A Dissertation on

# *"Prevalence of Metabolic Syndrome in Urban Low Socioeconomic Group Patients with Symptomatic Coronary Artery Disease"*

**submitted to**
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# Certificate

This is to certify that "***Prevalence of metabolic Syndrome in Urban Low Socio-economic Group Patients with Symptomatic Coronary Artery Disease***" is bonafide work done by **Dr. Jayaprakash K.P**., post graduate student, Department of Internal Medicine, Kilpauk Medical College, Chennai-10 under my guidance and supervision in fulfillment of regulations of the Tamilnadu Dr. M.G.R. Medical University for the award of M.D. Degree Branch I (General Medicine) during the academic period from March 2005 to March 2008.

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# CONTENTS


| Chapter No. | Titles | Page No. |
|---|---|---|
| 1. | Introduction | 1 |
| 2. | Aim of study | 3 |
| 3. | Review of Literature | 5 |
| 4. | Materials and methods | 27 |
| 5. | Results | 33 |
| 6. | Discussion | 59 |
| 7. | Conclusions | 67 |
| 8. | Limitations | 70 |

**Appendix**

Bibliography

Abbreviations

Questionnaire

Master Chart

# Introduction

It is estimated that more than one fifth of world's population lives in India. Today, India is one of the fastest growing economies in the world. Urbanization is rapid as ever. Young and old abandoning healthy Indian lifestyle and culture for western culture in the name of modern living. Sedentary lifestyle, low fibre, high fat and energy rich foods have penetrated even the rural India in the name of globalization. All these will come not without cost. India is now facing paradox of malnutrition on one hand and epidemic of obesity on the other.

Indians three times higher risk of developing Coronary Artery Disease (CAD) compared to Chinese and are 20 times more likely to die due to CAD compared to native black or white South Africans. [1, 2] The SHARE study demonstrated that South Asians had higher prevalence of cardiovascular disease compared to Europeans and Chinese living in Canada.[3] In India 2.78 million deaths are due to cardiovascular diseases, of which over 50% is due to CAD, making CAD the number one killer disease in our country.[4] In Jaipur Heart Watch – 2 study conducted in 2002, prevalence of CAD was reported to be 8.2%.[5]

Over 35 million diabetic patients live in India, making India the diabetic capital in the world. These numbers expected to double by the year 2030.[6] Thus India faces the dangerous dual epidemic of diabetes and CAD. The major root of both epidemics lies in "Metabolic Syndrome".

Lots of studies from west on metabolic syndrome represent middle and higher socioeconomic classes of society. Those studies which assess the burden of metabolic syndrome in CAD patients living below poverty line in India is still lacking. Thus it is worthwhile effort to find out the burden of metabolic syndrome in less privileged poor CAD patients of Chennai city. Kilpauk Medical College Hospital is being a Government run institution serves these patients either free of cost or with minimal fee. Majority of patients attending the OPDs of the hospital are poor, hence giving good opportunity to study the problem pertaining to these patients.

# Aim

1. To find out the prevalence of metabolic syndrome in urban low socioeconomic group patients with symptomatic coronary artery disease using modified International Diabetic Federation (IDF) consensus worldwide definition of the metabolic syndrome, 2005.
2. To analyze the differences in the prevalence of metabolic syndrome among age groups, sex, social class and chronic and acute coronary syndromes.

# Objectives

1. To diagnose symptomatic coronary artery disease in low socioeconomic group patients.
2. To classify patients in to social classes based on family income.
3. To measure waist circumference, blood pressure, fasting blood sugar, fasting high density lipoprotein (HDL) cholesterol and triglyceride.
4. To find out the prevalence of Central Obesity, Hypertension, Impaired Fasting Glucose or Diabetes mellitus, Hypertriglyceridemia and low HDL cholesterol and to analyze the differences in their prevalence among the age groups, sex, social class and chronic and acute coronary syndromes.
5. To apply modified IDF, 2005 definition for metabolic syndrome to the data and diagnose metabolic syndrome.

6. To find the prevalence of metabolic syndrome and analyze the differences in its prevalence among the age groups, sex, social class and chronic and acute coronary syndromes.

# Review of Literature

Some 250 years ago, JB Morgagni with the help of only a knife for anatomical dissection, an acute mind, and an observational skillfulness was able to identify the intraabdominal and mediastinal fat accumulation in android obesity.[7] He clearly described the association between visceral obesity, hypertension, hyperuricemia, atherosclerosis and obstructive sleep apnea syndrome, long before the modern recognition of this syndrome. The concept of insulin resistance is more than 250 years old and was first described in the 20th century by Himsworth, when in ***Lancet*** he wrote about subdivision of diabetes into insulin sensitive and insulin resistance in 1936. Yet it needed Prof. Gerald Raeven who delivered the famous Banting Oration[8] in 1988 to introduce the concept of Insulin Resistance. But he surprisingly missed obesity or visceral obesity from the definition which was later added as a crucial abnormality. Several terms are used for the same entity namely, Insulin Resistance Syndrome, Reaven's Syndrome, Metabolic Syndrome, Deadly Quartet, CHAOS (**C**oronary artery disease, **H**igh Blood Pressure, **A**dult Onset Diabetes (type 2), **O**besity, and **S**troke), New World Syndrome, Civilization Syndrome, Syndrome 'X' etc. The latest term used is 'Metabolic Syndrome' as per ATP III and WHO.[9] The clusters which make this syndrome and its etiopathogensis will keep getting varied in different ethnic populations, regions and countries. Factors like migration, socioeconomic status, lifestyle, nutrition habits play important role.

# Definitions of Metabolic Syndrome (MS)

Different definitions have been put forth by IDF, WHO, NCEP-ATP III and EGIR. While most definitions agree on essential components, i.e., glucose intolerance, obesity, hypertension and dyslipidemia, they differ in the cut-off point for criteria of each component of the cluster and the way of combining them to define MS. The definition used in WHO report, centers on diabetes and insulin resistance, whereas, the ATP III guidelines gives equal weightage to abdominal obesity, hypertension, hyperglycemia, hypertriglyceridemia and low HDL cholesterol. The IDF is closest to ATP III in that it includes the same variable but it differs in that central obesity is an essential component. Also waist measurement is set at a lower level than in ATP III and is ethnic-specific and the fasting hyperglycemia is set at the new American Diabetic Association (ADA) cut point for impaired fasting glucose (IFG). Moreover, it does not include of insulin resistance and hyperglycemia is not an obligatory component, which sets it apart from WHO and EGIR definitions.

The IDF, 2005, ATP III and WHO definitions are given in table 1. The European Group for the study of Insulin Resistance (EGIR) definition for metabolic syndrome is as follows:

1. Central obesity defined as waist ≥94cm (men), ≥80cm (women).
2. Blood pressure ≥140/≥90mmHg, or treated for hypertension.

3. Triglycerides >2.0 mmol/L, or HDL – cholesterol <1.0 mmol/L, or treated for dyslipidemia.
4. Fasting plasma glucose >6.1 mmol/L, but non-diabetic.
5. Presence of fasting hyperinsulinemia (i.e., levels falling in the highest 25% of the non-diabetic population).

Diagnosis of MS is made by presence of fasting hyperinsulinemia and two of the other factors mentioned above.

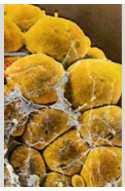
## Table 1

| Risk factors | IDF consensus (2005)[11] | ATPIII criteria (2001)[12] | WHO criteria (1999)[13] |
|---|---|---|---|
| **Obesity/abdominal obesity** | Waist circumference ≥90 cm (m)*, ≥80 cm (f)** – South Asians | Waist circumference ≥102 cm (m)*, ≥88 cm (f)** | Body mass index(BMI) ≥30 kg/m2 and/or waist-to-hip ratio >0.90 (m)*, >0.85 (f)** |
| **Blood pressure** | ≥130/≥85 mmHg | ≥130/≥85 mmHg | ≥140/≥90 mmHg or on Medication |
| **Fasting glucose** | ≥5.6 mmol/L or pre-existing diabetes | ≥6.1 mmol/L or on medication for diabetes | Diabetes, impaired glucose tolerance or insulin resistance |
| **Triglycerides** | ≥1.7 mmol/L | ≥1.7 mmol/L | Triglycerides ≥1.7 mmol/L and/or HDL-C <0.91 mmol/L (m)*, <1.01 mmol/L (f)** |
| **HDL cholesterol** | <1.04 mmol/L (m)*, <1.3 mmol/L (f)** | <1.04 mmol/L (m)*, <1.3 mmol/L (f)** | --- |
| **Microalbuminuria** | Not used for diagnosis | Not used for diagnosis | Urinary albumin excretion rate ≥20 μg/min |
| **Metabolic syndrome – definition** | Abdominal obesity plus two or more risk factors | At least three risk factors | Diabetes, impaired glucose tolerance or insulin resistance plus any two or more risk factors |

m*– males, f**- females

## Genetics of MS

Peroxisome proliferator-activated receptor γ 2 (PPAR γ 2) gene, Peroxisome proliferator-activated receptor γ co-activator-1 α (PPARGC1A), leptin, leptin receptor, resistin, uncoupling protein-1 (UCP-1), and UCP-2 genes have been implicated in common forms of obesity. A recent study conducted in Chennai looked at the Thr394Thr, Gly482Ser and +A2962G polymorphisms of the PPARGC1A gene showed that the A allele of the Thr394Thr(G→A) polymorphism was associated with increased total, visceral and subcutaneous body fat as measured by computerized tomography (CT) and dual energy X-ray absorptiometry.[14]



## Adipose Tissue in Metabolic Syndrome

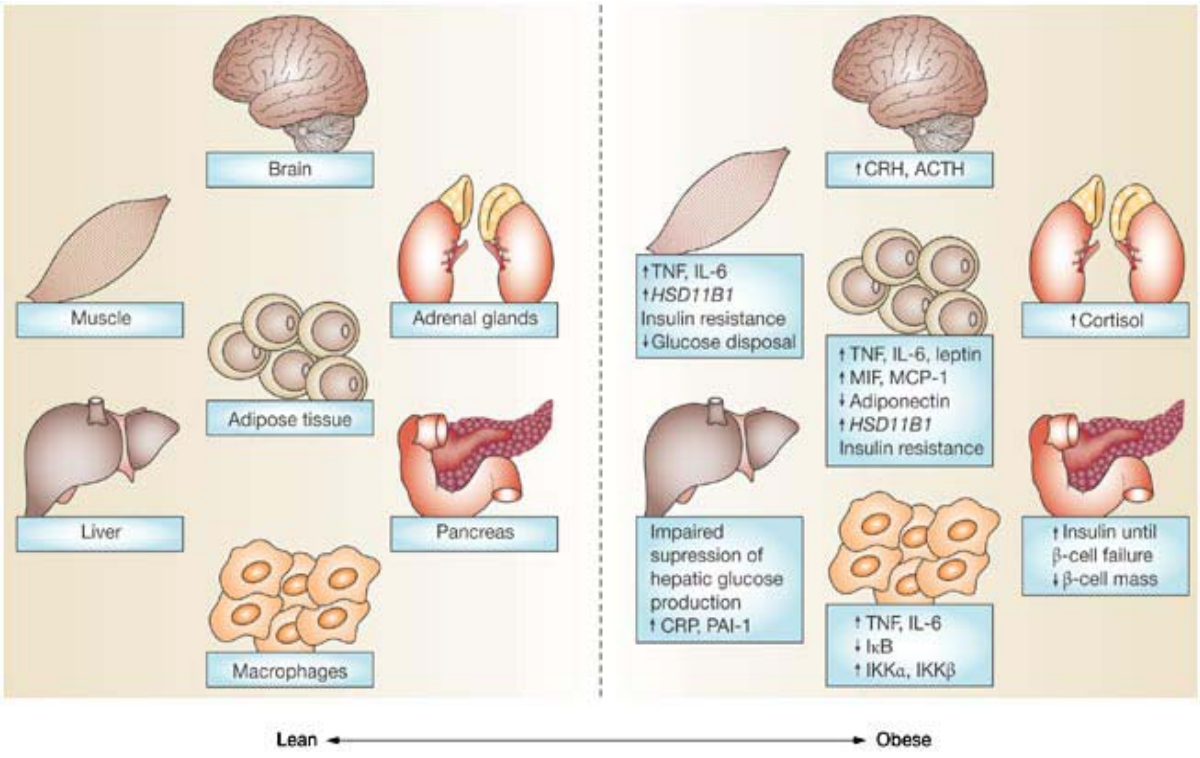



**Figure 1[15] - Tissues involved in the metabolic syndrome**

With weight gain (right-hand side of the figure), the number of macrophages in adipose tissue increases, as do the endocrine, paracrine, and autocrine secretory patterns for various tissues. Adipocytes and macrophages resident in adipose tissue increase secretion of adipokines and cytokines, including **IL-6, TNF and leptin.**[15] Obesity is associated with all of the risk factors of the metabolic syndrome.[16] They are mediated by products released by adipose tissue.[17]

The humoral changes that are brought about by adipose tissue in obesity include-

- ↑ Non-esterified fatty acid (NEFA)
- ↑ Inflammatory cytokines (TNF-$\alpha$, IL-6).
- ↑ PAI-I
- ↓ Adiponectin
- ↑ Leptin

Adeponectin reduces insulin resistance in target tissues. Leptin is an appetite suppressant.

The results of the changes are-

- TNF-$\alpha$ and IL-6 enhance inflammatory reactions in liver, muscle and arterial wall → ↑ CRP
- Increased TNF levels directly interfere with insulin signal transduction through effects on the insulin receptor and insulin receptor substrate 1, which contributes to insulin resistance.

- ❖ The most important factor responsible for lipoprotein overproduction and dyslipidemia that follows is an increased influx of NEFA into the liver.
- ❖ Obesity induces leptin resistance.
- ❖ ↓ Adeponectin induces severe insulin resistance in target tissues.
- ❖ The net result is a chronic inflammatory state associated with insulin resistance, dyslipidemia, altered hypothalamic–pituitary–adrenal sensitivity, and elevated cytokines.

