

**DISSERTATION**  
**ON**  
**STUDY OF PLASMA FIBRINOGEN IN ACUTE**  
**MYOCARDIAL INFARCTION**

**Dissertation submitted to**  
**THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY**  
**In partial fulfilment of the regulations**  
**for the award of the degree of**

**M.D. -GENERAL MEDICINE- BRANCH – I**



**THANJAVUR MEDICAL COLLEGE,**  
**THANJAVUR - 613 004.**

**THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY**  
**CHENNAI - 600 032.**

**APRIL - 2013**

## **CERTIFICATE**

This is to certify that this dissertation entitled “**STUDY OF PLASMA FIBRINOGEN IN ACUTE MYOCARDIAL INFARCTION.**” is the bonafide original work of **Dr. NARENDRAN.M** in partial fulfilment of the requirements for M.D Branch -I (General Medicine) Examination of the Tamilnadu Dr. M.G.R. Medical University to be held in APRIL - 2013. The period of study was from October– 2011 - November 2012.

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I, **Dr.NARENDRAN. M**, solemnly declare that the dissertation titled “**DISSERTATION ON THE STUDY OF PLASMA FIBRINOGEN IN ACUTE MYOCARDIAL INFARCTION** ” is a bonafide work done by me at Thanjavur Medical College, Thanjavur during October 2011 - November 2012 under the guidance and supervision of **Prof.Dr.C.GANESAN, M.D.**, Unit Chief M-5, Thanjavur Medical College, Thanjavur.

This dissertation is submitted to Tamilnadu Dr. M.G.R Medical University towards partial fulfilment of requirement for the award of **M.D. degree (Branch -I) in General Medicine.**

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Dissertation on study of plasma fibrinogen in acute myocardial  
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**INTRODUCTION**

Cardiovascular disease is one among the major global health problems presenting in epidemic proportions. Myocardial infarction is one of the commonest cause of death, including low and middle income countries. India is in a transition phase from the state of high incidence of communicable disease to a state of high incidence of non communicable disease. India's contribution to the rising global burden of coronary artery disease is significant.<sup>1</sup>

High risks of coronary artery disease reported in south Asian populations, particularly in Indians regardless of the country in which they live.

During the last twenty years it is noted that Indians have a higher incidence of coronary artery disease. Myocardial infarction claims a large number of lives even before they reach fifth decade of life. Myocardial infarction occurring at early age is associated with absence of usual risk factors such as systemic hypertension, smoking, diabetes mellitus and hyperlipidemia in about one third of them.<sup>2</sup>

The coronary artery disease manifest as acute coronary syndrome including unstable angina, ST elevation MI and Non ST elevation MI. There is increase in mortality and complications associated with ST elevation MI.

1

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## **ABSTRACT**

### **BACKGROUND AND OBJECTIVES OF THE STUDY**

Myocardial infarction is one of the commonest cause of death in the developing and developed countries. Indians are more prone to coronary artery disease but conventional risk factors do not explain the high rates of Coronary Artery Disease among Indians. Myocardial infarction is claiming a large number of lives in india. An impressive difference was absence of traditional risk factors in a third of them. Novel risk factors like homocysteine, lipoprotein (a), small LDL particle and fibrinogen may play a significant role in these patients. The aim of this study is to estimate fibrinogen levels in myocardial infarction patients and to study association of these novel risk factors with conventional risk factors.

### **METHODOLOGY**

The present study included 70 patients who were admitted to IMCU and ICCU of Thanjavur medical college hospital during the period of Oct 2011–Nov 2012 fulfilling WHO criteria for acute myocardial infarction, presenting within 48 hours. Traditional risk factors were studied in addition to studying plasma fibrinogen levels.

### **RESULTS**

This study was predominantly male oriented 49(80%). Mean age of the patients was 52.26 years. Chest pain was the most common presenting symptom present in all the patients followed by sweating 10 (14.3%). Dyslipidemia was the most

common 42 (60.9 %) risk factor in the present study followed by smoking 39 (55.7 %). High mean plasma fibrinogen ( $440.61 \pm 75.4$  mg/dl) levels was noted among patients. Significant association was noted between plasma fibrinogen and risk factors like dyslipidemia, obesity, diabetes and smoking. High plasma fibrinogen was observed in patients with chronic alcoholism, but not statistically significant.

### **INTERPRETATION AND CONCLUSION**

In addition to the conventional risk factors of myocardial infarction, a high plasma fibrinogen levels were noted in patients with acute Myocardial infarction.

However, larger studies need to be done to substantiate these findings.

**KEY WORDS:** Myocardial infarction, Fibrinogen, Smoking, Dyslipidemia, Obesity.

## CONTENTS

SL. NO.	TITLE	PAGE NO.
1	INTRODUCTION	1
2	AIM OF THE STUDY	3
3	REVIEW OF LITERATURE	4
4	MATERIALS AND METHODS	46
5	RESULTS	50
6	DISCUSSION	70
7	CONCLUSION	77
8	SUMMARY	79
9	ANNEXURES	
	ANNEXURE –I BIBLIOGRAPHY	
	ANNEXURE –II PROFORMA	
	ANNEXURE –III MASTER CHART	
	ANNEXURE –IV ABBREVIATIONS	
	ANNEXURE –V CONSENT FORM	

## INTRODUCTION

Cardiovascular disease is one among the major global health problems presenting in epidemic proportions. Myocardial infarction is one of the commonest cause of death, including low and middle income countries. India is in a transition phase from the state of high incidence of communicable disease to a state of high incidence of non communicable disease. India's contribution to the rising global burden of coronary artery disease is significant.<sup>1</sup>

High risks of coronary artery disease reported in south Asian populations, particularly in Indians regardless of the country in which they live.

During the last twenty years it is noted that Indians have a higher incidence of coronary artery disease. Myocardial infarction claims a large number of lives even before they reach fifth decade of life. Myocardial infarction occurring at early age is associated with absence of usual risk factors such as systemic hypertension, smoking, diabetes mellitus and hyperlipidemia in about one third of them.<sup>2</sup>

The coronary artery disease manifest as acute coronary syndrome including unstable angina, ST elevation MI and Non ST elevation MI. There is increase in mortality and complications associated with ST elevation MI.

Acute myocardial infarction is due to sudden interruption of coronary blood flow. It is the complication of thrombotic occlusion of already narrowed coronary artery due to atherosclerosis.

The mortality following the acute coronary event depends on the size of the infarct. The left anterior descending supplies wide areas including bundle branches, ventricular wall and septum hence its occlusion results in larger area of infarct.

Salient features of coronary artery disease among Indians when compared to other ethnic groups.<sup>3</sup>

- More than two fold higher prevalence
- A decade earlier onset of first MI
- Nearly fivefold higher incidence of MI and mortality in younger population less than 40 years
- Severity of the disease
- Lower prevalence of traditional risk factors
- Higher prevalence of newer risk factors including fibrinogen, homocysteine, lipoprotein (a) and apolipoprotein B<sup>3</sup>

## **AIM OF THE STUDY**

1. To study fibrinogen levels in subjects with acute myocardial infarction.
2. To compare the novel risk factors like fibrinogen with conventional risk factors like smoking, hypertension, diabetes mellitus, obesity and dyslipidemia.

## **REVIEW OF LITERATURE**

### **Myocardial infarction**

#### **Definition**

The World Health Organisation (WHO) definition includes the presence of two of the following<sup>4</sup>

1. Symptoms of myocardial infarction
2. Cardiac markers (enzymes) elevated
3. ECG showing characteristic electrocardiographic changes

Newer diagnostic criteria according to the American College of Cardiology and European Society of Cardiology.<sup>5</sup>

It requires the presence of one of the following diagnostic criteria to satisfy the diagnosis of acute, evolving or recent myocardial infarction.

1. Typical rise and gradual fall (troponin I/T) or more rapid rise and fall (CK-MBs) of biochemical markers of cardiac muscle necrosis with any one of the following:
  - a. Symptoms of myocardial ischemia
  - b. Appearance of pathological Q waves in ECG

c. ECG changes suggestive of ischemia (ST segment elevation / depression)

d. Coronary artery intervention (Eg. Coronary angioplasty)

2. Pathological findings of an acute Myocardial infarction

### **Risk factors**

According to American heart association (AHA) prevention conference held in 1999, risk factors are classified to three categories.<sup>6</sup>

#### **1. Traditional /Conventional risk factors.**

- Cigarette smoking,
- Low HDL cholesterol
- Elevated serum cholesterol
- Hypertension
- Diabetes mellitus

#### **2. Predisposing factors**

- Male sex
- Physical inactivity
- Family history of CAHD
- Overweight & obesity
- Insulin resistance



### **3. Conditional factors**

- Homocysteine
- Fibrinogen
- Small LDL particle
- C-reactive protein
- Lipoprotein (a)

### **Emerging risk factors**

- Nitrotyrosine
- Oxidative stress
- Asymmetric dimethylarginine
- Myeloperoxidase

### **Smoking**

Cigarette smoking is the one of the most important modifiable risk factor. It interacts with other risk factors to increase the risk multi fold. It accelerates coronary atherosclerosis in men and women, at all ages. Smoking increases the risk of thrombosis, plaque rupture, myocardial infarction, arrhythmias and sudden death.

It increases the oxygen demand of myocardial tissue and hence worsens angina. Coronary artery disease causes about 40% of smoking related deaths, and in addition to it around 8% of them attributable to passive smoke exposure.

The most important and modifiable cause of coronary heart disease and death is smoking. Smoking correlates strongly with atherosclerotic disease, usually in association with other risk factors.<sup>7</sup>

It has been found that 28% of all deaths from coronary heart disease are attributed to tobacco smoking. Compared with non-smokers, current smokers have a 70% increased risk of fatal coronary event and a two to four fold increased risk of non-fatal CAD.<sup>8</sup>

In a recent major overview, smoking cessation reduced coronary heart disease mortality by 36% as compared with mortality in subjects who continued smoking.<sup>9</sup>

Smoking was the most common risk factor (87%) in a study by Siwach SB et al. who studied the profile of acute MI in young patients (below 40 years).<sup>10</sup>

## **Hyperlipidemia**

Abnormalities in plasma lipoproteins and derangements in lipid metabolism rank as the most firmly established and best understood risk factor for atherosclerosis. The 4S trial demonstrated an approximately 40% reduction in incidence of myocardial infarction as well as a further reduction in the need of procedural intervention in hyperlipidemic individuals.<sup>11</sup>

In a study by Weinberger et al., hyperlipidemia was present in only four patients among 30 young patients.<sup>12</sup>

In a study by Kanitz et al., Hyperlipidemia was present in 20% of young adult patients.<sup>13</sup>

## **Hypertension**

The elevated blood pressure has been shown to be associated with accelerated atherosclerosis and coronary heart disease. Elevated systolic blood pressure/diastolic blood pressure is clearly associated with an increased risk of coronary heart disease.<sup>14</sup>

In Framingham heart study even high normal blood pressure augments risk of cardiovascular disease two fold compared with lower levels.

Hypertension is not a common risk factor in CAD in young adults. In a study by Zimmerman FH et al., hypertension and diabetes were more frequent in older men and women.<sup>15</sup>

In study by Al Khadra et al., hypertension was documented in 18.5% of young individuals with acute myocardial infarction.<sup>16</sup>

### **Diabetes mellitus**

Diabetes mellitus is the most important CAD risk equivalent. Most diabetic patients die of atherosclerosis and its complications.

The dyslipidemia present in diabetic patients is responsible for the elevated cardiovascular risk. The coronary artery disease is responsible for three fourths of all deaths in diabetic patients.<sup>17</sup>

There is endothelial and smooth muscle function impairment in diabetic patients. They also have increased adhesion of leukocytes to the vascular endothelial surface. This is very important step in atherosclerosis.

Patients with diabetes mellitus have two to eight fold higher rates of future cardiovascular events as compared with age and ethnically matched non-diabetic individuals.

In a study by Barbash GI et al. few young patients with MI had history of hypertension and diabetes mellitus.<sup>18</sup>

In a Nurse's health study, women who eventually developed type 2 DM, the relative risk of MI was increased 3 fold before the diagnosis of diabetes.<sup>19</sup>

In a study by Al khadra 30.8% of young patients with MI had diabetes mellitus.<sup>16</sup>

## **Gender**

Men have increased risk of atherosclerosis than women. It is the most important predisposing factor for coronary atherogenesis. The female sex have protection from coronary atherogenesis. This effect is due to the estrogen. After menopause however, coronary risk accelerates in women.<sup>20</sup>

The Framingham study found a greater than two fold age adjusted increase in risk for CAD among post menopausal females compared with premenopausal females. Data from the Framingham cohort also indicate that there are sex specific differences in the manifestations of CAD.<sup>21</sup>

Male : Female ratio was 20:1, in study of profile of acute MI in young patients by Siwatch SB et al.<sup>10</sup>

### **Physical activity and Obesity**

Regular physical activity is associated with cardio protective effect. It increases exercise capacity. It also reduces the oxygen demand of cardiac muscles. Hence it lowers the coronary risk. Cardioprotective effects of exercise include adiposity, diabetes incidence, lowered blood pressure, improved coronary endothelial function, lower CRP levels, and appears to benefit hemostatic variables including tissue plasminogen activator, fibrinogen, VWF, fibrin D dimer and plasma viscosity.<sup>26</sup>

A consistent series of prospective studies have demonstrated an association between levels of physical activity and reduced rates of cardiovascular mortality and morbidity.

