Introduction
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Coronary artery disease is the most common serious chronic life threatening illness in USA where more than 11 million persons have coronary artery disease. It continues to remain the leading cause of mortality and morbidity. Although the prevalence of CAD varies widely throughout the globe, prevalence is lowest in Japan, France and highest in USA & Finland.

Coronary artery disease (CAD) has become a major public health problem in India. CAD is emerging as a major killer in India. Some recent data have suggested that CAD will replace infections as the major killer by the year 2015.

CAD has become one of the most common cardiac disorders that affects the adult Indian population. In many cases, CAD afflicts Indians in prime of their lives. It is well known that the prevalence of CAD increases with age and recent studies have demonstrated that CAD is the leading cause of death in people above 55 years of age\(^1\). It should, however, be noted that, based on recent observations, the prevalence of CAD in younger age groups (often referred to as premature CAD) appears to be increasing in people of
Indian origin\textsuperscript{2,3}. It has been reported that some may develop clinical manifestations of CAD in the second or third decade of life. Even in women who are relatively protected from CAD in the premenopausal period, after 65 years of age, CAD becomes the leading cause of death. With improved survival and increased life expectancy, the number of patients with CAD is likely to increase. A recent metaanalysis also showed that there has been a ninefold increase in CAD in urban population from the 1960s to the 1990s and the two fold increase in rural population from the 1970s to the 1990s\textsuperscript{4}. The meta-analysis also showed that this increase is more in younger age groups (20-39 years) and it is also affecting men more than women.

Despite the recent increase in the incidence of premature CAD in Indians, little is known about the pathogenesis of atherosclerosis and premature CAD in Indians. Evaluation of major coronary risk factors in Indian patients undergoing coronary arteriography has shown that more than one third of patients with CAD have no major risk factor\textsuperscript{5}. There is an urgent need to examine the role of environmental factors, metabolic abnormalities and genetic factors responsible for premature CAD in Indians.
Recent epidemiologic observation have clearly demonstrated that of all ethnic groups, the people of Indian origin have one of the highest incidence of CAD\textsuperscript{6}. Most of these studies have also documented that CAD in Indians frequently occur at an early age (usually in prime years - the 3\textsuperscript{rd} or 4\textsuperscript{th} decade of life) and the disease is more diffuse and severe. In addition the results of some studies have shown that when compared with age and gender matched individuals living in a similar geographic location, the Indians with CAD have a significantly increased risk of myocardial infarction and cardiac death (often at a young age), which occurs earlier in the course of the disease process. The incidence of premature CAD has been documented to be up to 3 times higher when compared with people of similar age in western world. Of those Indian patients with CAD who are fortunate enough to come to clinical attention before a fatal coronary event occurs, many are considered poor candidates for myocardial revascularization (coronary bypass surgery and coronary angioplasty) because of the diffuse and advanced extent of angiographically demonstrated CAD.
It is also becoming increasingly apparent that the natural protection for premenopausal women is often lost for many women of Indian origin, particularly those residing in South Africa and England. The predilection for premature CAD in Indian women might well be because of increased incidence of diabetes and obesity and could provide important insight into the basic pathophysiologic process responsible for the accelerated premature CAD in Indians. The available data clearly indicate that premature and accelerated CAD is growing health problem for people of Indian origin. Although no specific data are available, it seems reasonable to consider that because the disease afflicts most Indian in the prime of their professional careers and early years of family life, it would have significant socio-economic consequences. Clearly then, there is an urgent need to pay close attention to the problem of premature CAD in Indians and define the underlying pathophysiologic processes involved so that potential solutions to resolve the problem can be implemented.

Coronary artery disease has been defined as "Impairment of heart functions due to inadequate blood flow to the heart compared to its needs, caused by atherosclerotic narrowing
and occlusion of coronary arteries of the heart. CAD may manifest itself in many ways.

A. Angina pectoris
   - Stable
   - Unstable
     - Prinzmetal’s variant
     - Silent ischemia

B. Myocardial infarction
   - Q-wave
   - Non Q-wave

C. Unexplained arrhythmias
D. Unexplained CCF
E. Abnormal X-ray chest, ECG, TMT, CART
F. Sudden death
G. Abnormal echo. Th. ventriculography & MRI.