**Interleukin-6:** Studies have demonstrated that about 35% of the production of interleukin-6 (IL-6) is from adipose tissue.[18] IL-6 decreases glucose uptake by insulin sensitive tissues, increases hepatic glucose production, production of NEFA and triglycerides.[19, 20] IL-6 has been shown to be increased in subjects with diabetes, coronary artery disease and in those who take a high fat meal.[21-26]

**Central (abdominal) Obesity** 65% of the body fat is subcutaneous, nearly 20% is abdominal and the rest is intramuscular, hepatic fat etc. Abdominal fat plays major role in metabolic abnormality.[27] Abdominal fat includes intra-abdominal fat (visceral) which constitutes approximately 80% and the rest as subcutaneous fat. Obesity is considered to be the link between insulin resistance and metabolic abnormalities which includes diabetes, hypertension and dyslipidemia, all of which are risk factors for coronary artery disease. [28] The visceral fat stored beneath the muscles and wrapped around the internal organs is considered to be the most

'atherogenic', 'diabetogenic', and 'hypertensinogenic' fat depot of the human body. [29-31]

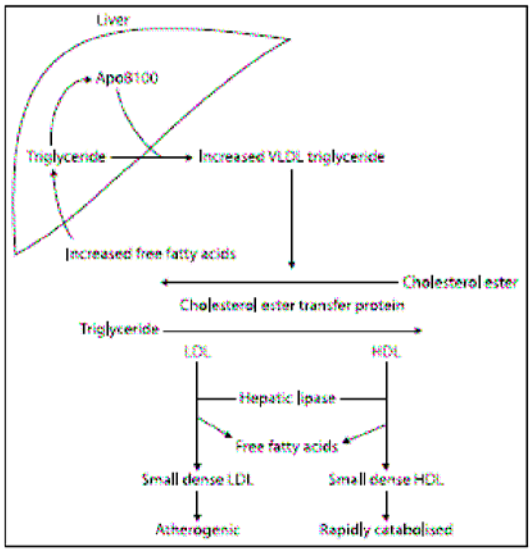



**Figure 2 [36] Development of atherogenic dyslipidemia**

**Atherogenic Dyslipidaemia** describes the combination of raised triglycerides (TG) and low concentrations of HDL-c together with elevated apolipoprotein B (Apo B), small dense LDL and small HDL particles, all of which are independently atherogenic[32], and which is commonly observed in patients with both type 2 diabetes and the metabolic syndrome. Low HDL-c and high TG levels are frequently found with insulin resistance, with or without type 2 diabetes[33], and both are risk factors for coronary heart disease (CHD). [34, 35]

**Prothrombotic State** Prothrombotic defects in MS involve increased levels of Plasminogen Activator Inhibitor- I (PAI-I), fibrinogen, factor VII and platelet abnormalities.[37] Some of the prothrombotic factors may be involved in the atherogenic process itself.[38] These and other likely enhance the thrombotic response to acute plaque ruptures or plaque erosions.[39]

**Proinflammatory State** Atherogenesis is an inflammatory process. This inflammatory process has two major components:

- Tissue injury – lipid abnormalities, hypertension, hyperglycemia and thrombotic factors inflict direct injury on the arterial wall.
- Response to injury – infiltration and cellular uptake of lipids, release of bioactive molecules by macrophages, and proliferation and collagen deposition by smooth muscle cells.[40]

These responses apparently elicit secondary inflammatory responses that include increased synthesis of acute phase reactant by the liver. Among the latter are C-reactive protein and fibrinogen, this may travel to site of arterial injury and enhance the inflammatory response.[41] Evidence is growing that an elevation of serum CRP levels predicts the occurrence of the major CVD events and development of type 2 diabetes. [42, 43] Persons with metabolic syndrome commonly have high levels of CRP. [44]

# "The Asian Indian Phenotype"

"South Asians can be classified as metabolically obese".[45]

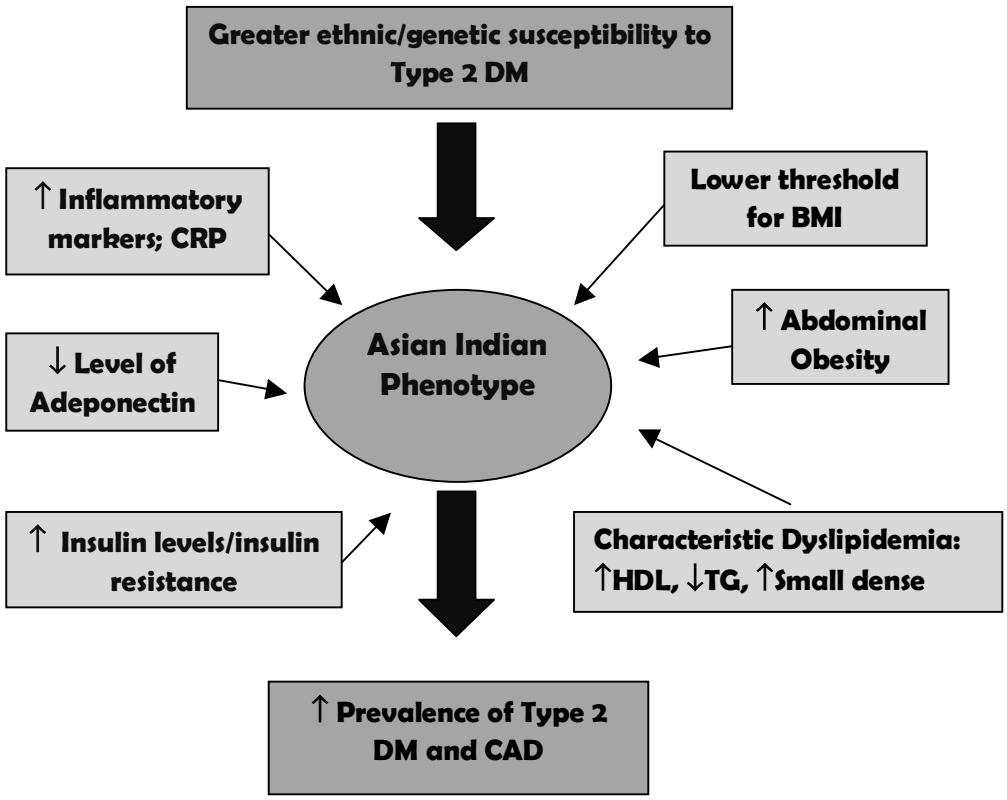



**Figure 3**

**Table 2**

| Associations of insulin resistance and other cardiovascular risk factors in South Asians | |
|---|---|
| Factors with evidence of positive association | Factors with weak or no evidence of association |
| Excess body fat<br>Abdominal obesity<br>High truncal subcutaneous fat<br>Low birth weight<br>High levels of procoagulant factors | C-reactive protein<br>Intramyocellular triglycerides<br>Leptin |

**Neel's "Thrifty Gene" Hypothesis[46]:** Increased ability of Asian Indians to store fat may have come as a survival advantage when subjected to famine during evolution.

This selective pressure would have enriched the genes that facilitate fat storage, predisposing them to obesity and hence glucose intolerance.

**Barker's "Thrifty Phenotype" Hypothesis[47, 48]:** In bad conditions, a pregnant female can modify the development of her unborn child such that it will be prepared for survival in an environment in which resources are likely to be short, resulting in a **thrifty phenotype.** Individuals with a thrifty phenotype will have a smaller body size and a lowered metabolic rate. **L**ow birth weight (LBW) predisposes to adult onset metabolic diseases.

**The Asian Indian Phenotype** is characterized by--

- Higher body fat per unit BMI.[49]
- Higher body fat for given waist circumference.[51-53]
- Lower prevalence of obesity as defined by body mass index.[50]
- Larger waist circumference and waist: hip ratio for given BMI.[50]
- Larger high waist-hip ratio for given waist circumference.[49]
- Greater degree of central obesity.[50]
- Increased insulin resistance for any given body fat.[51-53]
- Less lean body mass (particularly in lower limbs); Sarcopenia.[49,54, 55]

Mohan et al., have recently shown that CRP levels do not appear to mediate the relationship between the body fat and CHD.[56] Absence of any relationship between intramyocellular lipids (IMCL) and insulin sensitivity has been reported in South Asians in UK and Asian Indians in India[57, 58], but it is related to excess body fat and abdominal obesity.[57] High body fat, often at BMI values that are in non-obese

range is another characteristic phenotypic feature of Asian Indians, reported by several groups, including Banerji *et al* in Asian Indians in USA (mean BMI, 24.5 kg/m2, body fat ~33%) and Dudeja, Misra *et al* in Asian Indians in India (mean BMI 23.3 kg/m2, body fat ~35%).[49]

In the light of these new researches, **anthropometric values for Asian Indians are modified**. According to provisional recommendations of WHO, BMI should be maintained between 19-23 kg/m$^2$.[59] Waist circumference should be maintained <90cm for men and <80cm for women.

## MS as CVD Risk Factor

Individuals with MS have two times higher risk for mortality due to myocardial infarction or stroke and three times as likely to develop, myocardial infarction or stroke compared to people without MS. [60] The relation of insulin resistance to cardiovascular risk, particularly CAD has been well established in many prospective studies in the West. In 1209 Finnish men aged 42-60years, the 10-year CVD risk was increased 2.1- and 2.5- fold with the ATP III and WHO MS definitions, respectively. [61] The same study found that the risk of death from CVD was increased by 2.63-2.96 times and the risk of death from any cause was increased 1.87-2.11 times with the presence of the MS. The MS alone predicted ~25% of all new-onset CVD. [61] The DECODE study reported that the presence of MS increased all-cause and CVD mortality by 1.2-2.8 times. [62] In the WOSCOPS (West of Scotland Coronary Prevention Study), MS defined by ATP III definition was associated with

1.8-fold increase in CHD risk, but after adjusting for other risk factors, a more modest 1.3-fold increase was observed. [63]

## Recommendations for treatment [IDF]

Patients should undergo a full cardiovascular risk assessment (including smoking status) in conjunction with the following:

**Primary Intervention:** Healthy lifestyle promotion. This includes:

- moderate calorie restriction (to achieve a 5–10 per cent loss of body weight in the first year)
- moderate increase in physical activity
- change in dietary composition

The results of Finnish and American prevention of diabetes studies have shown the marked clinical benefits associated with a small weight loss in terms of preventing (or at least delaying by several years) the conversion to type 2 diabetes among high-risk individuals with glucose intolerance who were, generally, obese.[64, 65]

**Secondary Intervention:**

Drug therapy may be required to treat the metabolic syndrome in those who are considered to be at high risk for CVD. Specific pharmacological agents are not yet available that can modulate the underlying mechanisms of the metabolic syndrome as a whole. Current practice is to treat the individual components of the syndrome.

## Treatment of the Individual Components of the Metabolic Syndrome

### Atherogenic Dyslipidaemia

**Primary aims for therapy:**

- Lower TG (as well as lowering ApoB and non-HDL cholesterol)
- Raise HDL-c levels.
- Reduce LDL-c levels (elevated levels represent a high risk in the metabolic syndrome)

**Options:**

- **Fibrates (PPAR alpha agonists)** improve all components of atherogenic dyslipidaemia and appear to reduce the risk for CVD in people with metabolic syndrome. The Veterans Affairs High-Density Lipoprotein Intervention Trial (VA-HIT) showed that raising HDL-c concentrations using a fibrate in patients with well-established CHD and both a low HDL-c and a low LDL-c level will significantly reduce the incidence of major coronary events.[33]
- **Statins** to reduce all ApoB-containing lipoproteins and to achieve ATP III goals for LDL-c as well as for non-HDL-c (ATP III, 2001). Several clinical studies have confirmed the benefits of statin therapy.[66-68]
- Fibrates in combination with statins but may be complicated by side effects

**Elevated Blood Pressure**

**Primary aims for therapy:**

- **Categorical hypertension** (BP ≥140/≥ 90 mm Hg) should be treated according to the USA Seventh Report of the Joint National Committee on prevention, detection, evaluation and treatment of high blood pressure (JNC 7) recommendations.[69]
- In **patients with established diabetes**, antihypertensive therapy should be introduced at BP ≥130/≥80 mm Hg.

**Options:**

- **Angiotensin Converting Enzyme Inhibitors and Angiotensin Receptor Blockers** are useful antihypertensive drugs, with some clinical trials (but not all) suggesting they carry advantages over other drugs in patients with diabetes. At this time, however, the majority of clinical trials suggest that the risk reduction associated with antihypertensive drugs is the result of blood pressure lowering per se and not due to a particular type of drug.
- **No particular agents** have been identified as being preferable for hypertensive patients who also have the metabolic syndrome.

**Insulin resistance and hyperglycemia**

There is growing interest in the possibility that drugs that reduce insulin resistance will delay the onset of type 2 diabetes and will reduce CVD risk when metabolic syndrome is present. The Diabetes Prevention Program (DPP) showed that metformin therapy in patients with prediabetes will prevent or delay the

development of diabetes and recent thiazolidinedione studies have also demonstrated efficacy in delaying or preventing type 2 diabetes in patients with impaired glucose tolerance (IGT) and insulin resistance.[70-72] Similarly, other studies have shown that both acarbose and orlistat can be used to delay the development of type 2 diabetes in patients with IGT.[73, 74] Data do not yet exist to show whether any of the currently available thiazolidinediones reduce the risk of CVD in those with the metabolic syndrome, IGT or diabetes.