In a prospective Harvard study, those men with highest levels of activity at baseline had a 40% reduction in non-fatal cardiovascular events and 24% reduction in cardiovascular mortality compared with those with sedentary lifestyle.<sup>22</sup>

In the women health initiative, walking briskly for 30 mins, 5days/week associated with 30 % reduction in vascular events over a period of 3.5 years follow up.<sup>23</sup>

The American Heart Association has recommended an exercise energy expenditure approaching 2000 calories each week, a level of exercise that can be achieved with modest daily exertion.<sup>24</sup>

Recent studies indicate that waist / hip ratio, a surrogate marker for centripetal obesity is associated with coronary risk. This ratio holds good as a independent factor in both sex.<sup>25</sup>

### **Novel atherosclerotic risk factors**<sup>26</sup>

Several newer risk markers of atherothrombotic risk are identified. They are proved by epidemiological studies. They are useful clinically. They are fibrinogen, lipoprotein (a), plasminogen activation inhibitor-1, homocysteine and high sensitivity C reactive protein.

## **C reactive protein**

CRP is an acute phase reactant. CRP is a member of the pentraxin family. It plays an important role in the human innate response. Apart from this effect, it directly affects vascular vulnerability. Levels of CRP greater than 3 mg/L also appear to predict recurrent coronary events.

## **Lipoprotein(a)**

It was first described in detail by Berg et al. Its clinical importance was described by Mclean et al. They have structural similarity with apoprotein (a) and plasminogen.

It has LDL particle with apo B-100. This component is linked by a disulphide bridge to apoprotein (a).

Apoprotein (a) is a member of a family of 'KRINGLE' containing proteins. Other members of this family include proteins such as Plasminogen, Prothrombin, Factor XII, urokinase type Plasminogen activator and Macrophage stimulating factor.



Lipoprotein(a) acts by binding on the endothelium. It competes with plasminogen. It binds to plasminogen receptor on endothelium. Thus it reduces the activity of plasminogen. Many epidemiological studies prove positive relation between lipoprotein(a) and atherogenic risk.

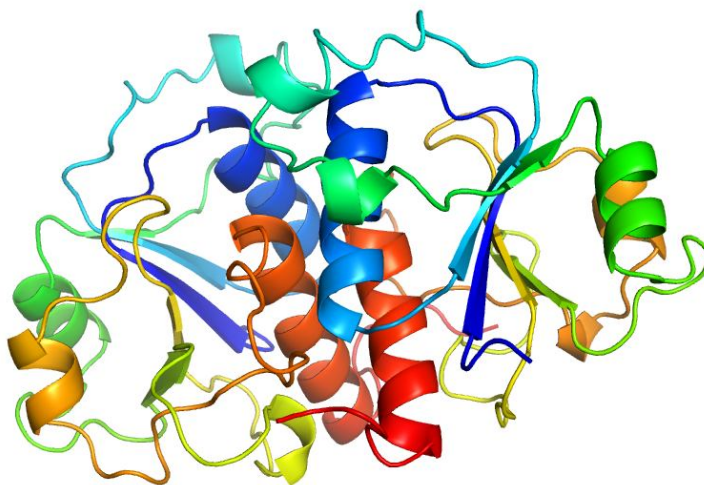
Their plasma concentration is inversely proportional to the size of apoprotein isoform. Thus small isoforms are associated with higher plasma Lp(a) concentration.

At birth Lp (a) levels are low and adult levels achieved in two years. Levels are high in Asian and African population. Levels above 30 mg/dl are significant.

Serum Lp(a) levels elevated in type 2 DM, renal failure, menopause, hypothyroidism and malignancy. Height, weight, BMI, diet, weight loss and physical activity do not affect the level of serum lipoprotein (a).

## HOMOCYSTEINE

Homocysteine was first described by botz and du vizwand in 1932, however a link to human disease was not suggested until 1962.



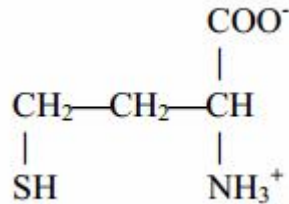
### *Structure of Homocysteine*

The person who first described pre mature atherosclerosis in children and young individuals is Dr. McCully .In 1960s he demonstrated that atherosclerosis is present in children with disorders of homocysteine metabolism.

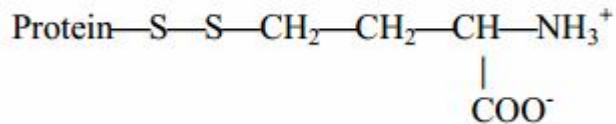
Dr. McCully demonstrated that atherosclerosis could be due to high homocysteine levels. He postulated the same cause for atherosclerosis in adults also. He hypothesized that elevated homocysteine levels is the cause for atherosclerosis, but this was not widely accepted.<sup>27</sup>

Homocysteine is an intermediate derivative in the metabolism of methionine. This amino acid contains a thiol-containing group. Less than 1% circulates as free form (reduced state). Nearly 75% is bound to serum albumin. Around 25% combines with other thiol-containing amino acids or with itself to form dimer compounds.<sup>28</sup>

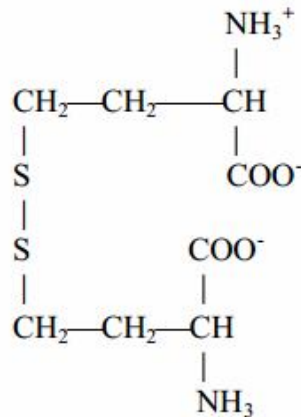
**Homocysteine (reduced) 1%**



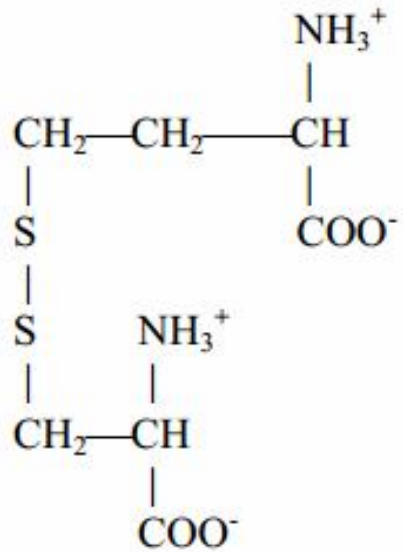
**Protein bound homocysteine mixed disulphide (oxidised) 70-80%**



**Homocysteine (oxidised) 5-10%**



## Homocysteine- cysteine mixed disulphide (oxidised) 5-10%



## Metabolism of homocysteine

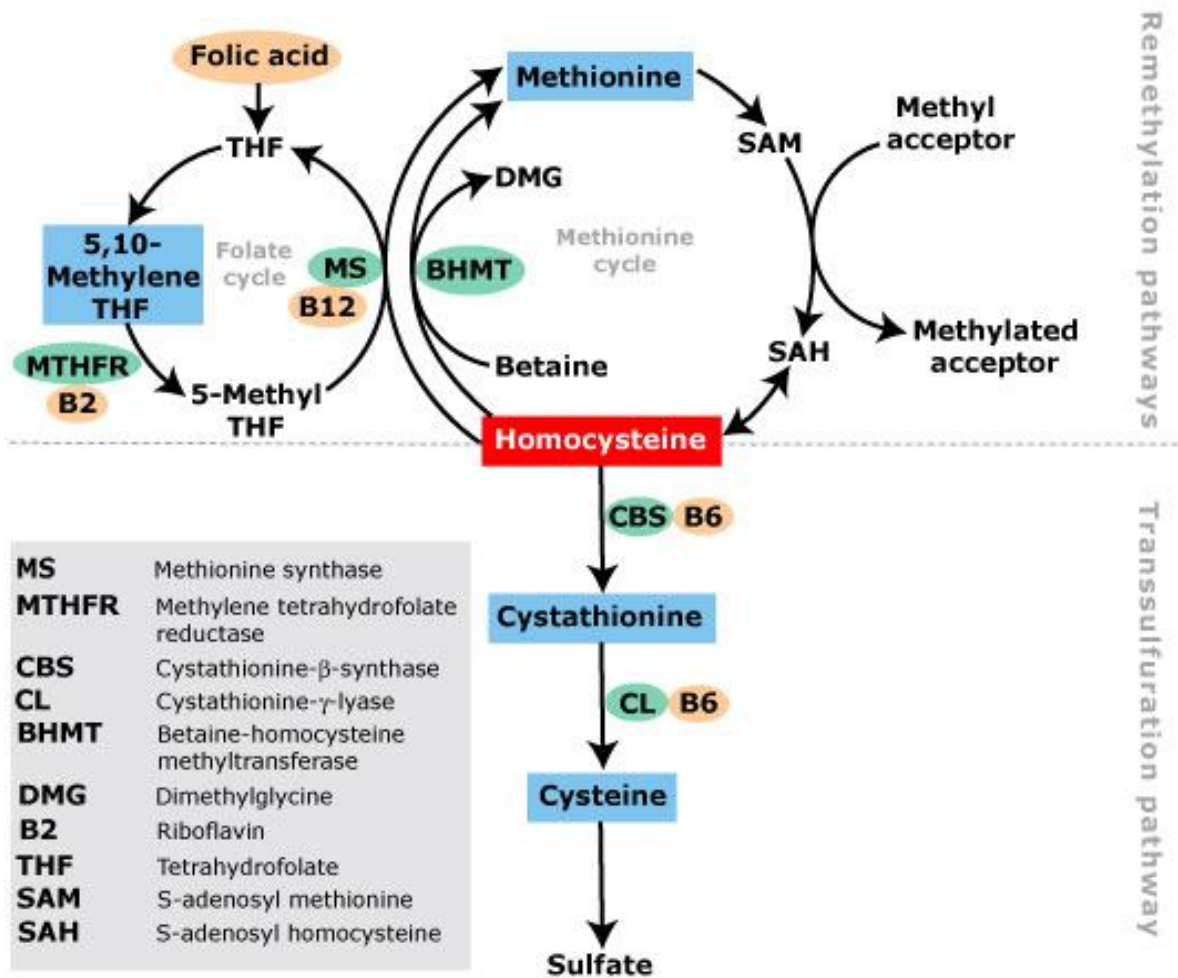
The important 3 processes involved are as follows<sup>28</sup>

- Demethylation
- Transmethylation
- Transamination

### Demethylation

In Demethylation methionine is converted to homocysteine .

In this process various intermediate metabolites are formed including S-adenosyl homocysteine & S-adenosyl methionine .



**Fig. 1 : Metabolism of Homocysteine**

This chart describes the metabolic pathways of Homocysteine in a nutshell. It describes both remethylation and transsulfuration pathways in our body.

## **Transmethylation**

In transmethylation pathway homocysteine is again converted to methionine. Homocysteine is again remethylated to methionine in liver, by enzyme betaine-homocysteine methyl transferase. This step is catalysed by methionine synthase. Vitamin B12 is used as a co-factor. Methyl tetrahydrofolate acts as a substrate.

## **Transsulfuration**

It is the process by which homocysteine is converted to cysteine. This reaction is irreversible process. In this pathway cystathionine  $\beta$  synthase which is vitamin B<sub>6</sub> dependent acts as catalyst. By this process cystathionine is formed as intermediate. Finally cystathionine is hydrolysed and it produces cysteine.

## **Measurement and Classification of Homocysteine Levels**

The normal plasma homocysteine is 5-15  $\mu$ moles/L. Plasma homocysteine level greater than 15  $\mu$ moles/L is considered as hyperhomocysteinemia.

The American Heart Association have defined hyperhomocysteinemia as being divided into<sup>29</sup>

<b>Moderate</b>	<b>:</b>	<b>15-30 µmoles/L</b>
<b>Intermediate</b>	<b>:</b>	<b>30 - 100 µmoles/L</b>
<b>Severe</b>	<b>:</b>	<b>&gt;100 µmoles/L</b>

### **Various methods of estimation of plasma homocysteine<sup>30</sup>**

- 1 High liquid chromatography
- 2 ELISA
- 3 Mass spectrometry
- 4 Fluorescence polarizaion immunoassay

### **Types of hyperhomocysteinemia**

They are broadly divided into 2 types of hyperhomocysteinemia.<sup>31</sup>

1. Primary &
2. Secondary

#### **1. Primary hyperhomocysteinemia**

Due to defect in homocysteine metabolism pathways like:

##### **a. Deficiency of Cystathionine beta synthase (CBS) :**

It is the commonest cause of hyperhomocysteinemia . It is transmitted as autosomal recessive trait. It occurs in frequency of 1 per 3 lakh live births.

