CHAPTER VI

DISCUSSION
The subjects for the present study were selected from Academy of Medical Sciences, Pariyaram, Kannur district, Kerala state. Clinically confirmed cases of myocardial infarction were included in this study, with an age limit up to 60 years and they had no previous history of myocardial infarction. This study includes a total number of 1221 subjects. Out of 1221 subjects 87.1% were males and 12.9% were females. There were 606 patients belonged to test group, and 615 normal healthy age and sex matched subjects belonged to the control group. In the test group 87.1% and 12.9% were males and females respectively with the mean age of 50.98 ± 8.41. Similarly in the control group 87.0% and 13.0% were males and females respectively with the mean age of 50.20 ± 8.74. In our study the maximum numbers (61.4%) of patients were between 51-60 years of age and 25.2% of patients were between 41-50 years of age. While 9.9% of patients were between 31-40 years of age and 3.5% of patients were even below 30 years of age. Present study shows the threat of coronary artery disease in productive age group of north Kerala. CAD in Kerala is premature and malignant resulting in death at very young age. Soman C. R et al\textsuperscript{23} found that approximately 60% of CAD death in men and 40% of CAD death in women occur before the age of 65 years in Kerala and this is higher than that of Andhra Pradesh and Chennai.
6.1. Rural/urban distribution

Rural urban distribution of myocardial infarction is very important. In present study we noticed that major numbers of our patients were residing in rural areas. Out of 606 patients 459 were residing in rural area. The institute where the study was performed is itself situated in remote area. The patients from Kasarkode, Kannur and some parts of Wyanad and Calicut districts of Kerala state were mainly admited in this hospital. Many studies show that CAD rates are increasing in Indian rural population. Gupta R et al\textsuperscript{261} reported that in India the prevalance of CAD is more in rural area than urban one because more Indians live in rural areas. Patients in urban areas had lower observed mortality rates for MI admissions when compared with hospitals in more geographically remote areas.

When considering the prevalence of MI in Kerala it is much more than that of national average. Thankappan et al\textsuperscript{262} reported that the overall prevalence of MI is 50-100\% higher in Kerala than the national average with narrower urban-rural gradient. In another study James PA et al\textsuperscript{263} reported that mortality from myocardial infarction in rural hospitals is not higher than that of urban ones.

Three fourth of our patients were from rural background. Out of 606 patients of our study only 147 were from urban area. This indicates that the burden of MI in rural area is much more than urban population of North
Kerala. The increased rate of CAD in rural population may be due to the change in lifestyles, ie more westernized lifestyle or due to the urbanization of our villages. Urban environments are associated with increased opportunities for mechanized and sedentary employment, consumption of energy-dense processed foods, and other life style characteristics associated with the development of CAD.

6.2. Obesity

Obesity is one of the leading risk factor for cardiovascular disease. Overweight and obesity are defined by body mass index (BMI; weight in kilograms/height in meters squared, kg/m$^2$). In adults, overweight is defined as BMI of 25–29.9 kg/m$^2$; obesity is defined as a BMI ≥30 kg/m$^2$. It is a conventional measure of obesity. Waist-to-hip ratio (WHR) is another less commonly used index, and it has more predictive power of obesity. It is a measure of visceral fat or abdominal obesity. High WHR was defined on the basis of World Health Organization (WHO) criteria as >0.85 for women and >0.90 for men.$^{157}$ As a measure of obesity we included BMI and WHR in our study, and our findings were interesting. While considering the BMI there was no significant obese group in MI patient. But the other parameter WHR was statistically significant. This means the weight of the patient is normal in relation with height, but exhibiting visceral fat or abdominal obesity. If we
were considering the BMI alone the obesity is less prevalent. So it is to be considered the WHR along with BMI in our population.

Some investigators have reported to lower BMI cutoffs for Indians based on visceral fat. They reported that the conventional cutoff limit of BMI might not define overweight and obesity optimally, because of their higher percentage of body fat and less lean mass. Moreover, WHO has redefined overweight (BMI ≥ 23 kg/m²) and obesity (BMI ≥ 25 kg/m²) for South Asians, based on the preliminary data, which are under debate. Many Asian Indians develop metabolic syndrome and diabetes at BMI <25 kg/m², which is generally considered normal among whites. BMI may underestimate the cardio metabolic risk which may be evaluated best by waist-hip ratio.

Although the degree of obesity was positively associated with CVD incidence, there are a sizeable proportion of individuals who are at an increased CVD risk state without being overweight or obese when considering only the BMI in our population of north Kerala. Still the classical concept for measuring obesity is BMI. Majority of our clinicians and researchers are adopting the same and the available datas based on this concept. Therefore, a further implementation and promotion of measure of waist-hip ratio are needed to bring about meaningful changes in the obesity
that may be useful in prevention activities. Exhibiting too much visceral fat is to be considered as one of the minor risk factors for MI.

6.3. Sedentarism

Lack of adequate physical activity or sedentarism is one of the risk factor for premature coronary artery disease. A large number of studies have proved the association between physical activity or exercise with risks of CHD and its morbidity and mortality. Williams PT et al\textsuperscript{268} have found a clear close response pattern, showing a continuously lower risk with higher levels of physical activity. The 2002 World Health Report estimated that over 20% of CHD in developed countries was due to physical inactivity.\textsuperscript{269} Recommended physical activity levels are 30 minutes of moderate physical activity on 5 or more days per week.\textsuperscript{270}

In our study we considered the physical activity of the subjects. 48.5% of the patients were coming under hard working group. Here we classified the physical activity into two principal categories - leisure time physical activity (LTPA) and occupational physical activity (OPA). LTPA is a broad descriptor of the activities one participates in during free time, based on personal interests and needs. These activities include formal exercise programmes as well as walking, hiking, gardening, sport, dance, etc. OPA is associated with the performance of a job, usually within the time frame of an 8 hour work a day. A similar classification was described by Howley \textit{et al.}\textsuperscript{271} Moderate and
high levels of LTPA and OPA are associated with a reduced CVD and all-cause mortality among both sexes, and promoting moderate levels LTPA and OPA are essential to prevent premature CVD and all-cause mortality.