# Recognition of Coronary Artery Disease

**Classification:**

1. Chronic stable Angina
2. Acute coronary syndrome
    - Unstable angina
    - Non-ST elevation MI
    - ST elevation MI

The first step is to a detailed description of the symptom complex in order to characterize the chest pain or discomfort. Five descriptors typically are considered.[75]

1. Location,
2. Quality,
3. Duration of the discomfort,
4. Inciting factors, and
5. Factors relieving pain.

**Clinical classification of angina**[76]

Typical angina (definite)

1. Substernal chest discomfort with a characteristic quality and duration that is
2. Provoked by exertion or emotional stress and
3. Relieved by rest or nitroglycerin.

Atypical angina (probable)

Meets two of the above characteristics.

Noncardiac chest pain

Meets one or none of the typical anginal characteristics.

**Stable Angina:** Stable angina is characterized by a deep, poorly localized chest or arm discomfort (rarely described as pain) that is reproducibly associated with physical exertion or emotional stress and relieved within 5 – 15 minutes by rest or sublingual nitroglycerine, or both. The characteristics of the stable angina usually **unchanged for 60 days**.

**Anginal Equivalent:** Symptoms of myocardial ischemia other than angina such as dyspnea, fatigue, faintness and eructations, are particularly common in the elderly.[77]

**Acute Coronary Syndrome:**

**Unstable Angina:** Angina pectoris (or equivalent type of ischemic discomfort) with at least one of the following three features[78]:

1. Occurring at rest (or with minimal exertion) and usually lasting more than 20 minutes (if not interrupted by nitroglycerin),
2. Being severe and described as frank pain and of new onset (i.e., **within 1 month**),
3. Occurring with a crescendo pattern (i.e., more severe, prolonged or frequent than previously).

**Crescendo Angina**[79]: worsening of angina can be defined as symptoms that result in at least 1 Canadian Cardiovascular Society (CCS) class increase or to at least CCS Class 3 severity.

**Secondary Unstable Angina**: This form of unstable angina is precipitated by an imbalance in myocardial oxygen supply and demand caused by condition extrinsic to the coronary arteries in patients with prior coronary stenosis and chronic stable angina. [79, 81]

## Canadian Cardiovascular Society (CCS) Grading of Angina Pectoris

**Table 3.**[80]

| Grade | Description |
|---|---|
| Grade I | "Ordinary physical activity does not cause angina."<br>• Walking and climbing stairs.<br>• Angina with strenuous, rapid or prolonged exertion at work or recreation. |
| Grade II | "Slight limitation of ordinary activity".<br>• Walking or climbing stairs rapidly.<br>• Walking uphill.<br>• Walking or stair climbing after meals.<br>• In cold, or in wind, or under emotional stress.<br>• During the few hours after awakening.<br>• Walking > 2 blocks on the level.<br>• Climbing >1 flight of ordinary stairs at a normal pace and in normal conditions. |
| Grade III | "Marked limitation of ordinary physical activity".<br>• Walking 1 or 2 blocks on the level and<br>• Climbing 1 flight of stairs in normal conditions and at normal pace. |
| Grade IV | "Inability to carry on any physical activity without discomfort -- anginal syndrome may be present at rest." |

**Non-ST elevation MI (NSTEMI)**: NSTEMI represents a clinical condition presenting very similarly to unstable angina but with the evidence of myonecrosis by some form of cardiac markers without ST segment elevation on ECG.

**ST elevation MI**: The classic World Health Organization criteria for an acute MI require that **two of the following three elements**[82] be present:

1. A history suggestive of coronary ischemia for a prolonged period (>30 min),
2. Evolutionary changes in serial ECGs suggestive of MI,
3. A rise and fall in serum cardiac markers consistent with myonecrosis.

The pain of myocardial infarction is typically substernal, diffuse, with a squeezing or pressure quality. It may radiate to the neck or jaw, shoulders, or arms. Most often, the pain is accompanied by additional symptoms, such as lightheadedness, nausea or vomiting, diaphoresis, or shortness of breath. The symptoms of myocardial infarction last longer than 30 minutes, and do not respond completely to nitroglycerin. Elderly or diabetic patients are prone to atypical symptoms, such as nausea or dyspnea as the sole symptoms of infarction. As many as one-fourth of myocardial infarctions are "silent" — that is, whatever symptoms were present did not impress the patient enough to seek medical care, or even to remember the incident.

## Secondary Precipitant of Myocardial Ischemia

### Table 4

| Increased Myocardial Oxygen Demand | Decreased Oxygen Supply |
|---|---|
| • Fever<br>• Thyrotoxicosis<br>• Tachycardia<br>• Malignant Hypertension<br>• Pheochromocytoma<br>• Hypertension<br>• Aortic Stenosis<br>• High Output State<br>• Pregnancy<br>• Drugs: Cocaine, Amphetamine | • Anemia<br>• Hypotension<br>• Hypoxemia (pneumonia, CCF etc.)<br>• Carbon Monoxide Poisoning<br>• Polycythemia Vera<br>• Hyperviscosity Syndromes |

## Braunwald Clinical Classification of Unstable Angina or Non-ST Elevation Myocardial Infarction.

### Table 5.[81]

| Clinical Circumstances | | | |
|---|---|---|---|
| **Severity** | A—**Develops in Presence of Extra cardiac Condition That Intensifies Myocardial Ischemia** (Secondary UA) | B—**Develops in Absence of Extra cardiac Condition** (Primary UA) | C—**Develops Within 2 wk of AMI** (Post infarction UA) |
| I—**New onset of severe angina or accelerated angina; no rest pain** | IA | IB | IC |
| II—**Angina at rest within past month but not within preceding 48 h** (angina at rest, sub acute) | IIA | IIB | IIC |
| III—**Angina at rest within 48 h** (angina at rest, acute) | IIIA | **IIIB-$T_{negetive}$**<br>**IIIB-$T_{positive}$** | IIIC |

UA indicates unstable angina; AMI, acute myocardial infarction.

# Socioeconomic Status and Poverty

Poverty is the most obvious problem in India. According 1987-88 estimates about 29.9% population of the country is living below "poverty line" of which 82.5% are living in the rural areas and 17.5% in urban areas. The "poverty line" is defined as the expenditure required for a daily calorie intake of 2400 per person in rural areas and 2100 in urban areas. This expenditure is officially estimated at Rs. 181.50 per capita per month in rural areas and Rs. 209.50 in urban areas at 1991-92 prices. It varies from place to place. The poverty line in different states, cities, villages is drawn at a different level.[83] When these values are adjusted to prevalent inflation of 2006-07, the values are Rs. 4438 per capita per month in rural areas and Rs. 5123 per capita per month in urban areas, respectively.

All over the world the social scientists have considered occupation as the most important determinant of the level of social standing of an individual in society. In India, Prasad's classification of 1961, further modified in 1968 [84] and 1970 [85] is based on per capita income is used. The income limits emphasize only the need for updating this classification with time. Realizing this need, P.Kumar [86] linked Prasad's classification (1961) with the All India Consumer Price Index (AICPI) as both of them shared the same base year of 1961.

To get modified social class adjusted to prevalent inflation, value in Prasad's Classification should be multiplied by a factor R.

R = Value of CPI (4.93) / 100.

CPI=Consumer Price Index

4.93 = A multiplication factor, which transforms current values of CPI into a hypothetical value of CPI in relation to the base year of 1961.

The All-India CPI (UNME) for January, 2007 is 496. [87]

Hence, R =24.4528.

**Table 6**

| Social Class | Monthly Income Limits (Rs) | |
|---|---|---|
| | Prasad's Classification (1961) | Modified classification for the month of January 2007 |
| I | 100 & above | 2445 - 5100 |
| II | 50 - 99 | 1225 - 2444 |
| III | 30 - 49 | 735 - 1224 |
| IV | 15 - 29 | 370 - 734 |
| V | Below 15 | Below 369 |

# Prevalence

The term "disease prevalence" refers to the total numbers of all individual who have an attribute or disease at a particular time (or during a particular period) divided by total the population at risk of having the attribute at this point of time or midway through the period. [88]

# Materials and Methods

## Study Design:

A cross sectional study, with analysis of the metabolic parameters for differences.

**Ethical Clearance:** Obtained

**Informed consent:** Obtained

## Criteria for MS:

Modified International Diabetic Federation consensus worldwide definition of the Metabolic Syndrome, 2005.

## Study Period:

September, 2006 to August, 2007 (12 months).

## Study Population:

All patients belonging to low socioeconomic group (family income <Rs.5100 per month), attending medical outpatient department or those who are getting admitted in medical ward of Govt. Kilpauk Medical College (KMC), Chennai with coronary artery disease (CAD).

## Sample Size:

113 patients, i.e. 38 female patients and 75 male patients.

## Inclusion Criteria:

Patients'

1. Those who attend medical outpatient department or getting admitted in medical ward at KMC.
2. With family income less than Rs.5100 per month.
3. Who live in Chennai city.
4. With age more than 20 years.
5. With symptoms suggestive of CAD.
6. With ECG features suggestive of CAD or significant CK-MB elevation.

## Exclusion Criteria:

Patients'

1. Children, adolescents and those with age less than 20 years.
2. With nonanginal chest pain.
3. With asymptomatic CAD.
4. With ECG changes which are not due to myocardial ischemia or infarction.

## Data Collection:

1. **Socio-demographic profile**.
    - ❖ Name, age, sex, address and family income recorded in the questionnaire.
    - ❖ Patients with family income less than Rs. 5100 per month are included and classified into 5 Modified Prasad's socio-economic

classes, which is adjusted for the existing inflation by multiplying with current All India Consumer Pricing Index (AICPI) (2006 – 07).

2. **Recognition of CAD**.

- Patients enquired for typical history of angina and its duration, previous history of CAD and treatment received for the same.
- Vital parameters recorded.
- Cardiac, Respiratory, Abdomen and Neurologic Systems examined for signs of complications of CAD.
- 2 ECGs (12 lead) taken 24 hours apart, looking for changes suggestive of myocardial ischemia and infarction (new or old).
- Simultaneously 2 venous blood samples are drawn, 24 hours apart and Creatine Kinase – MB (units per liter) levels assessed by commercially available CK – MB kit from Ranbaxy diagnostics.
- With information available patients classified into 2 groups, namely, Chronic CAD and Acute Coronary Syndrome (ACS).

3. **Screening for parameters of MS**.

**Waist Circumference**: It is measured at a level midway between the lower rib margin and iliac crest with the tape all around the body in horizontal position, at the end of normal gentle exhalation, in morning before breakfast after emptying bowel and bladder. Patients are asked

to remove their clothes, except for light underwear. If this is not possible cultural reasons, measurement taken without heavy outer garments. Tight clothing, including the belt, should be loosened and the pockets emptied, standing with their feet fairly close together (about 12-15 cm) with their weight equally distributed to each leg. The tape should be loose enough to allow the observer to place one finger between the tape and the subject's body. Measurements are recorded to the resolution of 0.1cm.

**Blood Pressure**: Blood pressure is measured in right arm supine position using mercury manometer using appropriate size cuff, recorded in mmHg to the precision of 0.2mmHg. 2 reading are recorded. Higher reading among systolic and diastolic blood pressure is taken for analysis. Patient is asked for previously diagnosed hypertension and response recorded.

**Fasting Plasma Glucose** measured (in mg/dL) by semi quantitative O' Toluidine method from venous blood sample drawn in morning following at least 8 hours of fasting. Patient is asked for previously diagnosed hypertension and response recorded.

Triglyceride measured (in mg/dL) by enzymatic colorimetric method and HDL measured (in mg/dL) by selective immune precipitation photometric method from venous blood sample drawn in morning following at least 8 hours of fasting at Thyrocare Technologies Limited,

Mumbai. Patient is asked for previously diagnosed lipid abnormality for which treatment is being taken and response recorded.

**4. <u>Statistical analysis.</u>**

- Statistical analysis is done using Windows based NCSS 97 software.
- Measures of central tendency, dispersion and distribution of the variables obtained.
- Prevalence of Central Obesity, Hypertension, Diabetes or Impaired Fasting Glucose (IFG), Hypertriglyceridemia, Low HDL and Metabolic Syndrome calculated in the study sample, among sexes, social classes and in chronic and acute coronary syndrome.
- $\chi^2$ test used as the test as significance to find difference between the proportions of discrete variables. $P<0.05$ taken as significant.

## The IDF consensus worldwide definition of the metabolic syndrome modified for Indians

**Central Obesity** (defined as waist circumference ≥ 90cm for Indian men and ≥ 80cm for Indian women)

**Plus any two of the following four factors**:

1. **Raised TG level**: >150 mg/dL (1.7 mmol /L), or **specific treatment for this lipid abnormality**
2. **Reduced HDL Cholesterol**: < 40 mg/dL (1.03 mmol/L) in males and < 50 mg/dL (1.29 mmol/L) in females, or **specific treatment for this lipid abnormality**
3. **Raised Blood Pressure**: systolic BP ≥130 or diastolic BP ≥85 mm Hg, or **treatment of previously diagnosed hypertension**
4. **Raised Fasting Plasma Glucose (FPG)** ≥ 100 mg/dL (5.6 mmol/L), or **previously diagnosed type 2 diabetes**

If above 5.6 mmol/L or 100 mg/dL, OGTT is strongly recommended but is not necessary to define presence of the syndrome.

# Results

**Baseline Characteristics:** Total 113 patients with coronary artery disease whose income less than Rs. 5100 per month participated in the study. 38 (33.6%) were females. 75 (66.4%) were males. Age groups were near normally distributed with the sample mean being 54.27years (CI: 54.3±23years). Maximum numbers of patients (70) are in the age groups 40 – 60 years. Youngest patient is 25years and oldest being 80years old.

Mean of age for males (CI: 55.49± 22years) and females (CI: 51.87±24.7years) lie within one standard deviation from sample mean. Males represent older age (>60 years) group more than females. Age distribution in males is negatively skewed.

Social class distribution is positively skewed, i.e., income being negatively skewed. Class I & II (i.e., Rs.1200 – 5100) represent > 70% of sample both in males and females. There has been no representation of lower income groups, i.e., social class IV and V, from < 40 years and >60 years. Since there is inadequate representation of the social classes, especially, class IV and V, social classes were excluded from further analysis.