The important clinical features are skeletal deformities, premature atherosclerosis, mental retardation and dislocation of lens. About one percent of the general population have cystathionine beta synthase deficiency, in heterozygous state. They have homocysteine levels elevated in the range of 20-40 micromol/L.

**b. Deficiency of MTHFR (5,10 methylene tetrahydrofolate reductase )**

The gene for enzyme MTHFR is mutated. It results in hyperhomocysteinemia associated with low folic acid.

**c. Deficiency of Methylene tetrahydrofolate homocysteine methyl transferase<sup>31</sup>**

**2. Secondary hyperhomocysteinemia**

**a. Physiological**

- Elderly age group
- Men
- Post menopausal

**b. Modifiable factors**

- use of Tobacco
- consumption of Coffee



**c. Vitamin deficiency -**

- Folate
- Vit B6 (pyridoxine),
- Vit B12 (cobalamine)

**d. Systemic disorders**

- (i) Psoriasis
- (ii) Anorexia nervosa
- (iii) Systemic lupus erythematosus
- (iv) Pernicious anaemia
- (v) Hypothyroidism
- (vi) Renal failure
- (vii) Liver failure
- (viii) Organ transplantation

**e. Drugs (toxins)**

- 1) Cholestyramine ,Colestipol ,Metformin (affect folate and cobalamin absorption)
- 2) Folate antagonists
  - Phenytoin
  - Carbamazepine

- 3) Vit B6 antagonists (Theophylline, Oestrogen containing OCP ,Niacin)
- 4) L-dopa (increases transmethylation)
- 5) Androgens
- 6) Cyclosporins ,Fibric acid derivatives (reduces renal function)
- 7) Nitrous oxide (inactivates methionine synthesis)

### Determinants of plasma total homocysteine<sup>32</sup>

		<b>Fasting plasma homocysteine</b>
<b>Sex</b>	Male	10.3
	Female	8.8
<b>Age (years)</b>	< 45	8.8
	45-54	9.2
	54-64	9.8
	> 65	10.4
<b>Serum creatinine (mol/L)</b>	< 79	8.7
	79-87	9.3
	87-96	9.3
	96-106	9.7
	> 106	10.5
<b>Alcohol intake (g/d)</b>	0.1-4.9	9.3
	5-14.9	9.4
	> 15	10.0
<b>Caffeine intake (mg/d)</b>	< 88	8.9
	> 420	9.9
<b>Current cigarette smoking</b>	0	9.3
	1-15	9.9
	16-25	10.1
	≥ 26	11.0
<b>Body mass index (kg/m<sup>2</sup>)</b>	< 23.2	9.4
	≥ 30.6	9.9

Dietary intake of folate in a dose of 0.5 to 5 mg reduces homocysteine levels by 24 %. Vitamin B12 in addition reduces to about 7%.

Renal failure raises plasma homocysteine due to reduced renal clearance .

Coffee intake and smoking showed positive association with homocysteine. Moderate alcohol lowers while chronic alcoholics have increased plasma homocysteine.

### **Effects of Homocysteine on vascular endothelium<sup>28</sup>**

It produces damage to vascular endothelial surface & accelerates atherosclerosis. It is also associated with thrombo embolism. It affects smooth muscle cells, coagulation factors, connective tissues , plasma lipoproteins and platelets. It also affects production of nitric oxide.

It stimulates the proliferation of vascular smooth muscle . It increases DNA synthesis and cyclin A. It causes platelet aggregation and increases platelet adhesion. The inhibition of Na<sup>+</sup> - K<sup>+</sup> - ATPase activity by Homocysteine is responsible for hemolysis of Red blood cells.

## **Hyperhomocysteinemia favours atherosclerosis**<sup>34</sup>

Endothelial cell dysfunction is prerequisite for development of atherosclerosis. Homocysteine is toxic to endothelial cell surface by generating oxygen free radicals. Sulfhydryl group reacts to ferric or cupric ions and gets oxidized to synthesis hydrogen peroxide. This reaction also produces oxygen free radicals and homocysteine radicals.

Homocysteine gets auto-oxidized to form Homocysteine mixed sulphides and homocysteine thiosulphates. There by it liberates hydrogen peroxide and superoxide anion. Hydrogen peroxide implicated in vascular injury of hyperhomocysteinemia.

The oxidation of LDL by Homocysteine causes vascular injury . Homocysteine thiolactone a byproduct oxidises native LDL. This step produces oxidised LDL which when taken up by intimal macrophages of vascular endothelium forms foam cells. This step initiates the early stage of atheromatous plaque formation. Homocysteine reduces synthesis of endothelial derived relaxing factor (NO). NO is a potent antiplatelet agent. It also inhibits production of hydrogen peroxide.

Hyperhomocysteinemia may interfere with antithrombotic and fibrinolytic mechanisms of the endothelium, making it prothrombotic. Homocysteine causes collagen deposition in atheromatous plaques . It also increases of proliferation of vascular smooth muscle cells .

Homocysteine decrease the activity of antioxidant enzymes. This effect is responsible for proliferation of smooth muscles of vascular endothelium by increasing their mitotic activity.

### **Complications of hyperhomocysteinemia<sup>31</sup>**

- Hypertension
- Cerebrovascular accidents
- Ischemic heart disease
- Peripheral vascular disease
- Venous thromboembolism

### **Stroke and peripheral vascular disease**

Their concentration is elevated in patients with CVA (stroke) and peripheral vascular disease (PVD) .

As regards cerebrovascular disease, eleven clinical studies looked at causal relationship between homocysteine levels and cerebrovascular disease. In nine studies, they have significant relationship while two prospective studies lacked evidence for an association.

### **Hyperhomocysteinemia and venous thrombosis**

Hyperhomocysteinemia can be considered as a factor which favours venous thromboembolism.

Martin Den Haijer et al.<sup>36</sup> studied the plasma homocysteine concentration of patients with venous thrombosis. It was found to be elevated. The combination of hyperhomocysteinemia and factor V further increases the likelihood of venous thromboembolism .

### **Homocysteine and diabetes mellitus**

Type 2 diabetes mellitus patients who had macrovascular disease had elevated homocysteine levels. It was shown that hyperhomocysteinemia appears to be a greater risk factor for cardiovascular disease in them, than the subjects with normal/impaired glucose tolerance.<sup>37</sup>

## **Homocysteine and hypertension**

Bortolotto LA et al, demonstrated that hypertensive patients with elevated levels of homocysteine associates positively with arterial stiffness.<sup>38</sup>

## **Homocysteine and renal disease**

Kidneys play an important role in homocysteine metabolism. Patients with renal failure have delayed clearance of homocysteine. This effect increases risk of atherosclerosis.

## **Homocysteine and ischaemic heart disease**

As regards CAD, 17 studies were evaluated, out of which in 14 studies, homocysteine was found to be a significant risk factor. The CAD risk was around ten percent attributed to be due to elevated homocysteine. It was studied that reduction of homocysteine levels by 3  $\mu\text{mol/L}$  results in 30% reduction of risk of ischaemic heart disease.<sup>39</sup>

Study done by Boushey et al. shows that increase in homocysteine levels is associated with an increased risk of peripheral arterial disease, ischaemic heart disease, CVA and venous thromboembolism.<sup>40</sup>

Studies by Arnesan et al illustrate that Homocysteine levels in study population was elevated than that of age and sex matched controls. This shows that ,it is an independent risk factor <sup>41</sup>

Nygaard et al studied 587 angiographically documented cases. He showed that there is positive relation between between their elevated levels and mortality. <sup>42</sup>

In Asian Indians, Chacko did his studies with CAD and plasma homocysteine. He stated that plasma homocysteine could not be statistically proven in Asian populations. <sup>43</sup>

Chambers et al. studied UK Indian Asians with CAD and compared them with Europeans having CAD. They studied 764 male patients (257 Indian Asian and 507 European). Their results revealed that plasma homocysteine concentrations were higher in Indian Asians compared with Europeans. <sup>44</sup>

Ford et al, analyzed the prospective trails and concluded that there was 20% increase in cardiovascular risk for every 5  $\mu\text{mol/L}$  increase in homocysteine levels. <sup>45</sup>



Enas A Enas et al found that women with homocysteine levels elevated above 16  $\mu\text{mol/L}$  have double the risk of acute coronary event .<sup>46</sup>

Stampher et al, studied about coronary atherogenesis in doctors. His results are such that a rise in homocysteine concentrations ten to twelve percent is positively associated with three times the risk of acute coronary event.<sup>47</sup>

### **Homocysteine and aute coronary event in young adults**

Myocardial infarction is claiming a large number of lives in young patients. Various studies have shown that homocysteine may be significant marker of risk in young patients lacking conventional risk factors .

In a study by ogawa et al, he discussed the role of homocysteine in myocardial infarction (young adults) and concluded that increased concentration of plasma homocysteine is absolutely a risk marker for myocardial infarction.<sup>48</sup>

Dr. Khare A. studied the role of homocysteine in patients with acute myocardial infarction less than 40 years age. He concluded that elevated homocysteine levels were independently associated with CAD.<sup>49</sup>

VK Katyal et al., studied 100 young patients (less than 40 years) admitted with acute MI and found hyperhomocysteinemia to be a significant contributor towards premature CAD.<sup>50</sup>

Study conducted by Puri A et al. showed that CAD is associated with homocysteine. He postulated that it can be taken as an important risk factor among young CAD patients.<sup>51</sup>

Stephen M Schwartz et al studied 79 women of age < 45 years diagnosed with MI and concluded that elevated plasma homocysteine and low plasma folate are risk factors for MI among young women.<sup>52</sup>

## **TREATMENT**

The effective way of reducing homocysteine concentration in plasma is to treat with folates, vitamin B6 and B12. A strong negative correlation between folic acid levels and their homocysteine levels has been proven.

Guidelines of the American heart association advocate the principle of screen and treat, i.e., screening for hyperhomocysteinemia is recommended only in high risk population (personal or family history of premature atherosclerosis, myocardial infarction, hypertension, diabetes).

It is recommended to keep the homocysteine levels to  $<10\mu\text{mol/L}$  in the high risk group. Those with hyperhomocysteinemia should be treated with dietary modification followed by vitamin supplementation or fortification of food with vitamins (400  $\mu\text{gm}$  of folic acid, 2mg of vitamin B6 and 6 $\mu\text{gm}$  of vitamin B12).<sup>53</sup>

In the vitamin intervention for prevention of stroke trial, the benefit of high dose vitamin therapy over vascular events was not established. The effect on stroke, CHD events, and death could not be proved.<sup>54</sup>

Results have shown that folic acid supplementation reduced plasma homocysteine by 41%, whereas Vit B12 supplement lowered homocysteine level by 14.8% and both were significant. But vit B6 therapy did not reduce homocysteine levels.

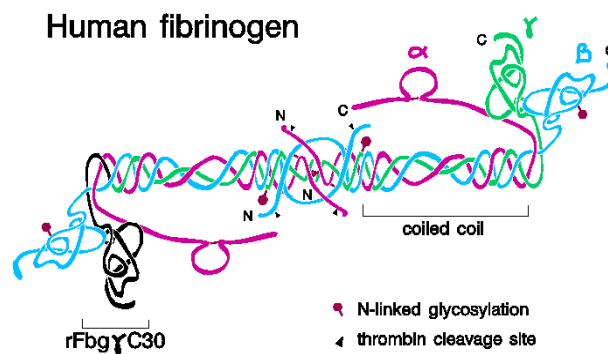
The combination of three vitamins reduced plasma homocysteine by 49.8%.<sup>55</sup>

## FIBRINOGEN

It is a part of coagulation cascade. It regulates blood flow and viscosity.

Now studies shows that elevated plasma concentration of fibrinogen is associated with vascular events like CVA , thrombo embolic phenomenon and coronary artery disease.

Nevertheless, the role of fibrinogen in causing, atherosclerosis is complicated. The atheroma formation is similar in process to thrombogenesis. This step involves various other thrombogenic factors also. The major contributor is fibrinogen. Thus it has detrimental effects on vascular endothelium.



(H. Cote, adapted from R. F. Doolittle)

**Fig. 2 : Schematic model of fibrinogen<sup>56</sup>**

## **STRUCTURE OF FIBRINOGEN MOLECULE**

The fibrinogen is a glycoprotein. Molecular weight around 340 kDa. Normal plasma concentration is 200 to 400n mg / dL. It is a precursor to fibrin. Length is 45 nm . Diameter 9 nm. It consists of three pairs of polypeptide chains . They are namely alpha, beta & gamma chains. They are held together by disulphide bonds.

The central nodule or E-domain is 5 nm in diameter and contains the NH<sub>2</sub>-terminal of all six polypeptide chains forming the NH<sub>2</sub>-terminal disulfide knot. The two outer D-domain nodules are composed of the C-terminal two thirds of both the B $\beta$  and  $\gamma$  chains. Between the E- and D-domains, there is a stretch of approximately 120 amino acids from each of the three chains that forms an  $\alpha$ -helical structure known as the coiled-coil domain. This region of the molecule is supported on both sides by a set of disulfide bonds called disulfide rings. These rings play an important role in making fibrin mechanically strong and resistant to proteolysis. Structural elements in each of the individual chains are needed for blood coagulation.

