LIFE STYLE RISK FACTORS OF MYOCARDIAL INFARCTION AND THE DRUGS THAT ARE COMMONLY USED TO PREVENT MYOCARDIAL INFARCTION

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A Thesis paper submitted to the Department of Pharmacy, East West University in conformity with the requirements for the Degree of Bachelor of Pharmacy.

Place of study: National Institute of Cardiovascular Disease (NICVD).

This thesis paper is dedicated to my parents

CERTIFICATE

This is to certify that, the thesis 'Life Style Risk Factors of Myocardial Infarction and the drugs that are commonly used to prevent MI' submitted to the Department of Pharmacy, East West University Mohakhali, Dhaka for the partial fulfillment of the requirements for the degree of Bachelor of Pharmacy (B.Pharm) was carried out by Farhana Ali Shorna (ID: 2005-2-70-102) under our guidance and supervision and that no part of the thesis has been submitted for any other degree. We further certify that all the sources of information and laboratory facilities availed of this connection is duly acknowledged.

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Farhana Ali Shorna

ABSTRACT

The term "myocardial infarction" focuses on the myocardium (the heart muscle) and the changes that occur in it due to the sudden deprivation of circulating blood. The main change is necrosis (death) of myocardial tissue.

Myocardial infarction is the commonest cause of heart disease and the most important single cause of death in world wide. Acute myocardial infarction is the leading cause of morbidity and mortality in developed countries and also emerging as a major health problem in developing countries like Bangladesh.

The goals of pharmacotherapy for myocardial infarction are to reduce morbidity and to prevent complications after having MI.

To find out the relationship between life style risk factors of myocardial infarction and the drugs that are commonly used for myocardial infarction, a study was performed in the National Institute of Cardiovascular Disease and Hospital (NICVD). The data were collected from patients of both sexes having MI. Duration of the study was from February 2008 to June 2009. Patient's personal and medical history such as blood pressure and diagnosis profile were also collected. All the patients were treated with the appropriate medicines. The patients were interviewed by asking question in Bengali, using a thoroughly pre tested questionnaires about the modifiable and non-modifiable risk factors of MI.

The results of the study showed that patients of age ranged from 56 to 60 years were more prevalent to MI. Among 60 MI patients, 88% were male and 12% were female. The results showed that 92% patients were married, 37% were not educated, and 13% were unemployed. About 25% patients were service holder, 18% were businessman and 12% were housewives. There were MI patients who suffered from other diseases such as Diabetes mellitus (DM) (12%); hypertension (11%); both asthma and Parkinson (8%); DM and hypertension (5%); both asthma & hypertension (5%); both DM & hypertension (8%).

Majority of the patients received Atorvastatin (71%), Clopidogrel (70%), Omeprazole (58%), Nitroglycerin spray (51%), Oxygen inhaler (38%), Diazepam (41%), Isosorbide mononitrate (25%), Beta-adrenergic blocking agent (25%), H2-blocking agent (13%), Trimetazidine Hydrochloride (5%), Losardil (1%), Atorpin injection (1%),

Cephalosporin (5%), Cephradin (3%)., Cardinex injection (10%), Captopril (15%), Acetaminophen (13%) for the control and prevention of MI.

According to the result, majority of the MI patients used atorvastatin and Clopidogrel for the prevention of MI. Atorvastatin was used for lowering blood cholesterol. It also stabilizes plaque and prevents strokes through anti-inflammatory and other mechanisms. Clopidogrel is an oral antiplatelet agent (thienopyridine class) to inhibit blood clots in coronary artery disease, peripheral vascular disease, and cerebrovascular disease.

The findings of the study suggest that the treatment with proper medicaments may be beneficial for the prevention of myocardial infarction in patients with other risk factors. The life style risk factors may have some important role to prevent MI.

CHAPTER 1

INTRODUCTION

1.1. Communicable Disease:

A communicable disease is carried by microorganisms and transmitted through people, animals, surfaces, foods, or air. Communicable diseases rely on fluid exchange, contaminated substances, or close contact to travel from an infected carrier to a healthy individual. Examples of communicable diseases include herpes, malaria, mumps, HIV/AIDS, influenza, chicken pox, ringworm, and whooping cough. Cancer, on the other hand, is not a communicable disease.

Parasites, bacteria, and viruses all qualify as pathogens, nicknamed "germs," and can cause a communicable disease. Their method of transmission, period of dormancy, ease of contagiousness, and relative danger can differ drastically from one disease to the next. A human-to-human communicable disease could be passed through blood, mucus, uterine fluid, breast milk, semen, saliva, or breath. Often, these are prevented by safer sex, frequent hand washing, proper disposal of waste, etc **(Mithra, S. 2003).**

"Communicable diseases" are those conditions that can be spread to others through air, touch or contact with contaminated body fluids. Some of the most common communicable diseases include Chlamydia, hepatitis A, B and C, giardia, salmonella, pertussis and campylobacter. It's not only important to be treated for infection, it is necessary for the health department to track communicable diseases in order to prevent disease outbreaks **(Leslie, A. 2008).**

Over 90 per cent of the world's disease burden occurs in developing countries and most is due to communicable diseases. While chronic diseases, such as heart disease and diabetes, are on the rise, communicable disease remains the major challenge. HIV and AIDS, malaria, and tuberculosis are important communicable diseases targeted by global control programmers. **(Pirozzi, G.2009).**

1.2. Non-communicable disease

A non-communicable disease or NCD is a disease which is not infectious. Such diseases may result from genetic or lifestyle factors. A non-communicable disease is an illness

that is caused by something other than a pathogen. It might result from hereditary factors, improper diet, smoking, or other factors. Those resulting from lifestyle factors are sometimes called affluence. Examples include hypertension, diabetes, cardiovascular disease, cancer, and mental health problems, asthma, atherosclerosis, allergy etc. The non-communicable diseases are spread by: heredity, surroundings and behavior. Non-communicable diseases such as heart attacks, strokes, cancers, diabetes, respiratory diseases and common injuries account for the vast majority of all global deaths **(World Health Organization-2009).**

Non-communicable diseases are usually thought of as chronic conditions that do not result from an acute infectious process. These conditions cause death, dysfunction, or impairment in the quality of life, and they usually develop over relatively long periods—at first without causing symptoms; but after disease manifestations develop, there may be a protracted period of impaired health. Generally, these conditions or diseases result from prolonged exposure to causative agents, many associated with personal behaviors and environmental factors. Non-communicable diseases also include injuries, which have an acute onset, but may be followed by prolonged convalescence and impaired function, as well as chronic mental diseases. Non-communicable diseases are the leading cause of functionary impairment and death worldwide **(Murray, C. J. L. & Lopez, A. D. 2000).**

Table 1

Causes of Death Worldwide: Estimates for 1999 (in thousands)	
Total Deaths	**55,965**
Communicable Diseases	17,380 (31%)
Non-Communicable Diseases	33,484 (59.8%)
Injuries	5,101 (9.1%)
Cardiovascular Diseases	16,970 (30.3%)
Cancers	7,065 (12.6%)
Respiratory Diseases	3,575 (6.4%)
Digestive Diseases	2,409 (3.7%)
Neuropsychiatric Disorders	911 (1.6%)
Genitourinary Diseases	900 (1.6%)

(Geneva: World Health Organization Report, 2000).

Cardiovascular disease is non-communicable disease and the general term used to describe several different conditions, all of which are potentially fatal, but are also treatable and/or preventable.

1.2.1. Cardiovascular diseases

Cardiovascular disease is a general term encompassing meanings for various ailments of the heart and the blood vessels surrounding the heart. The terms cardiovascular disease and heart disease are used interchangeably by many people and both are acceptable forms. It can be quite serious and often require serious medical attention from trained specialist. Most types of cardiovascular disease deal with the hardening and clotting of

arteries. This can lead to heart attacks and strokes in their most serious form. Both conditions are capable of resulting in death. While improvements have been made in cardiovascular disease treatment over the last 50 years in particular, the disease is still considered very dangerous **(Ken, B. 2003-2009).**

Cardiovascular disease or cardiovascular diseases refers to the class of diseases that involve the heart or blood vessels (arteries and veins) **(Maton, A.1993).**

Cardiovascular disease is a general category used for grouping diseases that involve the heart and blood vessels. Included under this designation are such diverse medical conditions as heart attack (myocardial infarction), stroke, coronary heart disease, cerebrovascular disease, atherosclerosis, hypertension, arrhythmia, and rheumatic heart disease.Cardiovascular disease is a major cause of death. In the United States, about 40 percent of all deaths in 1997, or about one million people, were attributed to cardiovascular disease (Friedewald 2002). It is one of two major causes of deaths, the other being cancer. Cardiovascular disease also has major economic costs, with an estimated direct health expenditure of $186 billion in 2000 in the United States, and an indirect cost of $190 billion.

While some risk factors cannot be modified (genetics, age, gender), there are a number of risk factors that can be addressed through lifestyle changes or medically. These controllable risk factors include cigarette smoking, high blood pressure, obesity, diabetes, physical inactivity, and high blood cholesterol level. Taking personal responsibility to address these risk factors also can be beneficial for good health in general **(Mcgill, H. 2000)**

a. Congenital Heart disease

A congenital heart defect is a problem or abnormality with the structure of any part of the heart that is present at birth. Congenital means present at birth. Heart defects originate in the early weeks of pregnancy when the heart is forming. Congenital heart defects are the most common type of major birth defect. A baby's heart begins to develop shortly after conception. During development, structural defects can occur. These defects can involve the walls of the heart, the valves of the heart and the arteries and veins near the heart.

Congenital heart defects can disrupt the normal flow of blood through the heart. The blood flow can

- Slow down
- Go in the wrong direction or to the wrong place
- Be blocked completely

Treatment for the defect can include medicines, surgery and other medical procedures and heart transplants. The treatment depends on the type and severity of the defect and a child's age, size and general health. Today, many children born with complex heart defects grow to adulthood and lead productive lives **(Rockville, P. B. 2009).**

Congenital heart disease (CHD) can describe a number of different problems affecting the heart. According to the American Heart Association, about 35,000 babies are born each year with some type of congenital heart defect. Congenital heart disease is responsible for more deaths in the first year of life than any other birth defects. Many of these defects need to be followed carefully. Some heal over time, others will require treatment.

Some congenital heart diseases can be treated with medication alone, while others require one or more surgeries. The risk of death from congenital heart disease surgery has dropped from about 30% in the 1970s to less than 5% in most cases today.

Congenital heart disease is often divided into two types: cyanotic (blue discoloration caused by a relative lack of oxygen) and non-cyanotic. The following lists cover the most common of the congenital heart diseases:

Cyanotic:

- Tetralogy of Fallot
- Transposition of the great vessels
- Tricuspid atresia
- Total anomalous pulmonary venous return

Non-cyanotic:

- Ventricular septal defect (VSD)
- Atrial septal defect (ASD)
- Patent ductus arteriosus (PDA)(**Zipes DP, Libby P, Bonow RO, Braunwald E. 2007)**

b. Acquired heart disease

Acquired heart disease is much more common in adults than in children. But the two most common acquired conditions among children are rheumatic heart disease and Kawasaki disease. Rheumatic heart disease is the result of rheumatic fever caused by streptococcal bacteria. Most likely to strike children between 5 and 15 years old, rheumatic fever can scar heart valves to the point where they may not function properly. Kawasaki disease primarily occurs in children under the age of five causing inflammation of the blood vessels that can result in damage to the coronary arteries and a widening of the vessel called an aneurysm. Other acquired heart disorders may occur in children treated for congenital heart defects. Like adults successfully treated for heart disease, these children have an increased risk of infective endocarditis and cardiomyopathy, damage to the valves and structure of the heart caused by infection or inflammation. Young children and teens also develop arrhythmias -- heartbeats that are slow, fast or irregular **(Pediatric Heart Center - 2007).**

Kawasaki disease (KD) is an acute self-limiting systemic vasculitis of unknown aetiology. It is the most common cause of acquired heart disease in young children. The intense inflammatory process has a predilection for the coronary arteries, resulting in the development of aneurysmal lesions, arterial thrombotic occlusion or, potentially, sudden death. There is no specific diagnostic test; however, treatment with immunoglobulin and aspirin effectively reduces cardiac complications from 25% to 4.7% in the UK. Several new pharmacological treatments may have important roles to play in managing KD in children and adolescents. Kawasaki Disease (KD) is an acute multi system vasculitis affecting mainly young children **(Kawasaki T. 1967).**

1.2.1.1. Types of Cardiovascular Disease

- Coronary Artery Disease
- Congestive Heart Failure
- Angina
- Cardiomyopathy
- Cardiac arrhythmias
- Atherosclerosis
- Myocardial infarction (Heart Attack)
- Peripheral vascular disease
- Hypertension
- Heart failure
- Valvular heart disease
- Hypertensive heart disease

Cardiovascular disease is a general term that describes many different diseases:

Congestive heart failure

Results when the heart muscle becomes weakened and can no longer pump blood efficiently. Common symptoms include shortness of breath, exercise intolerance, and edema (swelling of the legs). Congestive heart failure can result from damage induced by heart attack or cardiomyopathy (disease of the heart muscle).