49 (43.4%) patients had chronic CAD and 64 (56.6%) patients had ACS. Among males 37 had chronic CAD and 38 had ACS. Among females 12 had chronic CAD and 26 had ACS. Social groups IV and V had lesser representation in both chronic CAD and ACS.

# Distribution of Age Groups and Sex in the Sample

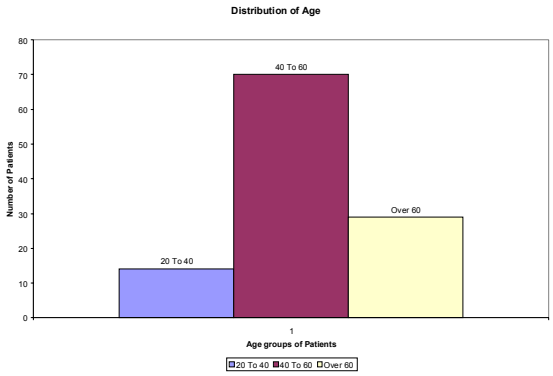



Figure 4

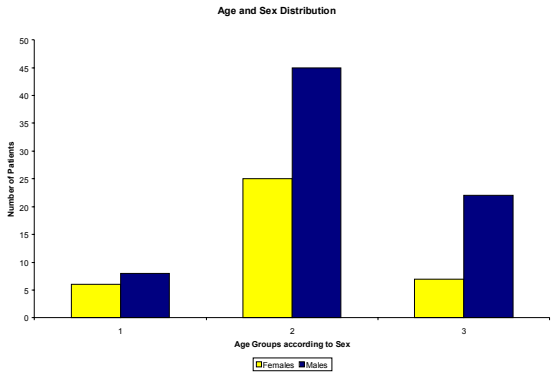



Figure 5

**Table 7**

| Age | Sex | | | | Total | |
|---|---|---|---|---|---|---|
| | Females | | Males | | | |
| | Count | % | Count | % | Count | % |
| **20 To 39** | 6 | 5.3 | 8 | 7.1 | 14 | 12.4 |
| **40 To 59** | 25 | 22.1 | 45 | 39.8 | 70 | 61.9 |
| **Over 60** | 7 | 6.2 | 22 | 19.5 | 29 | 25.7 |
| **Total** | 38 | 33.6 | 75 | 66.4 | 113 | 100.0 |

# Distribution of Social Class

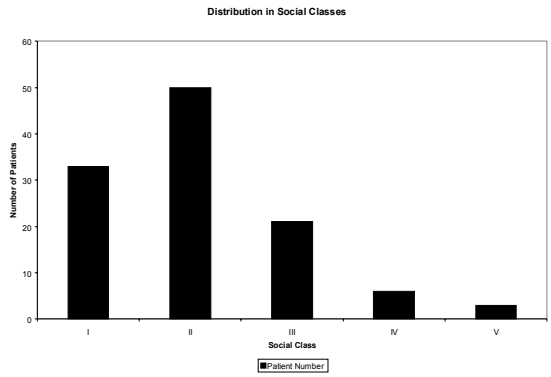



Figure 6

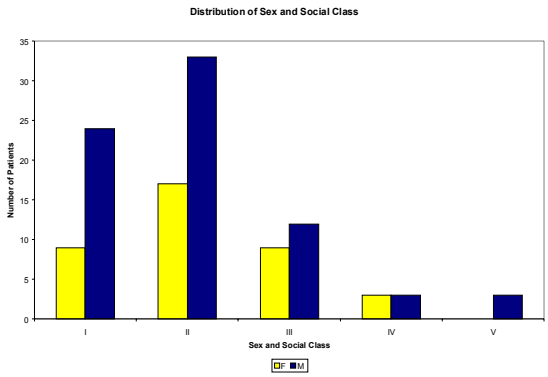



Figure 7

**Table 8**

| | Social Class | | | | | Total |
|---|---|---|---|---|---|---|
| | I | II | III | IV | V | |
| **Females** | 9 | 17 | 9 | 3 | 0 | 38 |
| **Males** | 24 | 33 | 12 | 3 | 3 | 75 |
| **Total** | 33 | 50 | 21 | 6 | 3 | 113 |

# Age Groups and Sex in Social Classes

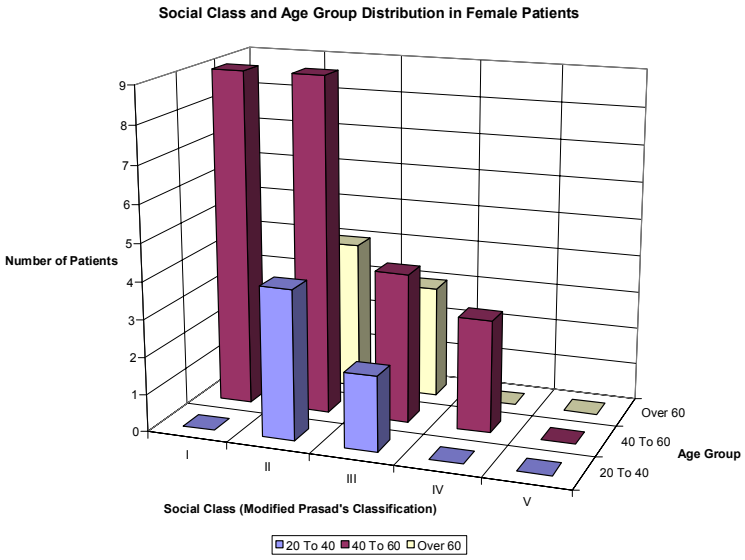



Figure 8

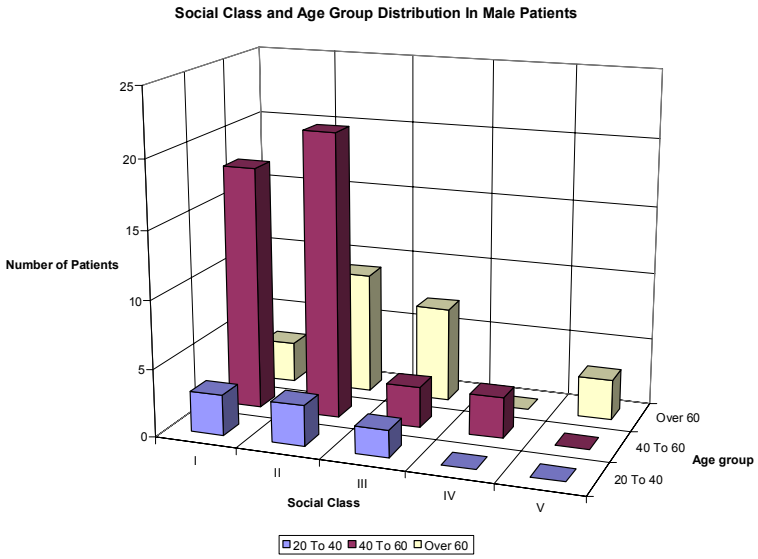



Figure 9

**Table 9**

| Age | Social Class | | | | | Total |
|---|---|---|---|---|---|---|
| | I | II | III | IV | V | |
| **20 To 39** | 3 | 7 | 4 | 0 | 0 | 14 |
| **40 To 59** | 27 | 30 | 7 | 6 | 0 | 70 |
| **Over 60** | 3 | 13 | 10 | 0 | 3 | 29 |
| **Total** | 33 | 50 | 21 | 6 | 3 | 113 |

# Females

**Table 10**

| Age | Social Class | | | | | Total |
|---|---|---|---|---|---|---|
| | I | II | III | IV | V | |
| **20 To 39** | 0 | 4 | 2 | 0 | 0 | 6 |
| **40 To 59** | 9 | 9 | 4 | 3 | 0 | 25 |
| **Over 60** | 0 | 4 | 3 | 0 | 0 | 7 |
| **Total** | 9 | 17 | 9 | 3 | 0 | 38 |

# Males

**Table 11**

| Age | Social Class | | | | | Total |
|---|---|---|---|---|---|---|
| | I | II | III | IV | V | |
| **20 To 39** | 3 | 3 | 2 | 0 | 0 | 8 |
| **40 To 59** | 18 | 21 | 3 | 3 | 0 | 45 |
| **Over 60** | 3 | 9 | 7 | 0 | 3 | 22 |
| **Total** | 24 | 33 | 12 | 3 | 3 | 75 |

# Distribution of Coronary Artery Disease

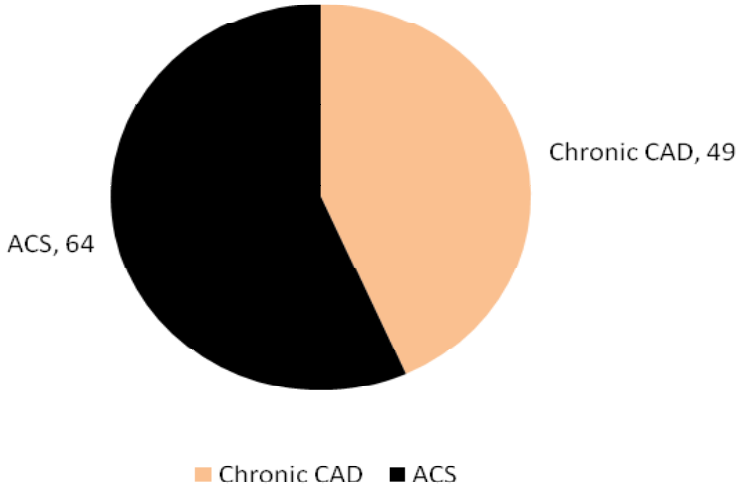



Figure 10

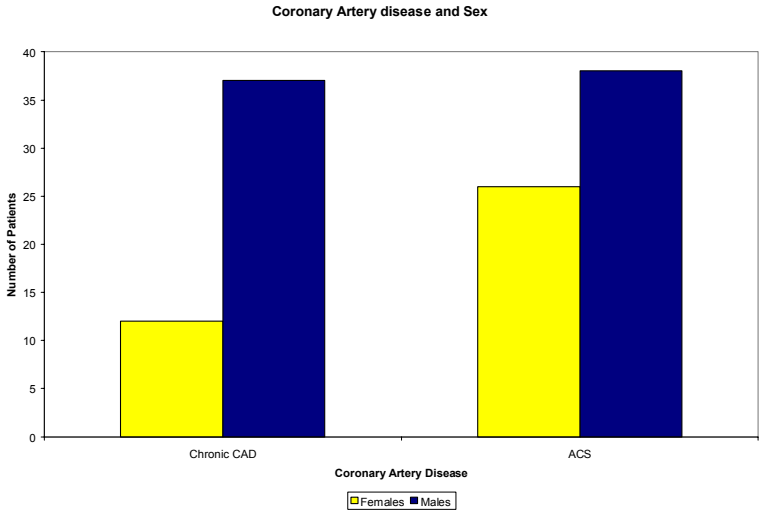



Figure 11

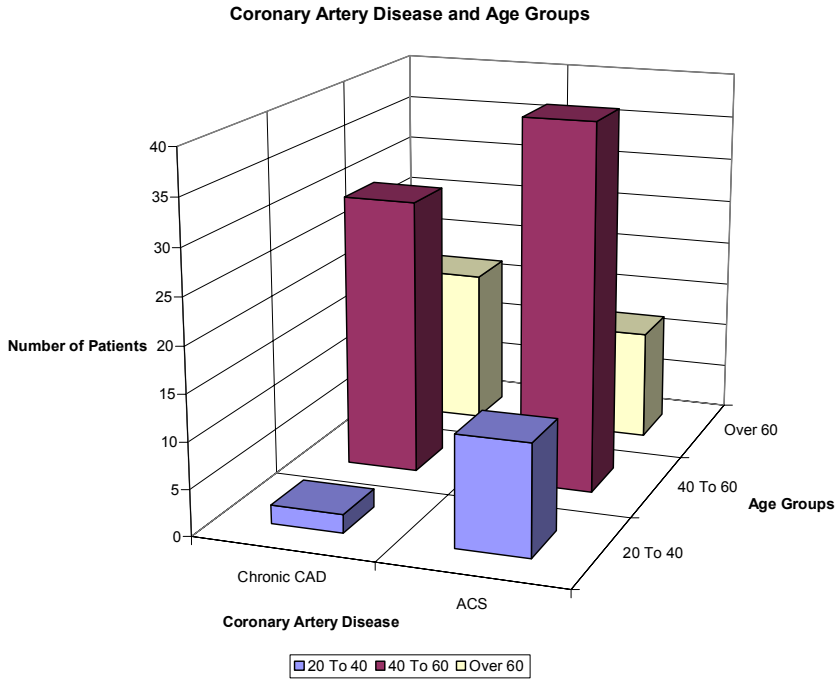



Figure 12

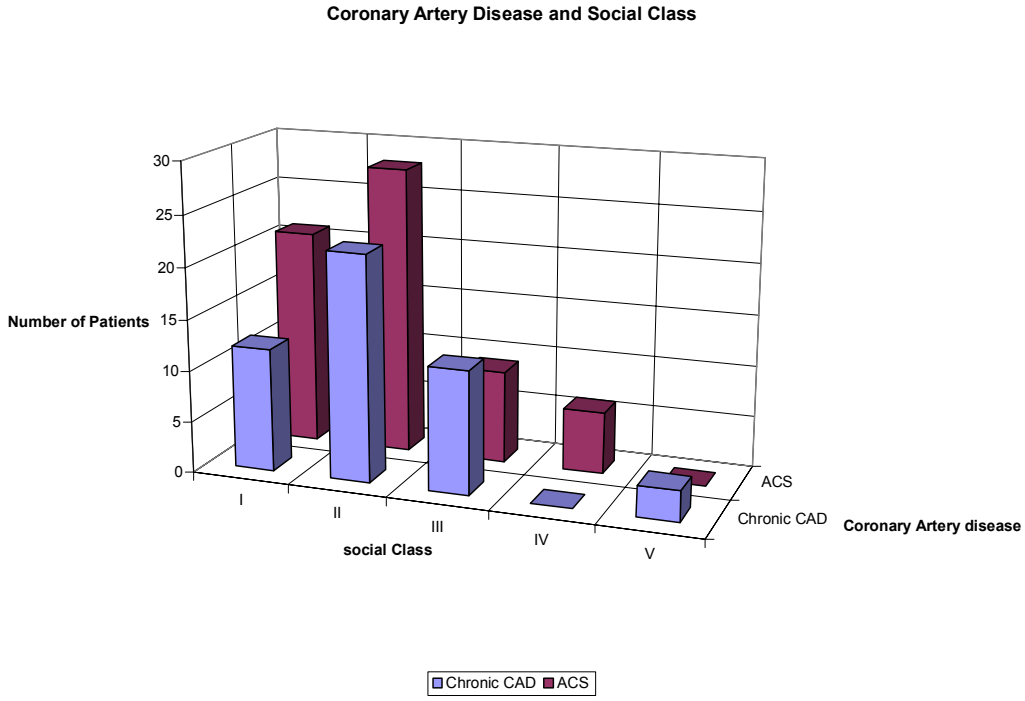



Figure 13

**Table 12**

| Sex | Chronic CAD | | ACS | | Total | |
|---|---|---|---|---|---|---|
| | count | % | count | % | count | % |
| **Females** | 12 | 10.6 | 26 | 23.0 | 38 | 33.6 |
| **Males** | 37 | 32.7 | 38 | 33.6 | 75 | 66.4 |
| **Total** | 49 | 43.4 | 64 | 56.6 | 113 | 100.0 |