The A $\alpha$  chain is a 610-amino acid polypeptide that can be divided into three distinct domains. The first section of the A $\alpha$  chain (residues 1-194) contains a region (residues 45-161) linked to the B $\beta$  and  $\gamma$  chains by disulfide bonds. This section forms part of the  $\alpha$ -helix or coiled coil domain. This first section also contains fibrinopeptide A (residues 1-16) and the polymerization site in the E domain.

The B $\beta$  chain is a polypeptide composed of 461 amino acids and is also divided into three sections. The first 80 residues contain the fibrinopeptide sequence (residues 1-15) and a site that supports endothelial cell spreading and proliferation (residues 15-42). The middle section (residues 81-192) is linked to the A $\alpha$  and  $\gamma$  chains through disulfide rings and forms part of the coiled-coil domain.

The  $\gamma$  chain is only 411 amino acids long and is also divided into three distinct sections. Unlike the A $\alpha$  and B $\beta$  chains, there is no fibrinopeptide at the NH<sub>2</sub>-terminus of they chain.

The first 18 amino acids of the  $\gamma$  chain form part of the NH<sub>2</sub>-terminal disulfide knot, the middle segment of this polypeptide consists of amino acids 19-135. This section contains the disulfide rings that link this region to the A $\alpha$  and B $\beta$  chains in the coiled-coil domain.

There are 2 distinct forms of  $\gamma$  chains in human plasma fibrinogen. Approximately 15% of the  $\gamma$  chain contains an extended C-terminal and are designated  $\gamma'$  chains. Although Fibrin polymerization and cross linking of  $\gamma'$  proceed normally, the  $\gamma'$  chain does not support platelet aggregation. The clinical significance of the  $\gamma'$  chain remains unknown, however, recent studies suggest that  $\gamma'$  is a carrier for the zymogen of factor XIII in circulating blood.

### **Synthesis**<sup>57</sup>

Plasma fibrinogen is synthesized in the liver by the hepatocytes. It is released into circulation with half life of nearly 100 hrs. it is degraded at rate of 24 % per day. The turnover rate of fibrinogen is about 1.7 to 5.0 gm/day.

## **Function**<sup>56, 57</sup>

It is the clotting factor I, according to the system for naming blood clotting factors. It plays vital role in coagulation pathway. It produces fibrin on activation.

Results in fibrin which binds to lipoprotein and LDL and retains lipid moiety in the plaque. It is also important mediator in inflammation and atherogenesis. It plays pivotal role in thrombogenesis. The possible mechanisms include increased blood viscosity and enhanced platelet aggregation. It also causes atherothrombosis by infiltrating the vessel wall. Thus they favour thrombus formation.

## **Role in Inflammation**

They interact with WBCs by 'integrins'. The integrins are surface receptors coated on the leukocytes. Mac1 and alpha X and beta 2 are the fibrinogen binding receptors. Mac1 is very specific for fibrinogen.

Fibrinogen also bind with intercellular adhesion molecule-1 (ICAM-1) . ICAM-1 is otherwise called CD54. It is present over vascular endothelium.



Fibrinogen attaches with Mac1 and also interacts with ICAM-1 to cause adhesion of monocytes over vascular endothelium. Fibrinogen also upregulates the expression of ICAM-1 or CD54 over the vascular endothelium.

Fibrinogen favours chemotaxis. Thus it is important in inflammation. This effect is mediated by binding with integrins receptors of leukocytes. As a consequence of this activation, the neutrophil activation markers are expressed. There is also increase in calcium concentration intracellularly.

Fibrinogen favours cell to cell adhesion and also facilitate cell to collagen (extracellular matrix). Thus it facilitates the inflammatory response.

### **Role in Thrombogenesis<sup>58</sup>**

There is a normal balance between coagulation and fibrinolytic pathways. Thrombosis initiated when the balance fails.

Activation of Factor X to Factor Xa is the final step in coagulation pathway. This in turn converts prothrombin to thrombin. Thrombin facilitates conversion of fibrinogen to fibrin monomers. They adhere to each other to form fibrin clot.

Fibrinogen plays definite role in platelet aggregation . they interact with glycoprotein IIb-IIIa receptor present on platelets to facilitate its aggregation.

## **Role in Atherogenesis<sup>58</sup>**

Fibrinogen plays pivotal role in causing endothelial damage. The fibrin formed upon activation of fibrinogen , initially acts over the intimal layer of the vessel wall and it promotes cellular proliferation.

They favour cell migration and cell adhesion. The fibrin degradation products are the main stimuli for chemotaxis, extracellular matrix synthesis and their proliferation. This affects the vascular permeability and their tone.

There is clear evidence for large amount of fibrin deposition in the atherosclerotic lesions in the human blood vessels. They are present either over the intact surface of plaque or buried within the fibrous cap.

## **Estimating fibrinogen levels<sup>58</sup>**

It is done by two methods .

### **1. Functional methods**

The Functional methods involves determining coagulation time. This is directly related to plasma fibrinogen concentration. Clauss method is widely accepted method. This is based on the time necessary for coagulation end point.

## **2. Direct method**

This method quantifies the plasma concentration directly. They are based on immunological or gravimetric methods. The disadvantage is that they do not give information about quality of their function.

The normal plasma concentration varies circulating from 200 – 400 mg/dl. The widely accepted method is Clauss method.

### **Determinants of fibrinogen<sup>59</sup>**

**1. Genetics:** There is genetic polymorphism which accounts for 30 to 50 percent variation.

**2. Gender :** According to Monica Ausburgs, women generally have their fibrinogen levels elevated when compared with age matched men. This is irrespective of pregnancy. It is also independent of use of oral contraceptive pills.

**3. Smoking :** There is clear evidence for elevation of fibrinogen associated with smoking. There is proportional increase of 350mg/dl with each cigarette smoked. Smoking causes inflammation of pulmonary alveoli and bronchus. This in turn increases concentration of IL-6 which promotes synthesis of acute phase reactants from liver.

**4. Alcohol** : Mild to moderate alcohol intake reduces plasma fibrinogen levels. According to DESIR study, those who do not take alcohol or heavy drinkers taking more than 70gms/day have more plasma fibrinogen values..

**5.Obesity** : They have positive relationship with body mass index, waist hip ratio and waist circumference in both men and women.

**6. Exercise** : Regular physical activity reduces the level of fibrinogen. This effect attributes to the cardiovascular benefits of regular physical exercise.

**7. Hormonal Influence** : The use of oral contraceptive pills is associated with elevated fibrinogen levels

**8. Age** : Fibrinogen has a tendency to increase with age. This is attributed to the delayed clearance from plasma.

**9. Role of Vitamins** : Dietary intake of Vitamin C reduces plasma fibrinogen to a great extent.

**10. Role of Infections:** Certain organisms like *Helicobacter pylori* and *Chlamydia* were implicated in causing coronary artery disease. The role of fibrinogen may be explained following these infections. Its level is also increased in periodontal infections.

#### **Factors increasing fibrinogen**

- Old age, women
- African and asian race
- Over weight and obesity
- Smoking
- Post menopausal women
- Combined oral contraceptives
- Heavy alcohol drinkers
- Sedentary life style

#### **Factors reducing fibrinogen**

- younger age group
- Caucasians
- Japanese race
- Smoking cessation
- Low to moderate alcohol intake
- Regular physical activity
- Weight reduction

## **Role of Fibrinogen in acute coronary event**

Many statistical analysis and prospective studies clearly shows that elevated plasma fibrinogen is associated with acute coronary event. This suggests the possibility of fibrinogen may be considered as a individual risk factor.<sup>59</sup>

In one meta analysis, which included a large number of prospective, cross sectional and case control studies concluded that the risk is about two times with elevated fibrinogen levels. Thus higher plasma levels are associated with increased risk of acute coronary event<sup>60</sup>

In Framingham study, the cardiovascular risk is directly related to their plasma fibrinogen levels. The risk of acute vascular event increases with levels above 4.5gm/dl<sup>61</sup>

In European concerted action on thrombosis and disabilities study, they concluded that plasma fibrinogen can be taken as an independent risk factor. They provided it for acute coronary event as well as for sudden death. They also included measurement of plasma VWF and t-PA, in their studies.

The relationship with acute coronary syndrome is much stronger. This is proved statistically when compared with LDL cholesterol.<sup>62</sup>

Deepa et al, studied prothrombogenic risk factors in south Indian with CAD and found that prothrombogenic risk factors particularly fibrinogen may be associated with CAD.<sup>63</sup>

### **Fibrinogen and young MI**

Khare A et al. studied fibrinogen levels in 120 patients with MI less than 40 years of age and concluded that fibrinogen is an independent risk factor.<sup>49</sup>

Von Eyben et al. studied fibrinogen levels in 22 patients with MI aged less than 41 years, came to conclusion that fibrinogen was independent risk factors.<sup>64</sup>

Elikowski W et al, studied thrombotic risk factor in 40 young survivors [aged 30-40 yrs] of myocardial infarction and found high fibrinogen levels among them.<sup>65</sup>

Lewandowski k et al, studied 99 male patients aged less than 40 yrs with MI and found that the frequency of BcII polymorphism of the beta-fibrinogen gene was significantly higher in MI patients along with higher plasma concentration of fibrinogen.<sup>66</sup>

### **Interventions to reduce its level**

Several drugs lower plasma fibrinogen concentrations, including some beta adrenergic blocking agents, platelet inhibitors, and fibric acid derivatives, but lifestyle modifications such as exercise and modest alcohol intake may be the most satisfactory initial treatment of choice.<sup>67</sup>

### **Intervention to decrease plasma fibrinogen<sup>59</sup>**

The most successful in reducing plasma fibrinogen levels includes drugs like fibrates, plasmapheresis, alcohol intake and most importantly by stopping smoking.

The other steps which yield doubtful benefits include hormone replacement in post menopausal women, weight reduction, lowering hypertension etc., Statins are not useful.

According to Bezafibrate Coronary Atherosclerosis Intervention Trial (BECAIT), the benefit of therapy is mediated by fall in fibrinogen levels.<sup>68</sup>



## **MATERIALS AND METHODS**

### **SOURCE OF DATA**

Cases for the present study were selected from the inpatients of ICCU ward, IMCU ward in Thanjavur medical college Hospital, Thanjavur between Oct 2011 to Nov 2012.

### **METHOD OF COLLECTION OF DATA**

Sample size: 70 cases

Present study involved 70 patient admitted to Thanjavur medical college Hospital with diagnosis of acute myocardial infarction. A detailed history and thorough clinical examination was done as per the proforma and were investigated further.

### **Inclusion Criteria**

1. Patients fulfilling WHO criteria for acute myocardial infarction .
2. At least two of the three elements presenting within 48 hours
  - a. History of ischemic chest discomfort
  - b. Typical ECG changes
  - c. Elevated cardiac enzymes

## **Exclusion Criteria**

1. Patients with renal dysfunction/ Liver disease
2. Patients with thyroid disease.

## **The following parameters were studied**

**Smoking :** Proper history of smoking obtained in terms of pack years & smoking index

## **Diabetes mellitus**

1. Known diabetics and their duration of disease.
2. Newly detected DM satisfying WHO criteria
  - a. Symptoms of diabetes mellitus with random blood glucose  $>200$  mg%
  - b. Fasting plasma glucose  $> 126$  mg%,
  - c. 2 hr plasma glucose  $> 200$  mg%

## **Hypertension**

1. Known hypertensives on treatment and their duration of disease
2. Newly detected hypertension according to JNC VII criteria

## **Family history of Ischemic heart disease**

**Obesity :** Patients were classified accordingly as overweight and obese based on body mass index.  $BMI = \text{Weight (kg)}/\text{height (m}^2\text{)}$

Obesity -  $BMI > 30$

Over weight -  $BMI \ 25 \ \text{to} \ 30$

## **Dyslipidemia**

According to NCEP-ATP III guidelines, patients were considered to have dyslipidemia when

1. Total cholesterol  $> 200 \text{ mg\%}$ ,
2. HDL  $< 40 \text{ mg\%}$ ,
3. LDL  $> 100 \text{ mg\%}$
4. Triglycerides  $> 150 \text{ mg\%}$ .

**Plasma fibrinogen level :** The levels were measured quantitatively by Coagulation method done by SYSMEX 500 series. Serum fibrinogen values greater than  $400 \text{ mg/dl}$  is considered as hyperfibrinogenemia.

## **Other investigations**

ECG

RBS,

Blood urea

Serum creatinine

Cardiac enzymes – CKMB

## **Method of Statistical Analysis**

The data were analysed by calculating percentages, mean values, standard deviation and standard error using one-sample T test, independent samples, chi-square T test and ANOVA – one way test.

