“STUDY OF LIPOPROTEIN (a) IN ACUTE MYOCARDIAL INFARCTION”

By

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Under the guidance of

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Dr Akshay M Kuchanur

LIST OF ABBREVIATIONS USED

CVD	:	Cardiovascular disease
CAD	:	Coronary Artery Disease
ACS	:	Acute Coronary Syndrome
CBC	:	Complete blood count
FBS	:	Fastng blood sugar
PPBS	:	Post prandial blood sugar
LDL	:	Low Density Lipoprotein
HDL	:	High Density Lipoprotein
STEMI	:	ST-segment Elevation Myocardial Infarction
NSTEMI	:	Non–ST-segment Elevation Myocardial Infarction
UA	:	Unstable Angina
PCI	:	Percutaneous Coronary Intervention
CAC	:	Coronary Artery Calcification
CFR	:	Coronary Flow Reserve
IMT	:	Intima-Media Thickness
AP	:	Angina Pectoris
TC	:	Total leucocyte Count
IHD	:	Ischemic Heart Disease
ECG	:	Electro Cardiographs

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INTRODUCTION

INTRODUCTION

Developing countries, especially countries like India are on the verge of twin epidemics of communicable diseases and non-communicable diseases [like hypertension and coronary artery disease (CAD)].

"The prevalence of coronary artery disease is high amongst Indians:- 2.2 to 5 times for myocardial infarction, 1.5 to 3.0 times for coronary heart disease mortality. Myocardial infarction also occurs at a younger age in Indians (50.2 year versus 55.5 years in whites)".(1)

"Age specific death rates (30-39) for Myocardial infarction in Indians were almost 10 times the rate observed for the white population. Autopsies also revealed more severe and extensive atherosclerosis and larger infarct size and increased frequency of triple vessel disease among Indians."(2)

"In CAD, 1st reported from Singapore in 1959 reveal that people hailing from Indian subcontinent had a higher probability of dying due to CAD. The overall age standardized mortality ratio of CAD in Asian males compared to whites was 37.3% higher in age group of 20-29 yrs, compared to 36% higher at all ages in the U.K."(3)

"Asian Indians belonging to different geographical culture and religious groups have the same high mortality. Further the prevalence of CAD is threefold higher in south India in comparison to north India."(4)

"An important cluster of metabolic risk factors seems to be responsible for the occurrence of extensive and early CAD in Indians. These include the greater occurrence of glucose intolerance, hyperinsulinaemia, hypertriglyceridemia, low HDL-C level, abnormal type of obesity and novel risk factor like high serum of lipoprotein-(a)."(3)

"Lipoprotein (a) constitutes an important inherited risk factor for atherosclerosis and is also regarded as biological marker for familial CAD."(5)

"Lipoprotein (a) is homologous with the fibrin binding domain of plasminogen, a plasma protein that dissolves blood clots when activated."(5)

"Lp(a) levels are also reduced by treatment with N-acetyl cysteine, danazol and ally sterol. Nicotinic acid and Neomycin also decrease levels of Lp (a), and are used for therapeutic purpose. LDL aphaeresis is useful modality of treatment of patients of homozygous familial hypercholesterolemia and ordinary hypercholesterolemia."(6)

This case control study was designed to explore the role of Lp (a) levels in young patients with myocardial infarction. Young patients in the study were defined as patients with age < 40 years.

AIMS OF STUDY

AIMS OF STUDY

- To study the Serum Lipoprotein (a) levels in patients of Acute Myocardial Infarction.
- To show the association of increase in risk of acute Myocardial Infarction with increasing levels of Lipoprotein (a).

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Coronary Artery Disease in Adult Indians

"At the threshold of the new millennium coronary artery disease (CAD) is looming large as the new epidemic afflicting Indians at a relatively younger age with severe and diffuse form of lesions. Recently, the subject of CAD in Indians has become a challenge for many research centers worldwide."(7)

"The prevalence of CAD has progressively increased in India during the latter half of the last century, particularly among the urban populations. The conventional risk factors namely Hypertension, Hypertriglyceridaemia, Diabetes mellitus (DM), Central obesity, Low levels of HDL-C, High LDL-C, Lipoprotein-a (Lp a), Low levels of antioxidants (vitamin A, E, beta - carotene), Rapid modernization associated with sedentary but stressful life style in summation are suggested as additional risk factors for CAD. They too do not fill all the blanks in information."(7)

CAD in Indians the emerging scenario

"The risk of CAD in Indians is 3-4 times higher than White Americans, 6 wtimes higher than Chinese, and 20-times higher than Japanese."(8) "Indians are prone as a community to CAD at a much younger age."(7)

The disease pattern is severe. CAD is affecting Indians 5-10 years earlier than other communities. Indians also show higher incidence of hospitalization, morbidity, and mortality than other ethnic groups. This global phenomenon of severity suggests that the disease starts at an early age and has a malignant and progressive course.(7)

"Patients from other communities do not show extensive disease",(9) "Whereas in Indians there is often three vessel diseases with poor prognosis".(7) "The postinfarction course is also worse in Indians as compared to whites. This is reflected by three-time higher rate of re-infarction and two-times higher rate of mortality.(10)

In an observation in the Middle East, out of patients admitted in CCU with acute MI, 80% were Indian expatriates as compared to 20% of native Arabs, whereas demographically Indian expatriates are about 10% of the local population."(10)

"The prevalence of CAD is two-times higher (10%) in urban than in rural India"(11) South Indians have higher prevalence, 7% in rural and 14% in urban areas. The vulnerability of urban Indians to CAD is possibly related to different environmental, nutritional, and life-style factors. The body mass index in urban Indians as compared to rural Indians is 24 Vs 20 in males and 25 Vs 20 in females. Unfortunately, the on-going urbanization of rural India is likely to narrow down these differences.(7)

Migration from rural to urban environment and migration from India to industrialized countries is another special risk-factor for our people. Migration is usually associated with stress of stress of coping with the new job expectations, and seeking and maintaining the new job and stress of competing with the peer group who is in the organization longer. New affluence is associated with sedentary life-style and higher consumption of calories, salt, saturated fats, tobacco, and alcohol. These factors contribute to Dyslipidaemias, Obesity, Hyperuricaemia, Hypertension, and Diabetes mellitus. Therefore, there has to be high index of suspicion for CAD in adult Indians. The risk-factor evaluation must start earlier. Investigations like treadmill, stress echo and coronary angiography should be more liberally recommended.(12)

Risk factors (conventional and new)

There is a need for identifying and correcting the conventional risk factors like diabetes mellitus, hypertension, hyperlipidaemia, smoking, tobacco consumption, and central obesity at much younger age. Male sex is more prone to CAD but post-

menopausal females need special attention as they constitute a distinct sub-group at a high risk for CAD.(7)

The prevalence of DM is about 20% in middle age and additional 20% may be having impaired glucose tolerance, even moderate elevation of glucose in Indians is associated with increased risk of CAD. In contrast to decreasing mean cholesterol levels in the USA, the mean serum cholesterol level in urban Indians in rising. In Delhi, the mean serum cholesterol level has risen from 160 mg/dl in 1982 to 199 mg/dl in 1994. Indians even with lower levels of serum cholesterol have higher risk of CAD.(13,14)

Hypertension remains a standard risk factor associated with CAD. Prevalence of hypertension is increasing in urban population, as compared to rural population. In metropolitan cities the prevalence is as high as ll%-27%. (15–17)

Central obesity, depicted by waist to hip ratio is an independent risk factor for CAD, even modest increase in body fat with central distribution increases the risk further.(18)

Smoking increases the risk of CAD by 3-5 times. In the first world countries, smoking has significantly decreased and is socially looked down-upon. In contrast, in India smoking is increasing particularly in the younger generation.(7,10)In the seventies, tobacco consumption in India per adult was 0.7 kg/year; it is likely to increase to 0.9 kg/adult/ year. In India the consumption of tobacco is 6.1% of the world's total un-manufactured tobacco, 20% is in the form of *cigarettes,* 40% is in the form of Beedis and the rest as smokeless tobacco products.(19–21) Studies have shown that 40-50% of the males in India are smokers. For Indians, tobacco remains a major risk factor as it is used in different forms.(22,23)

New risk factors

Lipoprotein-a (Lp-a) is now recognized as an independent risk factor for CAD. It has a genetic risk factor. In Indians, both in India and abroad, the levels of Lp-a are higher as compared to the whites in Great Britain, suggesting a genetic propensity.(5)

Lp-a is ten-times more atherogenic than LDL-C. It promotes early atherosclerosis and thrombosis. Lp-a is a stronger risk-factor than DM for CAD in women. It is not affected by any level of lifestyle modifications like changes in diet and exercise.(7)

Study of Lp-a levels in cord blood in Singapore showed that the levels are higher among Indian newborns than Chinese newborns and this difference is also associated with a four-fold higher CAD - related mortality in Indians than Chinese in Singapore.(24)

Lp-a level above 30 mg/dl are associated with three-fold higher risk of CAD. Lp-a levels over 40 mg/dl increases the risk associated with cigarette smoking by 1.9 times, with hypertension by 4.6 times, with high total cholesterol by 4.2 times, the risk associated with with DM by 3.4 times, with high total Cholesterol / HDL ratio by 6.9 times, and with hyper-homocysteinaemia by 9.3 times.(7,10,25,26)

In Indian patients with CAD, high triglyceride levels are found more often than high cholesterol levels. Triglycerides bring change in LDL particle size, density, distribution, and composition producing smaller, denser and more atherogenic particles.(27,28)

Estimation of triglyceride level gives an indirect measurement of LDL particle size. An increase of triglycerides from 90 mg/dl to 180 mg/dl is associated with doubling the incidence of CAD. Increase in triglycerides by 90 mg/dl has the same effect on coronary atherosclerosis, as increase in age by 10 years.(7,29)

Indians worldwide demonstrate a triad of high triglycerides with high LDL-C levels and low HDL levels. Earlier; there has been an under-emphasis on the significance of triglycerides as a risk factor for CAD. This triad combined with high levels of lipoprotein-(a) constitutes the deadly lipid quartet.(30,31)

Higher levels of Apolipoprotein-B (Apo-B) are reported in one third of Indians males. This factor in combination with low levels of HDL and hypertriglyceridaemia results in formation of small dense LDL which increases the risk of CAD more than three times.(32,33) The LDL-cholesterol types are described as phenotypes A, B, or C, which are genetically determined. Patients with LDL phenotype-B have predominantly small and dense LDL-particles which as mentioned above, constitute an important risk factor for CAD. A 75% prevalence of phenotype-B is seen in Asian Indians in contrast to 25% in White population. High levels of plasminogen activator inhibitor-1 (PAI-I) in Indians are reported in association with hypertriglyceridaemia and hyperinsulinaemia. This combination promotes thrombosis by impairing fibrinolysis.(34–37)

Indians, as compared to Europeans, have higher resistance to insulin mediated glucose uptake in association with hyperglycemia, hyperinsulinaemia, hypertriglyceridaemia, and low levels of HDL-C. Insulin resistance syndrome (IRS) is an important risk factor for early development of CAD in Indians.(38,39)

Serum fibrinogen is another independent and newer risk factor for CAD. Fibrinogen increases the blood viscosity and plays a key-role in thrombosis. Both factors promote coronary artery atherosclerosis.(7)

Hyper-homocysteinaemia

Homocysteine is a sulfur containing amino acid which is a new and independent risk factor for CAD and Stroke. Homocysteine causes vascular damage

by its deleterious effects on endothelial functions and its pro-thrombotic, pro-oxidant, and mitogenic effects. The risks are comparable with the cigarette smoking and dyslipidaemias.(40,41)

Infections and CAD

Various infections, viral and bacterial, have been implicated. Amongst them, *Chlamydia pneumoniae* is considered as an important risk factor for CAD.(42,43). This is so surmised because some patients with Chlamydia who had AMI had high antibody titers to Chlamydia lipopolysaccharide. It is thought that AMI may be precipitated by exacerbation of *Chlamydia pneumoniae* infection.(42,44)

Atherosclerosis represents an exaggerated inflammatory reaction to injury of the endothelial layer of the arterial wall. A systemic infective episode produces generalized arteritis including coronary arteritis with diffuse lesions. These lesions may be further worsened by pro-atherosclerotic factors like hypertension, smoking, diabetes and dyslipidaemias. The mechanism could be occurring other way round, i.e., coronary endothelium which has already developed atherosclerotic plaques due to conventional risk factors, on getting further inflamed by a systemic infection, undergoes aggravation of plaque activity and thrombosis, precipitating an acute coronary event.(7)

LIPOPROTEIN (a)

LIPOPROTEIN (a) was discovered in 1963 by Kave Berg while experimenting with Rabbits immunized with human LDL.(45) The association of Lipoprotein (a) with CAD was initially demonstrated in 1974. It constitutes an important inherited risk factor for atherosclerosis. And has also been regarded as biological marker for familial CAD.(46,47)

