 | 36 | 73.47 |
| **Total** | 23 | 100.00 | 26 | 100.00 | 49 | 100.00 |
| **P value** **Chi Squared Test** | | | | | 0.0342 | |

The study subjects on treatment with Metoprolol / Atorvastatin / Isosorbide Dinitrate are 21.74%, 7.69% and 20.41% in normal prolactin group, high prolactin group and control group patients respectively.

The association between the study groups and Metoprolol / Atorvastatin / Isosorbide Dinitrate intake status is considered to be statistically significant since $p < 0.05$ as per chi squared test.

## DISCUSSION

The incidence of Metoprolol / Atorvastatin / Isosorbide Dinitrate intake is significantly decreased in high prolactin group compared to control group by a percentage difference of 18.84(71% lower).

The incidence of Metoprolol / Atorvastatin / Isosorbide Dinitrate intake is significantly decreased in normal prolactin group compared to control group by a percentage difference of 4.79(18% lower).

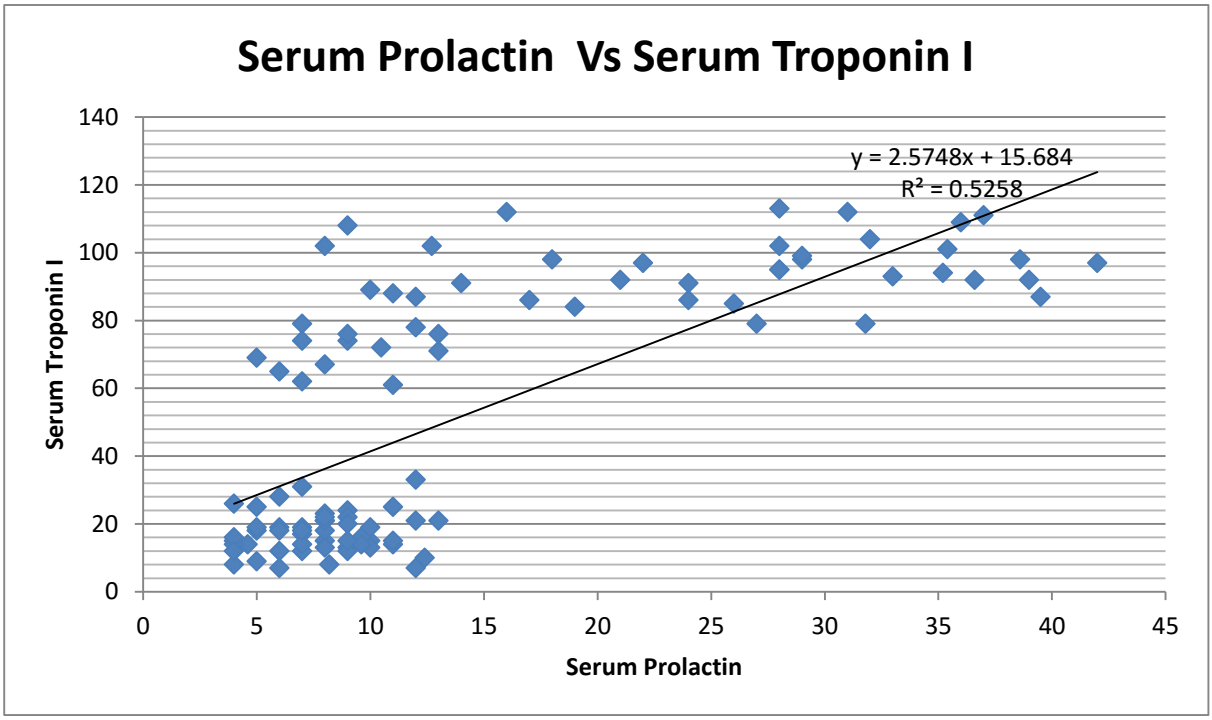
The incidence of Metoprolol / Atorvastatin / Isosorbide Dinitrate intake is significantly decreased in high prolactin group compared to normal prolactin l group by a percentage difference of 14.05(65% lower).

## CONCLUSION

In this study we can safely conclude that high and normal prolactin group had significantly decreased incidence of Metoprolol / Atorvastatin / Isosorbide Dinitrate intakecompared to control group and high prolactin group had significantly decreased incidence of Metoprolol / Atorvastatin / Isosorbide Dinitrate intakecompared to normal prolactin group among acute MI patients.