**Table 13**

| Age | Chronic CAD | | ACS | | Total | |
|---|---|---|---|---|---|---|
| | count | % | count | count | count | % |
| **20 To 39** | 2 | 1.8 | 12 | 10.6 | 14 | 12.4 |
| **40 To 59** | 30 | 26.5 | 40 | 35.4 | 70 | 61.9 |
| **Over 60** | 17 | 15.0 | 12 | 10.6 | 29 | 25.7 |
| **Total** | 49 | 43.4 | 64 | 56.6 | 113 | 100.0 |

**Table 14**

| | Social Class | | | | |
|---|---|---|---|---|---|
| | **I** | **II** | **III** | **IV** | **V** |
| **Chronic CAD** | 12 | 22 | 12 | 0 | 3 |
| **ACS** | 21 | 28 | 9 | 6 | 0 |
| **Total** | 33 | 50 | 21 | 6 | 3 |

# Central Obesity

Mean of waist circumference of the sample is 87.13 (95% CI: 87±21) cm and that of females and males being 84.31 (95% CI: 84±15.7) cm and 88.56 (95% CI: 88.6±22.6) cm, respectively.

59 patients (52.2%) had central obesity. 64.2% patients in age group <40years, 41.4% in age group 40-60years and 72.4% in age group >60years had central obesity. This increase in prevalence of central obesity among younger (<40year) and older age group (>60years) is significant ($X^2$- 08.82, p=0.01).

23(60.5%) female patients 36 (48%) male patients had central obesity, respectively. There is no significant difference in the prevalence of central obesity between females and males ($X^2$-1.59, p=0.21).

19 (38.78%) patients with chronic CAD and 40 (62.5%) patients with ACS had central obesity. The increase in the prevalence of central obesity in ACS is significant ($X^2$-6.26, p=0.01).

## Central Obesity in Age Groups

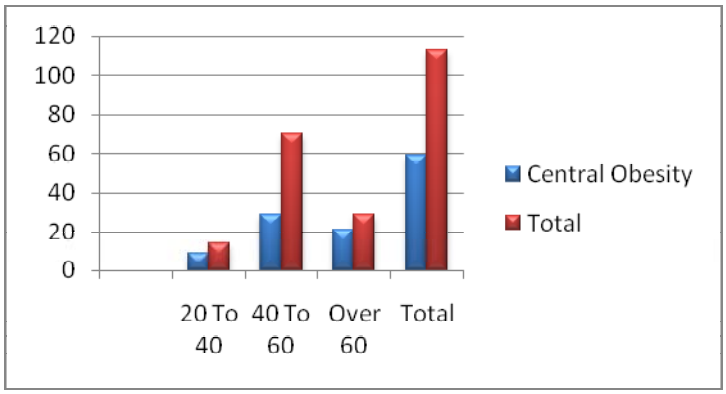



Figure 14

**Table 15**

| Age Groups | Central Obesity | | Total |
|---|---|---|---|
| | Absent | Present | |
| **20 To 39** | 5 | 9 | 14 |
| **40 To 59** | 41 | 29 | 70 |
| **Over 60** | 8 | 21 | 29 |
| **Total** | 54 | 59 | 113 |

## Central Obesity in Males and Females

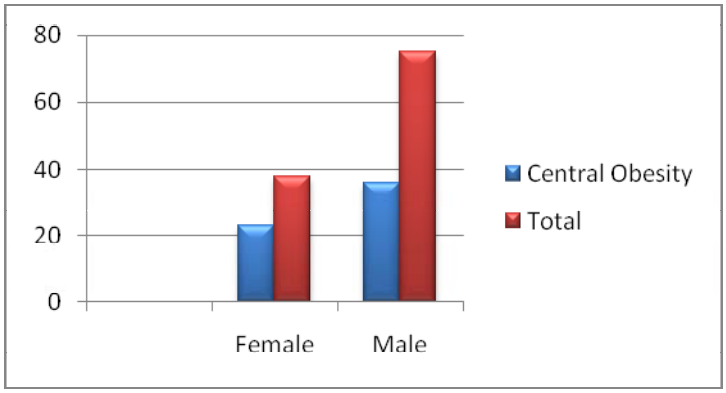



Figure 15

**Table 16**

| Sex | Central Obesity | | Total |
|---|---|---|---|
| | Absent | Present | |
| **Female** | 15 | 23 | 38 |
| **Male** | 39 | 36 | 75 |
| **Total** | 54 | 59 | 113 |

# Hypertension

Mean of SBP and DBP of the sample are 138.53 (95% CI: 138.5±44) mmHg and 88.85 (95% CI: 88.85±23.9) mmHg, respectively and that of females 145.26 (95% CI: 145±30.8) mmHg and 92.89 (95% CI: 92.89±21.8) mmHg, respectively and that of males being 135.12 (95% CI: 135±48) mmHg and 86.8 (95% CI: 86.8±24) mmHg, respectively.

84 patients (74.34%) had hypertension. 71.43% patients in age group <40years, 77.14% in age group 40-60years and 68.96% in age group >60years had hypertension. There is no significant difference in prevalence of hypertension among age group ($X^2$- 00.79, p=0.67).

33(86.84%) female patients 51 (68%) male patients had hypertension, respectively. This increase in prevalence of hypertension among females as compared to males is significant ($X^2$-04.69, p=0.03).

31 (63.27%) patients with chronic CAD and 53 (82.81%) patients with ACS had hypertension. Increase in the prevalence of hypertension in ACS is significant ($X^2$-05.56, p=0.02).

## Hypertension in Age Groups

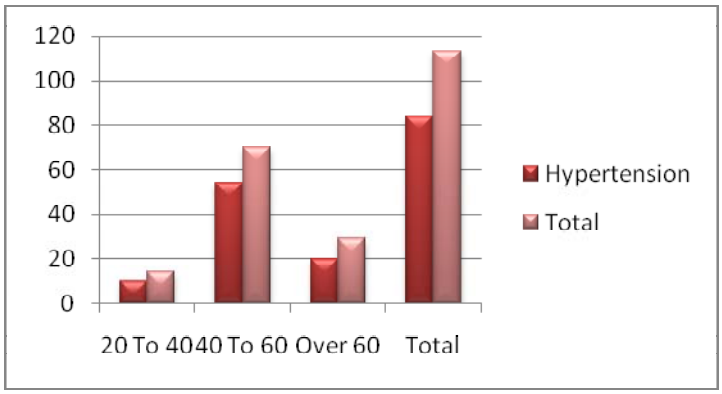



Figure 16

**Table 17**

| Age | Hypertension | | Total |
|---|---|---|---|
| | Absent | Present | |
| **20 To 39** | 4 | 10 | 14 |
| **40 To 59** | 16 | 54 | 70 |
| **Over 60** | 9 | 20 | 29 |
| **Total** | 29 | 84 | 113 |

## Hypertension in Males and Females

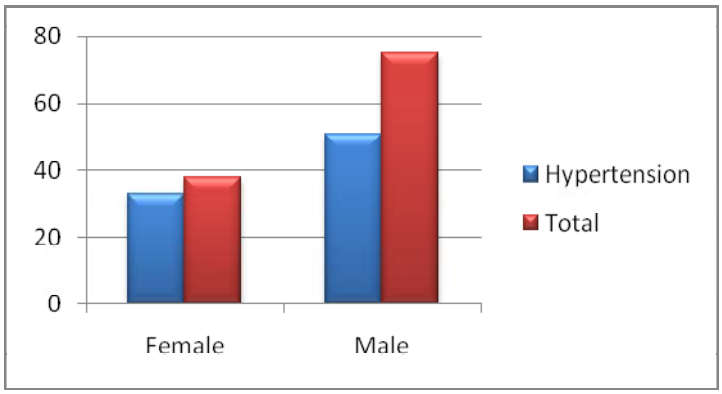



Figure 17

**Table 18**

| Sex | Hypertension | | Total |
|---|---|---|---|
| | Absent | Present | |
| **Female** | 5 | 33 | 38 |
| **Male** | 24 | 51 | 75 |
| **Total** | 29 | 84 | 113 |

# Diabetes and IFG

Mean of FBS of the sample is 130.31 (95% CI: 130.31±132) mg/dL and that of females and males being 126.72 (95% CI: 92.89±128.7) mg/dL and 137.39 (95% CI: 137.39±139) mg/dL, respectively.

57 patients (50.44%) had diabetes or IFG. 50% patients in age group <40years, 40% in age group 40-60years and 75.86% in age group >60years had diabetes or IFG. This increase in prevalence of Diabetes and IFG among younger (<40year) and older age group (>60years) is significant ($X^2$- 10.55, p=.005).

21 (55.26%) female patients 36 (48%) male patients had diabetes or IFG, respectively. There is no significant difference in the prevalence of diabetes and IFG between females and males ($X^2$-00.53, p=0.47).

22 (44.9%) patients with chronic CAD and 35 (54.69%) patients with ACS had diabetes or IFG. There is no significant difference in the prevalence of diabetes and IFG between chronic CAD and ACS ($X^2$-01.06, p=0.30).

## Diabetes and IFG in Age Groups

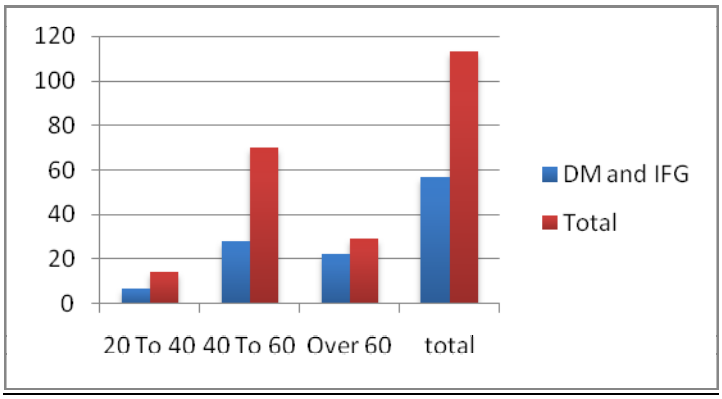



Figure 18

**Table 19**

| Age | DM and IFG | | Total |
|---|---|---|---|
| | Absent | Present | |
| **20 To 39** | 7 | 7 | 14 |
| **40 To 59** | 42 | 28 | 70 |
| **Over 60** | 7 | 22 | 29 |

## Diabetes and IFG in Males and Females

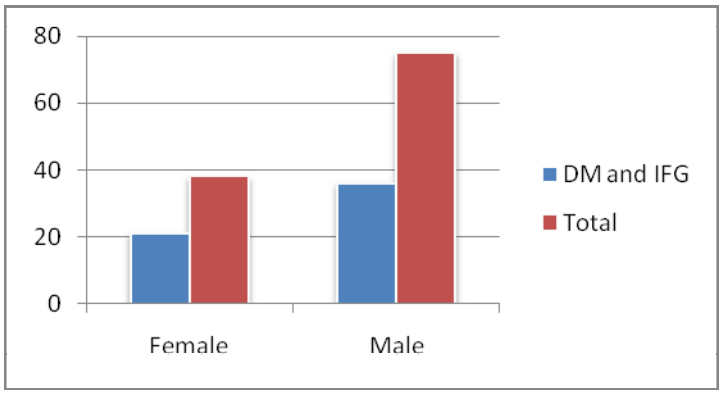



Figure 19

**Table 20**

| Sex | DM and IFG | | Total |
|---|---|---|---|
| | Absent | Present | |
| **Female** | 17 | 21 | 38 |
| **Male** | 39 | 36 | 75 |
| **Total** | 56 | 57 | 113 |

# Hypertriglyceridemia

Mean of triglyceride level of the sample is 159.71 (95% CI: 159.71±160.6) mg/dL and that of females and males being 150.14 (95% CI: 150.14±110.4) mg/dL and 164.56 (95% CI: 164.56±180.7) mg/dL, respectively.

48 patients (42.48%) had hypertriglyceridemia. 50% patients in age group <40years, 32.86% in age group 40-60years and 62% in age group >60years had hypertriglyceridemia. This increase in prevalence of hypertriglyceridemia among younger (<40year) and older age group (>60years) is significant ($\chi^2$- 07.53, p=0.02).