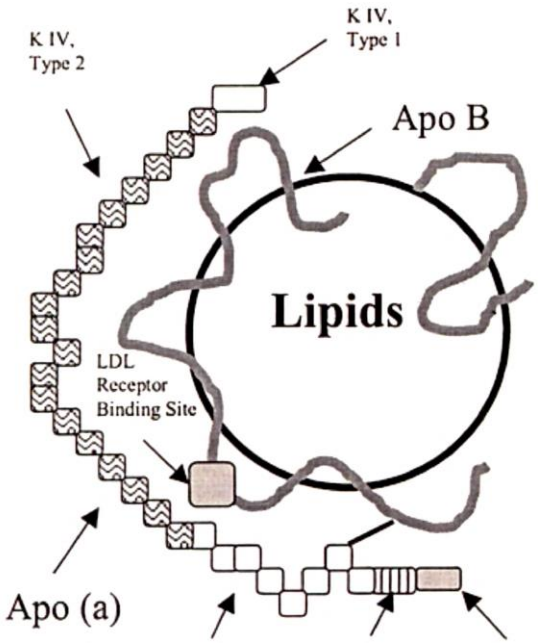
STRUCTURES OF LIPOPROTEIN (**a)**

Lipoprotein (a) [Lp (a)], is present only in humans, monkeys and the European hedgehog. Lp(a) has many properties in common with low-density lipoprotein (LDL) but contains a unique protein, apo (a), which is structurally different from other apolipoproteins. (48,49)

The size of the apo (a) gene is highly variable, resulting in the protein molecular weight ranging from 300 to 800 kDa (kilo Dalton); this large variation may be caused by neutral evolution in the absence of any selection advantage. Apo (a) influences to major extent, physicochemical and metabolic properties of Lp (a).(50)

And the size polymorphism of the apo (a) gene contributes to the pronounced heterogeneity of Lp (a). There is an inverse relationship between apo (a) size and Lp (a) levels; however, this pattern is complex. For a given apo (a) size, there is a considerable variation in Lp (a) levels across individuals, underscoring the importance to assess allele-specific Lp (a) levels. Further, Lp (a) levels differ between populations, and blacks have generally higher levels than Asians and whites, adjusting for apo (a) sizes. In addition to the apo (a) size polymorphism, an upstream pent nucleotide repeat (TTTTAn) affects Lp (a) levels.(51–57)

Lp(a) is modified form of LDL molecule with apo B-100 covalently linked and bound to a molecule of apoLp(a) i.e. Apo (a) by a single disulphide bridge to form Lp (a). The apo(a) chain contains five cystine rich domains known as kringles. The fourth kringle is homologous with the fibrin binding domain of plasminogen, a plasma protein that dissolves blood clots when activated. It is identical to LDL except for the addition of apo (a). The physiological function of Lipo (a) is not known.(58,59)



This LDL-like moiety consists of lipid core of cholesterol esters and triglycerides surrounded by a surface layer of phospholipids and free cholesterol. In addition to lipids, it also contains one molecule of apolipoprotein B, which is linked to apolipoprotein (a) through a single disulfide bond. The putative LDL receptor binding domain of apo B is shown. The apo (a) moiety consists of a single copy of kringles KIV, types 1 and 3 to 10, kringle V, and a protease domain analogous to plasminogen. In addition, it contains multiple copies of kringle IV, type 2.(56)

Lipoprotein (a) [Lp (a)] was first described 40 years ago, and interest in this entity is largely derived from its putative role as a cardiovascular risk factor. Underlying this concept is the realization that Lp (a) has many properties in common with low-density lipoprotein (LDL), a well-established atherogenic factor for coronary artery disease.(60)

Thus, the composition of the lipid moiety of Lp (a), including its cholesteryl ester-rich core, is similar to that of LDL, and the density distribution of the lipid moiety of Lp (a) in a given subject closely mirrors that of LDL.(61,62) Furthermore, like LDL, each particle of Lp (a) has 1 molecule of apolipoprotein B-100 (apo B-100); both apolipoprotein B (apoB) and the lipid core are pro-atherogenic.[51] Also, Lp (a) clearance rates are similar to those for LDL.(63–65)

However, Lp (a) also contains a unique protein, apolipoprotein (a) [apo (a)], which is structurally different from other apolipoproteins, having a hydrophilic, carbohydrate-rich structure with no amphipathic helices.(56,66) Apo (a) is linked to apoB through a single disulfide bond connecting their C-terminal regions.(67)

The presence of apo (a) influences to a major extent metabolic and physicochemical properties of Lp (a).(56,68) Notably, the cysteine residue in apoB is involved in the covalent bond between apoB and apo (a) and is close to the postulated LDL receptor-binding region of apoB.(69,70) It appears from many clinical studies that Lp (a) levels are not affected by LDL receptor activity.(63,71,72) Suggesting that the large, carbohydrate-rich apo (a) protein introduces a charge and/or stearic interaction affecting the binding potential of apoB in Lp (a) for the LDL receptor. This could at least partly explain why Lp (a) plasma levels are mainly determined by the synthesis rate in contrast to LDL in which catabolism through the LDL receptor is an important regulator of plasma levels, although overall clearance rates are similar

for the 2 lipoprotein fractions. Lp (a) levels are particularly affected by apo (a) synthesis rate, which is subject to strong genetic regulation. Because of this strong genetic impact, Lp (a) plasma levels are affected only to a minor extent by age, sex, and environmental factors.(73)

Lp (a): MOLECULAR PROPERTIES: -

Lp (a) is very heterogeneous and the underlying reasons for this heterogeneity were uncovered by the elegant work on the gene structure of apo (a) by Lawn, Scanu, and their collaborators.(48,71) They reported an analogy between the apo (a) and plasminogen genes; both genes have coding sequences for loop structures stabilized by intrachain disulfide bonds, so interestingly, the sequence coding for one of these Kringle called (K) domains. The plasminogen gene contains coding sequences for 5 different K domains (K1 to K5), and 2 of these are present in the apo (a) gene, K4 and domains, K4, is repeated many-fold in the apo (a).(74,75)

Altogether, the apo (a) gene has 10 different types of plasminogen- like K4 domains, referred to as K4 type 1 through 10. K4 types 1 and 3 to 10 are present as single copies, whereas K4 type 2 is present as multiple copies, varying in number from 3 to 40 copies. Each kringle contains 80 to 85 amino acids and has a molecular weight of -10 kDa, and the K4 repeat unit is thus unusually large. This heterogeneity in apo (a) gene size corresponds to a size variation in the apo (a) protein and apo (a) size isoforms containing from 12 to 50 K4 motifs have been reported, corresponding to a protein molecular weight ranging from 300 to 800 kDa. The size variability of apo (a) impacts on Lp (a) levels; there is a general inverse relation between apo (a) size and Lp (a) levels.(76–78) Thus, smaller apo (a) sizes tend to correspond to higher plasma Lp (a) levels; however, this pattern is complex. For a given apo (a) size, there is a considerable variation in Lp (a) levels across individuals. (26,48,67)

Lp (a) is found only in humans, in monkeys and in the European hedgehog. The hedgehog version of apo (a) appears to have evolved separately from -the primate and human apo (a) versions, because it contains the plasminogen K3 domain instead of the K4 domain and is not subject to size heterogeneity. Thus, although apo (a) is novel from an evolutionary standpoint, it appears nevertheless to have emerged twice. Despite this, there is currently a profound lack of understanding of any physiological function for Lp (a).(48)

GENETIC DETERMINANTS OF Lp (a):-

Serum Lp (a) levels are largely genetically determined with a single apo (a) gene, localized to the long arm of chromosome 6, accounting for more than 90% of variations in its serum level. Only part of plasma levels of Lp (a) is under genetic control. While the other part is environmentally influenced by factors like Renal function, Age , Hormonal status and Dietary habits. (79,80)

Lp (a) levels are also reduced by treatment with Danazol , N-acetyl cysteine and allylesterol.(81) Nicotinic acid and Neomycin also decrease levels of Lp (a), and are used for therapeutic purpose.(82,83) LDL aphaeresis is useful modality of treatment of patients of homozygous familial hypercholesterolemia and ordinary hypercholesterolemia. (81)

Although Lp (a) and LDL are rather similar in structure the 2 lipoproteins are metabolized differently. Lp (a) concentrations are resistant to most forms of LDL-lowering therapy. An exception is the antihyperlipidemic drug, Niacin, which decreases Lp (a) as well as LDL cholesterol. In addition anabolic steroids and alcohol decrease Lp (a) levels. The fact that Lp (a) is not affected by most lipid lowering drugs suggests that the regulation is different from that of LDL.(82)

Lp (a) does not have a precursor lipoprotein, because it is secreted in the blood directly from the liver. Lp (a) formation is a 2-step process involving an initial noncovalent interaction between apo (a) and apoB 100 that precedes specific disulfide bond formation. A possible coupling between the metabolism of triacylglycerol-rich lipoproteins (TRL) and that of Lp (a) was suggested. An inverse relation between Lp (a) and plasma triacyl glycerol (TAG) was reported in hyperlipidemics.(84,85)

Although an interaction between TRL and Lp (a) is plausible, the mechanism is not fully understood. Degradation of Lp (a) may be mediated through VLDL receptors or apo (a) may be cleaved from an Lp (a) particle in the kidney, leaving the lipid and apoB components to be cleared through the LDL receptor.(60,86)

Apolipoproteins

The protein moieties of Lipoproteins known as apolipoproteins have four major rules

1. Assemble and secrete Lipoproteins (apo B_{100} and B_{48})
2. They provide structural integrity to lipoproteins
3. Act as co-activators of enzymes
4. They bind or dock to specific receptors and proteins for cellular uptake

Table : Apolipoproteins

	Predominant Lipoprotein	**Role**	**Human Diseases**
Apo AI	HDL	ACAT activation, Structural	HDL deficiency
Apo AII	HDL	Structural	
Apo AIV	HDL	Structural, absorption	
Apo B100	LDL,VLDL	Structural, LDL-R binding	Hyperbetalipoproteinemia
Apo B 48	Chylomicrons	Structural	
Apo CI	Chylomicrons	TGL metabolism	
Apo CII	Chylomicrons, VLDL	LPL activation	Hyperchylomicronemia
Apo CIII	Chylomicrons, VLDL	LPL inhibition	Hypertriglyceridemia
Apo D	HDL	LCAT	
Apo E	Chylomicrons, LDL	LDL-R, ApoE-R binding	Type III
Apo J	HDL	Complement system	
Apo (a)	Lp(a)	Tissue injury	Hyper Lp(a)

LABORATORY ESTIMATION AND PLASMA LEVEL:-

The major source of circulating plasma Lp (a) level is derived from liver.(62,87) Laboratory estimation was obtained from radioimmunoassay, Immunoelectrophoresis and by ELISA method. There is marked variation in serum levels fluctuating from <0.1 mg/dl to a maximum of >150 mg/dl.

In the Framingham offspring study, distribution of serum levels of Lp (a) in Caucasians was found to be highly skewed. 10% had serum values of <1 mg/dl and more than 50% had, 10 mg/dl.(28,88)

A number of factors affect the serum levels including renal failure, alcohol consumption and nephrotic syndrome. Moderate alcohol drinking lowers plasma Lp (a) levels. Niacin and hormone replacement therapy lowers Lp (a) levels.(88,89)

FACTORS AFFECTING **Lp (a)** CONCENTRATION

1. PHYSICAL FACTORS:

   Age: High risk factor in young age.

   Menopause:- Estrogen reduces Lp (a) level.

2. CHEMICAL COMPOUNDS AND DRUGS :-

   Estrogen:- Reduces Lp (a) level

   Niacin:- Reduces Lp (a) level.

   Neomycin:- Additive effect along with Niacin to reduce Lp (a) level.

3. DISEASE:

   Myocardial infarction:- Risk factor for MI in young age.

Lp (a) AND ATHEROSCLEROSIS:-

Lp (a) promotes atherosclerosis by following mechanisms:

1. Enhancing susceptibility of LDL cholesterol to oxidative modification.
2. The VLDL receptors found on the macrophages present in atherosclerotic lesions can bind to and mediate the catabolism of Lp (a) by endocytosis, leading to its degradation within lysozomes. This would lead to a cellular accumulation of lipids within macrophages. Supporting this hypothesis is the observation that Lp (a) is ubiquitous in human coronary Atheroma, colocalizes with plaque macrophages, and is detected in large amount in tissue from culprit lesions in patients with unstable compared to stable coronary artery disease.(90)
3. With oxidation on modification by malondialdehyde, Lp (a) becomes a ligand, both in vitro &in vivo, for the scavenger receptor, & macrophages form cells may express a distinct Lp (a) clearance receptor. Lp (a) might interfere with the normal degradation of cholesterol by way of LDL receptor or itself be targeted to early atherosclerotic lesions, possibly through the macrophage scavenger receptor.
4. Interference with fibrinolysis by competition with plasminogen for binding sites on molecules and cells.
5. Binding to endothelium and components of the extra cellular matrix, leading to endothelial dysfunction due to selective impairment of vasodilators capacity of receptor mediated endothelial stimuli.
6. Inhibition of thrombolysis, which may prevent activation of transforming growth factor B, an inhibitor of vascular smooth muscle proliferation.