All statistical calculations were performed using the software SPSS for windows 14 evaluation version.

## RESULTS

In this study 70 patients with evidence of acute myocardial infarction were evaluated. Novel risk factor fibrinogen studied in comparison with other conventional risk factors.

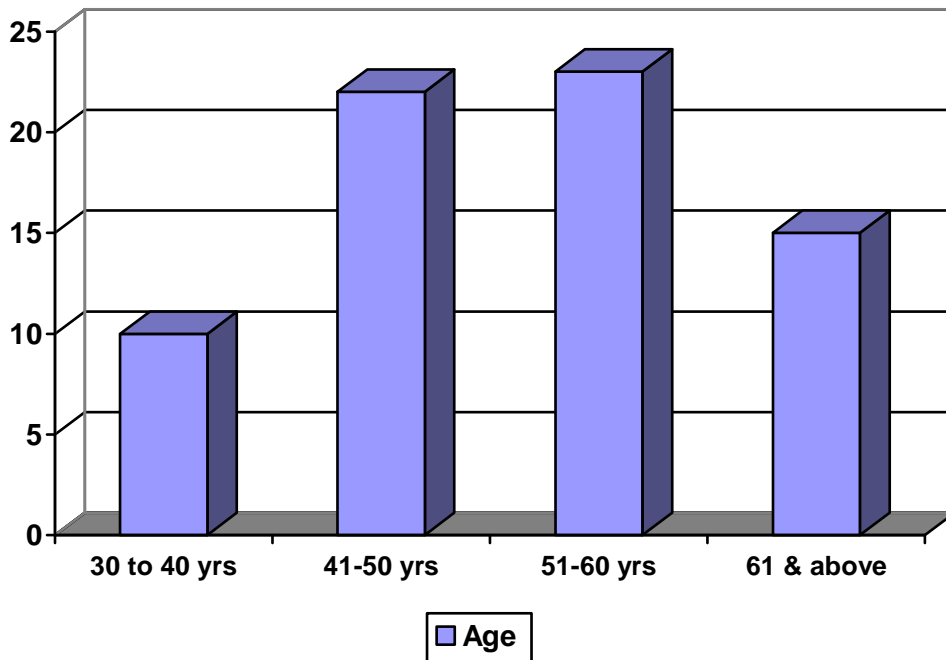
**Table – 1 : Age wise Distribution of the cases**

<b>Sl.no</b>	<b>Particulars</b>	<b>No.of respondents (n=70)</b>	<b>Percentage (100%)</b>
1	30 to 40yrs	10	14.3
2	41 to 50yrs	22	31.4
3	51 to 60yrs	23	32.9
4	61 & above	15	21.4

In this study most of the cases were between the age group of 51 to 60 years. Youngest patient in this study was 30 year old.

Mean age among the cases was 52.26 years

**Chart 1 : Age wise distribution of the cases**



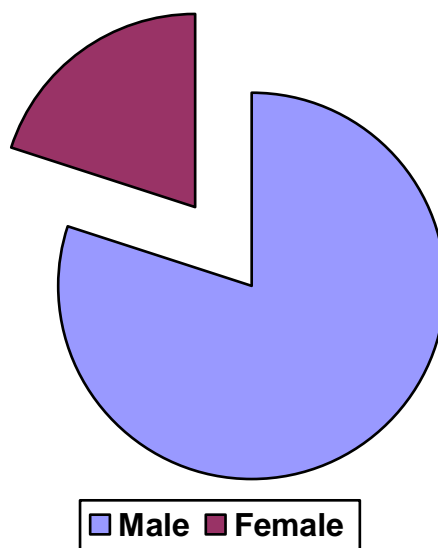
This graph shows age wise distribution of cases . Most of cases were in the age group 51 to 60 in our study.

**Table – 2 : Sex wise Distribution of the cases**

<b>Sl.no</b>	<b>Particulars</b>	<b>No.of respondents (n=70)</b>	<b>Percentage (100%)</b>
1	Male	56	80.0
2	Female	14	20.0

This was a male dominated study with males comprising 80% of the study group.

**Chart 2 : Sex wise Distribution of the cases**



This pie chart illustrates the sex wise distribution of cases. In our study males contribute to around 80% of cases.

**Table - 3 : Difference between gender of the respondents and their P.fibrinogen**

**T Test**

Sl.no	P.fibrinogen (mg%)	Mean	S.D	Statistical inference
1	Male (n=56)	439.54	72.104	T=-.238 .813>0.05 Not Significant
2	Female (n=14)	444.93	90.308	

**Df=68**

**Statistical test:** Student 't' test was used the above table

In our study the mean plasma fibrinogen of females is higher than males . But this is not statistically significant.

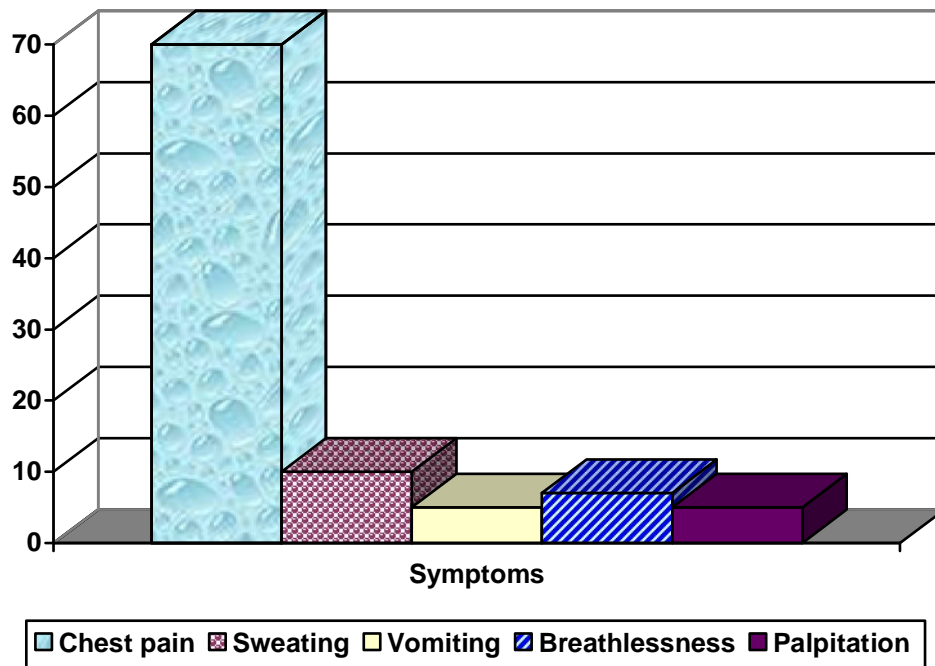


**Table – 4 : Symptoms at the time of admission**

<b>Symptoms</b>	<b>Number of cases</b>	<b>Percentage</b>
Chest Pain	70	100
Sweating	10	14.3
Vomiting / Nausea	5	7.1
Breathlessness	7	10
Palpitation	5	7.1

Chest pain was the most common symptom which was present in all patients (100%) followed by sweating (14.3%)

**Chart 3 : Symptoms at the time of admission**



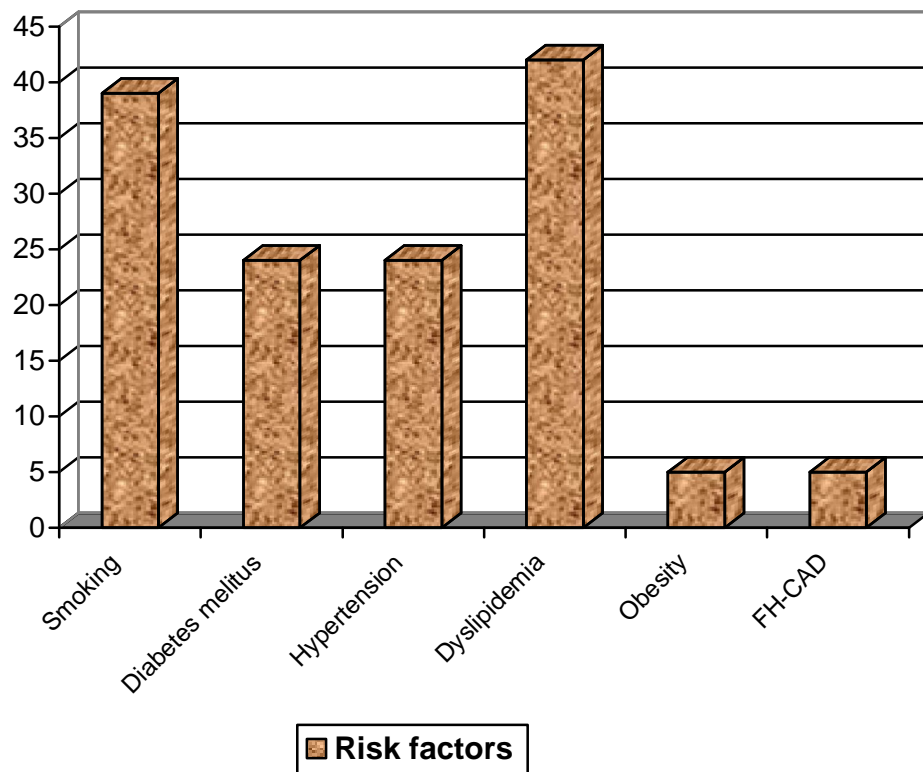
This bar diagram shows symptom wise distribution of cases. In our study most common symptom is chest pain.

**Table –5 : Comparison of risk factors among patients**

<b>Risk Factors</b>	<b>Number of Cases</b>	<b>Percentage</b>
Dyslipidemia	42	60.9
Smoking	39	55.7
Diabetes Mellitus	24	34.3
Hypertension	24	34.3
Obesity	5	7.1
F H – C A D	5	7.1

In this study dyslipidemia (60.9%) was the most common risk factor followed by smoking (55.7%). Diabetes mellitus and hypertension were observed in 24 number of patients. Overweight was present among 50 % of patients and only 5 (7.1%) patient was obese. 34.3% of the study group were alcoholics.

**Chart 4 : Comparison of risk factors among patients**



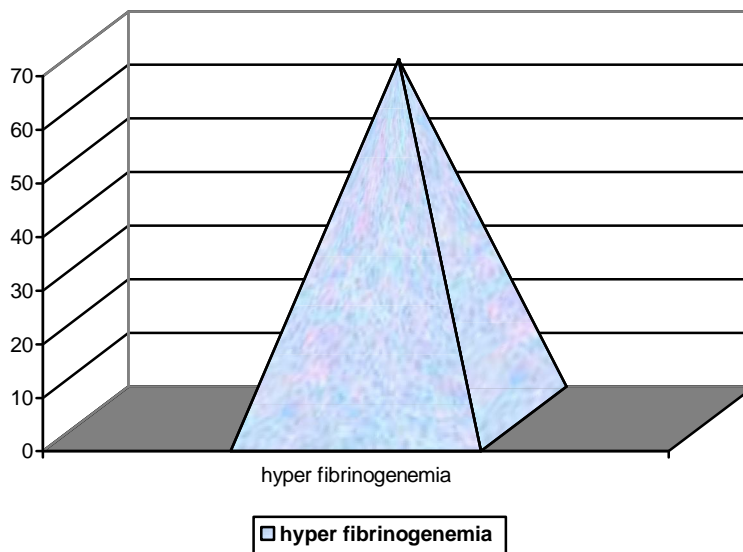
This bar chart shows the risk factor wise distribution of cases. In our study dyslipidemia is the most common risk factor ( 60 .9 % ) , followed by smoking (55.7 %).

**Table –6 : Percentage of cases with hyperfibrinogenemia**

<b>Risk factors</b>	<b>Number of Cases</b>	<b>Percentage</b>
Fibrinogen	47	67.1

In this study significant number of patients (67.1%) had hyperfibrinogenemia.

**Chart 5 : Percentage of cases with hyper fibrinogenemia**



**Table –7 : Study of plasma fibrinogen levels in our patients**

**T-Test**

**Study of level of P.fibrinogen of the respondents**

<b>Sl.no</b>	<b>P.fibrinogen (mg%)</b>	<b>Mean</b>	<b>S.D</b>	<b>Statistical inference</b>
1	<400 (n=23)	352.78	41.974	T=-11.847
2	>400 (n=47)	483.60	44.054	.000<0.05 Significant

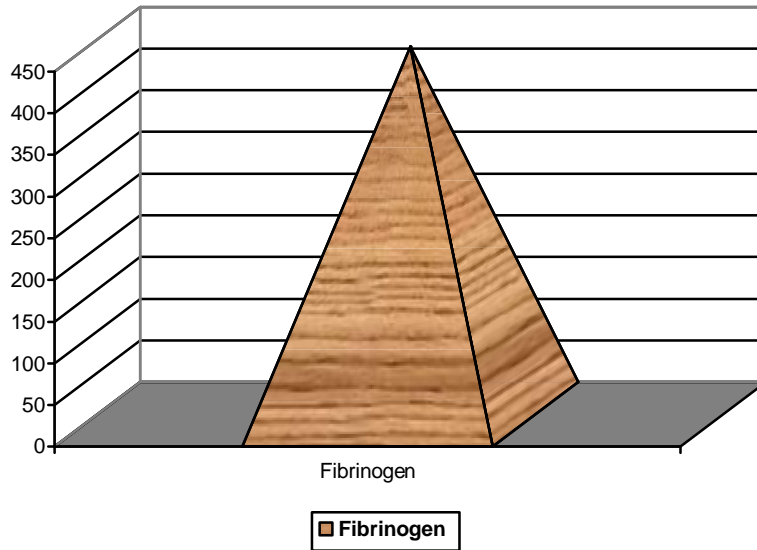
**Df=68**

**Statistical test:** Student ‘t’ test was used the above table

<b>Risk factors</b>	<b>Mean Values</b>	<b>P value</b>
Fibrinogen (Normal 180-400 mg/dl)	440.61± 75.4 mg/dl	0.000<0.05

In this study mean plasma fibrinogen level was (440.61± 75.4 mg/dl), which was high compared to the normal fibrinogen levels and was statistically significant.