The major risk factor for CAD includes:

Modifiable

(i) Cigarette smoking
(ii) Hypertension
(iii) Elevated LDL cholesterol
(iv) Diabetes
(v) Post menopausal status
(vi) Obesity
(vii) Left ventricular hypertrophy
(viii) Stress
(ix) Physical inactivity
(x) Personality
Non Modifiable

(i) Age

(ii) Sex

(iii) Family history of premature CAD & sudden death

There are only few studies on its prevalence in the general population in India. On screening of persons over the age of 30 years by a 12 lead ECG, in Chandigarh (urban population) the prevalence was found to be 65.4 and 47.8/1000 males and females respectively\(^{11}\). In a rural population from a village in Haryana the prevalence was 22.8 and 17.3 per 1000 males and females respectively\(^ {12}\). The current ICGR survey has shown a prevalence rate of about 80-120/1000 and it is estimated that there are about 40 millions patients of CAD in our country.

**Angina Pectoris**

Angina pectoris is the term used to describe discomfort due to transient myocardial ischemia and constitutes a clinical syndrome rather than a disease, it may occur whenever there is an imbalance between myocardial oxygen supply and myocardial oxygen demand (MVO2). Coronary atheroma is by far the most common cause but angina is also
a feature of aortic valve disease, hypertrophic cardiomyopathy and some other forms of heart diseases.

**Stable Angina**

Presents classically by left sided or central chest pain that is precipitated by exertion and promptly relived by rest. Most patients describe a sense of oppression or tightness in the chest- “like a band around the chest”. Pain may be denied. Angina victim often closes a hand around the throat, puts a hand or clinched fist on the sternum or places both hands across the lower chest, many patients report a choking sensation. Breathlessness is sometimes a prominent feature. The pain may radiate to the neck or jaw and is often accompanied by discomfort in the arms particularly the left, the wrists and some times the hands; the patient may also describe a feeling of heaviness or uselessness in the arm. Occasionally the pain is in epigastric or interscapular region. Angina may occur at any of these places of reference without chest discomfort but a history of precipitation by effort, and relief by rest or sublingual nitrate should still allow the condition to be recognised.
Symptoms tend to be worse after meal, in the cold, and when walking uphill or against a strong wind. Some patients find that the pain comes when they start walking and later it does not return despite greater effort (start-up angina) (walkthrough angina). Some experience the pain when lying flat (decubitus angina), and some are awakened by it (nocturnal angina).

Differential diagnosis of this includes musculoskeletal, pericardial and oesophageal pain. Musculoskeletal pain is provoked by specific movement rather than by walking and background pain often persists at rest, there may be associated chest wall tenderness. The pain of pericarditis is occasionally provoked by exercise.

Angina occurring at rest may be confused with oesophagitis with or without a hiatus hernia, but pain due to oesophagitis usually has a burning quality and is relieved by antacids.

Electrocardiogram may show evidence of previous myocardial infarction but is otherwise normal in most patients. Occasionally there is T wave flattening or
inversion in some leads providing non specific evidence of myocardial ischaemia or damage.

**Unstable Angina**

The term is used to described patients who present with rapidly worsening angina (crescendo angina), severe angina at rest or prolonged and severe ischemic chest pain without ECG or enzyme evidence of significant myocardial infarction. It may present as a new phenomenon or against a background of chronic stable angina.

The culprit lesion is usually a complex ulcerated or fissured atheromatous plaque with adherent thrombus and local coronary artery spasm. Episodes of myocardial ischemia are due to an abrupt reduction in coronary blood flow caused by thrombosis or spasm (supply-Led-Ischemia). In contrast the stable angina is related to a fixed obstruction and is usually precipitated by an increase in myocardial oxygen demand (Demand-Led-Ischemia) ECG usually shows acute ST segment elevation or depression during episodes of myocardial ischemia, the ECG changes are sometimes prolonged.
MYOCARDIAL INFARCTION

Myocardial infarction generally results from abrupt decrease in coronary blood flow. This generally follows a thrombotic occlusion of a coronary artery previously narrowed by atherosclerosis\textsuperscript{14,15}. Infarction occurs when an atherosclerotic plaque fissures, ruptures or ulcerates and with conditions favouring thrombogenesis (factors which may be local or systemic) a mural thrombus forms, leading to coronary artery occlusion\textsuperscript{16}. Coronary artery spasm may cause acute myocardial infarction in rare patients with normal coronary arteries. It has been postulated that spasm may cause the final damage that can initiate formation of an atherosclerotic plaque. An association between coronary artery spasm and coronary artery thrombosis has also been documented clinically.