Angina

Temporary discomfort or pain in the chest when the heart does not receive enough blood, due to narrowing in the blood vessel to the coronary artery. Angina usually occurs when the heart is working harder than usual, for example, during exercise or when a person is under stress. It can cause temporary discomfort, in the form of a dull ache, a feeling of pressure, squeezing or heaviness in the chest. This pain or discomfort may move down the arms, up the neck and jaw, or into the back.

Cardiac arrhythmias (abnormal heart rhythms)

Can be chronic and relatively harmless, but they can also be more serious, preventing the heart from pumping effectively. In the latter case, arrhythmias can contribute to congestive heart failure or cause cardiac sudden death.

Atherosclerosis

A condition that results from the gradual build-up of fatty substances, including cholesterol, on the walls of the arteries. This build-up, called plaque, reduces the blood flow to the heart, brain and other tissues, and can progress to cause a heart attack or stroke. This process is also referred to as hardening of the arteries.

Cardiomyopathy

Literally means "heart muscle disease" (Myo= muscle, pathy= disease) It is the deterioration of the function of the myocardium (i.e., the actual heart muscle) for any reason. People with cardiomyopathy are often at risk of arrhythmia and/or sudden cardiac death. Cardiomyopathy occurs when the heart muscle loses its ability to pump blood. Heart rhythm may be disturbed, resulting in arrhythmias. Cardiomyopathy can be caused by coronary atherosclerosis, but often the cause is unknown. Cardiomyopathy that is unrelated to coronary atherosclerosis is fairly uncommon, affecting about 50,000 Americans. However, unlike many other forms of heart disease, cardiomyopathy often occurs in young people. The condition tends to be progressive and can worsen fairly quickly. Cardiomyopathy is a leading reason for heart transplantation.

Less common forms of heart disease include valvular disease (problems with the valves in the heart) and aneurysm (abnormal widening of an artery) **(Fauci, A.S. Braunwald, E. Chaterjee, K. 1997-1998).**

Heart failure

Also called congestive heart failure (or CHF), and congestive cardiac failure (CCF), is a condition that can result from any structural or functional cardiac disorder that impairs

the ability of the heart to fill with or pump a sufficient amount of blood throughout the body **(Arialdi, M. Miniño, M.P.H and Melonie, P. 2004).**

Coronary artery disease

Coronary artery disease (CAD)(or atherosclerotic heart disease) is the end result of the accumulation of atheromatous plaques within the walls of the coronary arteries that supply the myocardium (the muscle of the heart) with oxygen and nutrients. It is sometimes also called coronary heart disease (CHD), but although CAD is the most common cause of CHD, it is not the only cause. CAD is the leading cause of death worldwide.[2] While the symptoms and signs of coronary artery disease are noted in the advanced state of disease, most individuals with coronary artery disease show no evidence of disease for decades as the disease progresses before the first onset of symptoms, often a "sudden" heart attack, finally arises **(Kaski, J.C. 2004).**

Coronary artery disease (or **coronary heart disease**) refers to the failure of coronary circulation to supply adequate circulation to cardiac muscle and surrounding tissue. It is already the most common form of disease affecting the heart and an important cause of premature death in Europe, the Baltic States, Russia, North and South America, Australia and New Zealand. It has been predicted that all regions of the world will be affected by 2020**(Walker B.R and Hunter J.A.A -2006).**

Coronary artery disease is caused by atherosclerosis an accumulation of fatty materials on the inner linings of the coronary arteries. Plaques in the coronary arteries can obstruct blood flow to the heart muscle which can produce angina (chest pain). If a coronary artery plaque ruptures then the resulting blockage restricts blood flow to the heart. When the blood flow is completely cut off, a heart attack can occur **(Jennifer M. 2008).**

Myocardial infarction is one of the most common cardiovascular diseases.

1.3. Myocardial Infarction (MI or AMI for acute myocardial infarction):

The term "myocardial infarction" focuses on the myocardium (the heart muscle) and the changes that occur in it due to the sudden deprivation of circulating blood. The main change is necrosis (death) of myocardial tissue.

The word "infarction" comes from the Latin "infarcire" meaning "to plug up or cram." It refers to the clogging of the artery. **(Daniel K. 2008).**

Myocardial infarction is necrosis, or tissue death, of a portion of cardiac muscle caused by obstruction in a coronary artery commonly known as a heart attack. It occurs when the blood supply to part of the heart is interrupted causing some heart cells to die. This is most commonly due to occlusion (blockage) of a coronary artery following the rupture of a vulnerable atherosclerotic plaque, which is an unstable collection of lipids (like cholesterol) and white blood cells (especially macrophages) in the wall of an artery

(Kosuge, M. 2006)

Myocardial infarction (MI) is the irreversible necrosis of heart muscle secondary to prolonged ischemia. This usually results from an imbalance of oxygen supply and demand. The appearance of cardiac enzymes in the circulation generally indicates myocardial necrosis. Myocardial infarction is considered, more appropriately, part of a spectrum referred to as acute coronary syndromes (ACSs), which also include unstable angina and non–ST-elevation MI (NSTEMI). Myocardial infarction may lead to impairment of systolic function or diastolic function and to increased predisposition to arrhythmias and other long-term complications **(Samer, G. 2009).**

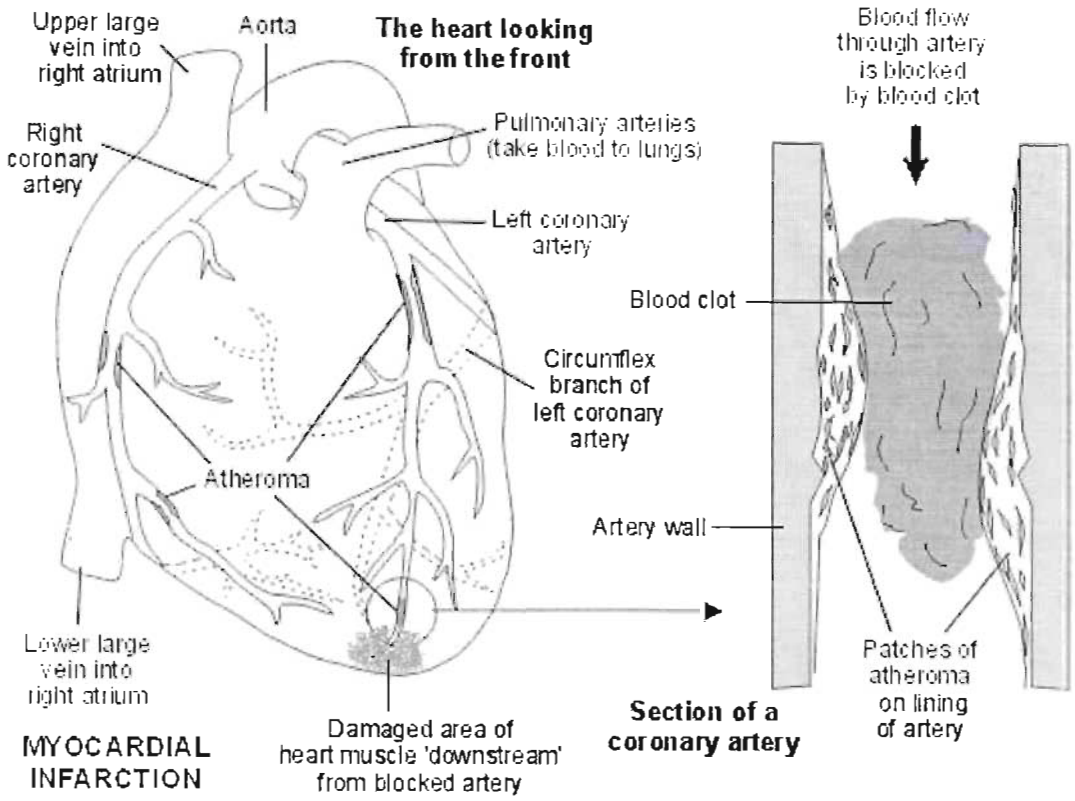

Fig1: Pathogenesis of Myocardial Infarction **(McKenna, C.J 2002).**

Myocardial infarction is becoming a serious public health problem in Bangladesh **(Abdul, F.1988).**

It generally affect middle aged person, so it cause economical problem for family due to untimely death of victim. Dietary fiber may have important effects on each of the major risk factors for heart diseases **(Kushi, L.H. and Lew, R.A 1986).**

Because of considerable side effects associated with currently available cholesterol lowering drugs and because of emerging suggestion from studies (the Ireland-Boston Diet Heart study, 1986) that dietary fibre may protect from coronary heart disease, therefore cholesterol lowering diet need more attention **(Albrink M.G. Newman, T.1979).**

Myocardial infarction now a day is one of the commonest causes of death all over the world. World Health Organization, in 1992, estimated that cardiovascular diseases take 12million lives every year and more importantly that about 6million of people deaths are

from the developing countries as against the previous belief that cardiovascular diseases occur in greater percentage in developed civilized countries.

It goes without saying that the incidence and evidence of cardiovascular disease in Bangladesh are on the increase **(Thom, T.J. Woltz, and M.1992).**

1.3.1. Types of Myocardial Infarction

Doctors use 3 different criteria to classify heart attacks.

I. **The part of the heart that was damaged.**

II. **The changes seen on an electrocardiogram.**

III. **The anatomic (or morphologic) extent of necrosis.**

I. **According to the first criterion, there are two types of heart attacks:**

1. **Anterior infarct**. Anterior infarct is the most dangerous type of heart attack and is caused by a blockage in the branch of the left coronary artery. It affects the lower chamber on the left side of the heart (left ventricle which pumps blood to all parts of the body) and damages the front part of the heart.

2. **Posterior or inferior infarct**. Posterior infarct is a less serious form of heart attack and is caused by a blockage in the right coronary artery or one of its branches. It affects the back or the base of the heart.

II. According to the second criterion, there are two types of heart attacks:

1. **ST segment elevation myocardial infarction (STEMI)**. This type of heart attack is caused by a prolonged period of blocked blood supply, and affects a large portion of the myocardium. It causes significant changes on the electrocardiogram and in the level of blood chemical markers.

2. **Non-ST segment elevation myocardial infarction (NSTEMI)**. This type of heart attack is caused by a partial or temporary blockage in the blood supply and the extent of the damages is minimal. NSTEMI does not cause changes on the electrocardiogram;

however the blood markers will indicate the occurrence of a heart attack by illustrating the tissue damage which has occurred.

III. According to the third criterion, there are two types of heart attacks:

1. Transmural myocardial infarction. This type of heart attack results in the death of the three layers of tissue (epicardium, myocardium, and endocardium) of the myocardial wall.

2. Nontransmural myocardial infarction. This type of heart attack results in the death of a limited area of myocardial wall tissue **(Alina M. 2008).**

1.3.2. Symptoms OF MI:

Severe chest pain is the usual main symptom. The pain may also travel up into jaw, and down into left arm, or down both arms. The pain may be similar to angina, but it is usually more severe and lasts longer. (Angina usually goes off after a few minutes. MI pain usually lasts more than 15 minutes - sometimes several hours.)
A small MI occasionally happens without causing pain (a 'silent MI'). It may be truly pain-free, or sometimes the pain is mild and people may think it is just heartburn or 'wind'
Some people collapse and die suddenly if they have a large or severe MI **(Stahmer S. 2007).**

Although chest pain or pressure is the most common symptom of a heart attack, heart attack victims may experience a variety of symptoms including:

- Pain, fullness, and/or squeezing sensation of the chest
- Jaw pain, toothache, headache
- Shortness of breath
- Nausea, vomiting, and/or general epigastria (upper middle abdomen) discomfort
- Sweating

- Heartburn and/or indigestion
- Arm pain (more commonly the left arm, but may be either arm)
- Upper back pain
- General malaise (vague feeling of illness)
- No symptoms (Approximately one quarter of all heart attacks are silent, without chest pain or new symptoms. Silent heart attacks are especially common among patients with diabetes mellitus.)