In conclusion, we observed that higher serum prolactin concentrations is associated acute MI patients with decreased incidence of Metoprolol / Atorvastatin / Isosorbide Dinitrate intake.

## CORRELATION - SERUM PROLACTIN VS SERUM TROPONIN I



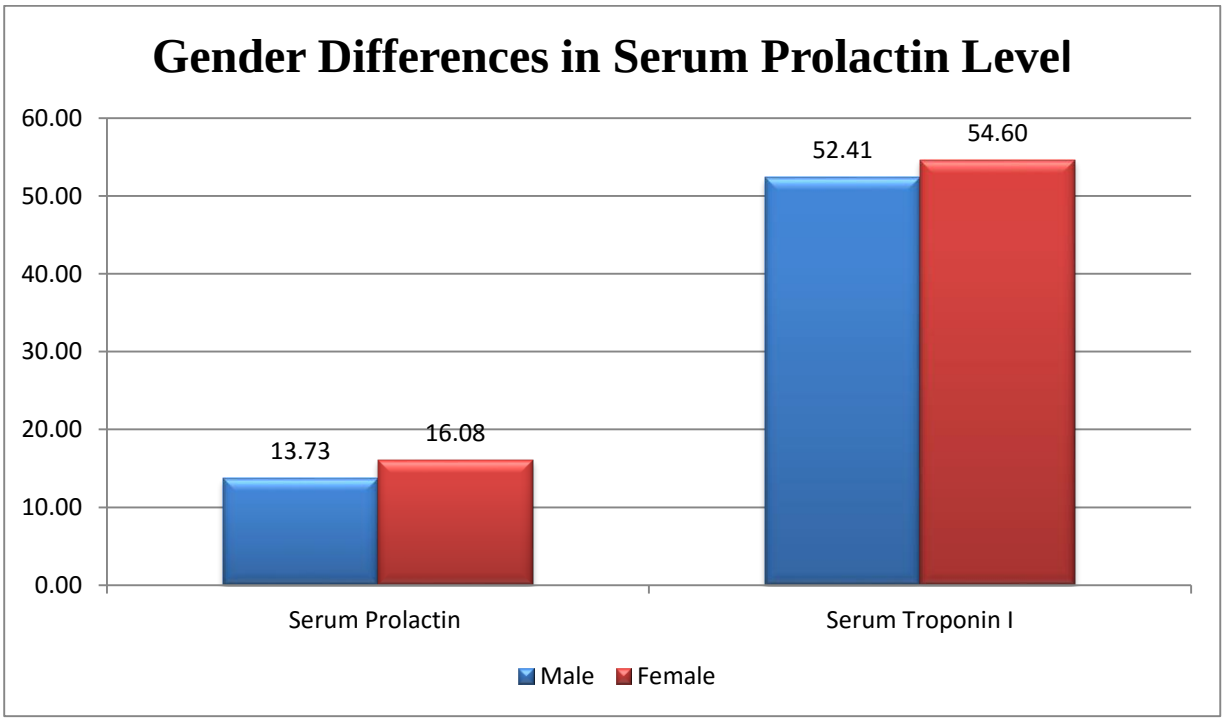

| *Correlation - Serum Prolactin Vs Serum Troponin I* | |
|---|---|
| **Pearson's R** | 0.73 |
| **R Square** | 0.53 |
| **P value**<br><br>**ANOVA** | <0.0001 |

The relationship in values between serum prolactin levels and serum troponin I levels is statistically significant as the p value is <0.0001 with a string and positive correlation as per pearson's coefficient of 0.73

The linear increase in serum prolactin levels in relation to increased serum troponin I levels is true 73% of times. But out of the 58% only 53% of the variation in mean increased serum troponin I

Serum prolactin levels can be predicted from the relationship serum troponin I levels. For every 1 unit increase in serum prolactin levels there is a corresponding 0.2 unit serum prolactin levels.

**GENDER DIFFERENCES IN SERUM PROLACTIN LEVEL**



| Gender Differences in Serum Prolactin Level | | Serum Prolactin | Serum Troponin I |
|---|---|---|---|
| **Male** | Mean | 13.73 | 52.41 |
| | SD | -10.72 | -37.27 |
| **Female** | Mean | 16.08 | 54.60 |
| | SD | 10.45 | 39.09 |
| **P value**<br>**Unpaired t Test** | | <0.0001 | >0.9999 |

The mean prolactin values in males was 13.73 and in females was 16.08. The association between the gender status and serum prolactin distribution is considered to be statistically significant since $p < 0.05$ as per unpaired t test.