7. Prothrombotic mechanisms: Given the extensive sequence homology between apo (a) and plasminogen, (euton et al 1987, Me Lean et al 1987), it has been suggested that much of the atherogenic potential of Lp (a) derives from interference in normal pathways of thrombolysis, to predispose patients to acute thrombotic complications. Prothrombotic effect of Lp (a) include interference with its binding to endothelial cells monocytes & thrombospondin, interference with the binding of tissue plasminogen activator to fibrin; & stimulation of synthesis of P AI - 1 (reviewed by stein &resenson, 1997, Ehapmann et al 1994, Loscalso 1990.)(90)
8. Oxidized Phospholipids: Relation to Lp (a) - Recently, a new possible mechanism for apo (a) atherogenicity has been suggested. In a series of studies, Witztum et al have demonstrated convincingly that key oxidized phospholipids are preferentially associated with Lp (a). Proinflammatory, oxidized phospholipids are covalently bound to kringle V in apo (a), a portion of apo (a) associated with macrophage IL-8 production. These results suggest that Lp (a) may act as a preferential acceptor that tightly binds oxidized phospholipids transferred from tissues or from other Lipoproteins. This could imply that Lp (a) functions as a scavenger absorbing potentially deleterious oxidized lipids, preventing an increased uptake in the vessel wall of other lipoproteins, primarily LDL, containing this factor. However, the presence of oxidized phospholipids in Lp (a), potentially being taken up by the vessel wall, could also accelerate development of atherosclerosis. Because kringle V is present as a single copy in the apo (a) molecule, the results suggest an apo (a) size-independent potential for binding of oxidized phospholipids, although it is possible that apo (a) size can affect the binding site through conformational

changes. Notably, Lp (a) levels have been found to be higheramong white centenarians, raising the possibility that Lp (a) may serve as alongevity factor, although opposite results have been reported in a Japanese cohort.(91,92)

9. Enhancement of expression of intracellular adhesion molecule 1, resulting in the recruitment of monocytes to the vessel wall and binding to macrophages. This can promote foam cell formation and the localization of Lp (a) in atherosclerotic plaque.
10. Other hypothesis includes a role for Lp (a) in cholesterol delivery to the injured vessel wall & stimulation of vascular cell proliferation. Pathogenic &laboratory evidence includes observations that Lp (a) binds lipoproteins containing apo B, avidly binds to arterial proteoglycans & fibronectin, accumulates in atherosclerosis lesions, stimulates SMC proliferation & promotes cholesterol accumulation in cells.
11. The interaction of Lp (a) with the vascular endothelial barriers has been serviced by Nordestgaard (1996). Lp (a) appears to enter the intima at aboutthe same rate as LDL but may be retained there to a greatest extent, particular at the sites of injury.

Lp (a) and CAD:

Lp (a) is considered to be 10 times more atherogenic than LDL-C.80 Relative risk of CAD is increased three fold in males if Lp (a) levels are above 30 mg/dl.81,82 Adverse effects are enhanced by High LDL-C and low values of HDL-C. There is six fold increased when LDL-C also elevated. Men with LDL-C >317 mg/dl and Lp (a) > 30 mg/dl have a 16 fold increased odds ratio of having CAD verses those having an LDL-C levels of >130 mg/dl, and Lp (a) levels of < 10 mg/dl. The levels also

correlate with presence and extent of severity and score of atherosclerotic lesions on coronary angiography.(93)

Lp (a) and Diabetes:

Diabetes is one of the most important disease, which has got significant impact on lipid profile. Studies from south India have shown good correlation between Lp (a) levels and risk of CAD in NIDDM.(71,94) Lipoprotein (a) is shown to be a powerful, independent risk factor for CAD in type 2 DM and this association is independent of all other known risk factor including TC, LDL-C, HDL-C and triglyceride.

Treatment:-

Primary goal of treatment: LDL reduction. If LDL concentration cannot be reduced to less than 130 mg/dl. Specific Lp (a) lowering therapy can be initiated in appropriate patient with Nicotinic acid (3-4 gm/day) or Neomycin (2-3 gm/day) in divided doses. Nicotinic acid reduces Lp (a) level by 38% versus 24% by Neomycin combined therapy produces addictive effect lowering Lp (a) and LDL by 45%.(95)

Estrogen replacement therapy is the treatment of choice for postmenopausal women with Lp (a) levels excess who do not have contraindication to its use.(96) ERT reduces Lp (a) levels up to 50%. Progesterone mitigates this effect. ERT appears to have more favorable effects on outcome in women with High Lp (a) levels then in women with low levels. Statins and bile sequestering agents do not reduce Lp (a) levels. Most fibric acid derivatives do not lower Lp (a) levels, except for Biz Fibrates. LDL aphaeresis in patients with homozygous familial hypercholesterolemia and in ordinary familial hypercholesterolemia can cause profound lowering of LDL-C.

RISK FACTORS FOR CAD

Current prediction estimates that by 2020, cardiovascular disease, notably atherosclerosis will become the leading global cause of total disease. The systemic study of risk factors in humans began in mid-century. The risk factors that emerged from such studies have seen classified into two categories.(96)

UNMODIFIABLE RISK FACTORS:

Age

Gender: (Male)

Genetics

MODIFIABLE RISK FACTORS:

By life style:

- smoking
- obesity
- physical inactivity

By pharmacological and or life style:

- Lipid disorders
- HT
- Insulin resistance
- Estrogen-status
- Mental stress

NOVEL RISK FACTORS:

- Homocysteine
- **Lp (a)**
- Fibrinogen
- Markers of fibrinolytic function: PA-1, t-PA
- Markers of inflammation: CRP, ICAM-1, IL-6

HYPERCHOLESTEROLEMIA:

This is considered as one of the prime risk factor for CAD. The earlier the age of detection, greater the risk of CAD. Elevated serum cholesterol is casually associated with risk of CAD specifically a 10% increase in serum cholesterol is associated with a 20-30% increase in risk of CAD.(97,98)

In man it has been found that 41% variants in CAD mortality was related to variation in serum cholesterol, 32% was related to variation in ratio of total cholesterol to HDL cholesterol. It is difficult to define safe basal level of serum cholesterol. A low risk level from the point of view of primary prevention should ideally be LDL-C <130 mg/dl, HDL >40 mg/dl, TG <150 mg/dl.

SMOKING:

Smoking increases CAD mortality by 50%, it doubles the incidence of CAD and the risk increases with age, and number of cigarettes smoked. Similar risk has been observed among women.

Smoking is a leading preventable cause of death and CAD worldwide. Those who quit smoking decrease the risk by 50% in 1-2 years and to normal levels by 5-15 years. Smokers have lower HDL-C levels and high VLDL and triglyceride levels.(99,100)

HYPERTENSION:

A well-established risk factor for CAD, both elevated SBP and DBP are associated with increased risk. A 7 mm Hg increase in diastolic blood pressure over any baseline reading was associated with 27% increased in CAD risk and 42% increase in stroke risk.86 Similarly lowering diastolic BP by 5-6 mm Hg results in a 42% reduction in risk of stroke and 15% reduction in risk of CAD.(99)

DIABETES:

It is a major risk factor for CAD. By age 40 years, CAD is the leading cause of death in both diabetic males and females. Age adjusted rates of CAD are 2-3 times higher in diabetic men and 3-7 times higher in diabetic women than their non-diabetic counterparts. In Danish Stars Hospital study, mortality from myocardial infarction alone was 12.5% after 35 years of diabetes regardless of age of onset.(99)

HDL AND TRIGLYCERIDES:

"HDL is an important independent predictor of CAD, every 1 mg decrease in HDL, causes 3-4% increase CAD. The ratio of HDL to LDL may be an even better predictor of CAD than LDL alone. Fasting triglyceride levels represents a useful marker of the risk of CAD particularly when the HDL levels are also considered".(101)

PHYSICAL INACTIVITY:

Regular physical activity protect against CAD. The risk of CAD in sedentary individuals was twice that in active individuals after controlling other coronary risk factors. The benefits are through weight reduction, BP and cholesterol reduction. (101)

OBESITY:

Obesity appears to have an independent risk for CAD, even after controlling the other risk factor. A higher BMI is associated with an increase in all the risk factor of CAD and stroke. "The distribution of body fat may also play role, with abdominal adiposity posing a substantially greater risk in both men and women. A waist circumference of 35 inches in women and 40 in men is an easily measured marker of CAD risk"(102,103)

ESTROGEN AND SEX:

A well-established fact that men have a higher risk of CAD than women.(8)The latter have high HDL-C level and lower LDL-C level. However there is striking increase in CAD in females after menopause. The beneficial effects are attributed to the higher estrogen levels in females, which drops after menopause.

ALCOHOL:

Heavy alcohol intake increase total mortality. However moderate alcohol consumption has a protective effect in CAD, 1-2 drinks/day, increases HDL, improves fibrinolytic capacity and platelets aggregation.

DIET:

Low fat diet decreases risk of CAD. "Saturated and Trans fatty acids appears to increase the risk of CAD".(104)

PSYCHOLOGICALFACTORS:

Type 'A' personality traits seem to predispose to CAD. Chronic emotional distress alters autonomic discharge and increase BP. "Depression, absence of social support and anger appear to contribute to an elevated risk of CAD."(104)

PATHOPHYSIOLOGY OF ATHEROSCLEROSIS WITH CAD

The intimate involvement of lipid at each step in the development of atheroma and its potentials for manifestations of disease has been brought out from extensive studies. Atheroma is circumscribed focal lesions in the intima of arteries. The vascular endothelium is endowed with special properties of contact inhibition, tight junction and elaboration of autacoids like, nitric oxide (NO), adhesion molecules and thrombolytic factors.-Several cytokines thus modulate the vascular tone and maintain the lumen for free flow of blood. Endothelial injury or dysfunction often alters these properties. Injury may occur from physical stress, infective agents, toxins or immunogenic inflammations.

Endothelial denudation leads to insudation of lipids and Atheroma formation. Endothelial dysfunction initiates the process. Hyperlipidaemia and excess of modified lipoprotein fractions have been recognized as important causes of endothelial dysfunction that leads to exaggerated transcytosis of lipoproteins mainly LDL more so,of the small dense type as well as chylomicron remnants, VLDL and Lp (a) from plasma into the sub endothelial zone of arterial intima. They are bound to proteoglycans, which present their egress from this site.

Within the intima, inaccessible to circulating plasma antioxidants, LDL particles are acted upon by oxygen free radicals from the surrounding tissue and form oxidized LDL (OX LDL) from minimally modified LDL. Both oxidized and glycated LDL tend to stimulate the endothelial cells to release adhesion molecules (E-Selectin,VCAM, ICAM), leading to pallisading monocytes and T lymphocytes along the endothelial surface, chemo attractants elaborate similarly, induce migration of the leucocytes across the endothelium. Under the influence of OX LDL the monocytes

turns into macrophages and develop scavenger, receptive for modified LDL molecules. Inhibition of lipids transforms such macrophages to foam cells.

FATTY STREAKS:

Accumulation of foam cells in the sub-endothelium appears as fatty dots or fatty streaks on the intimal surface of aorta in early life. Coronary arteries manifest fatty streaks by 3rd decade some may regress, but some will progress further to 'plaque' formation.

F1BROFATTY PLAQUE:

With time, the foam cells degenerate, releasing their contents into the extra cellular space within the intima, successive foam cell formation and release of contents leads to the creation of a lipid pool. Meanwhile, the released growth factors stimulate the proliferation of smooth muscle in the intima, as well as those recruited from media. These smooth muscle cells elaborate plenty of collagen, while inflammatory cytokines induces proliferation of fibroblast and lying down of fibers and intestinal matrix. These changes increase the size of lesions and they stand out as plaque over intimal surface, such lesions are common at branch point. Typically these plaques contain 40% lipids by volume, the rest being collagen tissue matrix and smooth muscle cells. The lipids are separated from vascular lumen by fibrous cap.

ADVANCED PLAQUE:

Calcification is common in advanced plaques. The deposits may be scanty, patchy, scarring cap develops from excessive fibrosis, cracks, fissures and erosion may develop over the fibrous cap. Endothelial denudation leads to platelet aggregation on its surface, rupture of cap exposes the circulating coagulation factor to highly thrombogenic core of the plaque leading to vascular thrombosis. Exudation of the core into the lumen may cause obstruction to blood flow in medium sized

muscular arteries whereas in larger vascular channels the material may flow out as cholesterol emboli. Hemorrhage into the plaques may occur from thin walled vascular channels within or blood may enter the plaque from the circulation through the dents in the fibrous cap.

Plaques with a tendency to develop complications leading to vascular occlusion are described as unstable. It has been observed that such plaque usually have large lipid cores and hence more susceptible to plaque rupture in contrast to those with excess calcification and scarring. Large lipid pools induce plaque instability and precipitate event such as unstable angina, and myocardial infarction and cerebral thrombosis.

Lp (a) and CAD

A number of studies carried out both in India and abroad, studying the level of Lp (a) and its relation to CAD.

The coronary artery-disease in India study first reported the existence of high levels of Lp (a) in Asian Indians when they compared the Lp (a) levels of 141 Asian Indian physicians with 136 white physician in U.S. Lp (a) levels >30mg/dl were found in 25% of Asian Indian and in 17% whites.

Sandholzer et al reported Lp (a) levels twice as high in Asian Indians compared to Caucasians, Malaysians and Chinese residents of Singapore from 1150 subjects.90 Bhatnagar et al have reported nearly identical high mean level of Lp (a) among Asian Indians living in the UK and their siblings in India.(104)

Shaukat et al have confirmed that mean Lp (a) level among Asian Indians is higher than whites with CAD and have also found a good correlation of levels of Lp (a) with the extent of CAD in Indian. It was found that Lp (a) levels were nearly double in 15-30 years old sons of Asian Indians suffering from CAD compared to

similar aged sons of white parents -19 mg/dl versus 10 mg/dl suggesting an important role of Lp (a) in CAD.(105)

Bahi et al, from Delhi, reported that only plasma lipids do not predict the severity of atherosclerosis and large vessels disease as demonstrated in angiography and only a trend for higher Lp (a) values in patients with severe CAD.(104)

A study from new Delhi, also showed higher lipoprotein (a) levels in 114 consecutive patients undergoing coronary angiography with mean levels of 42 mg/dl. Singh et al from Delhi have reported that Lp (a) alone would correctly discriminate a CAD individuals for control subjects by 95%. They also found that in female's atherothrombotic potential of lipoprotein (a) remains suppressed before menopause but after this stage women lose their advantage.(106)

Mary sed et al,found that in a prospective population based study, of asymptomatic — middle aged men in-UK that serum Lp (a) levels were an independent risk factor for coronary events.(107)

A study by **Sigudsson G et al**, of 1332 patients, who were followed for occurrence of coronary events showed that Lp (a) was an independent risk factor for the occurrence of myocardial infarction in men aged 45 to 72 years.(108)

The **Quebec cardiovascular study** found that high Lp (a) levels appeared to increase risk associated with other lipid risk factors. (109)

Studies by Boston et al have also shown that Lp (a) is a risk factor for CAD .(109)

Michael Shilpak et al have found Lp (a) to be an independent risk factor for recurrent CAD in postmenopausal women and that treatment with estrogen and progesterone lowers Lp (a).(109)

Recently a comprehensive lipid tetrad index has been proposed by enas as the best estimate of the total burden of dyslipidaemias. It is derived by the product of cholesterol, triglycerides and Lp (a) value divided by HDL level and may estimate the need for various cut off points and ratios involving these lipids. A high index indicates a highly atherogenic lipid profile and warrants aggressive treatment. (109)

Lipid tetrad index of Asian Indians

Population	Index = $\frac{TC \times TG \times Lp(a)}{HDL\text{-}C}$	TC	TG	Lp(a)	HDL
Men in India	12899	189	182	18	48
Women in India	10814	196	151	19	52
Men in UK	20629	251	186	19	43
Women in UK	15615	239	147	20	45
CAD in UK	34720	236	197	33	41
White CAD in UK	18085	233	163	20	42

Lipoprotein (a) Is an Independent Risk Factor for Myocardial Infarction.