Even though the symptoms of a heart attack at times can be vague and mild, it is important to remember that heart attacks producing no symptoms or only mild symptoms can be just as serious and life-threatening as heart attacks that cause severe chest pain **(Daniel Kulick, FACC, FSCAI and Dennis L).**

Women may display slightly different or less noticeable symptoms. The most common heart attack symptom in women is chest pain or discomfort, or "heartburn". Women more than men experience shortness of breath, nausea/vomiting, back or jaw pain, clammy skin, or unexplained fatigue.

A person can suffer a heart attack at any given moment (while working, resting, or engaged in physical activity). However, it was noticed that most cases of heart attack occur around the early hours of morning or during physical activity. In 50 percent of cases, a heart attack is warned by signs that occur hours, days, or weeks in advance **(Alina M. 2008)**

1.3.3. Causes of myocardial infarction:

Thrombosis - the cause in most cases

The common cause of an MI is a blood clot (thrombosis) that forms inside a coronary artery, or one of its branches. This blocks the blood flow to a part of the heart. Blood clots do not usually form in normal arteries. However, a clot may form if there is some atheroma within the lining of the artery. Atheroma is like fatty patches or 'plaques'

that develop within the inside lining of arteries. (This is similar to water pipes that get 'furred up'.) Plaques of atheroma may gradually form over a number of years in one or more places in the coronary arteries. Each plaque has an outer firm shell with a soft inner fatty core. A 'crack' develops in the outer shell of the atheroma plaque. This is called 'plaque rupture'. This exposes the softer inner core of the plaque to blood. This can trigger the clotting mechanism in the blood to form a blood clot. Therefore, a build up of atheroma is the root problem that leads to most cases of MI.

Uncommon causes

Various other uncommon conditions can block a coronary artery and cause an MI. For example: inflammation of the coronary arteries (rare); a stab wound to the heart; a blood clot forming elsewhere in the body (for example, in a heart chamber) and traveling to a coronary artery where it gets stuck; cocaine abuse which can cause a coronary artery to go into spasm; complications from heart surgery; and some other rare heart problems. There are not dealt with further.
The rest of this leaflet deals only with the common cause - thrombosis over an atheroma plaque **(McKenna CJ, Forfar JC; BMJ. 2002).**

A cause of MI is a condition in which plaque (plaque) builds up inside the coronary arteries. These arteries supply your heart muscle with oxygen-rich blood. Plaque is made up of fat, cholesterol (ko-LES-ter-ol), calcium, and other substances found in the blood. When plaque builds up in the arteries, the condition is called atherosclerosis (ATH-er-o-skler-O-sis) **(National heart, lung & blood institute in U.S.february 2009).**

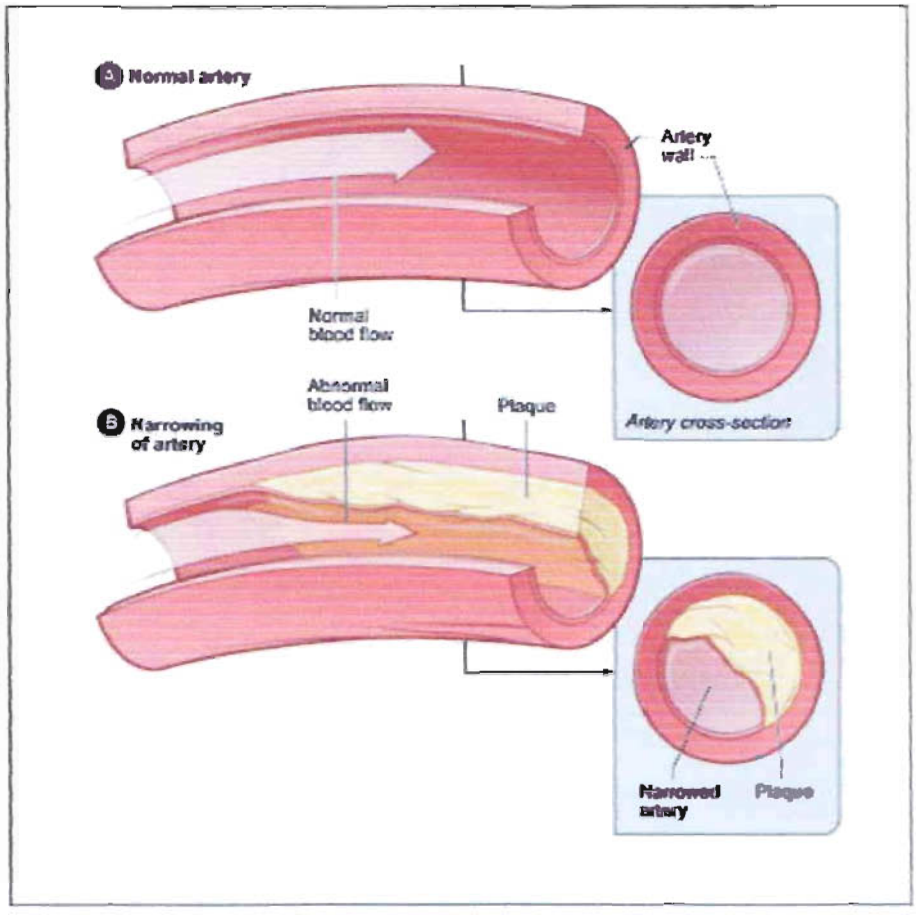

Fig 2: A show a normal artery with normal blood flow. Figure B shows an artery with plaque buildup.

Heart attack also can occur due to problems with the very small, microscopic blood vessels of the heart. This condition is called micro vascular disease. It's believed to be more common in women than in men. .Another less common cause of heart attack is a severe spasm (tightening) of a coronary artery that cuts off blood flow through the artery. These spasms can occur in coronary arteries that don't have CAD. It's not always clear what causes a coronary artery spasm, but sometimes it can be related to:

- Taking certain drugs, such as cocaine
- Emotional stress or pain
- Exposure to extreme cold
- Cigarette smoking **(Fauci, A.S. 1998)**

1.3.4. Risk factors for MI:

In 1981 a working group of national heart, lung & blood institute of U.S.A. defined a risk factor as any habit or trait that can be used to predict an individual probability of developing that disease **(Rashid K.M., 1999)**

Risk factors attribute or expose that significantly associate with the development of disease. Characteristics that are associated with an increased risk of becoming diseased are called "Risk factors" **(Flecher RH, 1996)**

Risk factors for atherosclerosis are generally risk factors for myocardial infarction:

1.3.4.1. Non-modifiable risk factors for MI

(The major risk factors that can't be changed)

Age (Four out of five patients with coronary artery disease are 65 years of age or older. After menopause, females are more likely to die within the first year of having a myocardial infarction than males.)

Sex/Gender (Males are at higher risk of myocardial infarction than women, and males are also more likely to suffer myocardial infarction earlier in life. However, heart disease kills more females each year than any other disease, including breast cancer. An alarming survey reported by the American Heart Association found that only 8% of women perceive heart disease as the greatest threat to their health despite the fact that heart disease is the leading cause of death among both women and men. Over 500,000 American women die from cardiovascular disease each year--twice the number of deaths from all cancers combined. Also, women are more likely to die within the first year of a heart attack than men.)

Family history of premature coronary heart disease (A family history of heart disease increases the risk of coronary artery disease and myocardial infarction. In the United States, African Americans tend to have more severe high blood pressure than Caucasians, increasing coronary artery disease/myocardial infarction risk. The incidence of heart disease is also higher among certain population groups such as Mexican

Americans, American Indians, native Hawaiians and some Asian Americans) **(J Am Coll Cardiol, 1988).**

1.3.4.2. Modifiable risk factors for MI

(The major risk factors that can be modified treated or controlled by changing lifestyle or taking medicine.)

Smoking or other tobacco use (Tobacco is probably the most important cause of coronary disease and therefore should be avoided. There is a strong consistent and dose linked relationship between cigarette smoking and ischemic heart disease. Cigarette smokers are twice as likely to experience myocardial infarction compared to non-smokers. Smokers also have a two to four time higher risk of sudden cardiac death (within an hour of a heart attack).

Alcohol (Heavy drinking is associated with hypertension and is the important risk factor of coronary artery disease.)

Diabetes mellitus (Diabetes (with or without insulin resistance) - the single most important risk factor for ischemic heart disease –IHD. Approximately two-thirds of patients with diabetes die from heart or blood vessel disease. Adults with diabetes are three to seven times more likely to develop heart disease. A recent recommendation from the U.S. government advocates aggressive treatment of high cholesterol in people with diabetes.)

Hypertension/High blood pressure (Alone or in association with obesity, smoking, high blood cholesterol levels or diabetes, high blood pressure increases the risk of myocardial infarction and stroke)

Stress (occupations with high stress index are known to have susceptibility for atherosclerosis. Research indicates a possible relationship between stress and coronary artery disease, which may lead to myocardial infarction Hypertension (high blood pressure) and high cholesterol are associated with stress, as are increased tendencies to smoke, gain weight and/or decrease physical activity.)

Obesity (defined by a body mass index of more than 30 kg/m², or alternatively by waist circumference or waist-hip ratio. Obesity increases coronary artery disease, myocardial infarction, and stroke risk. Obesity increases strain on the heart, raises blood pressure and cholesterol, and increases diabetes risk. Weight reduction can be achieved with modifications to diet and increased physical activity)

Hypercholesterolemia (more accurately hyperlipoproteinemia, especially high low density lipoprotein and low high density lipoprotein High total and low-density lipoprotein (LDL cholesterol) levels and low HDL cholesterol levels increase the risk of myocardial infarction Cholesterol levels can be lowered with dietary/lifestyle modifications such as exercise or medications.)

Physical inactivity(Regular exercise like brisk walking, cycling or swimming for 20 minutes two to three times a week appears to have protective effect which may be related to its ability to increase HDL cholesterol, lower blood pressure , reduce blood clotting and promote collateral vessel development)

Hyperhomocysteinemia (high homocysteine, a toxic blood amino acid that is elevated when intakes of vitamins B2, B6, B12 and folic acid are insufficient. Haemostatic factors Platelet activation and high levels of fibrinogen and factor VII are associated with an increase risk of myocardial infarction.) **(J Am Coll Cardiol, 1988)**

Dietary fact & coronary heart disease recent epidemiologic studies have shown a U-shaped curve for alcohol consumption & coronary heart disease mortality, with low-to-moderate alcohol consumption associated with lower overall mortality. High daily dietary intake of fat is associated with obesity & may act as an independent risk factor or may affect other stroke risk factors such as hypertension, diabetes, hyperlipidemia & cardiac disease. Homocysteine is another important dietary component associated with stroke risk, while other dietary stroke risk factors are thought to be mediated through the daily intake of several vitamins & antioxidants.

Despite the obstacles to the modification of lifestyle factors, health professionals should be encouraged to continue to identify such factors & help improve our ability to prevent stroke **(Boden-Albala B,Sacco RL,New York)**

1.3.4.3. New and other risk factors for MI

- Elevated homocysteine levels
- Male pattern baldness
- Sedentary lifestyle and/or lack of exercise
- Psychosocial stress
- Presence of peripheral vascular disease
- Poor oral hygiene

1.3.4.4. Nonatherosclerotic causes

- Vasculitis
- Coronary emboli
- Congenital coronary anomalies
- Coronary trauma
- Coronary spasm
- Drug use (cocaine)
- Factors that increase oxygen requirement, such as heavy exertion, fever, or hyperthyroidism
- Factors that decrease oxygen delivery, such as hypoxemia of severe anemia **(Braunwald E, Antman EM, Beasley JW September 2003)**

1.3.4.5. Other dietary factors

Diet deficient in fresh fruits, vegetables and polyunsaturated fatty acids are associated with an increased risk of coronary disease. Low levels of vitamin C and E and other antioxidants may enhance the production of oxidized LDL and are important risk factor for coronary artery disease **(J Am Coll Cardiol, 1988)**

1.3.5. Complication after having myocardial infarction:

- A number of arrhythmias occur after myocardial infarction, ranging from benign to fatal. Arrhythmias are common in the setting of myocardial infarction and are a major cause of morbidity and mortality. Close monitoring and immediate treatment

of arrhythmias may be the most important part of the treatment of a post–myocardial infarction patient within the first 48 hours. Pay close attention to exacerbating factors, such as electrolyte disturbances (especially potassium and magnesium), hypoxemia, drugs, or acidosis, and correct them accordingly.