The mean troponin I values in males was 52.41 and in females was 54.60. The association between the gender status and serum prolactin distribution is considered to be not statistically significant since $p > 0.05$ as per unpaired t test.

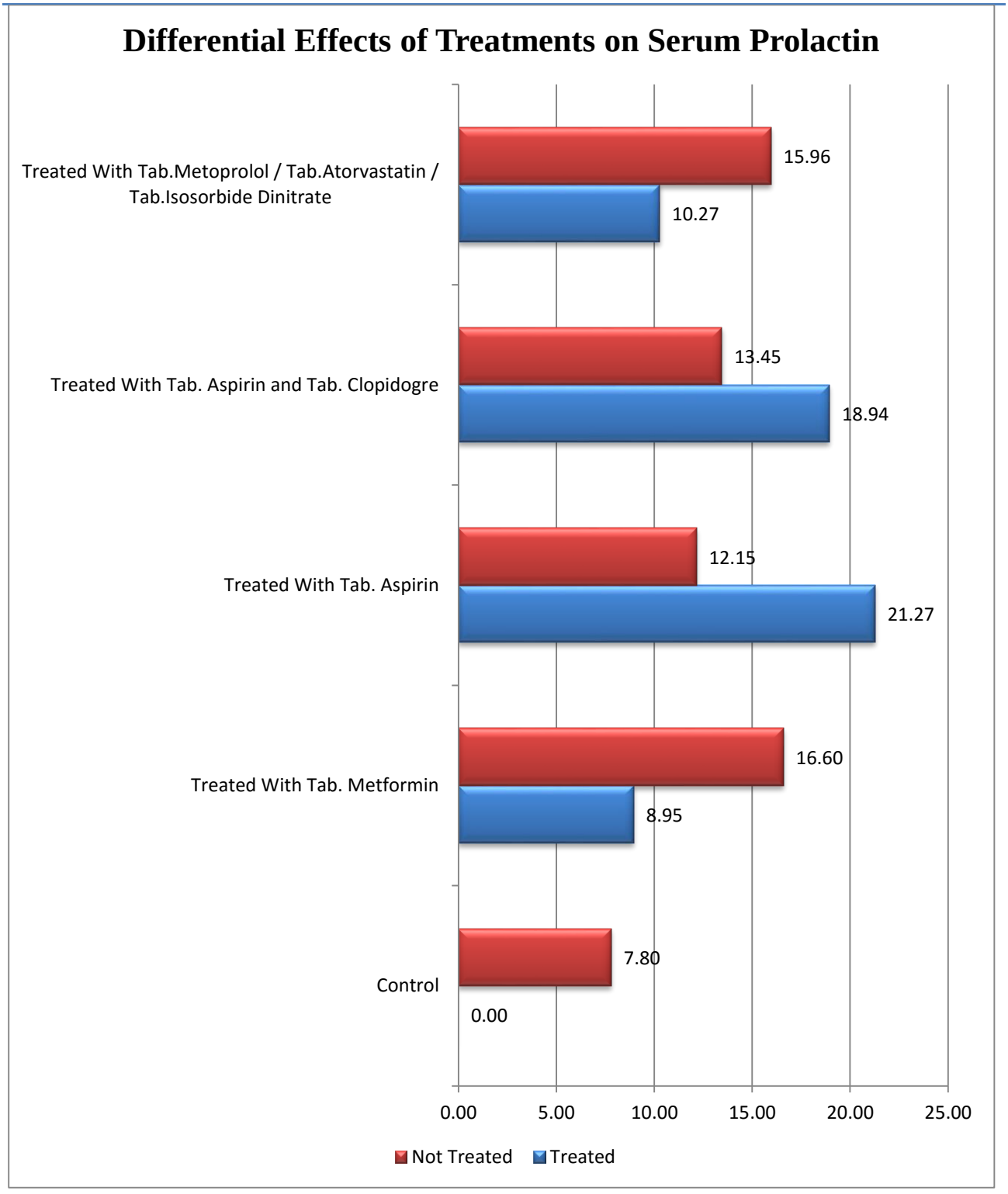
## DISCUSSION

The mean prolactin levels were significantly elevated in female group compared to male group by a mean difference of 2.36(84% higher).