12 (31.58%) female patients 36 (48%) male patients had hypertriglyceridemia, respectively. There is no significant difference in the prevalence of hypertriglyceridemia between females and males ($\chi^2$-02.78, p=0.09).

22 (44.9%) patients with chronic CAD and 26 (40.63%) patients with ACS had hypertriglyceridemia. There is no significant difference in the prevalence of hypertriglyceridemia between chronic CAD and ACS ($\chi^2$-00.21, p=0.65).

## Hypertriglyceridemia in Age Groups

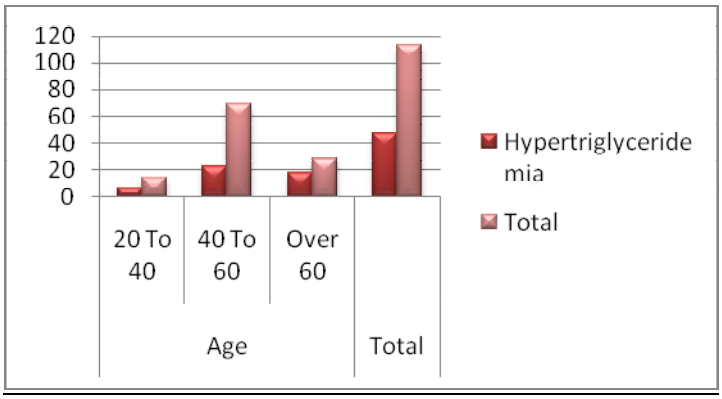



Figure 20

**Table 21**

| Hypertri glyceridemia | Age | | | Total |
|---|---|---|---|---|
| | 20 To 39 | 40 To 59 | Over 60 | |
| **Absent** | 7 | 47 | 11 | 65 |
| **Present** | 7 | 23 | 18 | 48 |
| **Total** | 14 | 70 | 29 | 113 |

## Hypertriglyceridemia in Males and Females

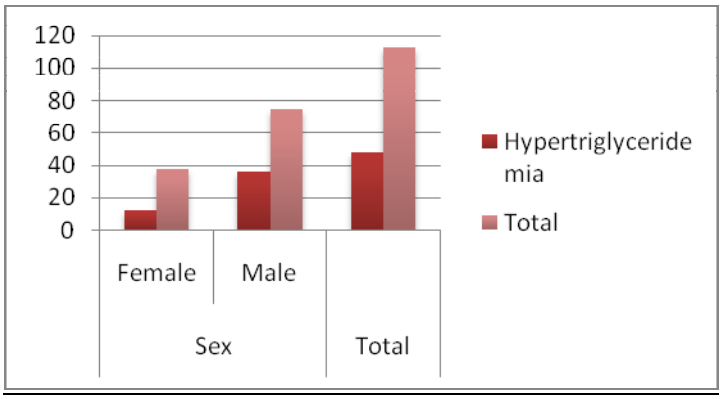



Figure 21

**Table 22**

| Hypertri glyceridemia | Sex | | Total |
|---|---|---|---|
| | Female | Male | |
| **Absent** | 26 | 39 | 65 |
| **Present** | 12 | 36 | 48 |
| **Total** | 38 | 75 | 113 |

# High Density Lipoprotein

Mean of HDL level of the sample is 44.32 (95% CI: 44.32±21.7) mg/dL and that of females and males being 48.07 (95% CI: 48.07±19.4) mg/dL and 42.4 (95% CI: 42.4±21.9) mg/dL, respectively.

54 patients (47.79%) had low HDL. 71.42% patients in age group <40years, 40% in age group 40-60years and 55.17% in age group >60years had low HDL. There is no significant difference in the prevalence of low HDL between age groups ($\mathcal{X}^2$-05.47, p=0.06).

21 (55.26%) female patients 33 (44%) male patients had low HDL, respectively. There is no significant difference in the prevalence of low HDL between females and males ($\mathcal{X}^2$-01.28, p=0.26).

25 (44.9%) patients with chronic CAD and 29 (40.63%) patients with ACS had low HDL. There is no significant difference in the prevalence of low HDL between chronic CAD and ACS ($\mathcal{X}^2$-00.36, p=0.55).

## Low HDL in Age Groups

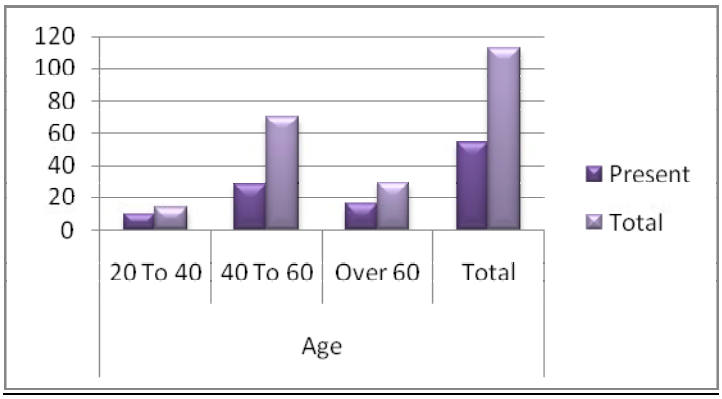



Figure 22

**Table 23**

| | Age | | | |
|---|---|---|---|---|
| **Low HDL** | **20 To 39** | **40 To 59** | **Over 60** | **Total** |
| **Absent** | 4 | 42 | 13 | 59 |
| **Present** | 10 | 28 | 16 | 54 |
| **Total** | 14 | 70 | 29 | 113 |

## Low HDL Males and Females

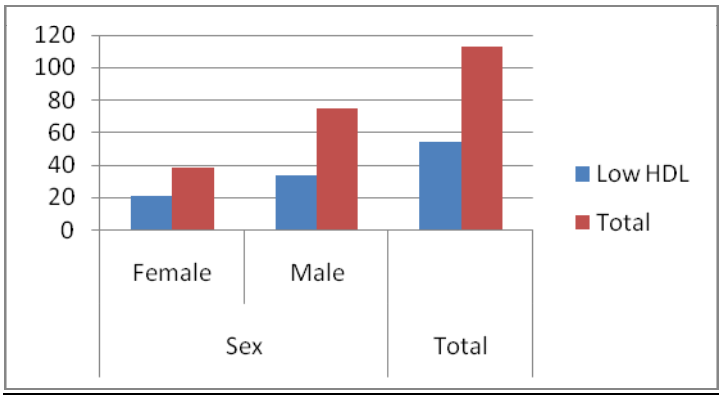



Figure 23

**Table 24**

| **Low HDL** | **Sex** | | **Total** |
|---|---|---|---|
| | **Female** | **Male** | |
| **Absent** | 17 | 42 | 59 |
| **Present** | 21 | 33 | 54 |
| **Total** | 38 | 75 | 113 |

# Measures of Central Tendency

**Table 25**

| | | total | female | Male |
|---|---|---|---|---|
| Age (years) | mean | 54.27 | 51.87 | 55.49 |
| | Std dev | 11.64 | 12.33 | 11.17 |
| | Std error | 1.10 | 2.00 | 1.29 |
| | 95% CI | 54.3±23 | 52±24.7 | 55.5±22 |
| Waist (cm) | mean | 87.13 | 84.31 | 88.56 |
| | Std dev | 10.44 | 7.84 | 11.30 |
| | Std error | 0.98 | 1.27 | 1.31 |
| | 95% CI | 87±21 | 84±15.7 | 88.6±22.6 |
| SBP(mmHg) | mean | 138.53 | 145.26 | 135.12 |
| | Std dev | 22.00 | 15.38 | 24.07 |
| | Std error | 2.07 | 2.49 | 2.78 |
| | 95% CI | 138.5±44 | 145±30.8 | 135±48 |
| DBP (mmHg) | mean | 88.85 | 92.89 | 86.8 |
| | Std dev | 11.93 | 10.88 | 11.99 |
| | Std error | 1.12 | 1.77 | 1.38 |
| | 95% CI | 88.85±23.9 | 92.89±21.8 | 86.8±24 |
| FBS (mg/dL) | mean | 130.31 | 126.72 | 137.39 |
| | Std dev | 66.07 | 64.43 | 69.52 |
| | Std error | 6.22 | 7.44 | 11.28 |
| | 95% CI | 130.31±132 | 92.89±128.7 | 137.39±139 |
| TG (mg/dL) | mean | 159.71 | 150.14 | 164.56 |
| | Std dev | 80.30 | 55.18 | 90.36 |
| | Std error | 7.55 | 8.95 | 10.43 |
| | 95% CI | 159.71±160.6 | 150.14±110.4 | 164.56±180.7 |
| HDL (mg/dL) | mean | 44.32 | 48.07 | 42.4 |
| | Std dev | 10.84 | 9.68 | 10.97 |
| | Std error | 1.02 | 1.57 | 1.27 |
| | 95% CI | 44.32±21.7 | 48.07±19.4 | 42.4±21.9 |

# $X^2$ Tests for Statistical Difference

**Table 26**

| | $^0$ Fr | $X^2$ | P value | $H^0$ | Difference |
|---|---|---|---|---|---|
| **1. Central Obesity in age groups** | 2 | 08.82 | 0.01 | Reject | Yes |
| **in sex** | 1 | 01.59 | 0.21 | Accept | No |
| **CAD** | 1 | 06.26 | 0.01 | Reject | Yes |
| **2.HTN in age groups** | 2 | 00.79 | 0.67 | Accept | No |
| **in sex** | 1 | 04.69 | 0.03 | Reject | Yes |
| **CAD** | 1 | 05.56 | 0.02 | Reject | Yes |
| **3.DM & IFG in Age groups** | 2 | 10.55 | .005 | Reject | Yes |
| **in sex** | 1 | 00.53 | 0.47 | Accept | No |
| **CAD** | 1 | 01.06 | 0.30 | Accept | No |
| **4.Hypertriglyceridemia in Age groups** | 2 | 07.53 | 0.02 | Reject | Yes |
| **in sex** | 1 | 02.78 | 0.09 | Accept | No |
| **CAD** | 1 | 00.21 | 0.65 | Accept | No |
| **5.Low HDL in Age groups** | 2 | 05.47 | 0.06 | Accept | No |
| **in sex** | 1 | 01.28 | 0.26 | Accept | No |
| **CAD** | 1 | 00.36 | 0.55 | Accept | No |
| **6.MS in Age groups** | 2 | 10.25 | .006 | Reject | Yes |
| **in sex** | 1 | 0.004 | 00.94 | Accept | No |
| **CAD** | 1 | 02.82 | 00.09 | Accept | No |

# Metabolic Syndrome

54 patients (47.78%) had metabolic syndrome. 50% patients in age group <40years, 37.14% in age group 40-60years and 72.41% in age group >60years had metabolic syndrome. This increase in prevalence of metabolic syndrome among younger (<40year) and older age group (>60years) is significant ($X^2$- 10.25, p=.006).

18 (47.37%) female patients and 36 (48%) male patients had metabolic syndrome, respectively. There is no significant difference in the prevalence of metabolic syndrome between female and male patients ($X^2$-0.004, p=00.94).

19 (38.78%) patients with chronic CAD and 35 (54.69%) patients with ACS had metabolic syndrome. There is no significant difference in the prevalence of metabolic syndrome between chronic CAD and ACS ($X^2$-02.82, p=00.09).

# Metabolic Syndrome in Age Groups

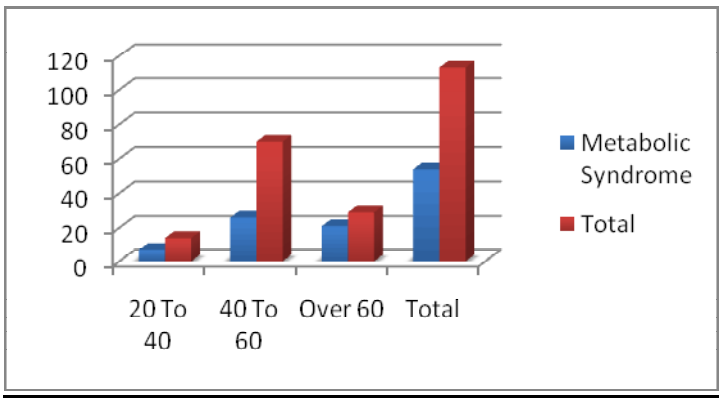



Figure 24

**Table 27**

| Age | Metabolic Syndrome | | Total |
|---|---|---|---|
| | Absent | Present | |
| **20 To 39** | 7 | 7 | 14 |
| **40 To 59** | 44 | 26 | 70 |
| **Over 60** | 8 | 21 | 29 |
| **Total** | 59 | 54 | 113 |

**Prevalence of Metabolic Syndrome in the population under study** =

(Number of patients with Metabolic Syndrome ÷ total number of patients involved in the study) ×100 = (54 ×100) ÷11

= **47.79%**

# Metabolic Syndrome in Males and Females

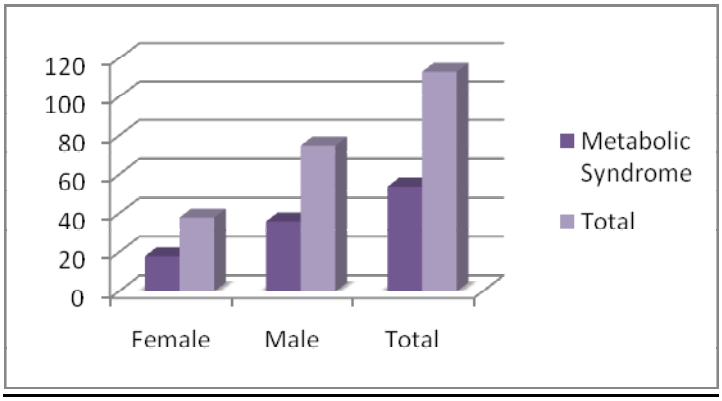



Figure 25

**Table 28**

| Sex | Metabolic Syndrome | | Total |
|---|---|---|---|
| | Absent | Present | |
| **Female** | 20 | 18 | 38 |
| **Male** | 39 | 36 | 75 |
| **Total** | 59 | 54 | 113 |