- Ventricular fibrillation, Ventricular rupture and/or ventricular tachycardia occurring within the first 48 hours may be due to ischemia; however, if ventricular arrhythmias occur later, then further workup is indicated. Immediate cardio version is the treatment of choice. Accelerated idioventricular arrhythmia is a ventricular arrhythmia that may occur in response to reperfusion. This rhythm has a benign prognosis and usually does not require therapy. **(Garas S. 2009).**

1.4. Diagnosis and treatment of MI

1.4.1. Diagnostic criteria

A heart attack is a process that spans over several hours and a fast diagnosis can increase the chance of survival and minimize the damages. A heart attack diagnosis involves a physical examination, a medical review of health problems, and diagnostic tests.

Diagnostic tests. Diagnostic tests are divided in two categories: non-invasive tests and invasive tests.

The category of non-invasive tests includes:
1. Electrocardiogram (or ECG). Electrocardiogram is the first test done by the medical team to diagnose a heart attack. This test establishes whether a heart attack is in progress or has already occurred by recording the electrical activity of the heart. When the heart muscle has suffered injuries, it doesn't conducts electrical impulses normally, and a special device registers these changes through a set of electrical sensors (leads) attached to certain location on the arms, legs, and chest **(Alina M. 2008).**

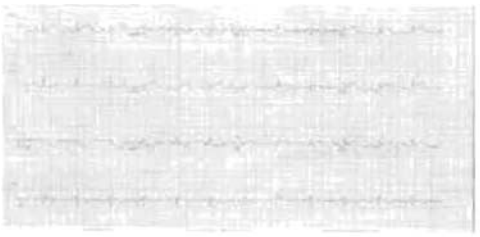

Fig 3: The ECG shows lateral ST-segment elevation that is consistent with a lateral wall AMI **(Samer G. 2009).**

2. Echocardiogram. Echocardiogram is a non-invasive diagnostic test that can determine whether the heart muscle has suffered changes and detect blood clots. This test can provide information regarding the heart's strength which is essential in determining the severity of the heart attack, which portion of the heart may have been affected, and what coronary artery is blocked. In normal conditions, approximately 60 percent of the blood in the left ventricle is pumped out each time the heart contracts.

3. Chest x-ray. This is an additional test used to visualize the shape and size of the heart, the width of aorta, and the condition of the lungs **(Alina M. 2008).**

The category of invasive tests includes:

Blood tests:

Cardiac enzymes are proteins that are released into the blood by dying heart muscles. These cardiac enzymes are creatine phosphokinase (CPK), special sub-fractions of CPK (specifically, the MB fraction of CPK), and troponin, and their levels can be measured in blood. These cardiac enzymes typically are elevated in the blood several hours after the onset of a heart attack. **(Daniel Kulick, FACC, FSCAI and Dennis L)**

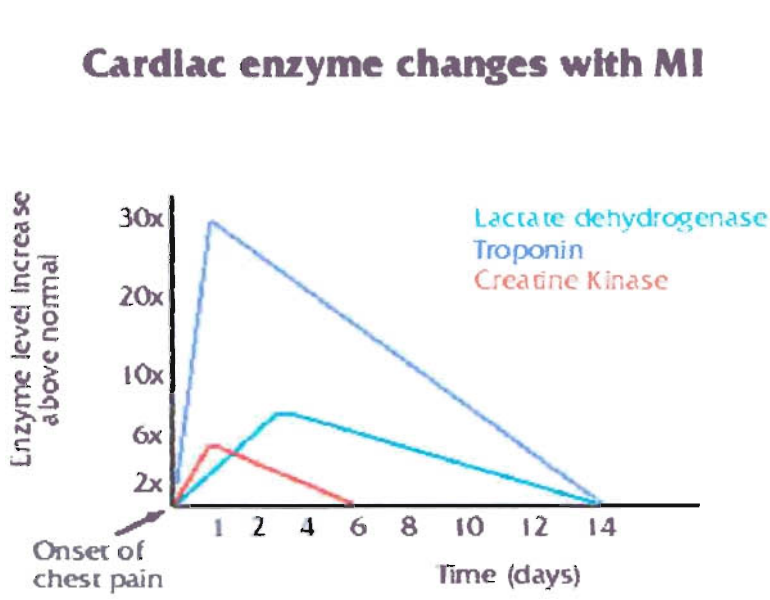

Fig 4: Cardiac enzyme changes with MI **(Kumm S, 2005)**

Creatine Kinase - MB Fraction:

Creatine kinase can be subdivided into three enzymes: MM, MB, and BB. The MM fraction is present in both cardiac and skeletal muscle, but the MB fraction is much more specific for cardiac muscle: about 15 to 40% of CK in cardiac muscle is MB, while less than 2% in skeletal muscle is MB. The BB fraction (found in brain, bowel, and bladder) is not routinely measured.

Thus, CK-MB is a very good marker for acute myocardial injury, because of its excellent specificity, and it rises in serum within 2 to 8 hours of onset of acute myocardial infarction. Serial measurements every 2 to 4 hours for a period of 9 to 12 hours after the patient is first seen will provide a pattern to determine whether the CK-MB is rising, indicative of myocardial injury. **(Mullner M 1996).**

1.4.2. Treatment and Medication of myocardial infarction

Once a heart attack diagnosis is established, the treatment procedure starts immediately. The primary goal of treatment is to restore the normal blood flow to the damaged portion of the heart muscle and preserve the ability to function normal for the rest of the myocardium **(Alina M. 2008).**

The most important factor in diagnosing and treating a heart attack is prompt medical attention. Rapid evaluation allows early treatment of potentially life-threatening abnormal rhythms such as ventricular fibrillation and allows early reperfusion (return of blood flow to the heart muscle) by procedures that unclog the blocked coronary arteries. The more rapidly blood flow is reestablished, the more heart muscle that is saved (**Daniel Kulick, FACC, FSCAI and Dennis L**)

Treatment is based on:

(1) Restoration of the balance between the oxygen supply and demand to prevent further ischemia,

(2) Pain relief, and

(3) Prevention and treatment of any complications that may arise.

(4) Medication

The most important goal of drug therapy early in the course of acute myocardial infarction is to improve the oxygen supply/demand ratio for the heart. The reduction in this ratio that occurs when coronary flow is compromised is the primary reason cardiac function is impaired, which leads to the clinical signs associated with myocardial infarction. There are two strategies to improve the coronary supply/demand ratio,

1) Restore normal coronary blood flow, and

2) Decrease myocardial oxygen consumption.

1.4.2.1. Classes of Drugs Used to Treat Myocardial Infarction

Drugs are prescribed after a myocardial infarction

- To reduce the chance of having another myocardial infarction (MI).
- To help prevent heart disease from getting worse.

- The drugs are usually taken each day for life (**British Heart Foundation -2006**).

Classes of drugs used in the treatment of myocardial infarction are given below.

1. Vasodilators (dilate arteries and veins)

- Alpha-adrenoreceptor antagonists (alpha-blockers)
- Angiotensin converting enzyme (ACE) inhibitors
- Angiotensin receptor blockers (ARBs)
- Beta$_2$-adrenoceptor agonists (β_2-agonists)
- Calcium-channel blockers (CCBs)
- Centrally acting sympatholytics
- Direct acting vasodilators
- Phosphodiesterase inhibitors
- Potassium-channel openers
- Renin inhibitors
- Endothelin receptor antagonists
- Ganglionic blockers
- Nitrodilators

2. Cardiac depressant drugs (reduce heart rate and contractility)

- beta-blockers

3. Antiarrhythmics (if necessary)

4. Anti-thrombotics (prevent thrombus formation)

- anticoagulant

- anti-platelet drugs

5. Thrombolytics (dissolve clots - i.e., "clot busters")

- plasminogen activators

6. Analgesics (reduce pain)

- morphine

1. Vasodilators (dilate arteries and veins)

As the name implies, vasodilator drugs relax the smooth muscle in blood vessels, which causes the vessels to dilate. Vasodilators are used to treat hypertension, heart failure and angina; venous dilators are very effective for angina, and sometimes used for heart failure, but are not used as primary therapy for hypertension. Most vasodilator drugs are mixed (or balanced) vasodilators in that they dilate both arteries and veins

Drug Classes

Vasodilator drugs can be classified based on their site of action (arterial versus venous) or by mechanism of action. Some drugs primarily dilate resistance vessels (arterial dilators; e.g., hydralazine), while others primarily affect venous capacitance vessels (venous dilators; e.g., nitroglycerine). Most vasodilator drugs, however, have mixed arterial and venous dilator properties (mixed dilators; e.g., alpha-adrenoreceptor antagonists, angiotensin converting enzyme inhibitors).

Nitrodilators

Nitrodilators are drugs that mimic the actions of endogenous Nitric oxide (NO), by releasing NO or forming NO within tissues. These drugs act directly on the vascular smooth muscle to cause relaxation and therefore serve as endothelial-independent vasodilators.

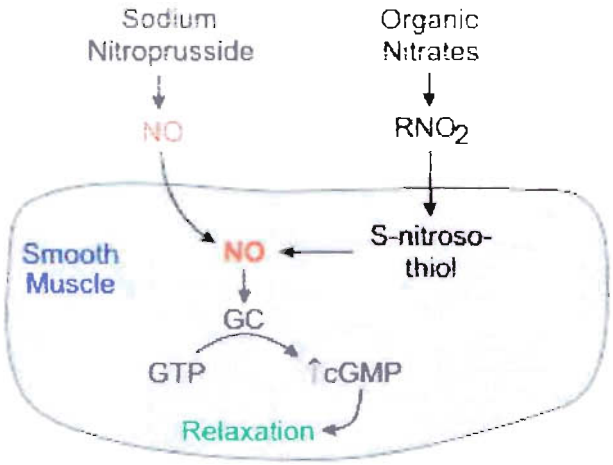

Fig 5: Action of Nitro dilators

Although nitro dilators can dilate both arteries and veins, venous dilation predominates when these drugs are given at normal therapeutic doses. Venous dilation reduces venous

pressure and decreases ventricular preload. This reduces ventricular wall stress and oxygen demand by the heart, thereby enhancing the oxygen supply/demand ratio.

The most common side effects of nitro dilators are headache (caused by cerebral vasodilation) and cutaneous flushing. Other side effects include postural hypotension and reflex tachycardia.

Angiotensin converting enzyme (ACE) inhibitors

ACE inhibitors reduce mortality rates after myocardial infarction. ACE inhibitors have the greatest benefit in patients with ventricular dysfunction. Angiotensin-receptor blockers may be used as an alternative in patients who develop adverse effects, such as a persistent cough, although initial trials need to be confirmed. An ACE inhibitor (Captopril) should be given orally within the first 24 hours of STEMI to patients with anterior infarction, pulmonary congestion, or left ventricular ejection fraction (LVEF) less than 40% in the absence of hypotension. ACE inhibitors produce vasodilation by inhibiting the formation of angiotensin II. This vasoconstrictor is formed by the proteolytic action of renin (released by the kidneys) acting on circulating angiotensinogen to form angiotensin I. Angiotensin I is then converted to angiotensin II by angiotensin converting enzyme. Angiotensin II constricts arteries and veins by binding to AT_1 receptors located on the smooth muscle, which are coupled to a Gq-protein and the the IP_3 signal transduction pathway. Angiotensin II also facilitates the release of norepinephrine from sympathetic adrenergic nerves and inhibits norepinephrine reuptake by these nerves. This effect of angiotensin II augments sympathetic activity on the heart and blood vessels.