## CONCLUSION

In this study we can safely conclude that high prolactin group are significantly associated with gender (more in women acute MI patients.)

## DIFFERENTIAL EFFECTS OF TREATMENTS ON SERUM PROLACTIN



| Differential Effects of Treatments on Serum Prolactin | | Control | Treated With Tab. Metformin | Treated With Tab. Aspirin | Treated With Tab. Aspirin and Tab. Clopidogre | Treated With Tab.Metoprolol / Tab.Atorvastatin / Tab.Isosorbide Dinitrate |
|---|---|---|---|---|---|---|
| **Treated** | Mean | 0.00 | 8.95 | 21.27 | 18.94 | 10.27 |
| | SD | 0.00 | 4.19 | 10.99 | 12.95 | 7.82 |
| **Not Treated** | Mean | 7.80 | 16.60 | 12.15 | 13.45 | 15.96 |
| | SD | 2.54 | 11.51 | 9.46 | 9.73 | 11.08 |
| **P value Unpaired t Test** | | | 0.0014 | 0.0001 | 0.0385 | 0.0218 |

The mean prolactin values in treated subjects was 8.95, 21.27, 18.59 and 10.27 in metformin, aspirin, aspirin and clopidogre and metoprolol / tab.atorvastatin / tab.isosorbide dinitrate groups. Similarly mean prolactin values in not treated subjects was 7.80, 16.00, 12.15 and 15.56 in metformin, aspirin, aspirin and clopidogre and metoprolol / tab.atorvastatin / tab.isosorbide dinitrate groups. The association between the treatment groups and serum prolactin distribution is considered to be statistically significant since $p < 0.05$ as per unpaired t test.

## DISCUSSION

The mean prolactin levels were significantly decreased in metformin treatment group compared to no treatment group by a mean difference of 7.65(46% lower).

The mean prolactin levels were significantly elevated in asprin treatment group compared to no treatment group by a mean difference of 9.12(46% lower).

The mean prolactin levels were significantly elevated in metformin treatment group compared to male group by a mean difference of 7.65(43% higher).

The mean prolactin levels were significantly elevated in asprin treatment group compared to male group by a mean difference of 5.49(29% higher).

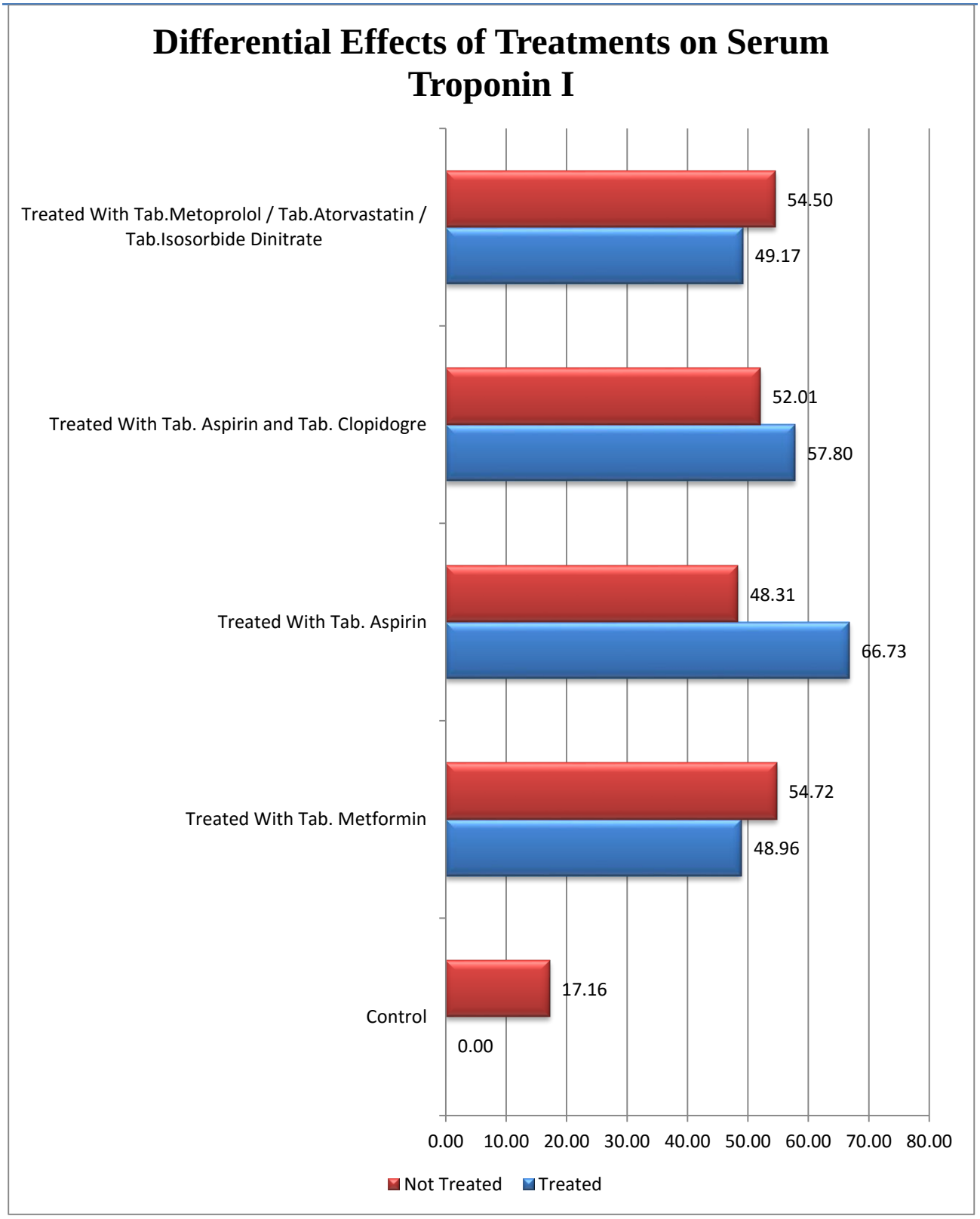
The mean prolactin levels were significantly elevated in metoprolol / tab.atorvastatin / tab.isosorbide dinitrate treatment group compared to male group by a mean difference of 5.69(36% higher). .