Additional infarction may be due to coronary artery occlusion secondary to coronary emboli. The causes of coronary embolism are numerous-infective and marantic endocarditis, mural thrombi, prosthetic valve fragmentation, neoplasms, air that is introduced at the time of cardiac surgery and calcium deposits from manipulation of calcified valves at operation. Oral contraceptive use also probably
can be associated with AMI in healthy women, the mechanism of this association may operate through an increased tendency of thrombosis. Viral infections, particularly with Coxsakie-B may be an uncommon cause of AMI. Syphilitic aortitis may produce marked narrowing or occlusion of one or both coronary ostia whereas Takayasu arteritis may result in obstruction of coronary arteries. Necrotizing arteritis, polyarteritis nodosa, muco-cutaneous lymphnode syndrome (Kawasaki disease), systemic lupus erythematosus and giant cell arteritis can cause coronary occlusion. Therapeutic levels of mediastinal radiation can cause thickening and hyalinization of the wall of coronary arteries, with subsequent infarction, AMI may also be the result of coronary arterial involvement in amyloidosis, Hurler syndrome, pseudoxanthoma elasticum and homocystinuria, cocain abuse may cause myocardial infarction in patients with normal coronary arteries.

A variety of hematological disorders causing in situ thrombosis in the presence of normal coronary arteries such as polycythemia vera, cyanotic heart disease with polycythemia, sickle cell anemia, DIC, thromcytosis and thrombotic thrombocytopenic purpura, can cause myocardial
infarction. The conditions which augment the oxygen demand (Thyrotoxicosis), amphetamine use, are also suggested causes, hypotension secondary to sepsis, blood loss, or pharmocological agents can precipitate myocardial infarction.

AMI may be precipitated by factors such as severe physical exercise, mental stress and medical or surgical illness. Other factors reported as predisposing to AMI include respiratory tract infection, hypoxaemia of any cause, pulmonary embolism, hypoglycemia, administration of ergot preparations, serum sickness, allergy and wast stings\textsuperscript{17}.

A circadian periodicity has been associated to the time of onset of AMI. The early morning hours 6.00 a.m. to 12.00 noon are associated with peak incidence of AMI and parallels the onset of other related phenomena including sudden cardiac death, thrombotic stroke and transient myocardial ischemia in early morning hours are associated with rise in plasma catecholamines and cortisol and increase in platelet aggregation\textsuperscript{19}. The characteristic circadian pattern is absent in patients receiving betablocker or aspirin therapy before the presentation with AMI.
AMI presents clinically as retrosternal or precordial pain, spreading frequently to both sides of the anterior chest, more on left side. The pain radiates down the ulnar aspect of the left arm, producing a tingling sensation in the left wrist, hand, and fingers. The pain is prolonged usually lasting for more than 30 minutes and frequently for a number of hours. The discomfort is described as constricting, crushing, oppressing, or compressing. The patient complains of a sensation of heavy weight or squeezing in the chest. The pain may also be characterized as a stabbing knife like, boring, or burning discomfort.

The discomfort may radiate to the shoulders, upper extremities, neck, jaw, and interscapsular region, again usually favouring the left side. Associated symptoms are dyspnoea, diaphoresis, nausea, vomiting belching, diarrhoea and an urge to defecate.

Population studies suggest that between 20-60% of non fatal MIs are unrecognized by the patient and are discovered only on subsequent routine electrocardiagraphic or postmortem examination. Of these unrecognized infarctions, approximately half are truly silent, with the patient unable to recall any symptoms. Unrecognized or silent infarction
occurs more commonly in patients without antecedent angina pectoris and in patients with diabetes and hypertension. Silent MI is often followed by silent ischemia. In elderly patients AMI may present as sudden onset of breathlessness which may progress to pulmonary oedema. Other less common presentations are sudden loss of consciousness and confusional state.

Patients suffering an AMI often appears anxious and in considerable distress. An anguish facial expression is common. Pallor associated with perspiration and coolness of the extremities occurs commonly. Although many patients have a normal pulse rate and blood pressure, within the first hour of infarction, about one fourth of patients with anterior infarction have manifestations of sympathetic nervous system hyperactivity (tachycardia and/or hypertension), and upto one half with inferior infarction shows evidence of parasympathetic hyperactivity (bradycardia and/or hyotension).

The precordium is usually quiet and the apical impulse may be difficult to palpate. In patients with anterior wall infarction, an abnormal systolic pulsation caused by dykinetic bulging of infarcted myocardium may develop in
the periapical area. Third heart sound ($S_3$) and fourth heart sound ($S_4$) may be present along with diminished intensity of $S_1$ and $S_2$. Rarely paradoxical splitting of second heart sound can be heard. A transient apical systolic murmur due to mitral regurgitation caused by dysfunction of papillary muscle is commonly audible during acute myocardial infarction. Jugular venous distention occurs commonly in patients with right ventricular infarction, Basilar rales are frequently detected. temperature upto 38°C may be found towards the end of first week of AMI. Pericardial friction rub is audible along the left sternal border or just inside the point of maximal impulse especially in patients with transmural infarction in approximately 10% cases.