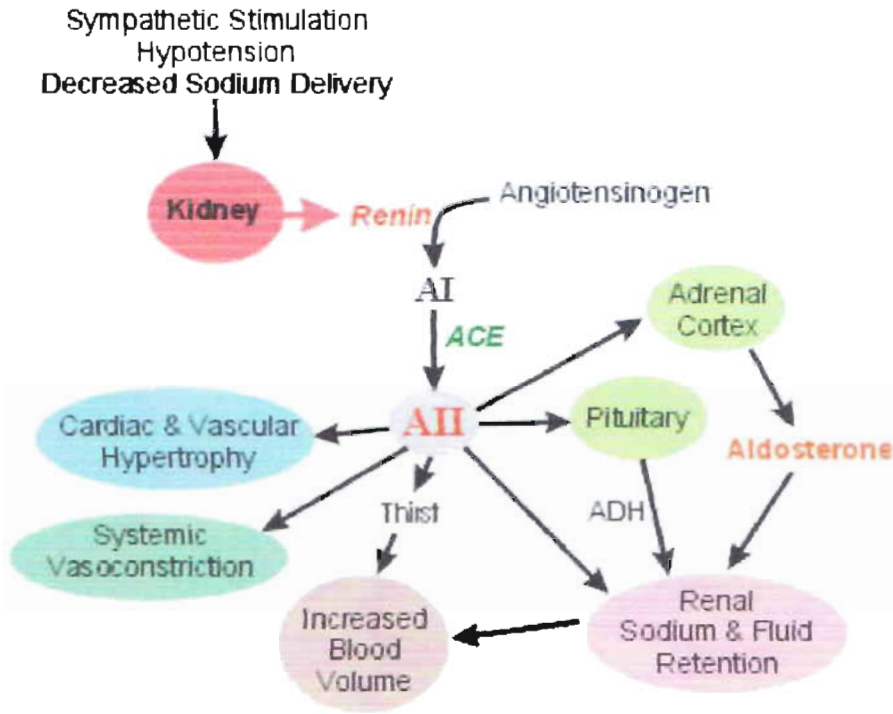

Fig 6: General pharmacology of ACE inhibitors

Cardiorenal Effects of ACE Inhibitors

- Vasodilation (arterial & venous)
  - reduce arterial & venous pressure
  - reduce ventricular afterload & preload
- Decrease blood volume
  - Natriuretic
- - Diuretic (Diuretics may also be given depending on the degree of heart failure and fluid retention).
- Depress sympathetic activity
- Inihibit cardiac and vascular hypertrophy

ACE inhibitors have the following actions:

- Dilate arteries and veins by blocking angiotensin II formation and inhibiting bradykinin metabolism. This vasodilation reduces arterial pressure, preload and afterload on the heart.

- Down regulate sympathetic adrenergic activity by blocking the facilitating effects of angiotensin II on sympathetic nerve release and reuptake of norepinephrine.
- Promote renal excretion of sodium and water (natriuretic and diuretic effects) by blocking the effects of angiotensin II in the kidney and by blocking angiotensin II stimulation of aldosterone secretion. This reduces blood volume, venous pressure and arterial pressure.
- Inhibit cardiac and vascular remodeling associated with chronic hypertension, heart failure, and myocardial infarction.

Specific Drugs

The first ACE inhibitor marketed, captopril, is still in widespread use today. Although newer ACE inhibitors differ from captopril in terms of pharmacokinetics and metabolism, all the ACE inhibitors have similar overall effects on blocking the formation of angiotensin II. ACE inhibitors include the following specific drugs:

- **Benazepril**
- **Captopril (Capoten)**-Has short half-life, which makes it important drug for initiation of ACE inhibitor therapy. Can be started at low dose and titrated upward as needed and as patient tolerates.
- **Enalapril**
- **Fosinopril**
- **Ramipril**

As a drug class, ACE inhibitors have a relatively low incidence of side effects and are well-tolerated. A common, annoying side effect of ACE inhibitors is a dry cough appearing in 10-30% of patients. It appears to be related to the elevation in bradykinin. Hypotension can also be a problem, especially in heart failure patients.

Angiotensin receptor blockers (ARBs)

ARBs are used in the treatment of hypertension and heart failure in a similar manner as ACE inhibitors (see ACE inhibitors for details). These drugs have very similar effects to angiotensin converting enzyme (ACE) inhibitors and are used for the same indications (hypertension, heart failure, post- myocardial infarction). Their mechanism of action, however, is very different from ACE inhibitors, which inhibit the formation of

angiotensin II. ARBs are receptor antagonists that block type 1 angiotensin II (AT_1) receptors on bloods vessels and other tissues such as the heart

ARBs have the following actions, which are very similar to ACE inhibitors:

- Dilate arteries and veins and thereby reduce arterial pressure and preload and afterload on the heart.
- Down regulate sympathetic adrenergic activity by blocking the effects of angiotensin II on sympathetic nerve release and reuptake of norepinephrine.
- Promote renal excretion of sodium and water (natriuretic and diuretic effects) by blocking the effects of angiotensin II in the kidney and by blocking angiotensin II stimulation of aldosterone secretion.
- Inhibit cardiac and vascular remodeling associated with chronic hypertension, heart failure, and myocardial infarction.

ARBs include the following drugs:

- Eprosartan
- Irbesartan
- Losartan
- **valsartan**

As a drug class, ARBs have a relatively low incidence of side effects and are well-tolerated. Because they do not increase bradykinin levels like ACE inhibitors, the dry cough and angioedema that are associated with ACE inhibitors are not a problem. ARBs are contraindicated in pregnancy. Patients with bilateral renal artery stenosis may experience renal failure if ARBs are administered.

Side-Effects of Vasodilators

Systemic vasodilation and arterial pressure reduction can lead to a baroreceptor-mediated reflex stimulation of the heart (increased heart rate and inotropy). This increases oxygen demand, which is undesirable if the patient also has coronary artery disease. Vasodilators can impair normal baroreceptor-mediated reflex vasoconstriction when a person stands up, which can lead to orthostatic hypotension and syncope upon standing. Vasodilators

can lead to renal retention of sodium and water, which increases blood volume and cardiac output and thereby compensates for the reduced systemic vascular resistance.

2. Cardiac depressant drugs (reduce heart rate and contractility)

- **Beta-blockers**

May reduce the rates of reinfarction and recurrent ischemia. Administer to patients with myocardial infarction unless a contraindication is present.

Beta-adrenergic blockers-This category of drugs has the potential to suppress ventricular ectopy due to ischemia or excess catecholamine. In the setting of myocardial ischemia, beta-blockers have antiarrhythmic properties and reduce myocardial oxygen demand secondary to elevations in heart rate and inotropy. These agents inhibit chronotropic, inotropic, and vasodilatory responses to beta-adrenergic stimulation and reduce blood pressure, which decreases myocardial oxygen demand. -**Metoprolol (Lopressor)**

Selective beta1-adrenergic receptor blocker that decreases automaticity of contractions. During IV administration, carefully monitor blood pressure, heart rate, and ECG.

3. Antiarrhythmics (if necessary)

The ultimate goal of antiarrhythmic drug therapy is to restore normal rhythm and conduction. When it is not possible to revert to normal sinus rhythm, drugs may be used to prevent more serious and possibly lethal arrhythmias from occurring. Antiarrhythmic drugs are used to:

- decrease or increase conduction velocity
- alter the excitability of cardiac cells by changing the duration of the effective refractory period
- suppress abnormal automaticity

All antiarrhythmic drugs directly or indirectly alter membrane ion conductance, which in turn alters the physical characteristics of cardiac action potentials. For example, some drugs are used to block fast sodium channels. These channels determine how fast the membrane depolarizes (phase 0) during an action potential. Since conduction velocity is

related to how fast the membrane depolarizes, sodium channel blockers reduce conduction velocity.

.Antiarrhythmic drug classes:

- Class I - Sodium-channel blockers
- Class II - Beta-blockers
- Class III - Potassium-channel blockers
- Class IV - Calcium-channel blockers
- Miscellaneous - adenosine
  - electrolyte supplement (magnesium and potassium salts)
  - digitalis compounds (cardiac glycosides)
  - atropine (muscarinic receptor antagonist)

4. Anti-thrombotics (prevent thrombus formation)

These agents prevent the formation of thrombus associated with myocardial infarction and inhibit platelet function by blocking cyclooxygenase and subsequent aggregation. Antiplatelet therapy has been shown to reduce mortality rates by reducing the risk of fatal myocardial infarctions, fatal strokes, and vascular death.

- **Anticoagulant**

- **Heparin** (anticoagulant agents) has an established role as an adjunctive agent in patients receiving t-PA, but not in patients receiving streptokinase. Heparin is also indicated in patients undergoing primary angioplasty.

- **Anti-platelet drugs**

-Salicylates-The antiplatelet effects of these agents may improve mortality rate.

-Aspirin and/or antiplatelet therapy

Aspirin has been shown to decrease mortality and re-infarction rates after myocardial infarction.Continue aspirin indefinitely unless an obvious contraindication, such as a bleeding tendency or an allergy, is present. Clopidogrel may be used as an alternative in cases of a resistance or allergy to aspirin. Recent data from the CLARITY trial suggest

that adding clopidogrel to this regimen is safe and effective. The clopidogrel dose used was 300 mg. Further studies suggest that a higher dose of clopidogrel may have added benefit **(Chen ZM, Jiang LX, Chen YP, Xie JX, Pan HC Nov 5 2005).**

5. Thrombolytic (Fibrinolytic)(dissolve clots - i.e., "clot busters") therapy:

Thrombolytics agents the main objective is to restore circulation through a previously occluded vessel by the rapid and complete removal of a pathologic intraluminal thrombus or embolus that has not been dissolved by the endogenous fibrinolytic system. These agents prevent recurrent thrombus formation and rapid restoration of hemodynamic disturbances. When given within 12 h of symptom onset, they restore patency of occluded arteries, salvage myocardium, and reduce morbidity and mortality rates of AMI. Thrombolytic treatment should be started within 30 min of arrival (door-drug time). Maximum benefit occurs when administered within 1-3 h of symptom onset **(Samer G).**

Thrombolytic drugs are used to dissolve blood clots (thrombi). Blood clots can occur in any vascular bed; however, when they occur in coronary, cerebral or pulmonary vessels, they can be immediately life-threatening - coronary thrombi are the cause of myocardial infarctions, cerebrovascular thrombi produce strokes, and pulmonary thromboemboli can lead to respiratory and cardiac failure. Therefore, it is important to rapidly diagnose and treat blood clots **(Richard E. K. 2007).**

Mechanisms of Thrombolysis

Thrombolytic drugs dissolve blood clots by activating plasminogen, which forms a cleaved product called plasmin. Plasmin is a proteolytic enzyme that is capable of breaking cross-links between fibrin molecules, which provide the structural integrity of blood clots. Because of these actions, thrombolytic drugs are also called "plasminogen activators" and "fibrinolytic drugs."

There are three major classes of fibrinolytic drugs:

Tissue plasminogen activator (TPA),

This family of thrombolytic drugs is used in acute myocardial infarction, cerebrovascular thrombotic stroke and pulmonary embolism. For acute myocardial infarctions, tissue plasminogen activators are generally preferred over streptokinase.

- Alteplase (Activase®; rtPA)
- Retaplase (Retavase®) it is usually administered as IV bolus injections. It is used for acute myocardial infarction and pulmonary embolism.
- Tenecteplase (TNK-tPA) has a longer half-life and greater binding affinity for fibrin than rtPA. Because of its longer half-life, it can be administered by IV bolus. It is only approved for use in acute myocardial infarction

Streptokinase (SK)

Streptokinase and anistreplase are used in acute myocardial infarction, arterial and venous thrombosis, and pulmonary embolism. These compounds are antigenic because they are derived from streptococci bacteria.

Urokinase (UK).

Urokinase (Abbokinase®; UK) It has limited clinical use because, like SK, it produces considerable fibrinogenolysis; however, it is used for pulmonary embolism.

While drugs in these three classes all have the ability to effectively dissolve blood clots, they differ in their detailed mechanisms in ways that alter their selectivity for fibrin clots.