## CONCLUSION

In this study we can safely conclude that high prolactin group are significantly associated with increased intake of aspirin and metoprolol / tab.atorvastatin / tab.isosorbide dinitrte treatment group

In this study we can also safely conclude that high prolactin group are significantly associated with decreased intake of aspirin and metoprolol / tab.atorvastatin / tab.isosorbide dinitrate treatment group.

## Differential Effects of Treatments on Serum Troponin I



| Differential Effects of Treatments on Serum Troponin I | | Control | Treated With Tab. Metformin | Treated With Tab. Aspirin | Treated With Tab. Aspirin and Tab. Clopidogre | Treated With Tab.Metoprolol / Tab.Atorvastatin / Tab.Isosorbide Dinitrate |
|---|---|---|---|---|---|---|
| **Treated** | Mean | | 48.96 | 66.73 | 57.80 | 49.17 |
| | SD | | 35.71 | 40.44 | 37.96 | 36.13 |
| **Not Treated** | Mean | 17.16 | 54.72 | 48.31 | 52.01 | 54.50 |
| | SD | 5.95 | 38.57 | 35.76 | 37.84 | 38.39 |
| **P value Unpaired t Test** | | | 0.5075 | 0.0321 | 0.5434 | 0.5502 |

The mean troponin I values in treated subjects was 48.96, 66.54, 57.89 and 49.17 in metformin, aspirin, aspirin and clopidogre and metoprolol / tab.atorvastatin / tab.isosorbide dinitrate groups. Similarly mean troponin I values in not treated subjects was 54.72, 48.31, 37.83 and 54.50 in metformin, aspirin, aspirin and clopidogre and metoprolol / tab.atorvastatin / tab.isosorbide dinitrate groups. The association between the treatment groups and serum troponin Idistribution is considered to be statistically not significant since $p > 0.05$ as per unpaired t test.

## OVERALL CONCLUSION

- The association between the study groups and age distribution is considered to be not statistically significant.
- Serum Prolactin level higher among acute myocardial infarction patients.
- Prolactin is associated with a comprehensive panel of incident cardiovascular disease risk factors. Measurement of circulating prolactin levels on a routine basis among high risk individuals is more likely to provide substantial insight into cardiometabolic risk.
- Elevation of Serum Prolactin level is associated with a chronic inflammatory state
- T.Metformin treated group patients showed significantly reduced serum prolactin level in acute MI patient compared to control group.
- T.aspirin treated group patients showed significantly high Serum Prolactin level in Acute MI patient compared to control group,this is mainly due to aspirin increases prostaglandin generation in hypothalamic region which stimulate high serum prolactin.
- Serum Prolactin was not affected by T.Clopidogrel.
- Other drugs like T.Metoprolol, T.Atorvastatin, T.ISDN shows reduced Serum Prolactin level.