The ECG changes in acute myocardial infarction present as Q waves or loss of R waves in patients with Q-wave MI and only ST segment and/or T-wave changes in non Q-wave MI. Total occlusion of the infarct related artery produces ST segment elevation, and ultimately evolves in a Q-wave MI. a small proportion may sustain only a non Q-wave MI. A minority of patients who present initially without ST segment elevation may develop a Q-wave infarction.
The initial chest X-ray can detect signs of ventricular failure and cardiomegaly. Signs of pulmonary congestion may be present. The serum cardiac markers are useful indicators for diagnosing acute myocardial infarction. These are released in large quantities into the blood from necrotic heart muscle following myocardial infarction. Among them the important are creatine Kinase (CK), serum aspartate transaminase (AST) and SGOT, lactic dehydrogenase (LDH), cardiac specific troponins and myoglobin.

Creatinine Kinase (CK) rises within 4-8 hours following the onset of AMI and declines to normal within 2-3 days. The peak CK occurs on average at about 24 hours, CK is not specific because it may also increase in patients with muscle disease, alcohol intoxication, diabetes mellitus, skeletal muscle trauma, vigorous exercise, convulsion, intramuscular injections, thoracic outlet syndrome and pulmonary embolism. Two isoforms of CK viz CK-MB₁ and CK MB₂ has been identified.

In one study an absolute level of the CK-MB₂ isoform of >1.0 U/L or ratio of CK-MB₂/CK-MB₁ > 1.5 had a sensitivity for diagnosis of AMI of 59 percent at 2-4 hours and of 92 percent at 4-6 hours.²²
Serum aspartate transaminase (AST) starts to rise about 12 hours after infarction and reaches a peak on the first or second day, returning to normal within 3-4 days. False positive elevations occur frequently with most hepatic or skeletal muscle disease, following intramuscular injections, pulmonary embolism & with shock. Because the time course of elevation offers no advantage relative to other serum markers, its incremental benefit for the diagnosis of AMI is negligible, and it is no longer routinely used.

Lactic dehydrogenase (LDH) starts to rise after 24-28 hours of the onset of AMI, reaches a peak at 3-6 days and returns to normal levels 8-14 days after the infarction. Total LDH, although sensitive, is not specific, false positive elevations, occur in patients with hemolysis, megaloblastic anemia, leukemia, liver disease, hepatic congestion, renal disease, a variety of neoplasms, pulmonary embolism, myocarditis, skeletal muscle disease, shock. LDH comprises of five isoenzymes. LDH₁ is found predominantly in the heart. Therefore increased LDH₁ is a more specific indicator of myocardial infarction than total LDH. Its sensitivity exceeds 95%. However, LDH isoenzymes need to be measured only when the initial CK or CK-MB elevation
might have been missed (after 48 hours). Because they are not more sensitive than CK-MB, newer & more cardiac-specific late markers such as cTnI or cTnT have also emerged.

Myoglobin is a protein released into the circulation from injured myocardial cells and can be demonstrated within few hours after onset of infarction. Peak levels are reached considerably earlier (1-4 hours) than peak values of serum CK. A more rapid rise in serum myoglobin has been observed following reperfusion and its measurement has been suggested as a useful index of successful reperfusion.

Cardiac-specific Troponins (cTnT and cTnI) are antibodies produced against the cardiac muscle, in patients with AMI, cTnT and cTnI first begin to rise above the upper reference limit by 3 hours from the onset of chest pain. Elevation of cTnI may persists for 7-10 days followings AMI elevations of cTnT may persist for upto 10-14 days, the kinetics of release of cTnT are similar for patients with Q-wave and non Q-wave AMI, patients with AMI who undergo successful recanalization of the infarct-related artery have a rapid release of cTnT, this may be useful as indicator for reperfusion23.
Other promising serum cardiac markers that are under study include heart fatty acid binding protein (hFABP), myosin light chain (MLC), myosin heavy chains (MHC) and glycogen phosphorylase isoenzyme BB (GPBB).

The mortality with acute myocardial infarction is approximately 30% with more than half the death occurring before the stricken individual reach the hospital. An additional 5-10% of the survivors of AMI die in the first year, despite major therapeutic advances in the treatment of ischemic heart disease.