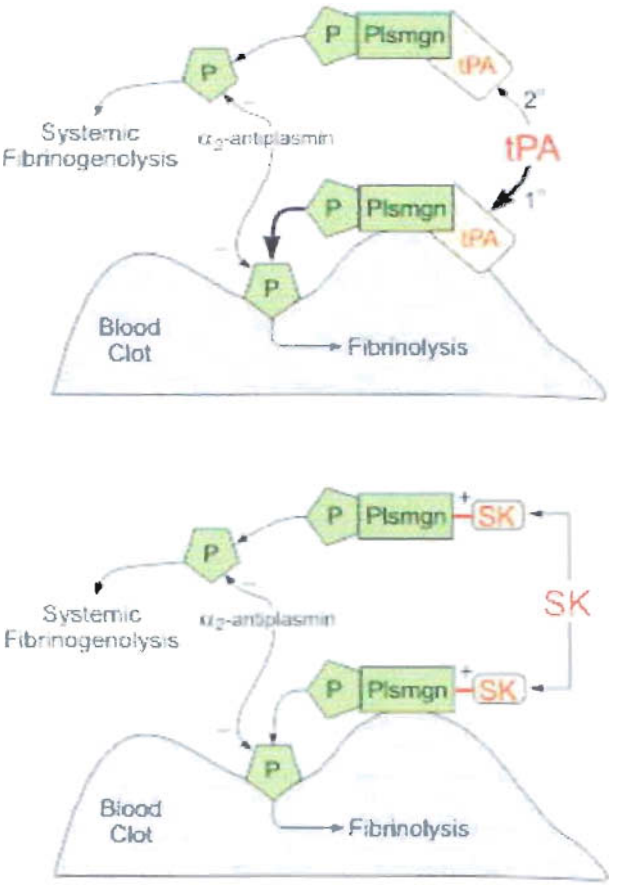

Fig 7: Fibrinolytic mechanisms for TPA and SK

The figure to the right illustrates the fibrinolytic mechanisms for TPA and SK. Derivatives of TPA are the most commonly used thrombolytic drugs, especially for coronary and cerebral vascular clots, because of their relative selectivity for activating fibrin-bound plasminogen. Tissue plasminogen activator produces clot lysis through the following sequence:

1. tPA binds to fibrin on the surface of the clot
2. Activates fibrin-bound plasminogen
3. Plasmin is cleaved from the plasminogen associated with the fibrin
4. Fibrin molecules are broken apart by the plasmin and the clot dissolves

Common adverse effects of all the thrombolytic drugs is bleeding complications related to systemic fibrinogenolysis and lysis of normal hemostatic plugs. Therefore, patients who have experienced trauma injury or who have a history of cerebral hemorrhagic stroke are not usually administered thrombolytics. Re-thrombosis can occur following

thrombolysis, and therefore anticoagulants such as heparin are usually co-administered and continued after thrombolytic therapy for a period of time.

6. Analgesics (reduce pain)

- morphine

Pain management is an important consideration because pain and associated anxiety stimulates sympathetic activity, which can be deleterious to the heart. Therefore, analgesic drugs such as morphine are often given in the acute setting to reduce pain. Morphine also has other beneficial effects as a vasodilator.

1.4.2.2. Drugs are used in addition to any relevant lifestyle changes:

Other drugs are sometimes advised. Some people take fish oil supplements. There is some evidence that eating oily fish (or taking fish oil supplements) that helps to protect the heart and reduces the risk of having a further MI. Drugs are used in addition to any relevant lifestyle changes which also help to prevent heart disease from getting worse. These include:

- Stop smoking if person is a smoker.
- Take regular exercise (unless advised otherwise by doctor).
- Lose weight if person is overweight.
- Eat a healthy diet, including oily fish at least 2-3 times a week.
- Drink alcohol in moderation **(British Heart Foundation 2006)**

1.5. Magnitude of the cardiovascular problem:

1.5.1. Global & World wide problem of MI:

Globally, non- communicable diseases (NCDs) are increasingly recognized as a major cause of morbidity and mortality. According to estimates in the World Health Report 2001, CVD accounts for 29% of all deaths and 115 of disease burden in the region. The incidence of CVD is increased in urban areas than in rural areas reflecting the acquisition of several risk factors such as tobacco consumption, lack of physical activity, unhealthy

diet and obesity. There was growing evidence to show that CVD posse a serious health threat to disadvantaged and poor segments of the population.

The World Health Report 2001 has indicated that non communicable diseases account for almost 60% deaths and 46% of the global burden of disease. 75% of total deaths due to non communicable diseases occur in developing countries. Coronary Heart Disease (CHD) rank no. 1 among the 10 leading cause of mortality estimated for 1999(WHO Report). In UK one in four men and one in five women die from this disease, an estimated 3000,000 people have a myocardial infarction each year and approximately 1.7 million people have angina **(Haslete C.1999).**

In early twentieth century diseases of the heart ranked fourth as a cause of death in the USA. Mortality from IHD reached its peak in 1963 in USA and since then there has been a progressive and steady decline in mortality. By 2020 this is expected to rise to 73%death and 60% of the disease burden. Most people suffering from non-communicable diseases are at the age in between 45-65 years **(Rashid K.M. 1999).**

1.5.2. In Asia:

Regionally, the countries of the East Asia Region are thus fasting a double burden with a heavy load of infectious diseases and an added burden of non communicable diseases. Cardiovascular diseases ranked third as a cause of death in South- East Asia. In the year 2000, 16.7 million people died from cardiovascular diseases, accounting for 30.3% of all deaths worldwide; more than half of those deaths taking place in the developing countries (**WHO, 2001).**

The burden of disease in disability- adjusted life years (DALYs) lost due to cardiovascular disease in South-East Asian Region. Cardiovascular diseases are responsible for 25% of the non- communicable disease in this region. Of the cardiovascular disease, ischemic heart disease accounts for 40% of DALYs Measurement of disease burden is often measured by the disability- adjusted life years (DAlYs) and is defined as the years of life lost to premature deaths(YLL) and years lived with a disability of specified severity and duration(YLD) **(World Health Organization-2002).**

In indigenous population of South Asia, high prevalence of rates for CHD risk factors is also apparent (table-1.1.2). In India, prevalence of coronary artery disease has been reported as being 11% in 2001; prevalence of coronary artery disease and its relationship to lipid in a selected population in South India; the Chennai Urban population Study **(Mohan V. 2001).**

1.5.3. In Bangladesh

In Bangladesh, Coronary Artery Disease ranked third among the cardiovascular diseases. Prevalence of the disease was found to be 3.38 and 14 per thousand in two different studies carried out in 1976 and 1984 (unpublished) respectively. Ami is the leading cause of morbidity and mortality in developed countries and also emerging as a major health problem in developing countries like Bangladesh.

MI is the most common disease in our country. About 180,000 people in the Bangladesh are admitted to hospital each year with an MI. Most MI occurs in people over 50, and become more common with increasing age. Sometimes younger people are affected. An MI is three times more common in men than women **(Rashid, K.M. 1999).**

With industrialization and development of the country, now days, like other developing countries, there are more causes of myocardial infarction in Bangladesh. An important observation among hospitalized patients in the country is that as many as 32% of the patients belongs to 41 and 50 years age group indicating premature occurrences of the disease. Male to female ratio is 8:1, which is higher as compared to that in other countries **(Rashid AKMH, 1997).**

Table 2: percentage of Hypertension, Cigarette Smoking, oral Smokeless Tobacco and Diabetes of different countries of South Asia

	Pakistan **(Gentller MM, White PD, 1995)**	India **(Nefzger MD, Hrubee, 1969)**	Bangladesh **(Denbrough MA, 1962)**	Nepal **(Meshalkin EN, 1981)**	Sri Lanka **(WHO, 1988)**
Hypertension*					
Men	17%	36.4%	9.8%	....	17%
Woman	....	37.5%	15.6%	....	....
Cigarette Smoking	....	....	....	73.7%	....
Men	34%	36.5%	50.3%		57.9%
Woman				57.95%	
Oral Smokeless Tobacco	10%	22%	....	....	....
Men	....	....	16.3%	....	....
Woman	....	....	21.4%	....	....
Diabetes	5%	....	....	....	....
Men	....	13.1%	2.9%	....	5.8%
Woman	....	11.3%	0.7%	....	....
Hyper cholesterolaemia	12.6%	..	..	..	..
Men	..	37.4%	2.8%	..	12.6%
Women	..	4.15	3%	..	..

(Mohan V.2001)

CHAPTER 2

Objectives of MI

2.1. Objectives of the study

Several drugs are used to treat the MI patients admitted in NICVD. The main objectives of the study are:

1. To find out the commonly used drugs for the treatment of MI.

2. To find out the life style risk factors such as smoking habit, habitual physical activity, body mass index, food habit, alcohol consumption, extra salt intake, social class etc responsible for myocardial infarction.

Other objectives of the study are -

- To assess systolic and diastolic blood pressure level of the respondents.
- To determine the lipid profile of MI patients admitted to NICVD.
- To determine the habit of smoking, alcohol consumption and other life style risk factors of MI patients.

2.2. Significance of the study:

Myocardial infarction (MI) is the rapid development of myocardial necrosis caused by a critical imbalance between oxygen supply and demand of the myocardium. This usually results from plaque rupture with thrombus formation in a coronary vessel, resulting in an acute reduction of blood supply to a portion of the myocardium. Myocardial Infarction is one of the commonest causes of death all over the world. The prevalence of Myocardial Infarction is increasing day by day.
The most common cause of MI is narrowing of the epicardial blood vessels due to atheromatous plaques.

The most important factor in diagnosing and treating a heart attack is prompt medical attention. Once a heart attack diagnosis is established, the treatment procedure starts immediately. The most important goal of early drug therapy in the course of acute myocardial infarction is to improve the oxygen supply/demand ratio for the heart. Drugs

are prescribed after a myocardial infarction to reduce the chance of having another MI, to help prevent heart disease from getting worse. Some common drugs used in the treatment of myocardial infarction are: Heparin, Salicylates, Aspirin, Streptokinase and anistreplase, Nitro dilators etc.

This study was carried out to observe the situation of MI patients admitted in NICVD and to find out the most commonly used drugs for the prevention of MI in NICVD. This study provides all the possible information about life style risk factors of MI the use of drugs to prevent MI.

This study is expected to provide important information to better understand the harmful effect of some modifiable life style risk factors which ultimately cause MI. Thus the result of this study will contribute to the public health by making awareness about the damaging effect of modifiable risk factors which can be changed by changing the life style of MI patients and the importance of use of different drugs which will ultimately reduce the risk of MI.

CHAPTER 3

MATERIALS AND METHOD

3.1. Type of study:

This study was attempted to find out the life style risk factors of Myocardial Infarction and the drugs that are used to treat MI. In addition to this, the study examined for other risk factors and presence of MI.

3.2. Place of study:

The study was being conducted in National Institute of Cardiovascular Diseases & Hospital (NICVD). This hospital is the largest and the pioneer cardiac hospital in Bangladesh .It was established in 1981, situated at the heart of the Dhaka city composed of 400 beds, offering 24 hours of services. This institute comprises of Outdoor, Emergency, highly specialized Coronary care unite, Post coronary care unit Intensive care unite and has a full fledged indoor. A good number of Doctors and medical specialists and other supporting staffs are providing cardiac medical and surgical care services to all categories of patients from different parts of the country- including referred patients from other medical college hospitals & district hospitals.

3.3. Study population:

All admitted patient of MI diagnosed by the hospital physicians.

Inclusion Criteria of the cases:

- Patient of diagnosed MI ages 25-85yers
- Both sexes irrespective of religion and occupation.

Exclusion Criteria of the cases:

- Patients of cardiac disease other than Myocardial Infarction.
- Post operative patient
- Any other chronic diseases.

3.4. Sample size:

Sample size was 60

3.5. Sampling Technique:

In this study, purposive sampling technique was followed.

3.6. Research Approach:

After getting the approval of the research proposal from the honorable faculty members, formal permission was obtained from the competent authorities of NICVD. The data were collected from the wards 3, 4, 5, 6, and 7, (Medicine Ward).

3.7. Research Equipments:

The following equipments were used in this study,

- Interview schedule
- Measuring Tape.
- Weighing machine (Bathroom Scale)
- Sphygmomanometer. (Aneroid type)
- Stethoscope.

3.8. Data collection method:

After explaining the purpose of the study to the respondents and obtaining their verbal consent, the researcher interviewed all the respondents by asking question in Bengali and using a thoroughly pre –tested questionnaires the questionnaires was be consists of three parts. Part -1 was consists of the respondents general information, part-2 behavioral characteristics and Part-3 was consists of Physical examination, recording blood pressure and anthropometrical measurements examination by checklist, clinical examination and laboratory tests.