## SUMMARY

This study “EVALUATION OF SERUM PROLACTIN LEVELS INACUTE MYOCARDIAL INFARCTION: THE ROLE OFPHARMACOTHERAPY” was carried out in government Stanley medical college and hospital , Chennai from March 2017 to October 2017

- 50 Acute MI patients were selected and their serum prolactin levels and serum troponin levels were studied correlated with 50 normal healthy individuals.the role of pharmacotherapy in serum prolactin level was assessed.
- In acute MI patient showed significant elevation of serum prolactin level.
- According to various pharmacotherapy drugs like Metformin decreases the serum prolactin,Aspirin increases the serum prolactin and other drugs like Clopidogrel no effect.
- So serum prolactin level increased in acute MI reflects underlying cardiovascular complications.

**LIMITATIONS**

1. Low sample size. So little space for robust statistical analysis.
2. Study population restricted to patients referred for acute MI to our department, so a selection may have influenced the results.
3. Poor financial support

4. Inability to use research design like cohort study due to paucity of time and resources

**AREAS FOR FUTURE RESEARCH:**

**1.** Prospective studies are needed to further study the association between Serum Prolactin , Atherosclerosis and Acute Myocardial Infarction.

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## PROFORMA

NAME: AGE: SEX:

ADDRESS: CONTACT NO:

**OCCUPATION** :

**COMPLAINTS:**

**PAST H/O**

CARDIAC ILLNESS 1. Yes 2. No If yes specify_____

DIABETIC ILLNESS 1.Yes 2. No If yes specify

**PERSONAL H/O:**

**H/O SMOKING:**

**FAMILY HISTORY**:

**RELEVANT CLINICAL EXAMINATION**

BP: PR: RR: BMI:

CVS: RS:

PA:

CNS:

**INVESTIGATIONS:**

COMPLETE BLOOD COUNT:

ECG:

FBS:

SERUM TROPONIN I:

SERUM PROLACTIN:

ECHO:

RENAL FUNCTION TEST:

SERUM ELECTROLYTES:

LIVER FUNCTION TEST:

FASTING LIPID PROFILE:

**COURSE OF PRESENT ILLNESS:**

**COMPLICATIONS :**

**COMMENT:**

**GOVT. STANLEY MEDICAL COLLEGE, CHENNAI – 600001**

**INFORMED CONSENT**

**"EVALUATION OF SERUM PROLACTIN LEVEL IN ACUTE MYOCARDIAL INFARCTION :ROLE OF PHARMACOTHERAPY "**

AT GOVERNMENT STANLEY MEDICAL COLLEGE AND HOSPITAL, CHENNAI**.**

Place of study: Govt. Stanley medical college, Chennai

I ……. have been informed about the details of the study in my own language.

I have completely understood the details of the study.

I am aware of the possible risks and benefits, while taking part in the study.

I agree to collect samples of blood/saliva/urine/tissue if study needs.

I understand that I can withdraw from the study at any point of time and even then, I can receive the medical treatment as usual.

I understand that I will not get any money for taking part in the study.

I will not object if the results of this study are getting published in any medical journal, provided my personal identity is not revealed.

I know what I am supposed to do by taking part in this study and I assure that I would extend my full cooperation for this study.

| Volunteer: | Witness: |
|---|---|
| Name and address | Name and address |
| Signature/thumb impression: | Signature/thumb impression |
| Date: | Date: |

Investigator Signature and date

**GOVT. STANLEY MEDICAL COLLEGE, CHENNAI – 600001**

**INFORMED CONSENT**

**"EVALUATION OF SERUM PROLACTIN LEVELS IN ACUTE MYOCARDIAL INFARCTION: THE ROLE OF PHARMACOTHERAPY"**

நான் இந்த ஆராய்ச்சியில் விவரங்களை முற்றிலும் புரிந்து கொண்டேன். ஆய்வில் பங்கு எடுத்து போது, சாத்தியமான அபாயங்கள் மற்றும் பயன்களை பற்றி நான் அறிந்துள்ளேன்.