**Prevalence of Metabolic Syndrome among female patients under study** =

(Number of female patients with Metabolic Syndrome ÷ total number of female patients involved in the study) ×100

= (18 ×100) ÷ 38

= **47.37%**

**Prevalence of Metabolic Syndrome among male patients under study** =

(Number of male patients with Metabolic Syndrome ÷ total number of male patients involved in the study) ×100

= (36 ×100) ÷ 75

= **48%**

# Metabolic Syndrome in CAD

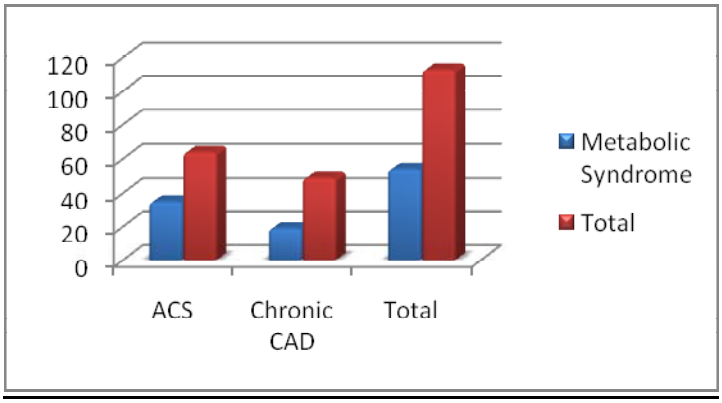



Figure 26

**Table 29**

| | Metabolic Syndrome | | Total |
|---|---|---|---|
| | Absent | Present | |
| ACS | 29 | 35 | 64 |
| Chronic CAD | 30 | 19 | 49 |
| **Total** | **59** | **54** | **113** |

**Prevalence of Metabolic Syndrome among patients Chronic CAD** =

(Number of Chronic CAD patients with Metabolic Syndrome ÷ total number of Chronic CAD patients involved in the study) ×100

= (19 ×100) ÷ 49

= **38.78%**

**Prevalence of Metabolic Syndrome among patients with ACS** =

(Number of ACS patients with Metabolic Syndrome ÷ total number of patients ACS involved in the study) ×100

= (35×100) ÷ 64

= **54.69%**

# The Prevalence of Metabolic Syndrome and Metabolic Parameters

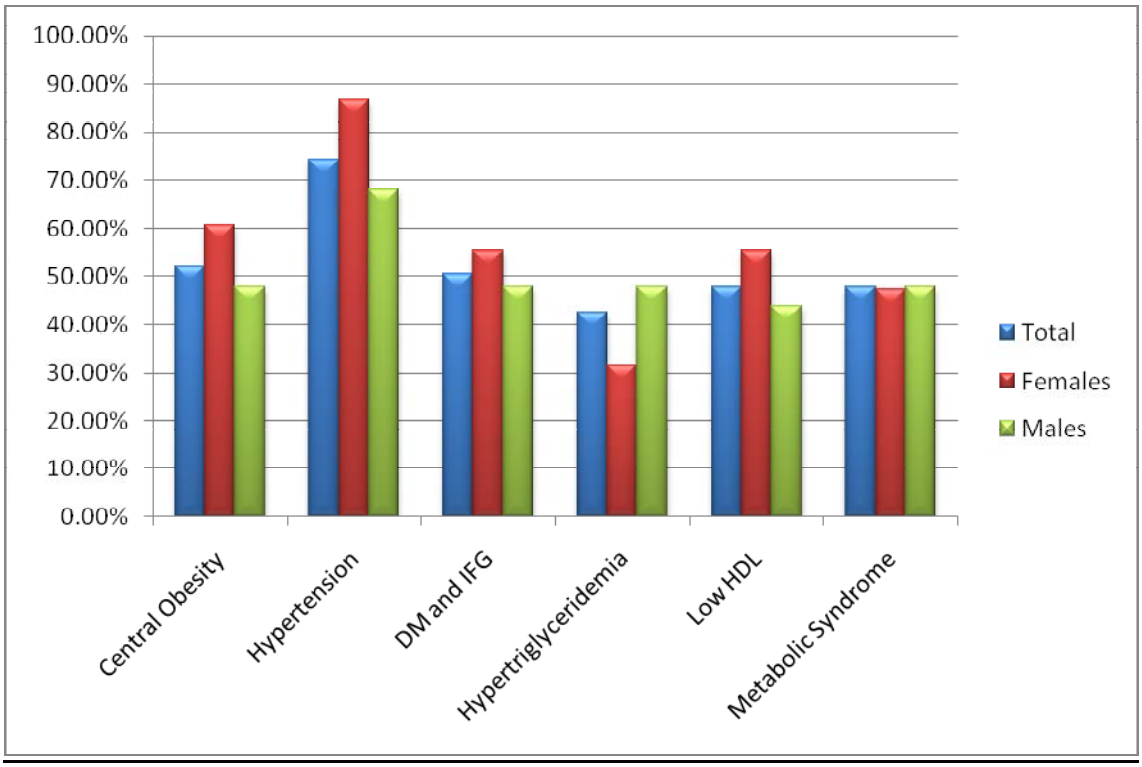
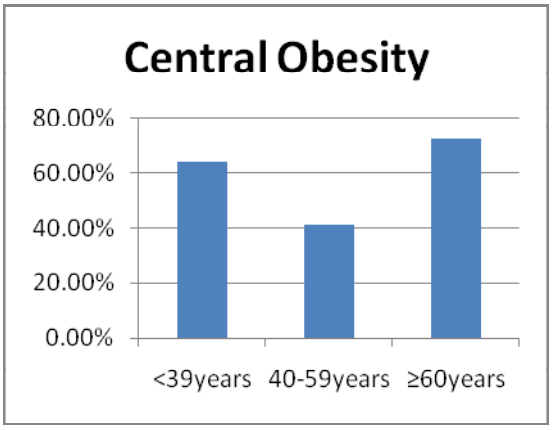



Figure 27

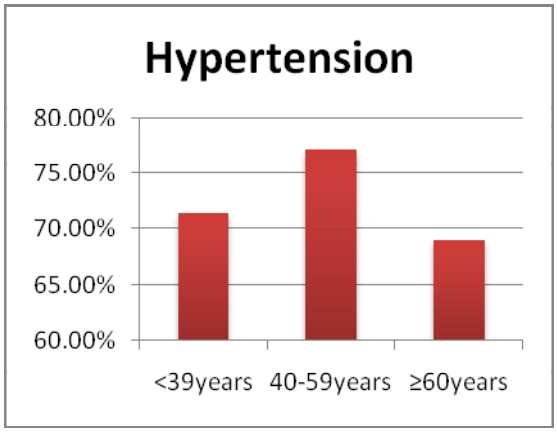
**Table 30**

| Prevalence | Total | Females | Males |
|---|---|---|---|
| **Central Obesity** | 52.21% | 60.53% | 48% |
| **Hypertension** | 74.34% | 86.84% | 68% |
| **DM and IFG** | 50.44% | 55.26% | 48% |
| **Hypertriglyceridemia** | 42.48% | 31.58% | 48% |
| **Low HDL** | 47.79% | 55.26% | 44% |
| **Metabolic Syndrome** | 47.79% | 47.37% | 47.79% |

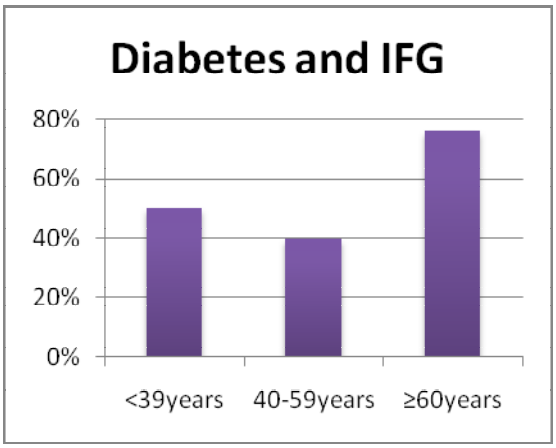
# The "U" shaped Distribution in Age Groups



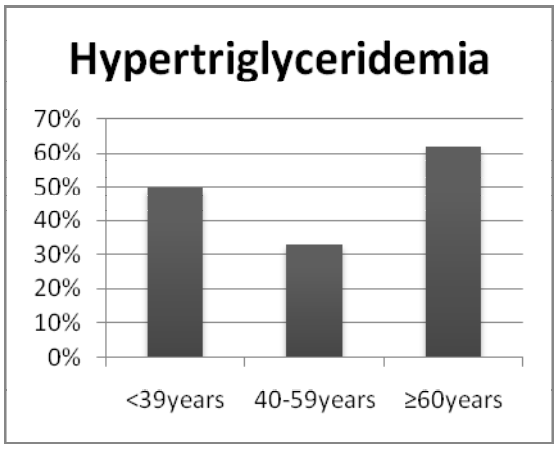

$X^2$ Significant



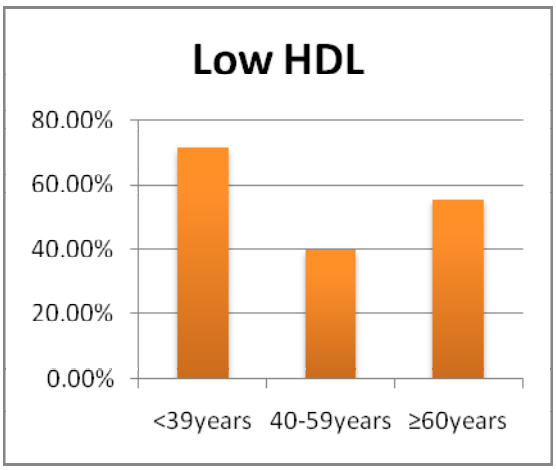

$X^2$ not Significant



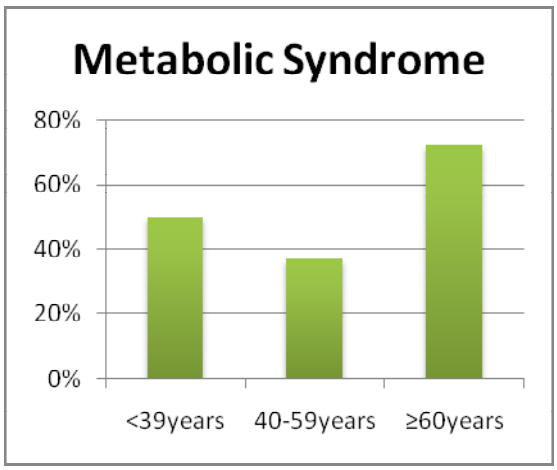

$X^2$ Significant




$X^2$ Significant




$X^2$ not Significant




$X^2$ Significant

**Table 31**

# Discussion

Mean age of the sample being 54.27years (CI: 54.3±23years). The mean age of an Asian Indian patient suffering a myocardial infarction is only 50 years.25% of all MIs in this population occur under the age of 40 years. [89]

## Obesity

This study shows higher prevalence of obesity (52.2%) in those suffering from CAD and living below poverty line. This is much higher compared to a study conducted in the intracountry migrant population that resides in urban slums, where obesity prevalence was 13.9%.[49]Even in males (48%) and females (60.5%), prevalence of obesity is markedly higher compared to the corresponding figures from the Nutrition Foundation of India, where the prevalence of obesity is 1% for males and 4% for females in the slums while corresponding figures for the middle socioeconomic class was 32.2% and 50%, respectively.[90] Using EGIR criteria, the Chennai Urban Population Study (CUPS), over 35% of the males in the middle-income group were obese compared to 13% in the low income group. The corresponding figures for females were 33% and 24% respectively.[91]

In my study, there was no significant difference in the prevalence of central obesity between females and males. Obesity prevalence was significantly higher (p=0.01) in ACS (62.5%) as compared to chronic CAD (38.78%).Interestingly, there significant increase (p=0.01) in prevalence of

central obesity among patients with premature CAD (<40years) and older age group (>60 years) forming a "U" shaped distribution.

**Hypertension**

Prevalence of hypertension in my study was 74.34%, whereas overall prevalence of hypertension in Chennai Urban Population Study (CUPS) was 21.1%, where hypertension was diagnosed using JNC 6 criteria. [92] In another study conducted in the intracountry migrant population that resides in urban slums, where prevalence of hypertension was 11.7%.[49] There is no significant difference in prevalence of hypertension among age group. But virtually all studies of blood pressure carried out in different populations including India have shown a rise of blood pressure with age in both men and women.[93] 86.84% of female patients 68% male patients had hypertension, respectively. This increase in prevalence of hypertension among females as compared to males is significant (p=0.03). Studies have shown that, greater prevalence of hypertension among urban Indian population of women compared to men.[94] 63.27% patients with chronic CAD and 82.81% patients with ACS had hypertension. Increase in the prevalence of hypertension in ACS is significant (p=0.02).

**Diabetes and IFG**

50.44% had diabetes or IFG. This is higher compared to 13.5% [95, 96] in a study conducted in Chennai city and 10.3%[49] in another study conducted in the

intracountry migrant population that resides in urban slums. But in these figures IFG is not included. There was significant increase (p=0.005) in prevalence of Diabetes and IFG among patients with premature CAD (<40years) and older age group (>60 years) forming a "U" shaped distribution. 55.26% of female patients 48% of male patients had diabetes or IFG, respectively. A recent cross-sectional cohort study conducted in Mysore, India found the prevalence of type 2 diabetes to be 40% in women, versus 34% in men.[97] Again this figures do not include IFG. 44.9% of the patients with chronic CAD and 54.69% of the patients with ACS had diabetes or IFG. There was no significant difference in the prevalence of diabetes and IFG among sexes and between chronic CAD and ACS.