3.9. Blood pressure Measurement:

Measurement of blood pressure was made on each study participant with an aneroid type of sphygmomanometer using a standardized technique.

3.10. Diagnosis of Myocardial Infarction patients:

This study was performed on 60 consecutive patients of acute Myocardial Infarction (AMI) admitted to the Department of cardiology, NICVD, for treatment and irrespective of age and Sex. All patients of acute anterior, inferior both anterior and inferior, and right ventricular infarction with inferior were included in the study. Patients were diagnosed on the basis of following criteria:

- Chest pains that characteristic of AMI.
- Increased level of cardiac enzymes in serum. Creatine kinase (CK)

3.11. Treatment

- Bed rest
- Sedative
- Beta- blocker
- Anti coagulant drug
- Anti ulcer drug
- Inhalers
- Injections

3.12. Study period:

Study period will be one year commencing from February 2008 to May 2009. To complete the study in time a work schedule is prepared depending on different task of the study .The six months were spent on board meeting for literature review, selection of topic, development of the protocol. Subsequent months spent on official correspondence, data collection, data analysis, report writing and submission of report.

3.13. Data analysis:

All the data were checked after collection. Then data was entered into computer and the different risk factors (%) of MI were calculated using Microsoft Excel. The result are given as table, bar and pie chart.

CHAPTER 4

RESULT

To find out the relationship between life style risk factors of myocardial infarction and the drugs that are commonly used for myocardial infarction, a study was performed in the National Institute of Cardiovascular Disease and the data were collected from the selected purposively from admitted patients with MI at NICVD. A total of 60 respondents were included in the study. Among them 53 were male and 7 were female.

4.1. Gender distribution of patients suffering from myocardial infarction (%).

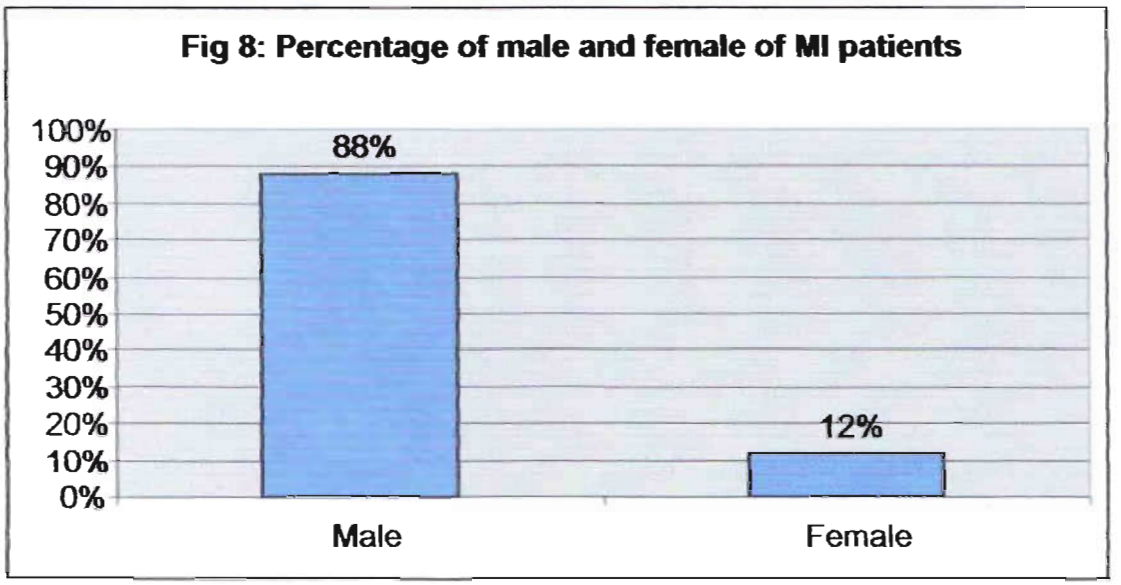

Fig 8 shows that among 60 patients 88% male and 12% female patients suffered from myocardial infarction.

4.2. Age distribution of patients suffering from Myocardial Infarction:

Age Range	Patients (%)
25-30	3
31-35	0
36-40	5
41-45	7
46-50	9
51-55	4
56-60	18
61-65	5
66-70	2
71-75	4
76-80	2
81-85	1

Table 3 shows different age of patients with myocardial infarction.

This study was conducted among 60 respondents of both sexes and patients age ranged from 25-85 years. But prevalence of MI was higher in the age group of 56-60. So there was a high risk of MI in this age group.

4.3. Different religions of patients suffering from MI (%)

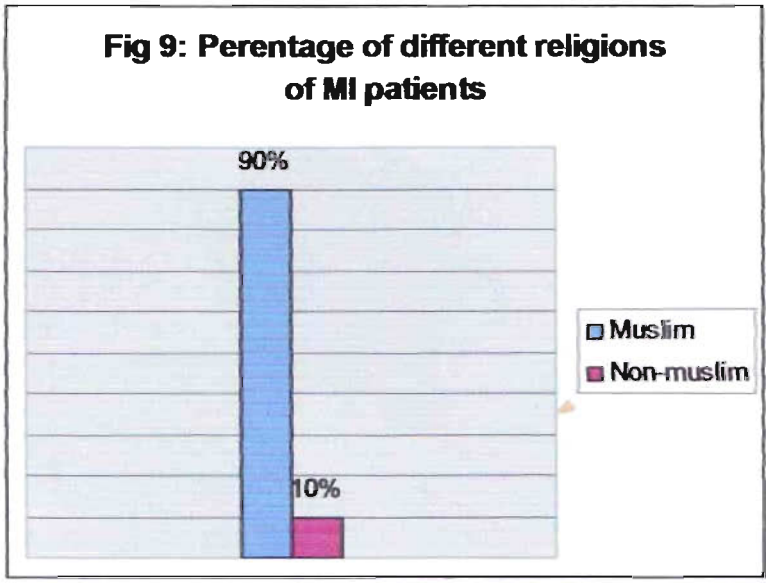

Fig 9 shows that among 60 patients ninety (90%) were Muslims, and ten (10%) were Non Muslims.

4.4. Different marital status of MI patients (%).

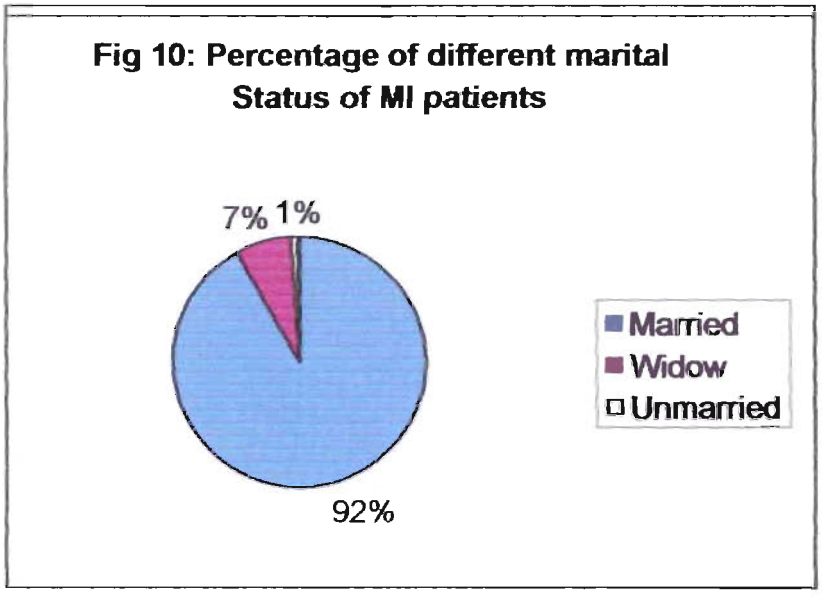

Fig 10 shows 92% patients were married, 7% were widow and 1% was unmarried with myocardial infarction.

Patients were grouped according to marital status. Majority were married. The result of the study showed that myocardial infarction was more common in married patients.

4.5. Educational status (%) of patient suffering from Myocardial Infarction

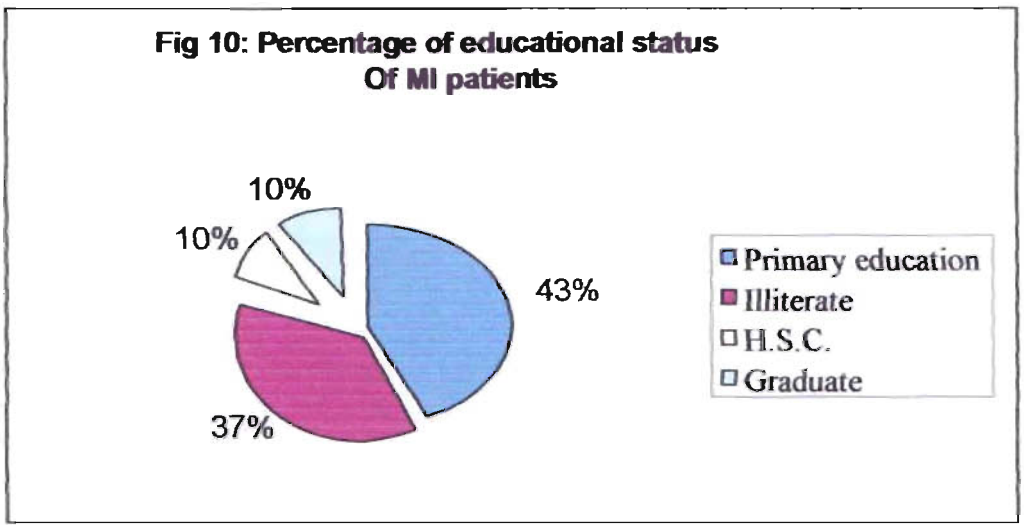

Fig 11 shows 37% patients were illiterate, 43% received primary education, 10% passed H.S.C., and 10% were graduated. The result of the study showed that myocardial infarction was more common in illiterate patients.

4.6. Occupation of MI Patient (%):

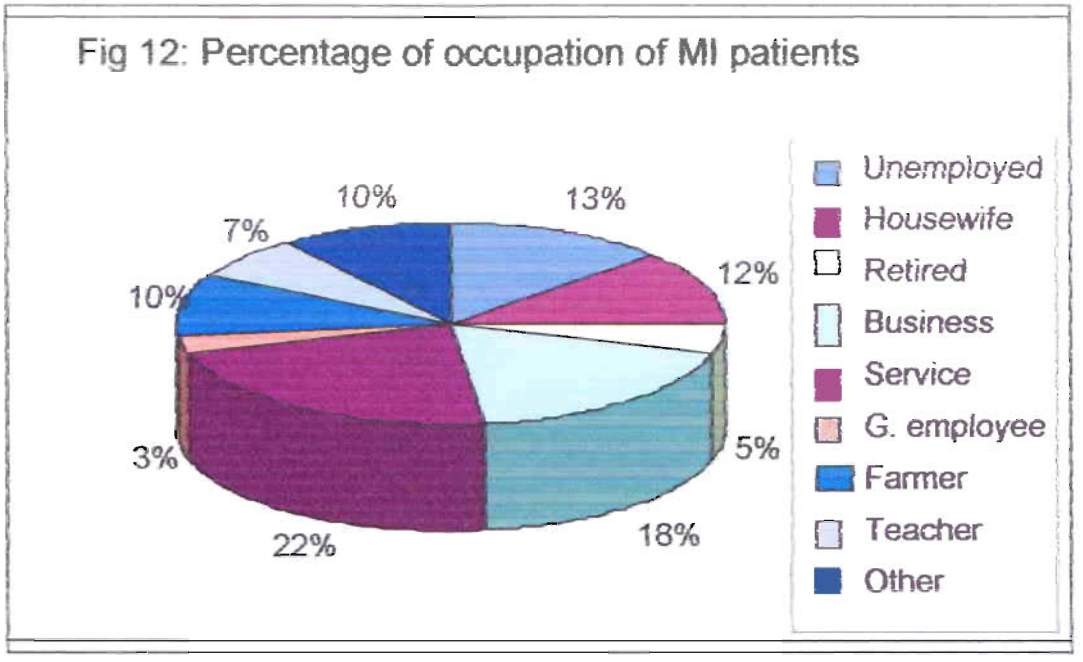

Fig 12 shows 13% patients were unemployed, 12% were housewife, 5% were retired, 18% were businessman, 22% were service holder, 3% were government employee, 10% were farmer, 7% were teacher, and 10% were other occupation of MI patients with myocardial infarction were present.