நான் எந்தவொரு வேளையிலும் ஆய்வில் இருந்து திரும்ப முடியும், அதன்பின்னர், நான்வழக்கம்போல் மருத்துவ சிகிச்சை பெறமுடியும் என்று புரிந்து கொள்கிறேன்.

நான் ஆய்வில் பங்குஎடுத்து பணம் எதையும் பெற முடியாது என்று அறிந்துள்ளேன். இந்த ஆய்வின் முடிவுகள் எந்தமெடிக்கல் ஜர்னலில் வெளியிடப்பட இருந்தால் நான் எதிர்க்கவில்லை, என்தனிப்பட்ட அடையாளத்தை வெளிப்படுத்தப்பட்டு இருக்ககூடாது.

நான் இந்த ஆய்வில் பங்கெடுப்பதன் மூலம் நான் என்ன செய்ய போகிறேன் என்று தெரியும். நான் இந்த ஆய்வில் என் முழு ஒத்துழைப்பையும் கொடுப்பேன் என்று உறுதியளிக்கிறேன்.

**தன்னார்வளர்** **சாட்சி**

பெயர்மற்றும்முகவரி பெயர்மற்றும்முகவரி

கையொப்பம் /விரல்ரேகை: கையொப்பம் / விரல்ரேகை:

ஆராய்ச்சியாளராக
கையொப்பம்மற்றும்தேத

MASTER CHART

| AGE | SEX | BMI | FBS | BP | Sr. Prolactin | Sr.troponin I | Triglyceride | Total cholestrol | T.Metformin | T.Aspirin | T.Aspirin and T. Clopidogrel | T.Metop,T.Atorv,T.ISDN |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 56 | M | 31 | 201 | 140/90 | 10.48 | 72 | 142 | 184 | YES | NO | NO | NO |
| 63 | M | 29 | 103 | 120/80 | 12.7 | 102 | 153 | 187 | NO | YES | NO | YES |
| 50 | M | 27 | 184 | 160/100 | 31 | 112 | 184 | 207 | NO | YES | NO | NO |
| 52 | F | 25.3 | 121 | 140/90 | 12 | 78 | 127 | 162 | NO | NO | NO | YES |
| 48 | M | 28 | 197 | 110/70 | 8 | 67 | 134 | 157 | YES | NO | NO | NO |
| 57 | F | 28.4 | 104 | 150/90 | 29 | 98 | 188 | 204 | NO | YES | NO | NO |
| 66 | M | 31 | 169 | 130/90 | 11 | 61 | 124 | 147 | NO | NO | YES | NO |
| 67 | F | 27.8 | 94 | 110/70 | 13 | 76 | 178 | 212 | YES | NO | NO | NO |
| 53 | M | 32 | 108 | 140/90 | 36 | 109 | 183 | 247 | NO | NO | YES | NO |
| 62 | M | 27 | 106s | 180/100 | 39 | 92 | 172 | 203 | NO | NO | YES | NO |
| 52 | F | 28.5 | 96 | 150/90 | 19 | 84 | 168 | 221 | NO | NO | NO | YES |
| 72 | M | 29 | 182 | 160/100 | 42 | 97 | 132 | 167 | NO | YES | NO | NO |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 61 | F | 27.8 | 112 | 140/90 | 10 | 89 | 143 | 154 | NO | NO | NO | YES |
| 65 | M | 27.5 | 101 | 150/90 | 33 | 93 | 155 | 172 | NO | YES | NO | NO |
| 49 | M | 28.5 | 205 | 160/100 | 7 | 79 | 128 | 178 | YES | NO | NO | NO |
| 64 | F | 26.2 | 98 | 130/80 | 11 | 88 | 119 | 152 | YES | NO | NO | NO |
| 59 | M | 29.5 | 104 | 110/70 | 6 | 65 | 123 | 148 | NO | NO | YES | NO |
| 51 | F | 28.6 | 106 | 130/80 | 9 | 74 | 152 | 203 | YES | NO | NO | YES |
| 66 | M | 27 | 100 | 110/70 | 7 | 62 | 119 | 143 | NO | NO | NO | YES |
| 61 | M | 31 | 173 | 140/90 | 32 | 104 | 182 | 219 | NO | YES | NO | NO |
| 52 | M | 28.5 | 91 | 150/90 | 12 | 87 | 124 | 128 | NO | NO | NO | NO |