Martin Sandkamp, Harald Funke, Helmut Schulte, Eckhard Kohler, and Gerd Assmann,quantified Lipoprotein (a) [Lp (a)] immunochemically in male survivors of myocardial infarction and in Age-matched controls recruited from participants of the Prospective Cardiovascular study. They further determined apolipoprotein E polymorphism and measure triglycerides, total cholesterol, high- and low-density lipoprotein cholesterol (HDL and LDL), and apolipoproteins Al, All, and B in the serum of these subjects. Lp (a) concentrations in serum were not correlated with other well-recognized risk factors for early myocardial infarction such as

apolipoproteins Al and B, LDL cholesterol, and HDL cholesterol. Apolipoprotein E polymorphism did not affect Lp (a) concentrations, but had a major influence on apolipoprotein B concentration. Lp (a) concentrations were not influenced by age. Our data suggest that (a) an increased concentration of Lp (a) constitutes an independent risk factor for early myocardial infarction and *(b)* the concentrations of Lp (a) and LDL cholesterol (apolipoprotein B) in serum are under separate metabolic control. (109)

Recent studies also shown the role of Lp (a) in CAD in Indian patients **Geetanjali et al** have found a level of 33.4±26,1 mg/dl in angiography proven coronary artery disease.(109)

A study by **Reddy Vit. K et al**, from Hyderabad of CAD patients showed a mean level of 26.4 mg/dl.(110)

A study of unstable angina patients from Amristsar by **Dr. BAL B.S. Et Al** showed mean level of 36.2±4.2 mg/dl (111)

A recent study from Kolkata by **Guha et al** of 30 proven CAD patients, showed a very high lipid profile tetrad index of 52350.2 and a mean Lp (a) levels of 59.2 mg/dl.(112)

MATERIAL AND METHODS

MATERIAL AND METHODS

This section includes

a) Subjects (patients and controls)

b) Blood sampling and preparation of Serum

Subjects :

Study of Lp (a) levels in patients with Acute Myocardial infarction was carried out at Shri B M Patil Medical College, Hospital and Research center, Vijayapura during the period of June 2016 to October 2018.

A total of 90 patients with Myocardial Infarction were included in the study. The patients included all admissions of patients aged > 18 yrs with Acute Myocardial infarction in ICCU of Shri B M Patil Medical College, Hospital and Research center, Vijayapura.

Control group included individuals without Ischemic heart disease.

Study population:

Study population consisted of 90 patients with Acute Myocaridal Infarction. The diagnosis in each case was established by History, clinical sign and symptoms, 12-lead ECG with or without ECHO and appropriate biochemical markers like CK-MB, Troponin T or Troponin I. Control group included 60 individuals without Ischemic heart disease, fitting in the same age bracket were involved.

Inclusion criteria:-

Patient above 18 years of age with

1. Symptoms of Ischemia with :
2. Detection of Cardiac biomarkers (preferably cardiac troponin [cTn]) with at least one of the following:
3. New or presumed new significant ST-segment T-wave (ST-T) changes. [≥2 mm rise in 2 consecutive leads]
4. Development of pathologic Q waves in the electrocardiogram (ECG)

Any two out of the above must present to be included in the study.

AND

Age, sex and risk factor matched non AMI patients / individuals for Control group.

EXCLUSION CRITERIA:

1. Patients of age less than 20 years.
2. Stable Angina and Unstable Angina.
3. Cardiovascular diseases resembling MI like pericarditis, aortic dissection.

The purpose of elimination of patients with exclusion criteria was to get a pure picture of relationship between Myocardial infarction and lipids as the above conditions alter lipid levels. In all patients with MI, collection of blood for Lipid Estimation and Lp(a) level estimation was drawn within 12 hours of the event.

No other limitations were imposed. After having been selected for the study each patient was subjected to the following procedures.

Methodology:

After admission, a relevant history and clinical examination was carried out and 12-lead ECG was taken in every patients of MI. Patients were treated with Thrombolysis, Anticoagulation, Aspirin, Clopidogrel, Nitroglycerin, Beta blockers, ACE inhibitors, Ionotropic support, Atropine and Laxatives wherever applicable.

Following investigations were carried out in all patients and controls:

1. SERUM LIPOPROTEIN (A)
2. COMPLETE BLOOD COUNT (WITH DIFFERENTIAL COUNTS)
3. FASTING LIPID PROFILE
4. ECG
5. SERUM CK-MB & TROPONIN - T / I
6. ECHOCARDIOGRAPHY
7. BLOOD SUGAR LEVEL
8. SERUM CREATININE
9. URINE ANALYSIS

Along with the above investigations other relevant investigations were performed if required.

SAMPLE COLLECTION AND PREPARATION

The blood sample was drawn from all patients within 12 hours of Mi. The venipuncture was done in antecubital fossa. About 10 ml of blood was drawn using a sterile syringe. Within 2 hours of drawing blood, serum was separated to prevent artefactual changes in HDL concentrations. For the estimation of triglycerides the serum was transferred to centrifuge at 5000 RPM for 10 minutes. Supernatant clear serum was then extracted and sample was analyzed the same day. Care was taken to exclude hemolysed serum.

METHODS FOR DIFFERENT PARAMETERS USED IN STUDY:

SERUM CHOLESTEROL:

Method: PAP method

Principle:

Cholesterol esterase hydrolyses esterified cholesterol to free cholesterol. The free cholesterol is oxidized to form hydrogen peroxide which further reacts with phenol and 4-aminoantipyrine by the catalytic action of peroxidase to form a red coloure dquinoneimine dye complex. Intensity of the colour formed is directly proportional to the amount of cholesterol present in the sample.

Cholesterol esters+H20 $\xrightarrow{\text{Cholestsro1 Esterase}}$» Cholesterol + Fatty acid

Cholesterol + $0_2 \xrightarrow{\text{Cholesterol oxidase}}$> cholest-4-en-3one + H_2O_2

H_2O_2+ 4-Aminoantipyrine + Phenol $\xrightarrow{\text{Peroxidase}}$> Red Quinoneimine dye + H_20

Procedure:

Wavelength	520 (490-540)
Reaction type	End point
Reaction Temperature	37° C
Incubation Time	20 min

Pipette in tubes according to following table

	Reagent blank (µl)	**Standard (µl)**	**Test (µl)**
Test	**--**	**--**	**10**
Standard	**--**	**10**	**--**
D/W	**10**	**--**	**--**
Reagent	**1000**	**1000**	**1000**

Mix, incubate for 20 min at 37° C. Measure the absorbance of the sample (Abs-T) and standard (Abs-S) against the reagent blank within 60 min.

Calculation:-

Serum cholesterol concentration (mg/dl) = $\frac{\text{Abs-T x Cone. Of standard}}{\text{Abs-S}}$

TRIGLYCERIDE:

Method: GPO method

Principle:

The triglycerides present in the serum are catabolised into glycerol and free fatty acids by lipoprotein lipase. Liberated glycerol is converted to glycerol-3-phosphate in presence of glycerol kinase and ATP Glycerol-3 -phosphate is acted upon by glycerol-3-phosphate oxidase to form hydrogen peroxide. This together with phenolic compound and 4-aminoantipyrine in presence of peroxidase gives the purple colour complex. The intensity of the colour is measured at 546 nm (530-570 nm) or green filter and corresponds to the triglycerides concentration.

Triglycerides $+H_2O$

Triglycerides +H3O $\xrightarrow{\text{Lipoprotein lipase}}$ Glycerol + Fatty acid

Glycerol + ATP $\xrightarrow{\text{Glyecrol phosphate}}$ Glycerol-3-phosphate + ADP

Glycerol-3-phosphate $+ H_20 \xrightarrow{\text{Gly-3-phosphate kinase}}$ Dihydroxyaeetone Phosphate $+ H_2O_2$

H_2O_2+4-Aminoantipyrine+Phenol $\xrightarrow{\text{Peroxidase}}$ Red Quinoneimine dye+ H_2O

Procedure:

Wavelength	546 (530-570) nm
Reaction type	End point
Reaction Temperature	37° C
Incubation Time	10 min

Pipette in tubes according to following table

	Reagent blank (µl)	Standard (µl)	Test (µl)
Test	--	--	**10**
Standard	--	**10**	--
D/W	**10**	--	--
Reagent	**1000**	**1000**	**1000**

Mix, incubate for 10 min at 37° C. Measure the absorbance of the sample (Abs-T) andstandard (Abs-S) against the reagent blank within 30 min.

Calculation:-

$$\text{Serum Triglyceride concentration (mg/dl)} = \frac{\text{Abs-T x Cone. Of standard}}{\text{Abs-S}}$$

HDL-CHOLESTEROL:

Method: PTA method

Principle:

The chylomicron, VLDL and LDL are precipitated by addition of phosphotungstic acid magnesium chloride. After centrifugation, high density lipoproteins fraction recovered as clear supernatant its cholesterol content is estimated by enzymatic method.

Serum + Phosphotungstic acid ----------> Supernatant (HDL) + ppts (other fractions)

Procedure:

Wavelength	505 (490-530)
Reaction type	End point
Reaction Temperature	37° C

Pipette in tubes according to following table

Sample	200 µl
Precipitating Reagent	200 µl

Mix well, incubate it for 10 min and then after centrifuge. Separate the clear Supernatant and proceed as below with it.

	Reagent blank (µl)	**Standard (µl)**	**Test (µl)**
Test	**--**	**--**	**50**
Standard	**--**	**50**	**--**
D/W	**50**	**--**	**--**
Reagent	**1000**	**1000**	**1000**

Mix, incubate for 10 min at 37° C. Measure the absorbance of the sample (Abs-T) and standard (Abs-S) against the reagent blank within 30 min.

Calculation:-

$$\text{Serum HDL-cholesterol concentration} = \frac{\text{Abs-T x Conc. Of standard (mg/dl)}}{\text{Abs-S}}$$

VLDL-CHOLESTEROL:

This was calculated by using Friedewald's equation as below.

Serum VLDL - Cholesterol conc (mg/dl) = $\frac{\text{Triglyceride}}{5}$

LDL-CHOLESTEROL:

This was calculated by using Friedewald's equation as below.

Serum LDL-Cholesterol conc, (mg/dl) = Total cholesterol - [HDL- Cholesterol+ VLDL-Choleterol]

SERUM LIPOPROTEIN (a)

Method: Turbidimetric test

Principle:

Latex particles coated with antibodies anti-Lp (a) are agglutinated when mixed with samples containing Lp (a). The agglutination causes an absorbance change, dependent upon the Lp (a) contents of sample that can be quantified by comparison from a calibrator of known Lp (a) concentration.

Procedure:

Wavelength	578 (540-600)
Reaction type	End point
Reaction Temperature	37° C

Pipette into a cuvette:

Diluent	800 µl
Latex	200 µl
Sample	15 µl

Mix and read the absorbance after 10 seconds (Al) and after 4 minutes (A2) of the samplea ddition.

CALCULATIONS:-

Lp (a) concentration in the sample is calculated by interpretation of its (A2-A1).

RESULTS

RESULTS

Statistical analysis:

All characteristics were summarized descriptively. For continuous variables, the summary statistics of mean, standard deviation (SD) were used. For categorical data, the number and percentage were used in the data summaries. Chi-square (χ^2)/ Freeman-Halton Fisher exact test was employed to determine the significance of differences between groups for categorical data. The difference of the means of analysis variables between two independent groups was tested by unpaired t test. The t test (also called Student's T Test) compares two averages (means) and tells if they are different from each other. If the p-value was < 0.05, then the results were considered to be statistically significant otherwise it was considered as not statistically significant. Data were analyzed using SPSS software v.23.0. and Microsoft office 2007.

Observations and Analysis :

A total number of 90 cases were studied. Among which 56.7% were male and female 43.3%. The youngest patient in the study was 30 years old and the oldest was 84 years old.

Also, 60 age and sex matched Controls were studied.