In USA, steady decline in the mortality rate from AMI has been observed across several population group. This drop in mortality appears to be caused by a fall in the incidence of AMI and a fall in the case fatality rate. Now clinicians are more astute at identifying those patients who are at increased risk of AMI and benefit from more aggressive prophylactic cardiovascular treatment to prevent it from occurring e.g. use of intravenous nitroglycerine during non cardiac surgery.

Several landmarks in the management of patients have contributed to the decline in mortality from AMI. In the mid
1960's the concept of coronary care units was introduced. The first decade of coronary care was notable by detailed analysis and vigorous management of cardiac arrhythmias. Subsequently introduction of the pulmonary artery balloon flotation catheter set the stage for bedside hemodynamic monitoring and more precise management of heart failure and cardiogenic shock associated with AMI. The modern reperfusion era of coronary care was ushered in by intra coronary and then intravenous thrombolysis, increased used of aspirin and the development of transluminal coronary angioplasty PTCA for AMI.

Drug therapy continues to be an integral aspect of the treatment of patients with AMI, with note worthy advances in the use of beta-adrenoceptor blockers, antithrombotic regimens, nitrates and angiotensin converting enzyme (ACE inhibitors).

**NEED FOR SYSTOLIC & DIASTOLIC FUNCTION ASSESSMENT**

In patients of CAD left ventricular dysfunction remain the single most important pridictor of mortality\(^\text{24}\). In patients with acute myocardial infarction, heart failure is characterized either by systolic dysfunction alone or by both
systolic and diastolic dysfunction. Clinically LV diastolic dysfunction leads to pulmonary congestion (by pulmonary venous hypertension) which cause breathlessness. Where as systolic dysfunction is principally responsible for depression of cardiac output and ejection fraction leading to hypotension and fatigue. Clinical manifestation of left ventricular failure become more common as the extent of the injury to left ventricle increases. Mortality increases in association with the severity of the haemodynamic deficit\textsuperscript{25}. This shows the importance of assessment of left ventricular function.

\textit{Assessment of LV function:} can be done with following techniques:

- Echocardiography
- Radionuclide angiography
- Gated SPECT (single photon emission computed tomography)
- Gated MRI
- Contrast ventriculography
ECHOCARDIOGRAPHY

Of all the non-invasive techniques available for the assessment of regional & global left ventricular function at rest, echocardiography is the most versatile, reproducible modality, it provides the most ancillary information, at a low cost\textsuperscript{26}.

Two dimensional echocardiography provides images of the heart and great vessels. When good window are obtained, it is superbly well suited for evaluation of global and regional LV systolic function because of its high spatial and temporal resolution and its ability to define both regional wall thickening and inward endocardial excursion.

When compared with all other techniques, it is the preferred initial test to diagnose heart muscle disease of yet unknown etiology like ischemic cardiomyopathy, nonischemic dilated cardiomyo-pathy, hypertrophic cardiomyopathy and restrictive heart disease. Echocardiography also permits the simultaneous assessment of valvalar and pericardial abnormalities.

Echocardiography has an advantage over others techniques for assessing LV function in its ability to
accurately assess regional myocardial thickening. Regional thickening is better marker of regional function than the regional wall motion. The only other technique that perhaps permits a more accurate assessment of regional systolic thickening is gated MRI. But it is more expensive than two dimensional echocardiography and can not be performed at the bed side in clinically ill patients.

**OTHER ADVANTAGES OF ECHOCARDIOGRAPHY**

- Early diagnosis of AMI can be made.
- Complication of AMI can be detected like- RV infarction, acute MR due to papillary muscle rupture or dysfunction, VSD, true or false aneurysm, pericardial effusion etc.
- It is more sensitive as well as specific than ECG for detection of left ventricular hypertrophy and is an excellent technique for estimating LV mass which has been shown to independently predict cardiovascular morbidity and mortality\(^{27}\).
- It can also be performed in emergency room in patients with chest pain and a possible acute ischemic syndrome.
- Transesophageal echo. can be performed at the bed side in an acutely ill patient with shock in intensive care unit
setting to help to identify the etiology of haemodynamic disturbances.

- Doppler echo. is excellent for detection of diastolic dysfunction.
- No ionizing radiation or contrast material is needed.
- Low cost & non invasive.

**LIMITATIONS**

- Poor acoustic windows in some patients like- COAD, obesity.
- High operator dependence
- Inability to visualize all regions of left ventricle in every patients.

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