| 57 | M | 32.5 | 102 | 130/90 | 8 | 102 | 132 | 122 | YES | NO | NO | YES |
| 63 | F | 29 | 185 | 160/90 | 13 | 71 | 102 | 159 | YES | NO | NO | NO |
| 71 | M | 27.4 | 101 | 140/90 | 21 | 92 | 172 | 234 | YES | NO | NO | NO |
| 59 | M | 26.4 | 93 | 120/70 | 9 | 76 | 111 | 196 | YES | NO | NO | NO |
| 62 | M | 26.6 | 86 | 110/70 | 5 | 69 | 131 | 149 | NO | NO | NO | YES |
| 58 | F | 29 | 154 | 150/90 | 35.4 | 101 | 187 | 253 | NO | NO | YES | NO |
| 61 | F | 28 | 87 | 140/90 | 18 | 98 | 122 | 273 | NO | YES | NO | NO |
| 52 | M | 27.6 | 84 | 130/80 | 9 | 108 | 138 | 162 | NO | NO | NO | YES |
| 72 | M | 28.5 | 102 | 150/100 | 29 | 99 | 176 | 217 | NO | YES | NO | NO |
| 64 | F | 26.4 | 109 | 160/100 | 16 | 112 | 187 | 209 | YES | NO | NO | NO |
| 54 | M | 31 | 97 | 140/90 | 28 | 95 | 162 | 212 | NO | YES | NO | NO |
| 69 | F | 27.6 | 142 | 170/100 | 37 | 111 | 183 | 264 | NO | NO | YES | NO |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 68 | F | 32.6 | 79 | 140/80 | 14 | 91 | 123 | 186 | YES | NO | NO | NO |
| 52 | F | 31 | 94 | 160/90 | 39.5 | 87 | 168 | 205 | NO | YES | NO | NO |
| 65 | M | 29 | 126 | 170/100 | 27 | 79 | 175 | 254 | NO | NO | NO | YES |
| 73 | M | 28.6 | 178 | 160/100 | 28 | 113 | 183 | 237 | NO | YES | NO | NO |
| 55 | F | 28.5 | 86 | 140/90 | 36.6 | 92 | 156 | 251 | NO | NO | YES | NO |
| 56 | M | 27.4 | 99 | 130/80 | 7 | 74 | 124 | 173 | YES | NO | NO | NO |
| 51 | M | 25.5 | 110 | 140/90 | 17 | 86 | 141 | 186 | NO | NO | YES | NO |
| 65 | M | 27 | 113 | 150/90 | 22 | 97 | 164 | 208 | NO | YES | NO | NO |
| 63 | F | 30 | 169 | 170/100 | 24 | 86 | 156 | 182 | NO | YES | NO | NO |
| 71 | M | 28 | 121 | 130/90 | 31.8 | 79 | 142 | 175 | NO | NO | YES | NO |
| 64 | M | 29 | 119 | 150/90 | 28 | 95 | 197 | 253 | NO | YES | NO | NO |
| 51 | M | 28 | 91 | 110/70 | 35.2 | 94 | 168 | 203 | NO | YES | NO | NO |
| 62 | M | 27.5 | 97 | 140/80 | 26 | 85 | 198 | 209 | NO | NO | YES | NO |
| 67 | F | 26 | 94 | 120/70 | 38.6 | 98 | 185 | 212 | NO | NO | NO | YES |
| 65 | F | 29.8 | 85 | 140/80 | 28 | 102 | 179 | 217 | NO | NO | YES | NO |
| 55 | M | 26 | 116 | 150/90 | 24 | 91 | 201 | 276 | NO | YES | NO | NO |

## ABBREVIATIONS

SMC-Smooth Muscle Cell

ECM-Extra Cellular Matrix

ICAM-Intracellular Adhesion

TNF-Tumour Necrosis Factor

MI-Myocardial Infarction

IL-Interleukin

PAPP-A-Pregnancy Associated Plasma Protein

EDRF-Endothelin Releasing Factor

PGI-Prostaglandin I

TXA2-Thromboxin A2

AMI-Acute Myocardial Infarction

ISDN-Isosorbide Dinitrate

DVT-Deep Vein Thrombosis

MMP-Matrix Metalloproteinase

IHD-Ishaemic Heart Disease

ACE-Angiotensin Converting Enzyme