TABLE 1: COMPARISON OF THE PRESENTATION AT PRESENTATION

SYMPTOM	NO OF CASES	PERCENTAGE
Chest Pain	79	87.7
Abdominal Pain	4	4.44
Radiating pain to shoulders	36	39.99
Vomitting	28	31.11
Sweating	54	59.99
Breathlessness	57	63.33
Hypotension	42	46.66
Hypertension(SBP>140 mmhg)	21	23.33
Bradycardia	58	64.44
Tachycardia	18	19.99

TABLE 2: CARDIAC BIOMARKER DETECTION

Biomarker	No of cases	Percentage
Troponin I / T	84	93.3
CPK – MB	69	76.66

TABLE 3: COMPARISON OF SEX DISTRIBUTION BETWEEN CASES AND CONTROLS

Sex	CASES		CONTROLS		p value
	N	%	N	%	
Male	51	56.7	31	51.7	0.547
Female	39	43.3	29	48.3	
Total	90	100.0	60	100.0	

FIGURE 1: COMPARISON OF SEX DISTRIBUTION BETWEEN CASES AND CONTROLS

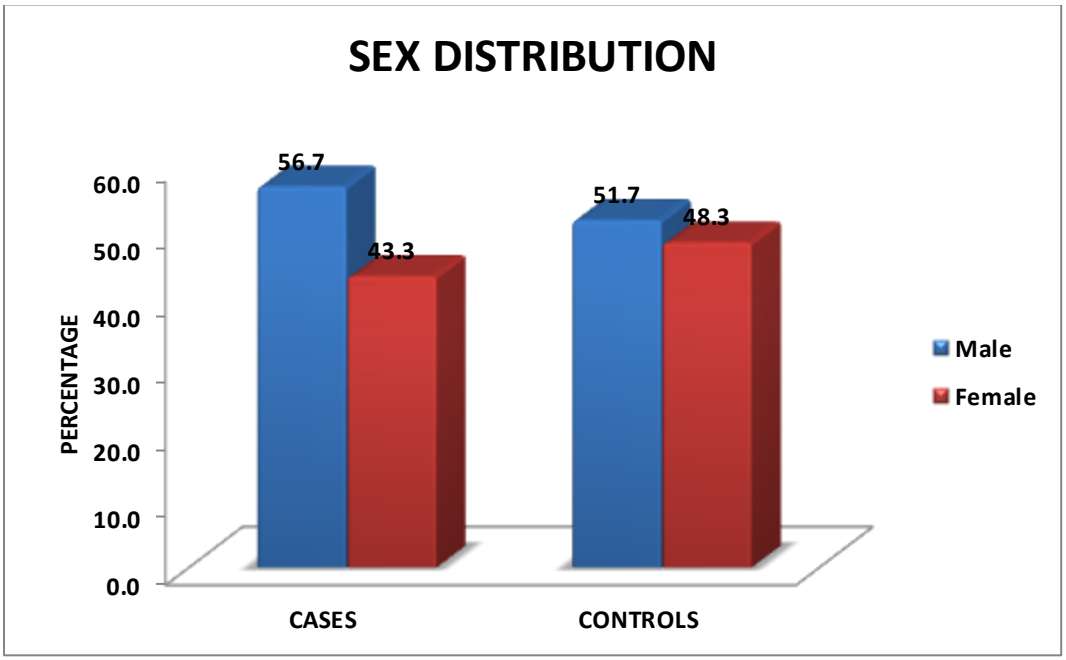


TABLE 4: COMPARISON OF MEAN AGE BETWEEN CASESAND CONTROLS

PARAMETER	CASES		CONTROLS		p value
	Mean	SD	Mean	SD	
Age	58.5	13.4	52.6	15.2	0.013*

Note: * significant at 5% level of significance ($p<0.05$)

FIGURE 2 : COMPARISON OF MEAN AGE BETWEEN CASES AND CONTROLS

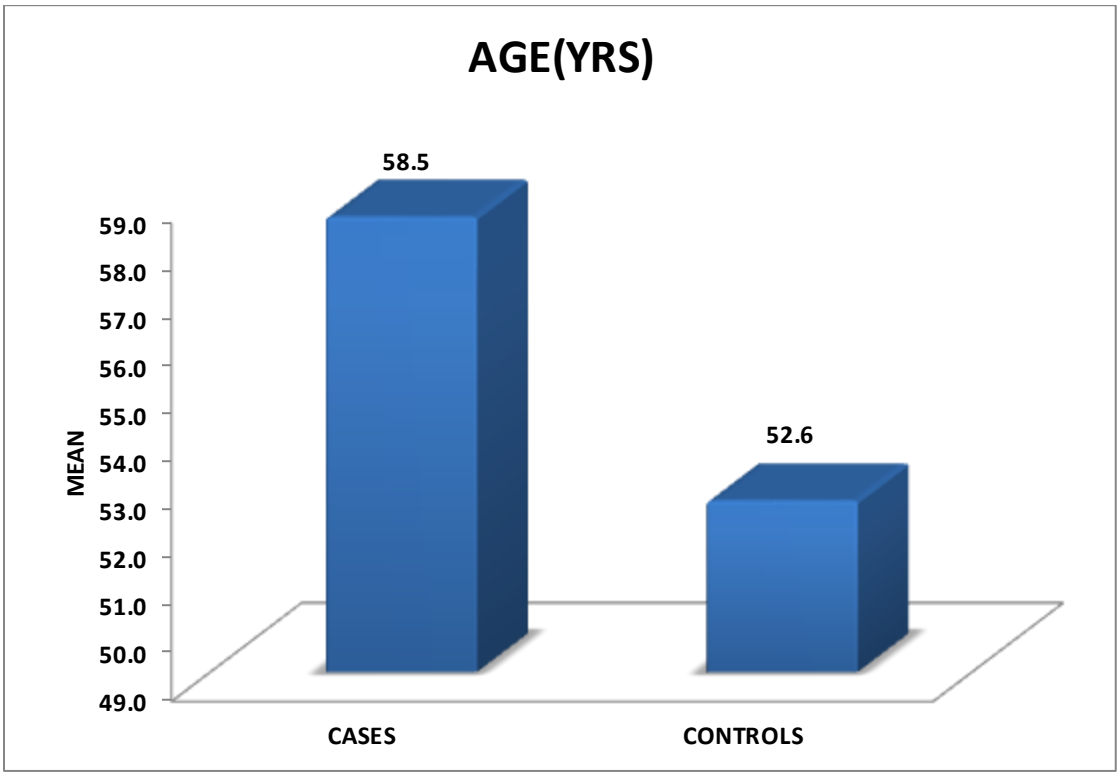
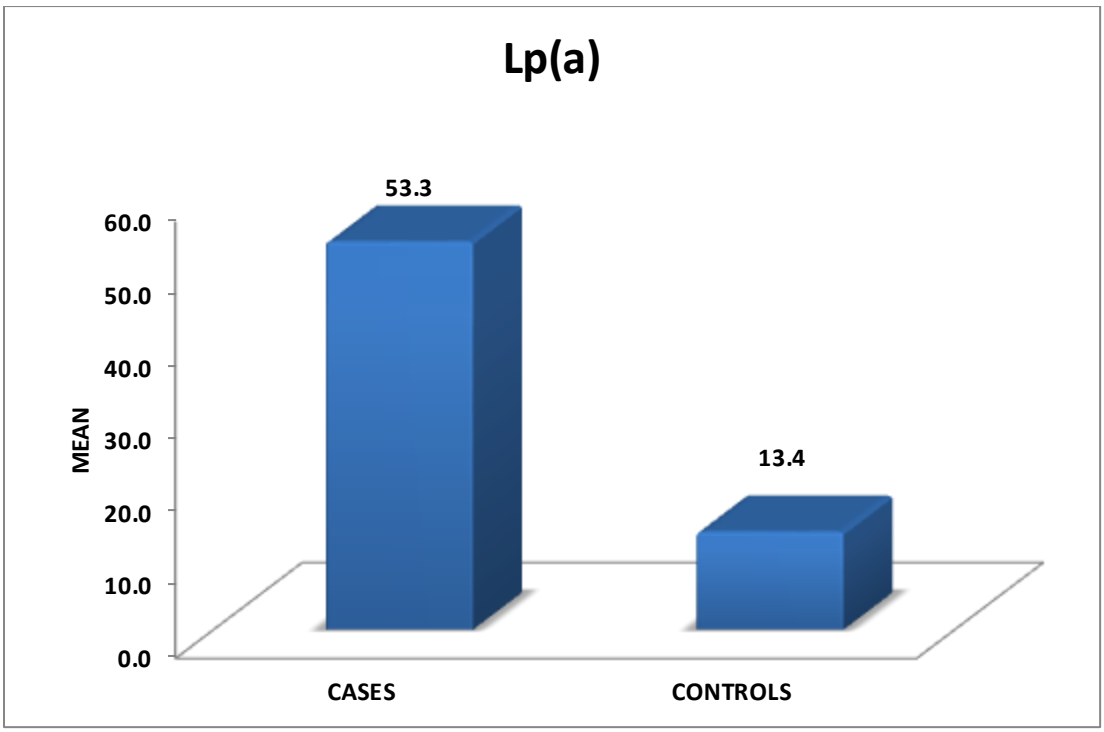


TABLE 5 : COMPARISON OF MEAN Lp(a) BETWEEN CASESAND CONTROLS

PARAMETER	CASES		CONTROLS		p value
	Mean	SD	Mean	SD	
Lp(a)	53.3	18.1	13.4	8.4	<0.001*

Note: * significant at 5% level of significance (p<0.05)

FIGURE 3: COMPARISON OF MEAN Lp(a) BETWEEN CASES AND CONTROLS

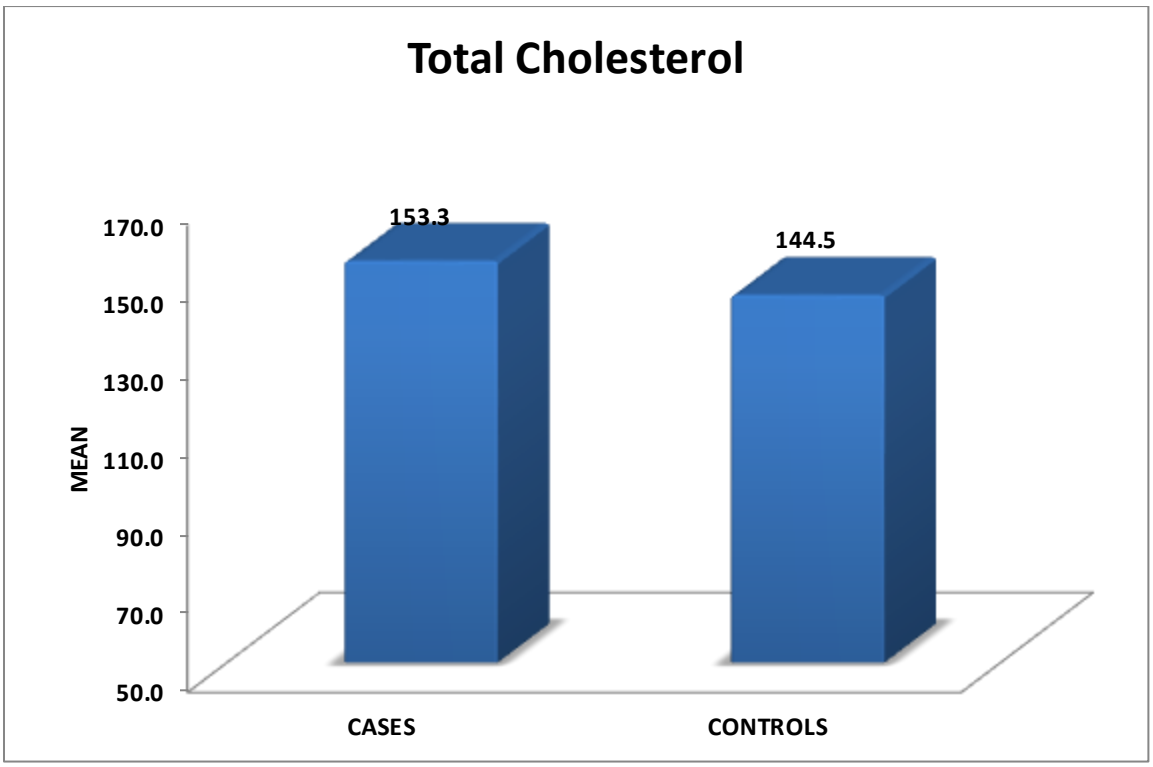


Mean value of **Lipoprotien (a)** was 53.3 in Myocardial Infarction patients, compared to mean of 13.4 of the heathy subjects, which was of a significance value of 0.001, which was highly significant.