**Chart 6: Mean plasma fibrinogen in our study**



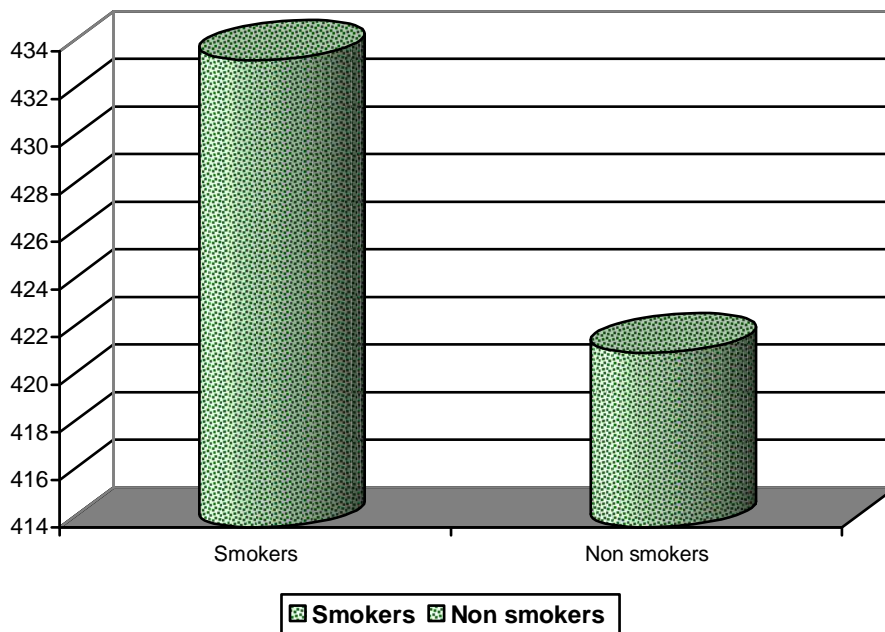
This chart shows mean plasma fibrinogen in our study (440.61 mg/dl)

**Table – 8 : Comparison of mean plasma fibrinogen levels among smokers and non-smokers**

	<b>Smokers</b>	<b>Non – smokers</b>	<b>P value</b>
Fibrinogen (mg/dl)	433.64± 72.08	421.3± 71.02	0.035<0.05

Mean fibrinogen level (433.64mg/dl) was high among smokers when compared to non-smokers (421.3mg/dl), and was statistically significant

**Chart 7 : Comparison of mean plasma fibrinogen level among smokers and non smokers.**



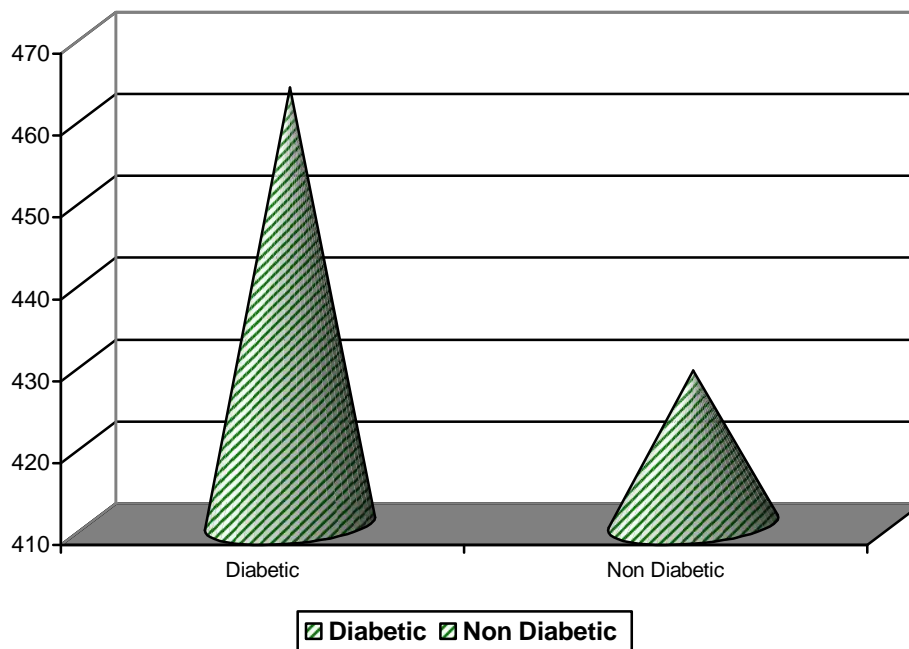


**Table – 9 : Comparison of mean plasma fibrinogen levels among diabetics and non diabetics**

	<b>Diabetics</b>	<b>Non – Diabetics</b>	<b>P value</b>
Fibrinogen (mg/dL)	463.33 ± 77.31	428.76± 72.4	0.046<0.05

Diabetics had higher values of fibrinogen (463 mg%) when compared to non-diabetics (428 mg%) , which was statistically significant. ( p value 0.046 < 0.05 ) .

**Chart 8 : Comparison of mean plasma fibrinogen levels among diabetics and non diabetics**



**Table-10 : Comparison of mean plasma fibrinogen among hypertensives and non hypertensives**

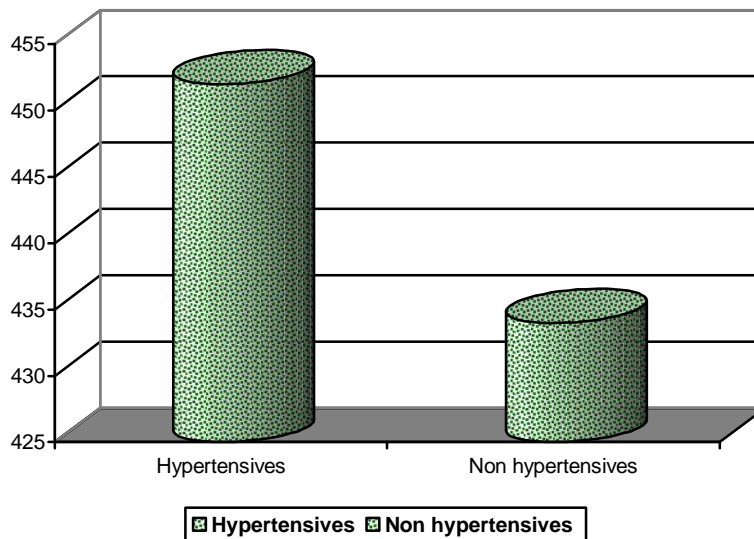
Sl.no	P.fibrinogen (mg%)	Mean	S.D	Statistical inference
1	Hypertensive (n=24)	452.13	78.751	T=.922 .360>0.05 Not Significant
2	Non hypertensive (n=46)	434.61	73.759	

**Df=68**

**Statistical test:** Student ‘t’ test was used the above table

The mean plasma fibrinogen in hypertensives ( 452.13 mg/dl ) was high when compared with non hypertensives ( 434.61 mg/dl ), but this difference is not statistically significant.

**Chart 9: Mean plasma fibrinogen among hypertensives and non hypertensives**



**Table 11: Comparison of mean plasma fibrinogen of alcoholics and non alcoholics**

**Oneway ANOVA difference between alcohol of the respondents and their P.fibrinogen**

Sl.no	P.fibrinogen (mg%)	Mean	S.D	SS	D f	MS	Statistical inference
1	Between Groups			11616.973	2	5808.486	F=1.022 .365>0.05 Not Significant
2	Nil (n=46)	446.85	75.4 19				
3	CR (n=13)	443.69	56.6 96				
4	OCC (n=11)	410.91	92.8 15				
5	Within Groups			380677.613	6 7	5681.755	

**Statistical test:** Oneway ANOVA 'f' test was used the above table

The mean plasma fibrinogen of chronic alcoholics is higher than occasional alcoholics , but it is not statistically significant.

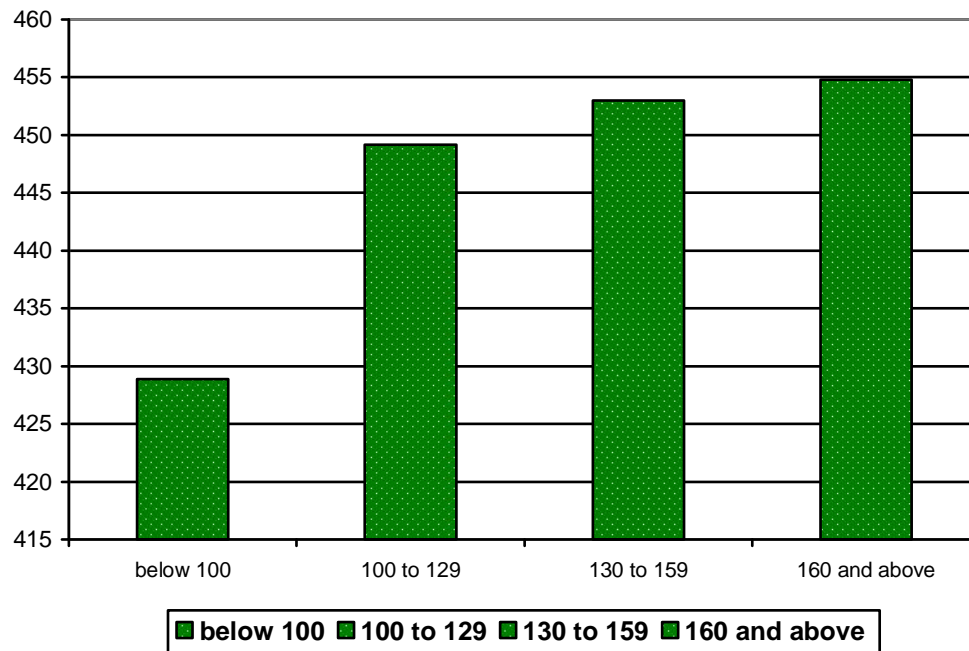
**Table – 12 : Comparison of mean plasma fibrinogen levels among patients with high LDL level and patients with normal LDL**

<b>Sl.no</b>	<b>Particulars (LDL mg %)</b>	<b>No.of respondents (n=70)</b>	<b>Percentage (100%)</b>
1	Below 100	28	40.0
2	100 to 129	26	37.1
3	130 to 159	11	15.7
4	160 & above	5	7.1

<b>Sl.no</b>	<b>P.fibrinogen (mg%)</b>	<b>Mean</b>	<b>S.D</b>	<b>SS</b>	<b>Df</b>	<b>MS</b>	<b>Statistical inference</b>
1	Between Groups			7622.973	3	2540.991	F=4.436 .031<0.05 Significant
2	Below 100 (n=28)	428.86	79.774				
3	100 to 129 (n=26)	449.15	73.408				
4	130 to 159 (n=11)	453.00	69.146				
5	160 & above (n=5)	454.80	67.059				
6	Within Groups			384671.613	66	5828.358	

Subjects with high LDL (> 100 mg %) had their Plasma fibrinogen Concentration ( 445. 65 mg % ) higher than persons with normal LDL (428.86 mg %)

**Chart 10 : Comparison of mean plasma fibrinogen levels among patients with dyslipidemia and patients with normal lipids**



**Table 13 : Comparison of HDL level and mean plasma fibrinogen**

**T-Test**

**Difference between level of HDL of the respondents and their  
P.fibrinogen**

<b>Sl.no</b>	<b>P.fibrinogen (mg%)</b>	<b>Mean</b>	<b>S.D</b>	<b>Statistical inference</b>
1	Less than 40 (n=15)	456.20	82.755	T=.902
2	More than 40 (n=55)	436.36	73.507	.601>0.05 Not Significant

**Df=68**

**Statistical test:** Student 't' test was used the above table

In our study subjects with HDL level above 40 mg/dl ,their plasma fibrinogen level is lower . But this difference is not statistically significant.