**Dyslipidemia**

42.48% had hypertriglyceridemia, in contrast to 14.5%[49] in the intracountry migrant population that resides in urban slums. There was significant increase (p=0.02) in prevalence of hypertriglyceridemia among patients with premature CAD (<40years) and older age group (>60 years) forming a "U" shaped distribution. 31.58% of female patients 48% of male patients had hypertriglyceridemia, respectively. 44.9% patients with chronic CAD and 40.63% patients with ACS had hypertriglyceridemia. There was no significant

difference in the prevalence of hypertriglyceridemia among sexes and between chronic CAD and ACS.

47.79% had low HDL as compared to 16.2%[49]in the intracountry migrant population that resides in urban slums. 55.26% female patients 44% male patients had low HDL, respectively. 25 (44.9%) patients with chronic CAD and 29 (40.63%) patients with ACS had low HDL. There was no significant difference in the prevalence of hypertriglyceridemia among age groups, sexes and between chronic CAD and ACS.

**Metabolic Syndrome**

Overall prevalence of metabolic syndrome among the study population was 47.79% using IDF, 2005 definition. There was significant increase (p=0.006) in prevalence of metabolic syndrome among patients with premature CAD (<40years) and older age group (>60 years) forming a "U" shaped distribution. 47.37% of female patients and 48% of male patients had metabolic syndrome, respectively.

Various studies have described prevalence of MS using different definitions ranging from 11.2-41.1% as given below. All of them reported decreased prevalence of MS in low socioeconomic class people.

1. Using EGIR criteria, the Chennai Urban Population Study (CUPS -4), reported overall prevalence of MS to be 11.2% with the significant

difference between the middle income (18.7%) and low income groups (6.5%).[91]

2. An earlier study in urban Indian adults aged 20-75years, reported a prevalence of MS to be 41.1% using NCEP definition.[98]
3. In CURES study, prevalence of MS were 23.2%, 18.3% and 25.8% according to the WHO, ATP III and IDF definitions respectively. Prevalence of MS was higher in women using ATP III criteria (men 17.1%, women 19.4%) and IDF criteria (men 23.1%, women 28.2%); but it was higher in men by WHO criteria (men 27.3%, women 19.7%). The prevalence of MS increased with age until the age of 69years and decreased thereafter based on all three criteria.[99]
4. The age-adjusted prevalence of MS based on ATP III criteria in Jaipur (urban north Indian population) was 24.9%.[100]
5. In a study conducted in the intracountry migrant population that resides in urban slums, the prevalence of insulin resistance was 22.5-26%.[49]

38.78% patients with chronic CAD and 54.69% patients with ACS had metabolic syndrome. There is no significant difference in the prevalence of metabolic syndrome between males and females and between chronic CAD and ACS.

Since there was inadequate representation of the social classes, especially, class IV and V, social classes were excluded from analysis.

My study concentrates on CAD patients living below poverty line and in this study prevalence of MS and its individual metabolic components, i.e., central obesity, hypertension, diabetes or IFG, hypertriglyceridemia and low HDL, were all found to be high compared to various studies conducted in India, but all of them have been conducted in community which include subjects with and without CAD. Relation between MS and CVD risk has been explained unequivocally in different studies.[60-63] Conversely, there must be an increased prevalence of MS and its individual metabolic components in patients with coronary artery disease as compared to its prevalence in general population in the community. The result of my study confirms this fact.

Prevalence of central obesity and hypertension were significantly higher in patients with ACS as compared to patients with chronic CAD. Thus presence of these risk factors means more severe disease to a patient with CAD. This finding not observed in hypertriglyceridemia, low HDL, diabetes and IFG. Interestingly, it was observed that central obesity, hypertriglyceridemia, diabetes and IFG and metabolic syndrome form a significant “U” shaped distribution in age groups. The proximal limb of this U

is formed by patients with premature coronary artery disease (age<40). This finding not observed on case of hypertension and low HDL.

Hence clustering of these metabolic risk factors result in the onset of CAD earlier in these patients. Asian Indians have an earlier and more severe course of CHD compared to other ethnic groups.[102]A striking predisposition to premature coronary artery disease and early myocardial infarction has been observed among Asian Indians.[1, 102] The mean age of an Asian Indian patient suffering a myocardial infarction is only 50 years.25% of all MIs in this population occur under the age of 40 years.[89] Increased prevalence of metabolic syndrome and related risk factors could explain these facts that are observed in above mentioned studies.

It is not clear why subjects who are generally manual labourers hence physically active, poor and cannot afford costly products of food industry should develop these clusters of metabolic risk factors. A simple explanation could be marked changes in their diets and lifestyle. Some data suggest that diets presently consumed by them were highly imbalanced. Specifically, the dietary consumptions of saturated fat and cholesterol were high and fiber and antioxidants were low.[49] Globalization and urbanization definitely has made an impact in their food habits, nutrition and physical activity. According to the "genetically unknown foods" hypothesis, adopting western dietary habits with a high fat and sucrose intake could lead to an epidemic of the IRS.[103] Maladaptation, 'stress response' causing

hypothalamic pituitary activation, increased smoking and alcohol drinking may be additional contributory factors. Moreover we Indians form a special "Asian Indian phenotype".

Another explanation would be that urban poor living below poverty line due to inadequate nutrition especially during antenatal period leading to fetal immaturity thus acquiring thrifty phenotype that leads to increased risk of acquiring obesity and insulin resistance at an earlier age.

Studies on the relationship of birth weight with insulin resistance syndrome variables in Indian children revealed that a lower birth weight is associated with insulin resistance.[104] It has been hypothesized that lower birth weight followed by increased obesity could lead to IRS during adulthood.[104]

# Conclusion

The result of present study suggests that in urban patients who live below poverty line with symptomatic coronary artery disease there in increased prevalence of metabolic syndrome, central obesity, hyperglycemia, hypertension and dyslipidemia. The higher prevalence particularly noticeable in those with the premature coronary artery disease and that might have resulted in earlier onset of CAD in them. Moreover presence of central obesity and other risk factors might lead to more severe CAD, i.e., acute coronary syndrome.

It is assumed that adapting unhealthy life styles such as sedentary work, rich calory and imbalanced diet, malnutrition among antenatal mothers might be the cause for this occurrence.

Coronary artery disease and its management pose a significant economical challenge and these patients who poor may not be able to meet the challenge, resulting in higher mortality and morbidity. Metabolic syndrome which is the emerging as a major risk factor for coronary artery disease in rich and poor further complicates the situation for these patients. So prevention of metabolic syndrome is better than cure for metabolic syndrome in these patients.

There is an urgent need to explore nutrition and physical activity and their role in the prevention and treatment of disorders directly or indirectly related to the metabolic syndrome. It is possible that by diet, exercise, changes in lifestyle, and most impotantly by education the prevalence of metabolic syndrome and hence prevalence of coronary artery disease can be reduced and such a preventive strategy is urgent need of the hour for our country which is facing a twin epidemic of diabetes and coronary artery disease.

This study identifies a class of society, which is in urgent need of such preventive measure.

## Prevention of MS

- Intensive efforts should be made to make them aware that they are at more risk for development of type 2 diabetes and CAD.
- Preventive measures should be particularly vigorous for those with the family history of type 2 diabetes and premature CAD.
- Overweight individuals and those with abdominal obesity should be actively managed to lose weight by life style measures.
- Detection of one component of metabolic syndrome should prompt the search of other components and its management.
- Adequate nutrition during the intrauterine period should be given to prevent early life adverse events, which may promote insulin resistance in adulthood.

Early identification and treatment of metabolic syndrome and other metabolic risk factors goes long way in preventing coronary artery disease in these patients.

# Limitations

1. Due to inadequate representation from class IV and V of modified Prasad's classification, the effect of social class in metabolic risk factors could not be studied.
2. Sample size was 113. This might have resulted in type 2 error in the study due to small sample size.

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# Proforma

Name | Hospital No.
Age | Date of admission
Sex | Date of discharge
Address

## Socio-economic Status

Occupation
Income (monthly)
Modified Prasad's Classification

## Diagnosing Coronary Artery Disease

### (I) History

### Chest pain

Site
Character
Onset (new i.e. with in 1 month/old)
Duration (<20min/ 20-30min/ >30 min)
Progression in past 60 days (crescendo pattern)
Frequency
Aggravating factor
Rest

- Angina at rest within past 1 month but not within preceding 48 h
- Angina at rest within 48 h

S/L nitroglycerine
CCA Class

### Angina equivalents

Dyspnea, fatigue, faintness and eructation
Pregnancy (in females of reproductive age)
Drug abuse

### Past History

MI within 2 weeks
MI after 2 weeks
Thrombolysis
IHD and Rx

### Examination

Pulse /min
BP mmHg
RR /min
Temperature degree Fahrenheit
SaO2 %
JVP cm
Pallor
Thyroidomegaly
Edema
Height
BMI
CVS
RS
Abdomen
CNS

Hemoglobin
Hematocrit

## (II) Electrocardiogram

| | First ECG | | ECG after 24 hours |
|---|---|---|---|
| | **leads** | **Myocardial localization** | |
| T inversion | | | |
| ST elevation | | | |
| ST depression | | | |
| Q wave | | | |
| LBBB | | | |

## (III) Creatinine Kinase - MB

| At presentation | 24 hour later |
|---|---|
| | |

**Secondary causes**

- Fever
- Thyrotoxicosis
- Tachycardia
- Hypertension
- Aortic Stenosis
- High Output State
- Pregnancy
- Drugs: Cocaine, Amphetamine
- Anemia
- Hypoxemia (pneumonia, CCF etc)
- Hypotension

## Diagnosis

1. **Chronic coronary artery disease**
    - **Stable angina**
    - **Old MI**

2. **Acute coronary Syndrome**
    - **Unstable angina – Braunwald Class.**
    - **NSTEMI.**
    - **ST elevation MI.**

## DIAGNOSING METABOLIC SYNDROME

### Waist Circumference

| First reading | Second reading | Average |
|---|---|---|
| | | |

### Blood pressure (in mm Hg)

| Day 1 | Day 2 | Average |
|---|---|---|
| | | |

**Treatment of previously diagnosed hypertension**

### Fasting blood sugar (in mg per dL)

| Day 1 | Day 2 | Day 3 | Average |
|---|---|---|---|
| | | | |

**Previously diagnosed type 2 diabetes**

### Fasting lipid profile

| TGL | LDL | HDL | TC | VLDL | LDL/HDL Ratio |
|---|---|---|---|---|---|
| | | | | | |

**Specific treatment for this lipid abnormality**

## Diagnosis Metabolic syndrome

# Abbreviations

ACS → Acute Coronary Syndrome

ADA → American Diabetic Association

AICPI → All India Consumer Price Index

Apo B → Apo lipoprotein B

ATP III → Adult Treatment Panel III

BMI → Body Mass Index

CAD → Coronary Artery Disease

CCS → Canadian Cardiovascular Society

CHD → Coronary Heart Disease

CHAOS → **C**oronary artery disease, **H**igh Blood Pressure, **A**dult Onset Diabetes (type 2), **O**besity, and **S**troke

CI → Confidence Interval

CK-MB → Creatine Kinase – MB

CPI → Consumer Price Index

CRP → C - reactive protein

CUPS → Chennai Urban Population Study

CVD → Cardiovascular disease

DBP → Diastolic Blood Pressure

DPP → Diabetes Prevention Program

ECG → Electrocardiogram

| | | |
|---|---|---|
| EGIR | → | European Group for the study of Insulin Resistance |
| FBS | → | Fasting Blood Sugar |
| HDL | → | High Density Lipoprotein |
| IDF | → | International Diabetic Federation |
| IFG | → | Impaired Fasting Glucose |
| IGT | → | Impaired Glucose Tolerance |
| IL-6 | → | Interleukin-6 |
| IMCL | → | Intramyocellular lipids |
| JNC 7 | → | Joint National Committee |
| KMC | → | Govt. Kilpauk Medical College |
| LDL | → | Low density Lipoprotein |
| MS | → | Metabolic Syndrome |
| MI | → | Myocardial Infarction |
| NCEP | → | National Cholesterol Education Program |
| NEFA | → | Non-esterified Fatty Acid |
| NSTEMI | → | Non-ST elevation MI |
| PAI-I | → | Plasminogen Activator Inhibitor- I |
| PPAR γ 2 | → | Peroxisome proliferator-activated receptor γ 2 |
| PPARGC1A | → | Peroxisome proliferator-activated receptor γ co-activator-1 $\alpha$ |
| SBP | → | Systolic Blood Pressure |
| STEMI | → | ST elevation MI |
| TG | → | Triglyceride |

| | | |
|---|---|---|
| TNF-$\alpha$ | → | Tumour Necrosis Factor- $\alpha$ |
| UCP-1 | → | Uncoupling Protein-1 |
| UA | → | Unstable Angina |
| VA-HIT | → | Veterans Affairs High-Density Lipoprotein Intervention Trial |
| WHO | → | World Health Organization |
| WOSCOPS | → | West of Scotland Coronary Prevention Study |

# Abbreviations in Master Chart

| | | |
|---|---|---|
| SN | → | Serial Number |
| HospNo | → | Hospital Number |
| SocClass | → | Social Class |
| ChrCAD | → | Chronic Coronary Artery Disease |
| ACS | → | Acute Coronary Syndrome |
| STEMI | → | ST elevation myocardial infarction |
| NSTEMI | → | non- ST elevation myocardial infarction |
| UA | → | Unstable Angina |
| Waist | → | Waist Circumference |
| SBP | → | Systolic Blood Pressure |
| DBP | → | Diastolic Blood Pressure |
| c/oHTN | → | known case of hypertension |
| FBS | → | Fasting Blood Sugar |
| c/oDM | → | known case of diabetes mellitus |
| TG | → | Triglyceride |
| HDL | → | High Density Lipoprotein |
| c/oDyslipid | → | known case of Dyslipidemia |
| MS | → | Metabolic Syndrome |
| M | → | Male |
| F | → | Female |