TABLE 6: COMPARISON OF MEAN TOTAL CHOLESTEROL BETWEEN CASESAND CONTROLS

PARAMETER	CASES		CONTROLS		p value
	Mean	SD	Mean	SD	
Total Cholesterol	153.3	40.9	144.5	44.3	0.216

FIGURE 4: COMPARISON OF MEAN TOTAL CHOLESTEROL BETWEEN CASES AND CONTROLS

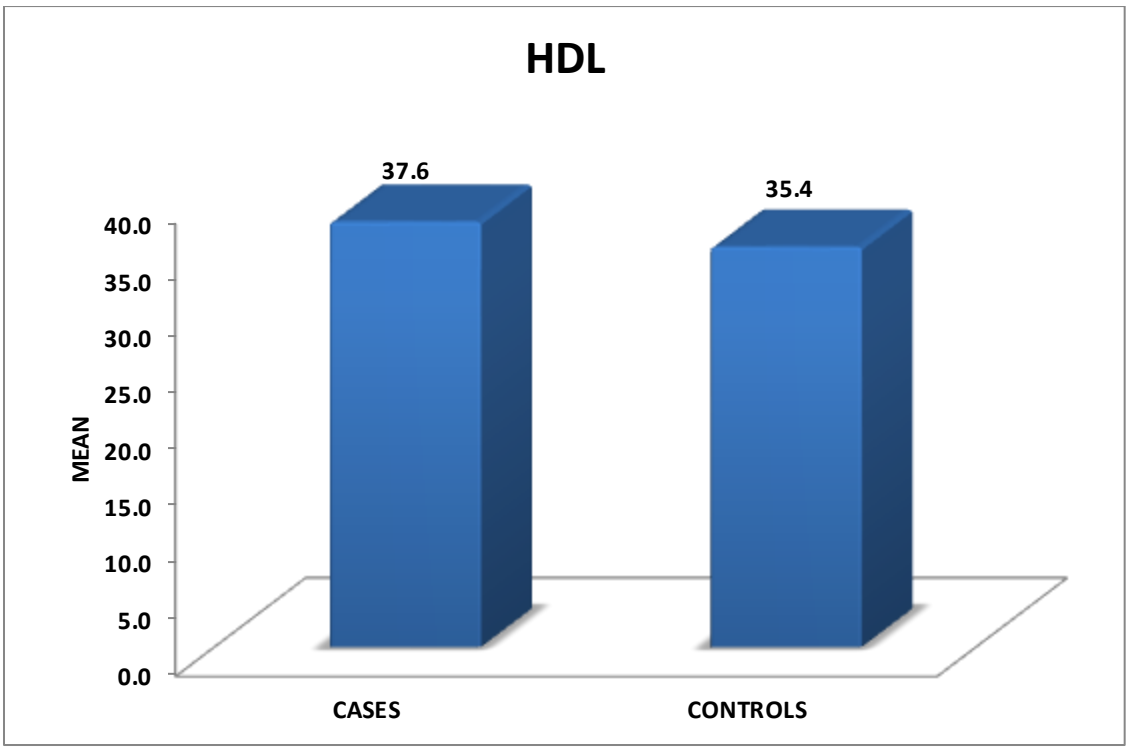


Mean value of **Total cholesterol** was153.3 in Myocardial Infarction patients, compared to mean of 144.5 of the heathy subjects, which was of a significance value of 0.216.

TABLE 7: COMPARISON OF MEAN HDL BETWEEN CASESAND CONTROLS

PARAMETER	CASES		CONTROLS		p value
	Mean	SD	Mean	SD	
HDL	37.6	14.1	35.4	11.4	0.310

FIGURE 5: COMPARISON OF MEAN HDL BETWEEN CASES AND CONTROLS



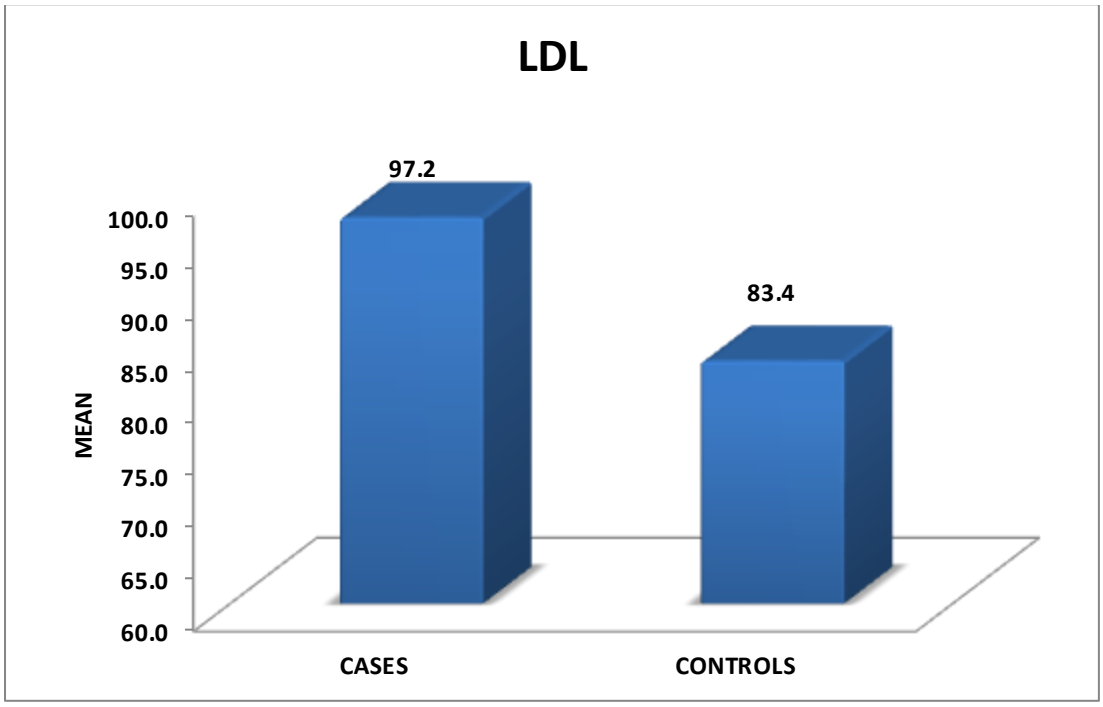
Mean value of **HDL** was37.6 in Myocardial Infarction patients, compared to mean of 35.4 of the heathy subjects, which was of a significance value of 0.310.

TABLE 8: COMPARISON OF MEAN LDL BETWEEN CASESAND CONTROLS

PARAMETER	CASES		CONTROLS		p value
	Mean	SD	Mean	SD	
LDL	97.2	31.7	83.4	30.3	0.009*

Note: * significant at 5% level of significance ($p<0.05$)

FIGURE 6: COMPARISON OF MEAN LDL BETWEEN CASES AND CONTROLS

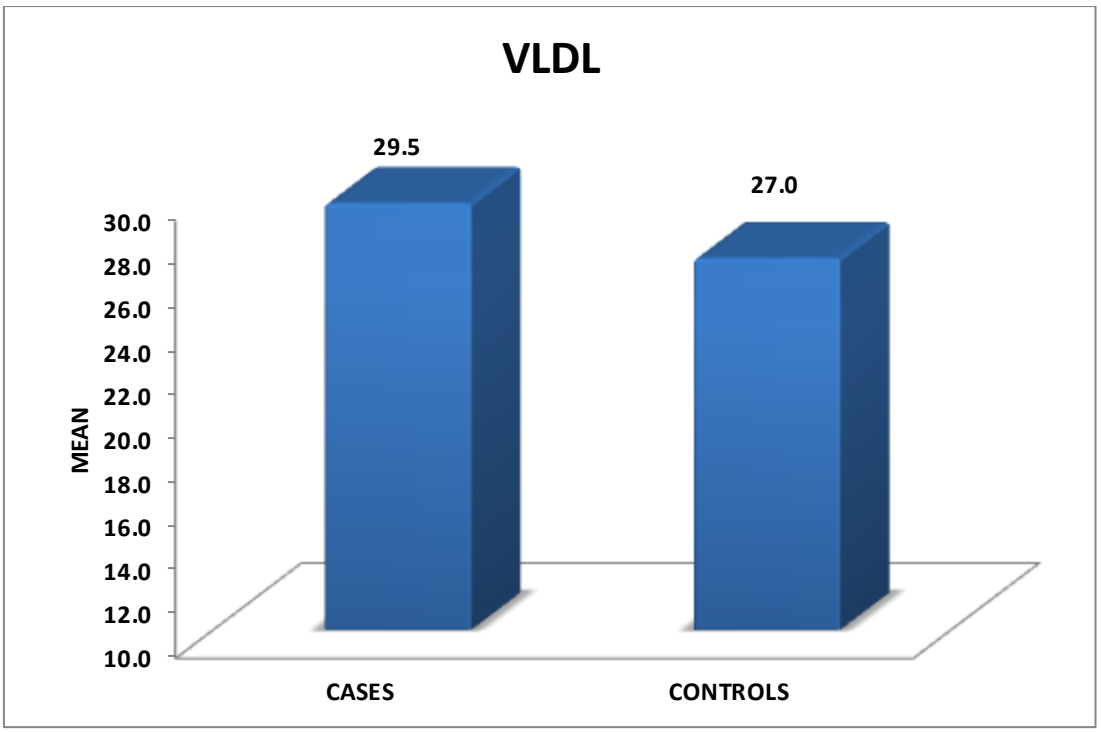


Mean value of **LDL** was31.7 in Myocardial Infarction patients, compared to mean of 30.3 of the heathy subjects, which was of a significance value of 0.009. which was highly significant.

TABLE 9: COMPARISON OF MEAN VLDL BETWEEN CASESAND CONTROLS

PARAMETER	CASES		CONTROLS		p value
	Mean	SD	Mean	SD	
VLDL	29.5	18.9	27.0	13.4	0.374

FIGURE 7: COMPARISON OF MEAN VLDL BETWEEN CASES AND CONTROLS

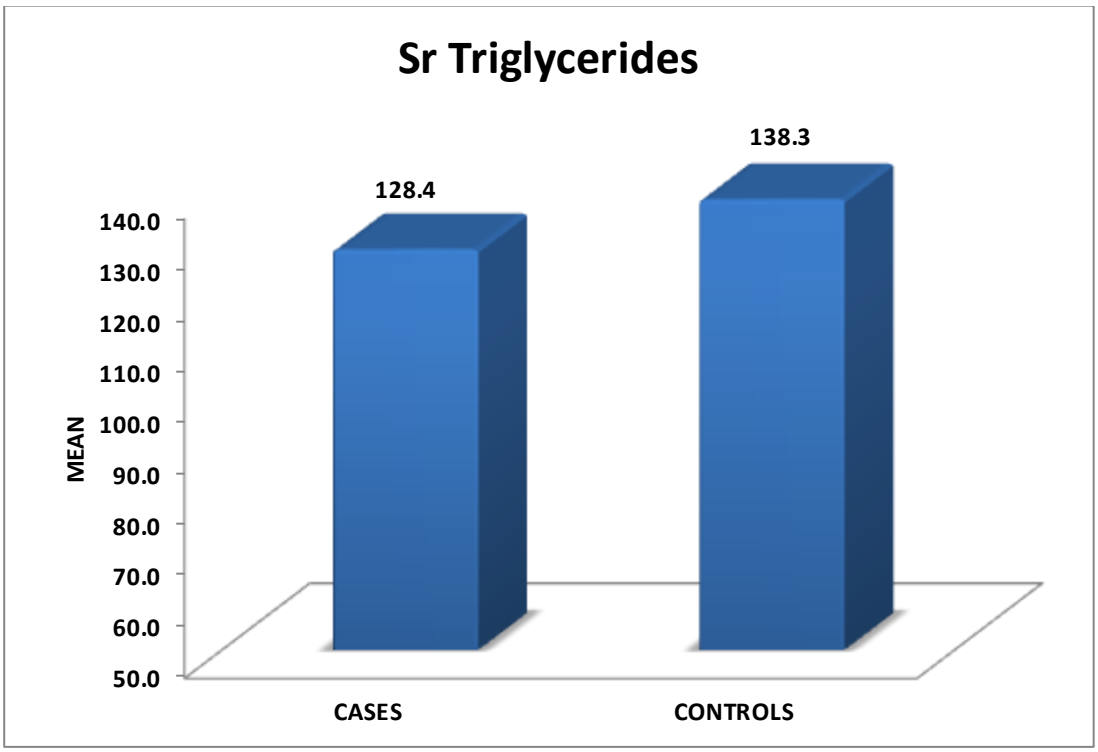


Mean value of **VLDL** was 29.5 in Myocardial Infarction patients, compared to mean of 13.4 of the heathy subjects, which was of a significance value of 0.374.

TABLE 10: COMPARISON OF MEAN SR TRIGLYCERIDES BETWEEN CASESAND CONTROLS

PARAMETER	CASES		CONTROLS		p value
	Mean	SD	Mean	SD	
Sr Triglycerides	128.4	44.4	138.3	67.8	0.286

FIGURE 8: COMPARISON OF MEAN SR TRIGLYCERIDES BETWEEN CASES AND CONTROLS



Mean value of **Triglycerides** was 128.4 in Myocardial Infarction patients, compared to mean of 138.3 of the heathy subjects, which was of a significance value of 0.286

TABLE 11: AGE WISE GROUPING OF PATIENTS

Age	Male	%	Female	&	Total
18-39	4	4.4	3	3.3	7
0-59	23	25.55	13	14.32	36
>60	24	27.76	23	25.56	47
	51	56.7	39	43.3	90

TABLE 12: COMPARISION OD LIPID LEVELS BETWEEN MEN AND WOMEN WITH MYOCARDIAL INFARCTION.

	AGE GROUP	Lp(a)	TC	TGL	HDL	LDL	VLDL
Men	**18-39 yrs**	72 ± 25.55	162.7 ±23.4	140 ± 61.4	36.67 ± 11.24	80.33 ± 40.1	27 ± 13
	40-60	55.7 ±12.8	161.1 ±47.3	133.2 ±54.6	36.7 ±16.6	36.78 ±16.6	34.04 ±26.8
	>60	68.3 ±13.1	153.1 ±45.6	139.6 ±38.8	39.6 ±13.9	95.9 ±38.5	30.4 ±13.3
Women	**18-39 yrs**	35.87 ± 2.76	139.67 ±43.01	121 ±45.1	34 ± 5.66	111.7 ±5.23	24.1 ±12
	40-60	34.9± 3.1	140.7 ±42.1	123.6 ±44.1	32.6 ±11.1	88.9 ±21.8	31.8 ± 6.5
	>60	41.4 ±5.4	152.8 ±30.3	114.1 ±36.9	39.5 ±14.4	98.2 ±28.6	24.1 ±9.4

DISCUSSION

DISCUSSION

Patients in our study presented with classical signs / symptoms of Ischemia like Chest pain, Sweating, Breathlessness, Radiating pain to neck/ shoulders, Hypotension, etc. Most predominant was Chest pain with87.7% of patients. Breathlessness was the second most seen presentation with 63.3% patients. 59.9% had associated Sweating with chest pain. And 39.9% had Radiating pain to shoulders. Whereas only 4.4% presented with severe abdominal pain.