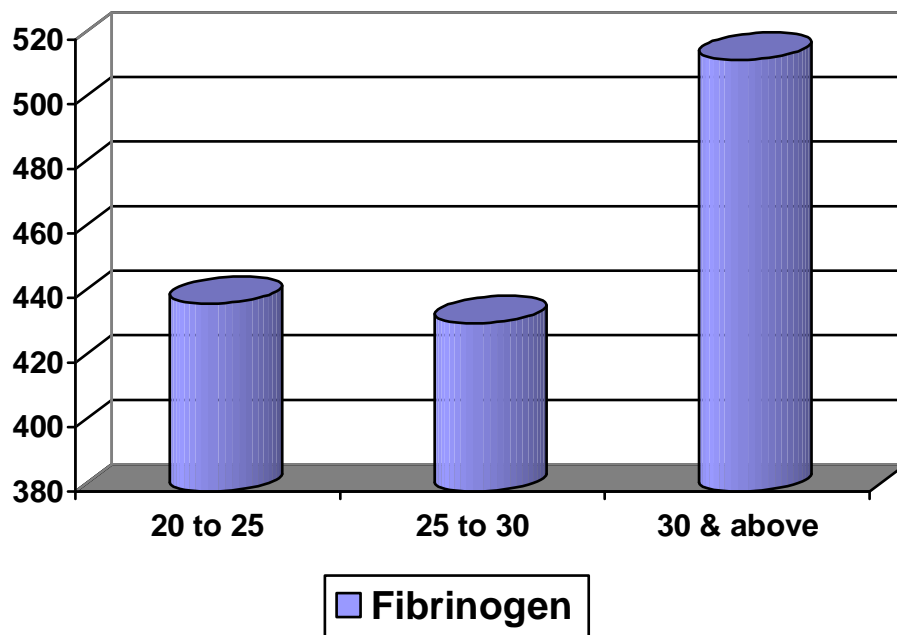
**Table – 14 : Comparison of mean fibrinogen levels among patients with obesity and patients with normal BMI**

<b>Sl.no</b>	<b>Particulars</b>	<b>No.of respondents (n=70)</b>	<b>Percentage (100%)</b>
1	20 to 25	30	42.9
2	25 to 30	35	50.0
3	30 & above	5	7.1

<b>Sl.no</b>	<b>P.fibrinogen (mg%)</b>	<b>Mean</b>	<b>S.D</b>	<b>SS</b>	<b>Df</b>	<b>MS</b>	<b>Statistical inference</b>
1	Between Groups			29428.819	2	14714.410	F=4.717 .043<0.05 Significant
2	20 to 25 (n=30)	438.23	73.520				
3	25 to 30 (n=35)	432.20	77.393				
4	30 & above (n=5)	513.80	24.823				
5	Within Groups			362865.767	67	5415.907	

The mean plasma fibrinogen in BMI < 25 is 438.23 mg/ dl . The mean plasma fibrinogen in BMI between 25 to 30 is 432.20 mg /dl. In obese group plasma fibrinogen is around 513.80 mg/dl. The difference is statistically significant.

**Chart 11 : Comparison of mean fibrinogen levels among patients with obesity and over weight and patients with normal BMI**



This chart describes the correlation between BMI and the plasma fibrinogen of the study group which is statistically significant.



## DISCUSSION

70 patients of with evidence of acute MI admitted to ICCU and IMCU were studied and the following data were compared.

**Table - 15 : Comparison of sex wise distribution of the cases**

Study	Males %	Females %
SK mishra et al <sup>69</sup>	90	10
Khare A et al <sup>49</sup>	91.67	8.33
AL Khadra et al <sup>16</sup>	96.9	3.1
Ranjit N <sup>72</sup>	86	14
Present Study	80	20

Sl.no	Particulars	No.of respondents (n=70)	Percentage (100%)
1	Male	56	80.0
2	Female	14	20.0

The study was predominantly male (80%) dominated. This may be attributed to the protective effects of estrogen in pre-menopausal women. This was comparable to the other studies.

**Table - 16 : Comparison of age wise distribution of the cases**

<b>Sl.no</b>	<b>Particulars</b>	<b>No.of respondents (n=70)</b>	<b>Percentage (100%)</b>
1	30 to 40yrs	10	14.3
2	41 to 50yrs	22	31.4
3	51 to 60yrs	23	32.9
4	61 & above	15	21.4

In our study, mean age of the patients was 52.26 years.

Most of the patients were in the age group between 51 to 60 years (32.9%).

<b>Study</b>	<b>Age (Mean) in years</b>
Present Study	52.26
Romero M et al <sup>50</sup>	56.4
Hampten et al <sup>71</sup>	57.03

**Table – 17 : Comparison of symptoms at admission**

<b>Symptoms</b>	Mishra SK et al. <sup>69</sup>	Patil CN et al. <sup>71</sup>	Present Study
Chest Pain	83.4%	93.3%	100%
Sweating	61%	50%	14.3%
Vomiting / Nausea	5%	16.7%	7.1%
Breathlessness	29%	16.7%	10%
Palpitation	-	3.3%	7.1%
Stroke	0.8%	-	-
Syncope	6%	-	-

In our study chest pain (100%) was the most common symptom followed by sweating (14.3%). Similar findings were noted in study by Mishra et al and Patil et al .

**Table - 18 : Comparison of risk factors**

<b>Risk Factors</b>	Al. Khadra et al <sup>16</sup>	Puri et al <sup>70</sup>	Mishra SK et al <sup>69</sup>	Present Study
Dyslipidemia	33.8%	58.8%	52%	60.9%
Smoking	76.9%	52%	75%	55.7%
Diabetes	30.8%	21.5%	16.5%	34.3%
Hypertension	18.8%	54.9%	23%	34.3%
Obesity	15.4%	23.3%	37%	7.1%
F H – C A D	-	-	33.8%	7.1%

Dyslipidemia (60.9%) was the most common risk factor which was comparable with other studies, Al. Khadra et al (33.8%), Mishra et al (52%).

In our study smoking is present in 55.7 % and 7.1 % patients are obese. Other risk factors like hypertension, Diabetes mellitus and family history of CAD were present in a few patients.

**Table - 19 : Comparison of mean plasma fibrinogen level with other studies**

<b>Study</b>	<b>Mean Fibrinogen (mg /dl)</b>
Cristal N et al <sup>49</sup>	466 ± 89.5
Puri et al <sup>50</sup>	447.68 ± 142.35
Romero M et al	457 ± 46.22
Present study	440.61± 75.40

High mean plasma fibrinogen (440.61 ±75.40 mg/dl) level was noted which is statistically significant. This is comparable with other studies .

## **Comparison of mean plasma fibrinogen levels with conventional risk factors**

### **1) Smoking**

Mean plasma fibrinogen was high among smokers (433.64 mg/dl) compared to non smokers (421 mg/dl) and was statistically significant.

Kannel WB et al.,<sup>73</sup> in Framingham study noted higher values of fibrinogen among smokers.

### **2) Dyslipidemia**

Patients with dyslipidemia had higher mean plasma fibrinogen (445.65 ±73.48 mg/ dl) compared to patients with normal lipid levels (428.86 ± 79.77 mg/dl). Puri et al.<sup>70</sup> noted high fibrinogen levels among patients with dyslipidemia when compared to patients with normal lipids.

### **3) Over weight and obesity**

Significantly higher levels of fibrinogen was noted among patients with BMI > 30 (513.8 mg/dl) when compared to patients with normal BMI ( 438.23 mg/dl ). Difference was statistically significant.

Craveri et al <sup>74</sup> noted significantly higher plasma fibrinogen among patients with BMI > 30 compared to those with BMI < 25.

#### **4) Alcohol**

Significantly high levels of fibrinogen was noted among chronic alcoholics (443.44mg/dl) compared to occasional alcoholics (344.78 mg/dl). Mennen LI et al<sup>76</sup> in DESIR study found that moderate alcohol consumption was associated with lower plasma fibrinogen when compared with those who were non drinkers or who drinks >60gm of alcohol per day.

#### **5) Hypertension and Diabetes**

High levels of fibrinogen was noted among patients with hypertension but was not statistically significant. Higher levels associated with diabetic patients is statistically significant.

## CONCLUSION

- In our study males contribute around 80% of cases.
- All patients presented with chest pain.
- Dyslipidemia was the most common conventional risk factor followed by smoking
- Novel risk factors like fibrinogen were elevated in myocardial infarction patients in our study group when compared to normal levels.
- Significant number of patients in our study had hyperfibrinogenemia.
- Significant association was noted between fibrinogen and risk factors like Dyslipidemia , Obesity and Smoking
- Large scale randomized multicentre studies are yet to be done to understand the proper association between novel risk factors like fibrinogen with myocardial infarction.



## SUMMARY

In this study 70 patients with acute myocardial infarction were studied.

- Most of the patients were males (80%).
- Majority of the patients were between the age group of 41-60 years (64.3%).
- All patients presented with chest pain. Sweating was present in 14.3% of patients.
- Dyslipidemia was the most common risk factor, which was present in 60.9% of patients followed by Smoking (55.7%). Few number of patients had hypertension, diabetes and family history of coronary artery disease.
- The mean fibrinogen level was ( $440.61 \pm 75.40$  mg/dl) which was high compared to normal fibrinogen level.
- Smokers had higher mean fibrinogen level compared to non smoker and was statistically significant.
- Mean fibrinogen level was high among patients with high LDL and was statistically significant.
- Plasma fibrinogen was high among diabetics and was statistically significant.

- Hypertensive patients had higher fibrinogen levels when compared to non hypertensive patients, but was not statistically significant.
- Patients with overweight and obesity had higher levels of mean fibrinogen levels and was statistically significant.
- Patients who were chronic alcoholics had higher levels of fibrinogen when compared to occasional alcoholics.

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## PROFORMA

Name:

I.P.No.: Age:

Sex:

DOA: Occupation: DOD:

Address:

### Diagnosis

**Presenting Complaints** Chest pain / Dyspnoea / Palpitation

### History of presenting illness

#### Chest Pain

Site - Onset- Nature - Duration: Radiation - Continuous/intermittent

Severity - Aggravating/precipitating factors - Relieving factors

#### Dyspnoea

Duration /Onset/ Time of onset in relation to pain / NYHA Class / I/II/III/IV

PND / orthopnoea

#### Palpitations

Onset / nature/ duration/ Precipitating/Aggravating factors /Relieving factors

## **Past History**

**Diabetes Mellitus/ Hypertension / Dyslipidemia / Cerebrovascular accident**

**Thyroid disorder/ Rheumatic fever/ Liver disease /Renal disease.**

## **PERSONAL HISTORY**

Diet - vegetarian/non-vegetarian/mixed

Smoking - beedies/cigarettes

- duration

- number/day

Alcohol - duration

- quantity...../day

Tobacco chewing - Yes/No/ duration

## **Treatment History -**

### **Family History**

Coronary artery disease - Yes/No

Hypertension - Yes/No

Diabetes - Yes/No

Dyslipidemia - Yes/No

Sudden deaths - Yes/No

## **GENERAL PHYSICAL EXAMINATION**

Condition of the patient - Wt (in Kg) - Ht (in length)

- BMI (kg/m<sup>2</sup>)

Icterus / Pallor/ Cyanosis/ Clubbing /Pedal edema /Lymphadenopathy

### **Vitals:**

Pulse - / minute

BP - /mmHg in right upper limb

Respiratory rate - / minute

### **Pulse**

Rate / Rhythm / Volume /Radio-radial/radio-femoral delay

Other peripheral pulses:

Blood pressure (R) UL (R) LL (L) UL (L) LL



## **Systemic examination:**

### **1. Cardiovascular system**

#### **a. Inspection**

Shape of the precordium -

Precordial pulsation/ Other pulsation -

Apical impulse -

#### **b.. Palpation**

Apical impulse-site -

Apical impulse-character / Parasternal heave / Thrill

#### **c. Percussion**

Cardiac borders

#### **d. Auscultation**

Mitral area / Tricuspid area / Aortic area / Pulmonary area

### **2. Respiratory system**

Inspection / Palpation / Percussion / Auscultation

### **3. Per abdomen**

Inspection / Palpation / Percussion / Auscultation

#### **4. Nervous system**

Hb, TC, DC, ESR, RBS , UREA,

S. CREATININE

Lipid profile- LDL/ HDL/ TGL

**PLASMA FIBRINOGEN- mg/ dl**

**ECG:**

Rate Rhythm P wave

QRS complex PR interval QRS complex ST

segment

**Echocardiography**

## LIST OF ABBREVIATIONS

ATP	Adult treatment panel
BMI	Body mass index
CAD	Coronary artery disease
DBP	Diastolic blood pressure
ECG	Electrocardiogram
HDL	High density lipoprotein
ICAM	Intracellular adhesion molecule-1
IHD	Ischemic heart disease
JNC	Joint National Committee
LDL	Low density lipoprotein
MI	Myocardial infarction
MTHFR	Methylene tetrahydrofolate reductase
NCEP	National Cholesterol Education Programme
NO	Nitric oxide
PAI	Plasminogen activator inhibitor
PVD	Peripheral vascular disease
SBP	Systolic blood pressure
t-PA	Tissue plasminogen activator
USA	United States of America
WHO	World Health Organisation

**PATIENT CONSENT FORM**

Study detail : “STUDY ON PLASMA FIBRINOGEN IN ACUTE MYOCARDIAL INFARCTION”

Study centre : THANJAVUR MEDICAL COLLEGE & HOSPITAL

Patients Name :

Patients Age :

Identification Number:

Patient may check ( ✓ ) these boxes

I confirm that I have understood the purpose of procedure for the above study.