4.7. History of diseases in the family of MI Patients:

Disease name	No of patients
Diabetes	6
Hypertension	2
Asthma	2
Coronary heart disease	7
Both asthma and hypertension	3
Both diabetes and hypertension	2
Both coronary heart disease and hypertension	2

Table 4 shows the patient's family history. It is divided into eight groups. Twelve percent patient suffered from Coronary heart diseases (CHD), 10% suffered from Diabetes, 3% from asthma and 3% from hypertension. Both hypertension & diabetes were found in 3% patients, both CHD & hypertension were found in 4% patients and both asthma & hypertension were found in 5% patients. This result shows that coronary artery disease was the major cause of MI in patients.

4.8. MI patients suffering from other Diseases (%):

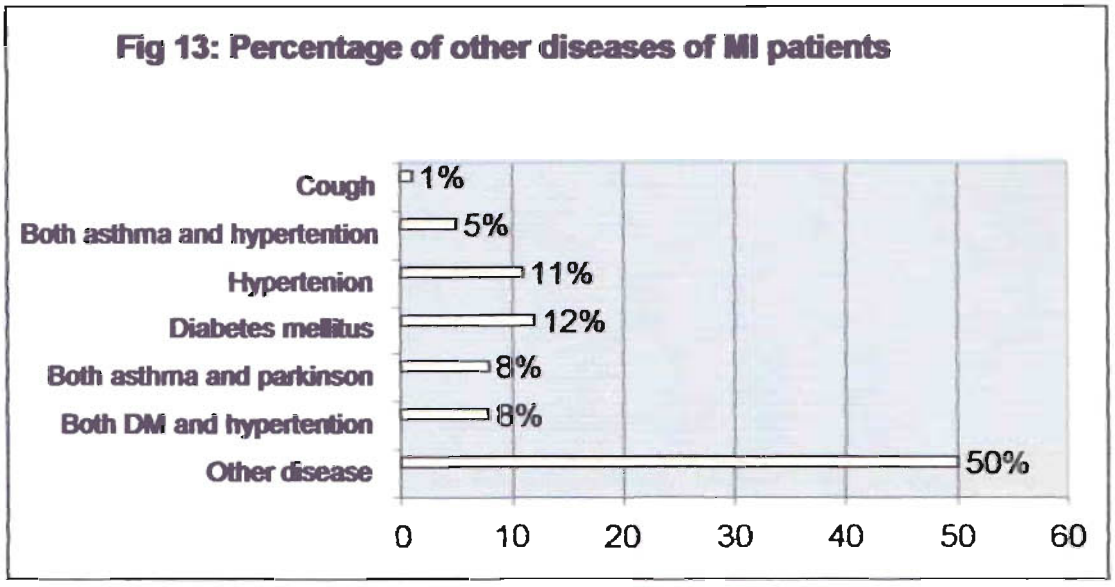

Fig 13 shows that there were MI patients who suffered from other diseases such as Diabetes mellitus (DM) (12%); hypertension (11%); both asthma and Parkinson (8%); DM and hypertension (5%); both asthma & hypertension (5%); both DM & hypertension (8%); cough (1%).There were many patients who suffered from other diseases.

4.9. MI patients suffering from blood pressure (%).

Diastolic Range	*Patients (%)*
50-60	*9*
61-70	*18*
71-80	*24*
81-90	*7*
91-100	*2*

Table 5: Percentage of Diastolic Range of the MI patients

High blood pressure increases the risks of the MI. Majority of the patients were more prevalent of MI who had suffered from high diastolic (71-80) and systolic (101-120) range. Hypertensions influences more risk of the MI.

Systolic Range	*Patients (%)*
80-100	*23*
101-120	*24*
121-140	*10*
141-160	*3*
161-180	*1*

Table 6: Percentage of systolic range of MI patients

4.10. Consumption of Table Salt by MI patients (%):

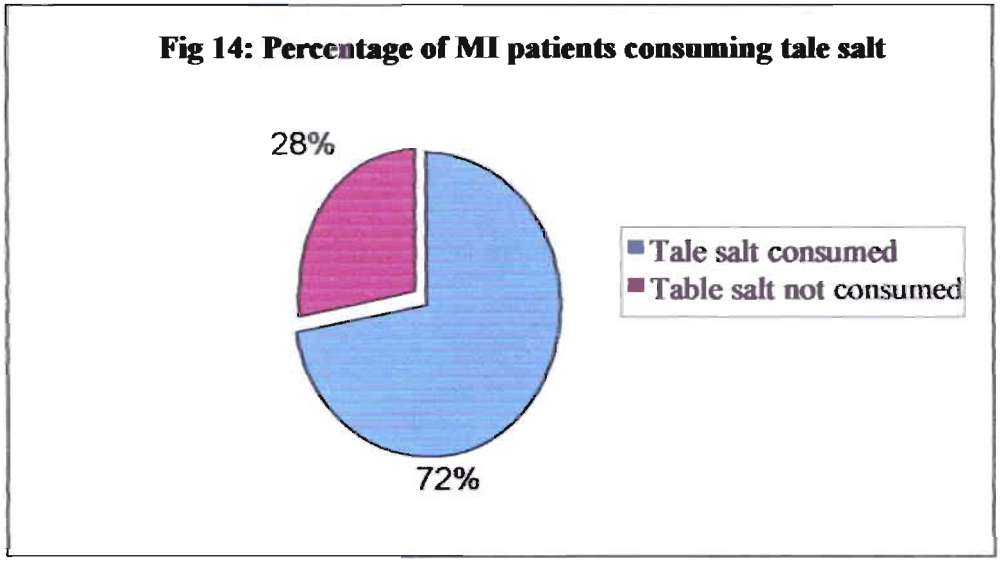

Fig 14 shows that percentage of consuming table salt by MI patients were 72%. Percentages of not consuming of table salt by MI patients were 28%. Consumption of table salt may be one of the risk factors of MI.

4.11. Commonly used medicine for MI patients (%).

Name of medicines commonly used for MI	Percentage of use
Atorvastatin	71%
Clopidogrel	70%
Omeprazole	58%
Nitroglycerin spray	51%
Oxygen inhaler	38%
Diazepam	41%
Isosorbide mononitrate	25%
Beta-adrenergic blocking agent	25%
H2-blocking agent	13%
Cardinex injection	10%
Captopril	15%
Acetaminophen	13%

Table 7 shows that the patients got different common medicines. MI patients received different medicines such as Trimetazidine Hydrochloride 5%, Losardil 1%, Atorpin injection 1%, Cephalosporin 5%, Cephradin 3%.

According to the result, majority of the MI patients used atorvastatin and Clopidogrel for the prevention of MI.

CHAPTER 5

DISCUSSION AND CONCLUSION

To find out the relationship between life style risk factors of myocardial infarction and the drugs that are commonly used for myocardial infarction, a study was performed in the National Institute of Cardiovascular Disease and Hospital (NICVD). The data were collected from patients of both sexes who were suffering from myocardial infarctions (MI). Patient's personal and medical history such as blood pressure and diagnosis profile were also collected. All the patients were treated with the appropriate medicines. The patients were interviewed by asking question in Bengali, using a thoroughly pre tested questionnaires about the modifiable and non-modifiable risk factors of MI.

The most important observation of the study is that the age group of 40-75 years had the highest incidence of MI. Five (5%) percents of patients belonged to age group of less than 40 years had suffered from MI. This observation has important implications that young and middle aged group also suffered from MI which is the most productive period of life. Another important finding of the study is that the female patients were only 7 in number. Majority of the females included in the study belonged to age group of over 50 years compare to male patients. This may be due to the sex hormones that protect female from getting on MI at an earlier age.

It is true that the prevalence of CAD among women is lower before menopause, the risk of CAD rises in women after menopause. At age 75, a woman's risk for CAD is equal to that of a man. CAD is the leading cause of death and disability in women after menopause. In fact, a 50-years-old woman faces a 46% risk of developing CAD and a 31% risk of dying from coronary artery disease.

After menopause, the production of estrogen by the ovaries gradually diminishes over several years. Along with this reduction, there is an increase in LDL ("bad" cholesterol) and a small decrease in HDL ("good" cholesterol). These changes in lipid levels are believed to be one of the reasons for the increased risks of developing CAD after menopause. Estrogen would protect women against CAD **(Daniel Kulick, FACC, FSCAI and Dennis L)**

The results of the study showed that patients of age ranged from 56 to 60 years were more prevalent to MI. Among 60 MI patients, 88% male and 12% female patients had been suffering myocardial infarction. The results showed that 92% patients were

married, 37% were not educated, and 13% were unemployed. About 25% patients were service holder, 18% were businessman and 12% were housewives. There were MI patients who suffered from other diseases such as Diabetes mellitus (DM) (12%); hypertension (11%); both asthma and Parkinson (8%); DM and hypertension (5%); both asthma & hypertension (5%); both DM & hypertension (8%).

Majority of the patients received Atorvastatin (71%), Clopidogrel (70%), Omeprazole (58%), Nitroglycerin spray (51%), Oxygen inhaler (38%), Diazepam (41%), Isosorbide mononitrate (25%), Beta-adrenergic blocking agent (25%), H2-blocking agent (13%), Trimetazidine Hydrochloride (5%), Losardil (1%), Atorpin injection (1%), Cephalosporin (5%), Cephradin (3%)., Cardinex injection (10%), Captopril (15%), Acetaminophen (13%) for the control and prevention of MI.According to the result, majority of the MI patients used atorvastatin and Clopidogrel for the prevention of MI.

Percentage of consuming table salt by MI patients was 72% and percentage of not consuming of table salt by MI patients was 28%. This result indicates that the people who were taking table salt with their food, they have increased chance of MI.

High blood pressure was increased the risk of the MI. Majority of the patients suffered from high diastolic (71-80) and systolic (101-120) pressure.

Including the above mentioned factors the study has been designed to explore the relationship between life style risk factors of myocardial infarction and the drugs that are commonly used for myocardial infarction. The outcome of this study may provide important information for future in depth study as well as may help in providing ideas for policy maker to formulate proper intervention strategies among the people having risk factors responsible for developing of cardiovascular disease in context of Bangladesh.

Further heart attacks can be prevented by aspirin, beta blockers, ACE inhibitors, discontinuing smoking, weight reduction, exercise, good control of blood pressure and diabetes, following a low cholesterol and low saturated fat diet that is high in omega-3-fatty acids, taking multivitamins with an increased amount of folic acid, decreasing LDL cholesterol, and increasing HDL cholesterol.

Greater public awareness about heart attacks and changes in lifestyle may contribute to a dramatic reduction in the incidence of heart attacks. The summary of the study suggests that properly taking medication and treatment are very important to prevent myocardial infarction in patients with other risk factors.

This is a hospital based study so it can not be taken as a prototype for the whole country, though it gives us idea about age, sex, life style, occupation, education etc. that influence MI in our country.

Myocardial infarction is the commonest cause of heart disease and the most important single cause of death in the affluent countries of the world **(Julian, DG. Cowan, JC. 1992).**

The commonly used criteria for the clinical diagnosis of myocardial infarction as defined by the world health organization include chest pain, classic ECG abnormalities and elevation of serum cardiac enzymes. Echocardiography has recently gained popularity as a noninvasive diagnostic aid in the evaluation of various forms of heart disease **(Horowitz, RS. Morganroth, J. 1982).**

The purpose of treatment of MI especially the thrombolytic treatment is to reopen the completely occluded coronary artery and to clear the clot and terminate myocardial ischemia and hence improving left ventricular function, reducing the complication and reducing the short term mortality.

Ischemic heart disease is a major health problem world wide. This disease kills and disables people in their most productive years in both sexes, in every racial and ethnic group extracting a toll in quality of life in old age **(Kennedy, JW. Ritchi, JL. Davis, KB).**

In our study we can conclude that administration of proper medicine for MI may reduce the complication and reducing the short term mortality.

Further studies are needed to explore the modifiable and non modifiable risk factors and the commonly used drugs to reduce the complication and short term mortality from MI.

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