86.6% of patients presented with significant ECG changes, (New significant ST-segment T-wave (ST-T) changes i.e., ≥2 mm rise in 2 consecutive leads). 93.3 percentage of them had elevated Troponin T / I biomarkers, while 76.6% had elevated CPK MB levels.

Our study had a male preponderance with 56.7% patients being male. And the mean age of the group was 58.5 years. The mean value for Lp (a) levels was 53.3, which was significantly high with p value < 0.001. The mean of LDL was 97.2 with a p value of 0.009, which was highly significant. The mean value for total Cholesterol levels was 153.3, which had p value 0.216. The mean value for HDL levels was 37.6 , which had p value of 0.310. The mean value for VlDL levels was 29.5 , which had p value of 0.374. The mean value for Sr Triglycerides levels was 128.4, which had p value of 0.286.

Our study correlated with that done by J. H. Gorasia C. P. Kamariyaet. al.,(6) where out of 50 patients diagnosed with AMI (by Signs, Symptoms, ECG and Bio-markers like CPK – MB & Trop-T), who participated in the study, there was no significant changes in total cholesterol (*P* = 0.8192), or high density lipoprotein-cholesterol (HDL-C) (*P* = 0.11), triglyceride (*P* = 0.1177) levels, and total cholesterol / HDL cholesterol ratio (*P* = 0.2129) were observed between the case and control

groups in this study . However , The difference in the Lp (a) levels between the case and control groups was highly significant (*P*-value = 0.0001). Concluding that, **Lp (a) level is an important and Independent risk factor for CAD. Serum Lp (a) level is not dependent on serum total cholesterol level**

Our study also correlated with that done by Angeline T., Aruna R et. al.(113) where 65 young male survivors of MI (< 45 years of age) with no traditional risk factors (diabetes, high cholesterol, hypertension, smoking, abnormal body mass index and non-vegetarians). None of the selected patients had a record of altered hypercholesterolemia, in comparison to the control group. Similar to our study where there was no significant variation in values of the cholesterols in MI and healthy individuals.

In our study there we noted an increased risk of MI with increasing levels of Lipoprotein (a), similar to the theThe Copenhagen City Heart Study conducted by P. R. Kamstrup, Marianne Benn, et.al.(114), where 9330 men and women from the general population were studied over a period of 10 years. Of these 498 participants developed AMI, where a stepwise increase in risk of MI with increasing levels of lipoprotein(a) was seen. And Extreme lipoprotein(a) levels predict a 3- to 4-fold increase in risk of MI.

Our study was similar to, a study by M.Gómez, V.Valle, et. al. conducted, The FORTIAM study,(115) which was a multi-center cohort study that includes 1371 AMI patients who were admitted within 24 hours of symptom onset. The prevalence of AMI without classical risk factors was 8.0%, The only emergent risk factors independently associated with a poor prognosis was the Lp(a). the results of our study showed that Lp (a) was an independently associated risk factor for MI.Similar to our study, a study by K. Miwa, K. Nakagawa, et. al. conducted estimation of Serum Lp(a)

levels were using a latex immunoassay(116) in 77 patients with coronary spasm. The study showed patients with higher Lp(a) levels had a higher incidence of prior MI than those without (41% vs. 13%, $p < 0.05$). Showing, **Elevated serum level of Lp(a) was found to be associated with a history of prior MI in patients with coronary spasm, suggesting that Lp(a) may play an important role in the genesis of thrombotic coronary occlusion and the occurrence of AMI.**

SUMMARY

SUMMARY

The study was designed:

1. To estimate the levels of Serum Lipoprotein (a) in patients with Myocardial infarction.
2. To compare Serum Lipoprotein (a) levels with conventional risk factors and to see for any significant association between them.
3. To carry out the statistical analysis to evaluate Lipoprotein (a) as an independent risk factor for Myocardial infarction.

Lp(a) in MYOCARDIAL INFARCTION:

Out of 90 patients with myocardial infarction, 51 were Males and 39 were Females. Thus there was a male preponderance. Chest pain was the most common presenting symptom & present in all the patients. The difference in Total Cholesterol levels between the case and control group was not significant (p value= 0. 216)

The difference in levels of HDL-C between the case and control groups was not statistically significant (p value = 0. 31). The difference in LDL-C levels observed between the case and control groups in this study was statistically significant (p value = 0.009). The difference in the serum triglyceride levels between the case and control groups was not significant (p value=0. 286). The difference in the cholesterol/HDL-C ratio between the case and control groups was not significant with the p value of 0.2129.

The difference in the Lipoprotein (a) levels between the case and control groups was highly significant (p value = 0.001) suggesting Lipoprotein (a) as an important predictor of coronary heart disease.

These all data shows that only Lipoprotein (a) is found significantly (99..9 %) higher in compare to controls in patients of Myocardial infarction, while S. Cholesterol, S.HDL-Cholesterol of S.VLDL- Cholesterol, S.LDL-Cholesterol & S. Triglyceride level does not have any significant difference. It means Lipoprotein (a) has played role as independent risk factor for Myocardial infarction.

The Lipoprotein (a) levels in case patients with S. Cholesterol <200 mg% was statistically significantly (p value = 0.001) higher in compare to controls suggesting that in patients who did not have high levels of S. Cholesterol, the higher levels of serum lipoprotein (a) triggered the coronary artery disease. Thus Lipoprotein (a) level is not dependent on serum cholesterol level. This is again means that Lipoprotein (a) can be an independent risk factor for myocardial infarction.

CONCLUSION

CONCLUSION

1. In patients with Myocardial infarction, there was a male predominance (56.7%).
2. Median age in Myocardial Infarction patients was 58.5 yrs.
3. Elevated levels of Lipoprotein (a) was found in all patients on Myocardial Infarction and it was an important and independent predictor of Myocardial infarction (Mean value of 53.3 with a significance value of $p < 0.001$).
4. Serum Lipoprotein (a) level is not dependent on Serum Cholesterol level.
5. Elevations in Total Cholesterol in Myocardial Infarction patients was not of significance, making it an unsuitable markers (Mean value of 153.3 with a significance value of p - 0.216).
6. LDL was significantly raised in the Myocardial Infarction patients (Mean value of 97.2 with a significance value of p 0.009).
7. The level of elevation of Triglycerides (Mean value of 128.4with a significance value of p 0.286) and VLDL (Mean value of 29.5 with a significance value of p 0.374) in Myocardial Infarction patients was not significant, making them a poor risk factor.
8. Selective screening for primary and secondary prevention should be considered for high - risk patients

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ANNEXURES

ANNEXURE-I

ETHICAL CLEARANCE CERTIFICATE

B.L.D.E. UNIVERSITY'S
SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR-586 103
INSTITUTIONAL ETHICAL COMMITTEE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 04/10/2016 *at* 3.00pm *to scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected & revised version synopsis of the Thesis has been accorded Ethical Clearance.*

Title " Study of Lipoprotein (a) in acute Myocardial infarction"

Name of P.G. student Akshay. M. Kuchanur
General Medicine

Name of Guide/Co-investigator Dr. R.M. Honnutagi
Professor of Medicine

DR.TEJASWINI. VALLABHA
CHAIRMAN
INSTITUTIONAL ETHICAL COMMITTEE
BLDEU'S, SHRI.B.M.PATIL
MEDICAL COLLEGE, BIJAPUR.

Following documents were placed before E.C. for Scrutinization
1) Copy of Synopsis/Research project.
2) Copy of informed consent form
3) Any other relevant documents.

ANNEXURE-II

INFORMED CONSENT FORM

TITLE OF RESEARCH : "STUDY OF LIPOPROTEIN (A) IN ACUTE MYOCARDIAL INFARCTION"

GUIDE : DR R.M. HONNUTAGI

CO – GUIDE : DR S. L. SAJJANAR

P.G.STUDENT : DR AKSHAY M. KUCHANUR

PURPOSE OF RESEARCH:

I have been informed that the purpose of this study is to access Lipoprotein (a) levels in Myocardial Infarction.

PROCEDURE:

I understand that I will undergo detailed history and clinical examination and investigations.

RISKS AND DISCOMFORTS:

I understand that there is no risk involved in this study and I may experience mild pain during the above mentioned procedures.

BENEFITS:

I understand that my participation in this study will help to study the association of Lipoprotein (a) in Acute Myocardial Infarction.

CONFIDENTIALITY:

I understand that the medical information produced by the study will become a part of hospital record and will be subjected to confidentiality and privacy regulation of hospital. If the data is used for publication the identity will not be revealed.

REQUEST FOR MORE INFORMATION:

I understand that I may ask for more information about the study at any time.

REFUSAL OR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and I may refuse to participate or withdraw from study at any time.

INJURY STATEMENT:

I understand in the unlikely event of injury to me during the study I will get medical treatment but no further medical compensation.

_____ _____

(Signature of Guardian) (Signature of patient)

STUDY SUBJECT CONSENT FORM

I confirm that Dr. Akshay M Kuchanur has explained to me the purpose of this research, the study procedure that I will undergo and the possible discomforts and benefits that I may experience, in my own language.

I have been explained all above in detail in my own language and I understand the same. I agree to give my consent to participate as a subject in this research project.

SIGNATURE OF PARTICIPANT DATE

SIGNATURE OF WITNESS DATE

ANNEXURE III

PROFORMA

Name of the patient :

Age in years :

Sex :

Address:

Religion:

Occupation:

IP no/OP no:

Presenting Complaints :

Past history:

Personal history:

1. Tobacco chewing
2. Smoking
3. Alcoholism
4. Diet- Veg/Mixed
5. No habits

Family history:

GENERAL PHYSICAL EXAMINATION :

Built :

Nourishment :

Ht(Cm) :

Wt(Kg) :

BMI:

Pallor

Icterus

Clubbing

Cyanosis

Edema

Vital parameters

Pulse :

BP :

Respiratory rate :

Temperature :

Waist circumference :

SYSTEMIC EXAMINATION:

ABDOMEN EXAMINATION

CARDIOVASCULAR SYSTEM

CENTRAL NERVOUS SYSTEM

RESPIRATORY SYSTEM

BIOCHEMISTRY

❖ Serum Lipoprotein (a)	
❖ Cardiac Markers • CK-MB • Troponin-T	
❖ LIPID PROFILE • Total Cholesterol • Triglycerides • HDL-Cholesterol • LDL-Cholesterol • VLDL-Cholesterol	
❖ Serum creatinine	
❖ Blood urea	
❖ Blood Sugar Levels ▪ RBS/FBS/PPBS	

PATHOLOGY

1)Urine Routine	
Urine albumin	
Urine sugar Urine bile salts Urine bile pigments	
Urine microscopy RBC's Pus cells Cast's Epithelial cells	
2)Complete blood count:	
Hb	gm/dl
Total count	Cells/cumm
Differential count Neutrophils	% %
Lymphocytes	%
Eosinophils	%
Basophils	%
Monocytes	%
ESR	At end of 1st hour.

2D-ECHOCARDIOGRAPHY

LVIVSd : cm	LVIDd : cm	Aorta : cm
LVPWd : cm	LVISd : cm	LA (AP): cm
RVIDd : cm	EF% : cm	PA : cm

VALVES :

Mitral Valve :

Aortic Valve :

Tricuspid Valve :

Pulmonary Valve :

CHAMBERS :

Left Ventricle :

Right Ventricle :

Left Ventricle :

Right Ventricle :

SEPTAE :

GREAT ARTERIES

Aorta :

Pulmonary Artery :

DOPPLER STUDY

Mitral Valve :

Aortic Valve :

Tricuspid Valve :

Pulmonary Valve :

REGIONAL WALL MOTION ABNORMALITIES :

PERICARDIAL EFFUSION :

CLOT/VEGETATION :

CONCLUSION :

FUNDOSCOPY:

ECG:

CONCLUSION:

SIGNATURE

DATE:

PLACE:

MASTER CHART – CASE GROUP

Sl no.	IP no	Name	Age	Sex	Lp(a)	cTn/CPK MB	Sr Triglycerides	Total Cholesterol	HDL	LDL	VLDL
1	915	Adiveppa G Jetagi	65	M	37	1.2/70	113	174	31	120	22.6
2	1730	Gangabai I Tamagond	84	F	51.7	86/P	140	114	43	43	28
3	4311	PREMA ASHOK MADHUBHAVI	43	F	31.9	43	98	175	37	119	19.6
4	2094	YALLAPPA D MASHYAL	64	M	51.9	53/P	143	123	48	127	24
5	1850	TANGEWWA K BANDIWADDAR	80	F	65.2	0.82	170	76	22	61	79
6	3013	SHARADA M BIRADAR	65	F	71	1.52/36	120	125	38	63	24
7	908	SAROJINI C PATIL	68	F	44.9	0.13	135	142	43	73	27
8	18855	CHAND ABDUL NADAF	60	M	45.5	136/P	80	216	62	138	16
9	19626	AMBREESH S KATTIMANI	50	M	52.2	p	98	114	31	127	79
10	19642	PAVITRAMMA C MALIPATIL	63	F	62.9	P	68	112	38	60.4	13.6
11	19946	KAMALAKSHI P PATTAR	55	F	48.9	36/P	68	112	38	60.7	136
12	18502	MAYAPPA SHIVAPPA HALLI	52	M	39.4	104/P	80	216	62	138	16
13	203568	LAKAPPA B HUNSHYAL	83	M	48.6	51/P	147	22	58.6	22	29.4
14	18007	SONAWWA R BIRADAR	65	F	36.4	35/P	105	160	32	107	21
15	15473	BORAMMA N BASTI	45	F	34.3	48/P	100	172	38	117	17
16	15564	PARVATIBAI R PATIL	70	F	43.7	78/P	110	150	37	109	27
17	15432	LAXMAN S PUJARI	75	M	32.9	81/P	174	102	37	102	21
18	15620	NINGAPPA A YADAWAD	95	M	42.8	50/P	105	155	31	103	21
19	14569	PRAKASH M HONWAD	39	M	33.8	P	110	136	27	35	19
20	13503	SHANKREMMA S BIRADAR	30	F	34.8	110/P	93	164	30	115.4	18.6
21	14432	LALSAB I GOUDAR	80	M	47.4	53/P	140	109	54	122	21
22	13980	MANABAI B LAMANI	62	F	36.2	42/P	140	109	54	122	21
23	12972	SUNANDA S BIRADAR	55	F	32.5	80/P	132	56	30	96.6	26.4
24	13046	RAMANGOUDA N KOLKUR	41	M	52.4	94/P	230	151	22	83	46
25	9665	RANIBAI M RATHOD	59	F	41	62/P	168	182	35	113	33.6
26	6166	SAHIRAHMED Z INAMDAR	58	M	31	66/P	128	136	25	85.4	25.6
27	6375	VITTAL L GUNAPUR	58	M	42	52/P	132	189	55	107.6	26.4
28	4754	SIDDU H TALWAD	40	M	48	51/P	75	164	50	99	15
29	5779	GURANNA B PATIL	60	M	44	45/P	177	132	28	68.6	35.4
30	8011	GIRIMALLAPPA R UMARGOL	65	M	37.1	41/P	108	128	27	79.4	21.6
31	10754	KAMALABAI H GUDALE	60	F	58.3	38/P	112	147	31	93.6	22.4
32	10420	BHEEMABAI G WALIKAR	60	F	39.8	300/P	85	213	55	141	17
33	10063	BAHUBALI M GUBACHI	30	M	48	72/P	173	90	low	-	34.6
34	9608	SHANKAR T DHADEKAR	59	M	52	36/P	107	120	45	53.6	21.4
35	41929	BASAPPA M ALLOLLI	70	M	31.4	P	218	207	31	145	41.4
36	6166	SAHIRAHMED INAMDAR	58	M	31	66/P	128	136	23	85.4	25.6
37	2388	NEELAMMA N HIREMATH	50	F	34	50/P	149	242	27	185.2	29.8
38	2267	RACHAYYA S HIREMATH	56	M	34	52/P	263	258	43	162.4	52
39	2583	MITHALI R DAS	55	F	68.4	P	82	200	70	113.6	16.4
40	42870	KANTABAI C NATIKAR	52	F	38	71/P	131	127	30	75.6	25.4
41	11227	BHIMU RAMCHANDRA	60	M	62	142/9.26	67	146	53	78	11
42	10383	MALLAPPA GURAPPA TELLI	60	M	76	0.342	69	148	55	79.6	13.4

43	6899	GURUNATH MADAYYA	48	M	65	0.314	60	205	57	138	12
44	5953	AKKATAI M GAYAKWAD	60	F	49	21/0.95	101	158	40	97	20
45	6927	KALAWWA CHANAPPA	65	F	82.3	77/2.43	153	157	35	91.4	30.6
46	6105	RUKMAWWA SABU	65	F	74.2	94/P	169	155	32	89	34
47	27056	DWARAKABAI DASRATH GADVI	60	F	60.4	47/P	97	215	40	155.6	19.4
48	17943	LAKSHMMAN NIVARTI DAGE	70	M	63	P	115	130	29	77	33
49	26934	KALLAPPA MADIWALAPPA BHAVIMANI	78	M	67.4	71/P	119	203	38	156	21
50	21727	SUBRAMANYYA DALWAI TALWAR	62	M	84.8	242/P	88	162	21	99.6	19.4
51	25819	CHANDBAG BHIMRAY LOGAVI	65	M	42.2	80/P	115	203	38	156	24
52	19796	SANGANGOUDA BALAVANTRAYAGOUDA	41	M	46.2	18/P	147	110	22	58.6	29.4
53	19881	CHANNAMA BHEEMANAGOUDA	60	F	37.5	45/P	217	190	21	124.6	43.4
54	27974	RAMESH KALLAPPA YALNDI	40	M	37.7	49/P	104	130	29	82.2	20.8
55	6365	BAGAWWA DUNDAPPA GIDAGANTI	20	F	63	50/0.67	97	165	38	108	19
56	6927	KALLAWWA C HADAGALI	62	F	82.3	77/2.43	153	151	35	91.54	30.6
57	6231	MALLARAYA GANGAPPA BADIGER	55	M	41.7	56/P	128	162	78	59	26
58	20558	KAMALA KASHIRAM SHINDE	76	F	54	23/P	201	197	65	91.8	40.8
59	20844	SIDAPPA NAGAPPA HOSAMANI	40	M	72.3	32/P	147	130	29	108	24
60	20852	SRIKANTH GULAPPA MALLI	80	M	82.4	287/P	114	190	32	135.2	22.8
61	17831	YENKAWWA GOVINDAPPA HOUCHIND	40	F	47	234/P	60	145	42	91	12
62	27835	KALLAPPA MUTAPPA KATAKAL	60	M	39.1	51.1/P	70	141	62	65	14
63	26703	HONNEGOWDAPPA KAVI	53	M	57.8	73/P	137	200	23	112	19
64	17998	RAMAPPA NINGAPPA SOUKAGOUDA	63	M	69.7	P	135	159	24	108	27
65	20387	MALLIKARJUN BIJAPUR	45	M	45.3	258/P	128	136	29	86.4	25.6
66	27027	BHARATI A SAJJAN	70	F	36.2	P	88	180	33	129.4	17.6
67	25627	NINGAWWA MUDAKAVI	56	M	39.6	35/P	82	132	25	96.3	16.4
68	27619	PARAPPA BIRADAR	76	M	78	31/P	115	203	36	146	23
69	19624	JAGADEVI M KUDLE	78	F	81.6	137/P	201	197	65	91.8	40.2
70	27516	NEELAKANTHAYYA S HIREMATH	60	M	53.1	30/P	115	150	28	99	23
71	20731	SHARAWWA YEMUNAPPA TALAKERI	32	F	105	79/P	100	180	49	111	20
72	27690	BASAYYA S STHAVARMATH	55	M	48.4	57/P	251	153	20	92.3	50.2
73	18108	MAHALINGAYYA CHANNAYYA PUJARI	55	M	52.3	122/P	95	110	24	67	19
74	17737	DONDILAL N KAPATKAR	64	M	40.7	235/P	106	134	32	77	41
75	3761	BHEEMANGOUDA D	70	M	51.7	72/1.32	114	115	29	40	23
76	4008	SARUBAI J PATTAR	65	F	38.8	41/P	53	170	61	104	10.6
77	5241	RATNABAI CHAVAN	65	F	114	/10.641	136	194	65	101.8	27.2
78	2228	PARAPPA S TILLHAL	65	M	49.3	28/P	116	147	18	26	48
79	4110	LAXMIBAI I KUMBAR	60	F	89.4	24/0.44	114	126	70	46	43
80	5696	SIDDARAYA S KASHETTI	40	M	71.3	47/1.4	116	145	36	75.8	23.2
81	4288	AMBUJAKSHI KALAL	55	F	67.3	49/0.137	156	167	21	115	31
82	4110	LAXMIBAI I KUMBAR	60	F	41.8	42/0.44	156	147	24	116	35
83	3895	NAJMA HUSSAIN	45	F	36.4	166/7.54	126	31	11	47	110
84	4277	ADIVEPPA G JETAGI	70	M	57.6	40/4.77	150	167	21	116	31
85	4642	SHIVAGANGAPPA IRSANGAPPA	55	M	79.2	156/80	143	165	33	103.4	26.6
86	5151	LAXMIBAI A DHUMLE	77	F	87.8	/4.63	192	143	38	66	38

87	5406	S CROSSWIN	50	M	39	41.4/14	238	183	26	109.4	47.6
88	4453	KUPPANNA C KAMBALMELI	45	M	84.9	191/P	152	199	46	100.1	39
89	5131	CHANNAMALLAPPA H MANAHALLI	35	M	39	29/0.187	211	172	34	95	42
90	4643	GUDAMA A JAMADEV	50	F	57.6	43/1.83	108	140	25	73.4	21.6

MASTER CHART FOR CONTROL GROUP

Sl no	IP no	Name	Sex	Age	Sr Lp(a)	Triglycerides	Cholesterol	HDL	LDL	VLDL
1	23177	Parvati Y Chambar	F	45	26	123	154	48	83	25
2	24712	Dayanand Chandrashekar	M	43	3.5	247	119	25	48	48
3	23644	Mallakuri I Koti	M	75	10.4	148	168	28	101	30
4	23229	Shantabai S Jevoor	F	42	6	302	120	38	74	8
5	24912	Indrabai I Javalgi	F	45	27	50	113	38	70	10
6	23507	Prema Ashok Madhabhavi	M	43	6	89	130	27	72	18
7	21120	Savitri B Shakapur	F	49	25	119	110	23	23.8	21
8	20465	Vijayalakshmi P	F	34	12	133	173	70	76	27
9	16524	Anand G Thulase	M	40	3	86	88	20	51	17
10	20520	Boramma H Ambiger	F	65	16	89	110	39	54	18
11	14563	Gurawwa S Hallur	F	74	11	117	99	34	42	23
12	21413	Satyappa N Samaga	M	32	3.4	227	169	45	79	45
13	20780	Yamanawwa P Karjol	F	79	7.4	83	187	47	134	17
14	14888	Kamala V Byakod	F	55	8	257	188	42	95	51
15	20800	Vidyavati H Baragi	F	58	18	108	158	39	98	22
16	15520	Neelavva B Gudag	F	70	25.8	112	138	37	96	22
17	15234	Bhimappa T Bajantri	M	81	29	160	208	58	118	32
18	10925	Suvarna C	F	40	20.5	199	247	48	113	49
19	8775	Rachawwa M Kumbar	F	70	5.9	91	104	45	41	18
20	8469	Parvati Y Biradar	F	25	19.4	87	120	21	82	17
21	7430	Gangabai I Gobbi	F	68	6	154	150	36	83	31
22	5780	Savitri P Aalkunte	F	70	23	87	180	39	123	17
23	7688	Lakappa Vittal Ambali	M	65	2.11	68	81	18	49.4	13.6
24	14605	Gurusidda B Gundal	M	79	24	75	62	28	19	15
25	14136	Gourabai C Sonnad	F	65	26	180	190	31	123	36
26	14274	Chandrashekar M Sonnad	M	77	29	135	138	50	62	27
27	26885	Basavaraj S Gubbi	M	47	8	167	102	40	79	33.4
28	26947	Anand G Tolashe	M	43	5	95	131	23	89	19
29	4434	Santosh B Biradar	M	22	12.5	374	175	18	82.2	74.8
30	3579	Rajashekar T Waddar	M	55	3	137	low	low	41	27.4
31	4234	Ambubai S Sanakki	F	38	14.2	156	167	21	116	31
32	4292	Ambruta S Jadhav	F	29	9.4	136	167	21	116	31
33	299	Lesappa S Patil	M	43	11	196	186	47	99	39
34	3127	Chandrashekar G Badiger	M	60	16	68	81	18	49.4	13.6
35	2834	Kavita T Rajaput	F	37	6	92	108	28	62	18
36	2738	Neelamma V Byakod	F	50	6	242	196	31	116	48
37	2677	Panchaksharayya Linagayat	M	60	13	98	172	35	117	20
38	1546	Yallappa K Soudi	M	31	12	116	156	30	102.8	23.2
39	3310	Ashok Alur	M	55	7	95	110	24	67	19
40	4103	Mantawwa S Kanse	F	75	19.8	156	178	31	115.8	31.2
41	3256	L Patil	M	42	21	305	250	42	147	61
42	4561	Vittal N Hadimani	M	53	23.2	119	100	21	78	20

43	9266	Saleem G Lalsab	M	36	2.2	78	109	22	114	15.6
44	8974	Sangappa D Kumbar	M	62	18.1	105	114	45	48	21
45	10524	Shivappa G Talawar	M	65	7.6	70	136	30	90.2	15.8
46	7555	Arjun B Walikar	M	72	11	107	120	45	53.6	21.4
47	4565	SIDRAM	M	40	6	86	88	20	51	17
48	15478	SIDRAMMAPPA	M	55	25	89	110	39	54	18
49	1269	SHANTABAI	F	60	12	117	99	34	42	23
50	3485	BASAVARAJ	M	38	3	227	169	45	79	45
51	24671	REKHA METI	F	30	16	83	187	47	134	17
52	2563	SATISH	M	48	6	257	188	42	95	51
53	4569	ANNAPURNA	F	35	6	108	158	39	98	22
54	7851	REKHA M	F	67	13	112	138	37	96	22
55	12496	ARUNKUMAR DESAI	F	56	12	160	208	58	118	32
56	6547	BHARATHI	F	45	7	199	247	48	113	49
57	3254	SHARANAPPA	M	54	2.11	91	104	45	41	18
58	7469	SUNITA	F	55	24	87	120	21	82	17
59	21456	SUDHA M K	M	49	26	154	150	36	83	31
60	12364	GURAPPA S R	M	59	29	87	180	39	123	17