I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction.

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected.

I understand that sponsor of the clinical study, others working on the sponsor’s behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study.

I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well being or any unexpected or unusual symptoms.

I hereby consent to participate in this study.

I hereby give permission to undergo complete clinical examination and diagnostic tests including haematological, biochemical, radiological tests.

Signature/thumb impression:

Patients Name and Address: \_\_\_\_\_ Place \_\_\_\_\_ Date \_\_\_\_\_

Signature of investigator :

Study investigator’s Name : \_\_\_\_\_ Place \_\_\_\_\_ Date \_\_\_\_\_

Sl.No.	Name	IP No.	Age yrs	Sex	Chest pain	Sweating	Vomiting	Breathlessness	Palpitation	Smoking	Diabetes mellitus	Hypertension	F - CAD	Alcohol	BMI (kg/m2)	RBS (mg%)	CK-MB (IU/L)	Lipid profile (mg%)				B.Urea (mg%)	S.creatinine (mg%)	P.fibrinogen (mg/dl)	ECG	ECHO	TREATMENT
																		TC	Trigl	LDL	HDL						
1	Murugaesan	1395932	33	M	Y	Y				y		Y		occ	25	144	38	220	170	130	56	34	1.1	440	IW MI	LV FN	thrombolysed
2	Pitchamuthu	1401941	25	M	Y									occ	23	102	42	133	86	72	44	30	0.9	420	AS MI	LVD EF50%	thrombolysed
3	Palanimanikam	1408493	36	M	Y	Y									21	170	60	170	140	92	50	24	0.9	480	EA W MI	LVD +MR	not thrombolysed
4	Ravichandran	1400506	41	M	Y					Y			Y	occ	22	129	145	240	295	131	50	28	1	294	AS MI	LV FN	thrombolysed
5	Suresh babu	1398653	30	M	Y										23	160	74	270	220	184	42	28	1.1	464	A W MI	LV FN	thrombolysed
6	Chellaiyan	1409078	40	M	Y					Y	y				22	168	42	148	88	86	44	32	0.9	448	AS MI	LVD EF50%	thrombolysed
7	Kaliyaperumal	1410197	42	M	Y	Y				Y		y			25	180	64	171	140	99	44	52	1.2	390	A W MI	LV FN	thrombolysed
8	Ravichandran	1415343	48	M	Y						ND			occ	23	320	64	160	85	90	53	40	1.1	334	IW MI	LVD EF60%	not thrombolysed
9	Selvam	1365388	36	M	Y					Y		ND			30	190	52	270	130	194	50	34	1	424	IW MI	LV FN	thrombolysed
10	Venkatesan	1378431	35	M	Y				Y	Y				cr	22	132	70	168	180	86	46	32	0.9	356	IW MI	LV FN	thrombolysed

11	Kajamaideen	1378804	38	M	Y	Y	Y			Y					24	156	38	175	126	97	53	35	0.9	416	IW MI	LV FN	thrombolysed
12	Sulaimaan	1378707	40	M	Y			Y		Y					29	146	183	220	200	133	47	24	1.2	487	EA W MI	LV FN	thrombolysed
13	Kumar	1379043	42	M	Y					Y	ND		Y	cr	21	258	95	260	216	179	38	49	1.2	484	IW MI	LVD EF60%	thrombolysed
14	Mohan	1382945	46	M	Y					y	y				25	158	70	148	110	80	46	40	1.3	394	A W MI	LVD EF55%	not thrombolysed
15	Lakshmanan	1377098	48	M	Y					Y	Y				27	250	90	154	140	77	49	36	0.8	440	A W MI	LV FN	thrombolysed
16	Kumaran	1365257	50	M	Y					y		y			26	150	70	152	100	96	36	30	1.1	280	IL MI	LVD EF50%	thrombolysed
17	Selvaraj	1365954	64	M	Y	Y				Y		ND		cr	27	178	76	240	200	135	65	25	1.1	455	A W MI	LV FN	not thrombolysed
18	Mohammed ismail	1366175	58	M	Y			Y		Y					24	107	60	148	88	86	44	20	1	442	A W MI	LV FN	thrombolysed
19	Tamil selvan	1366933	51	M	Y	Y				Y	y	Y			29	130	45	160	126	90	45	28	0.9	480	IW MI	LV FN	thrombolysed
20	Haseena begam	1369259	58	F	Y						y	y			31	126	146	180	86	113	50	22	1	488	A W MI	LVD EF48%	not thrombolysed
21	Puniyamoorthy	1370246	59	M	Y		Y			Y	y				27	182	66	171	80	110	45	26	1	476	AS MI	LV FN	thrombolysed
22	Thiyagarajan	1373215	58	M	Y							y		occ	23	170	80	154	120	88	42	25	1.2	398	IW MI	LVD EF45%	thrombolysed
23	Panjalai	1375473	42	F	Y					Y					28	152	42	196	82	124	46	42	1.1	532	IW MI	LV FN	thrombolysed
24	Bharkath nisha	1375375	45	F	Y						y				32	170	64	204	160	140	32	38	1.1	472	IW MI	LV FN	thrombolysed

25	Balakumar	1378253	53	M	Y			Y		Y			Y		21	104	34	169	110	102	45	24	1.3	338	EA WMI	LVD EF50%	thrombolys ed
26	Pappathy	1379243	60	F	Y	Y					y			.24.6	130	115	142	224	57	40	69	1.2	372	AS MI	LV FN	thrombolys ed	
27	Jayakumar	1385235	45	M	Y					Y		ND		cr	24	80	64	236	200	143	53	28	1.2	486	A WMI	LV FN	thrombolys ed
28	Andiyappan	1387090	68	M	Y					Y	y				29	124	40	183	116	118	42	24	1.1	438	A WMI	LVD EF50%	not thrombolys ed
29	Kuppusamy	1388141	57	M	Y					Y		y		cr	29	130	62	188	106	126	41	34	1	384	A WMI	LVD EF40%	thrombolys ed
30	Arumugam	1389034	45	M	Y					Y				cr	26	156	195	215	170	125	56	30	1.1	397	IW MI	LV FN	thrombolys ed
31	Manikkam	1390847	48	M	Y		Y		Y	Y	y			occ	30	136	130	250	200	170	40	38	0.9	290	AL MI	LV FN	thrombolys ed
32	Dhanam	1391771	62	F	Y							y			29	156	60	154	126	87	42	40	1.2	310	IW MI	LVD EF55%	thrombolys ed
33	Arumugam	1392229	60	M	Y							y		cr	28	186	70	181	110	117	42	26	0.8	390	AS MI	LV FN	thrombolys ed
34	Muthusamy	1392375	76	M	Y					Y		y	Y	occ	28	137	140	190	165	114	43	22	1	442	IW MI	LVD EF50%	not thrombolys ed
35	Mohandass	1394245	48	M	Y					Y					21	146	146	130	96	70	41	52	1.3	468	A WMI	LV FN	thrombolys ed
36	Gandhi	1419752	62	M	Y			Y			y	y			30	180	58	173	206	92	40	36	0.9	510	AL MI	LV FN	thrombolys ed
37	Vishwanathan	1418674	45	M	Y					Y		ND			25	215	265	180	116	106	50	23	1.2	426	AL MI	LVD EF45%	not thrombolys ed
38	Kamaraj	1420513	56	M	Y				Y		y				28	105	160	166	140	96	42	38	1.5	370	A WMI	LV FN	thrombolys ed

39	Iruthayamary	1419617	60	F	Y	Y									23	138	88	200	140	122	50	36	0.8	395	AS MI	LVFN	thrombolysed
40	Abdulkanni	1414855	68	M	Y				Y	y					31	230	56	188	88	132	38	28	1.1	446	AWMI	LVD EF45%	not thrombolysed
41	Balu	1395476	45	M	Y				Y	ND			cr		29	124	93	180	130	108	46	32	1.4	460	IWMI	LVFN	thrombolysed
42	Prabhakaran	1415127	59	M	Y										29	73	39	199	129	131	42	30	0.9	394	ILMI	LVFN	thrombolysed
43	Senthilnathan	1411150	49	M	Y					y			occ		28	185	153	184	210	83	59	22	0.8	448	AWMI	LVFN	thrombolysed
44	Rasu	1410483	49	M	Y				Y		ND				30	172	82	184	171	109	40	42	1.3	395	ASMI	LVD EF40%	thrombolysed
45	Rajakannu	1396826	70	M	Y					Y					29	210	76	169	138	100	41	34	1.1	482	IWMI	LVD EF40%	not thrombolysed
46	Dhanalakshmi	1397409	65	F	Y										29	95	68	138	110	74	42	22	0.8	280	AWMI	LVFN	thrombolysed
47	Habeeb rahaman	1400508	52	M	Y			Y					cr		29	112	74	158	110	98	37	20	0.9	484	IWMI	LVD EF50%	thrombolysed
48	Meenakshi	1400545	75	F	Y			Y							27	142	110	170	96	108	43	36	1.1	410	IWMI	LVFN	thrombolysed
49	Krishnamoorthy	1400525	52	M	Y				Y	y	y				30	138	50	208	158	138	39	23	1.2	398	IWMI	LVFN	thrombolysed
50	Sivabakiyam	1395178	61	F	Y						y				21	218	60	154	150	80	44	30	1	446	ALMI	LVFN	thrombolysed
51	Natarajan	1395486	74	M	Y	Y					y	y			26	130	115	241	224	157	40	69	1.2	465	ASMI	LVD EF45%	not thrombolysed
52	Suresh	1404683	31	M	Y										24	80	64	236	200	143	53	28	1.2	486	AWMI	LVFN	thrombolysed



53	Palaniammal	1396070	55	F	Y										21	124	40	153	116	88	42	24	1.1	390	AWMI	LVFN	thrombolysed
54	Akbarhussain	1395811	54	M	Y				Y		y		cr	30	130	62	188	106	126	41	34	1	448	AWMI	LVD EF40%	thrombolysed	
55	Paneerselvam	1396649	45	M	Y				Y				cr	27	156	195	215	170	125	56	30	1.1	450	IWMI	LVFN	not thrombolysed	
56	Selvaraj	1396797	55	M	Y		Y		Y	Y			occ	31	136	130	256	200	176	40	38	0.9	462	ALMI	LVFN	thrombolysed	
57	Ganesan	1396701	65	M	Y				y	y				31	156	60	184	126	117	42	40	1.2	460	IWMI	LVFN	thrombolysed	
58	Natarajan	1398275	57	M	Y						y		cr	23	186	70	171	110	107	42	26	0.8	382	ASMI	LVFN	thrombolysed	
59	Muthayan	1398705	65	M	Y				Y			Y	occ	27	137	140	170	165	124	43	22	1	420	IWMI	LVD EF45%	thrombolysed	
60	Pounammal	1398413	50	F	Y									24	146	146	136	96	76	41	52	1.3	376	AWMI	LVFN	thrombolysed	
61	Kunjammal	1398491	65	F	Y			Y						21	180	58	179	206	98	40	36	0.9	506	ALMI	LVD EF40%	not thrombolysed	
62	Ulaganathan	1398574	52	M	Y				Y	y				28	215	265	181	116	108	50	23	1.2	344	ALMI	LVD EF45%	not thrombolysed	
63	Sivamani	1398910	54	M	Y			Y			y			24	105	160	174	140	104	42	38	1.5	382	AWMI	LVFN	thrombolysed	
64	Saroja	1406988	51	F	Y	Y								30	138	88	190	140	112	50	36	0.8	332	ASMI	LVFN	thrombolysed	
65	Abdulsamath	1406860	50	M	Y				Y					28	230	56	137	88	82	38	28	1.1	462	AWMI	LVFN	thrombolysed	
66	Swaminathan	1405987	50	M	Y				Y				cr	28	124	93	174	130	102	46	32	1.4	446	IWMI	LVFN	thrombolysed	

67	Indirani	1408306	60	F	Y						y	y			26	73	39	193	129	126	42	30	0.9	438	IL MI	LVFN	thrombolysed
68	Ganapathy	1409480	47	M	Y				Y				occ	23	185	153	199	210	98	59	22	0.8	304	AWMI	LVD EF45%	not thrombolysed	
69	Pethuraj	1404684	53	M	Y		Y		Y		y			21	172	82	180	171	106	40	42	1.3	462	ASMI	LVD EF40%	thrombolysed	
70	Ponraman	1408570	65	M	Y					Y	y			23	210	76	176	138	108	41	34	1.1	398	IWMI	LVFN	thrombolysed	