Majority of the patients in present study were coolies or coming under hard working group (48.5%) and it was enough to explain OPA. Leisure time physical activity (LTPA) was inadequate in our study group, only 11.2% patients were having the habit of walking and only 4% patients were having the habit of playing to maintain their health. Several cross sectional studies have also found that leisure time physical activity is associated with decreased prevalence of established risk factors for CVD such as hypertension, dyslipidemia, inflammatory markers and obesity.\textsuperscript{272, 273}

A total of 63.7% of our study population were physically active when considering both OPA and LTPA. Further studies are required in depth regarding this risk factor in MI patients of our population while major number of our test subjects were physically active. Question have been raised whether physical activity are independently associated with CVD risk or they simply are associated with risk through known risk factors such as smoking, hypercholesterolemia, diabetes mellitus and hypertension.
6.4. Socioeconomic status (SES)

A relationship between socioeconomic position and morbidity/mortality is more than well documented. We considered the relative significance of education, occupational class and income for the risk analysis of myocardial infarction. So as a measure of this socioeconomic status we included education, job and monthly income of the subjects.\textsuperscript{274,275}

When considering the education, half of our study group were illiterate or educated only up to primary level. A significant number of the test subjects were unskilled workers (39.3%), unemployed (11.4%) or skilled workers (28.2%). While considering the monthly income 72.4% of test group subjects were earning Rs.< 5000. As a whole majority of the patients in the present study were coming in the group of low socioeconomic status.

It is well known that poverty is bad for health. Cardiovascular disease has now become a disease of the poor in rich countries and of the rich in poor countries. Considering the low social and educational status, the poor may have low risk factor awareness. In general, uneducated and less educated patients in our study have a low intake of fruits and vegetables, may due to poverty and lack of awareness, and they have also the threat of other risk factors of CAD. Again the access and affordability for acute care managements and long term secondary prevention practices and compliance may be lacking in these subjects. Similar findings were reported by Gupta et
According to them Asian Indians with low SES have a higher prevalence of CAD and risk factors such as smoking and hypertension. In another study Ali Janati et al\textsuperscript{277} suggested that in Iranian people from lower or middle social classes were in greater CHD risk than higher social classes. This epidemic might be halted through the promotion of a healthier lifestyle and the support of environmental and policy changes. Similar results have been reported from developed countries, where the lower SES groups suffer higher CHD and deaths due to non communicable diseases.\textsuperscript{278} Also the Studies carried out by Kaplan et al\textsuperscript{279} in developed countries provide credible evidence of an inverse relationship between socioeconomic status and cardiovascular disease, primarily CAD and stroke.

However, Kanala KR Reddy et al\textsuperscript{280} suggests that higher social classes in developing countries may have greater CHD risks than lower social classes. Rapid growth in industrialisation and urbanisation may have led to changes in dietary patterns and a reduction in physical activity in the study population. Their study showed that coronary risk factors such as hypercholesterolemia, hypertriglyceridemia and sedentary life style were more prevalent among higher SES groups. Low HDLC, on the other hand, was more common in lower SES groups. In contrast in the present study higher social classes were less in number. Only 6.9 % of patients were educationally qualified up to the level of graduation or above, 10.4 % of patients were earning an income of Rs
>10001 per month and 21.1 % of patients were government employees, pensioners, businessmen or farm owners.

Our findings were similar to Gupta R et al\(^{277}\), Ali Janati et al\(^{277}\) and Gwatkin et al.\(^{278}\) In our study a major number of patients were coming under low socioeconomic group and the reasons for CAD may be smoking, hereditary or dietary deficiency of vitamins along with other risk factors like dyslipidemia, diabetes, and hypertension. Our study demonstrates that socioeconomic status plays an important role in traditional cardiovascular risk factors in patients with MI. Future studies are needed under the heading of socioeconomic status and MI in rural population of north Kerala, to improve our understanding of cardiovascular disease. These risk factors are preventable up to certain extent by improving the socioeconomic status and so we have to consider the education, job and income as minor risk factors of MI.

6.5. Dietary habit

The dietary habits of the subjects were considered. A few numbers of patients were vegetarian (3.5 %) while the others were consuming mixed diet. In fact, majority of the patients were not consuming adequate amount of vegetables and fruits in their diet. Consumption of sufficient amounts of fruits and vegetables is recommended as part of a healthy diet. i.e., eating at least five servings of fruits and vegetables per day is recommended to reduce
risks for cardiovascular diseases. But we found that 69.3% of MI patients were not consuming seven serving of vegetables weekly and 84.2% of MI patients were not consuming a single serving of fruits daily. In the Nurses’ Health Study, each increase of one serving per day in the intake of fruits and vegetables was associated with 4% lower CAD risk. Those who had the highest intake had a 20% lower risk.

So an unhealthy dietary habit which may be a risk factor of MI, especially low consumption of vegetables and fruits, high consumption of trans FA, saturated FA and low consumption of PUFA, may categories under minor risk factor of MI. Fruits and vegetables may reduce risk of coronary heart disease (CHD) by means of their protective constituents. These nutrients act through a variety of mechanisms, such as reducing antioxidant stress, improving lipoprotein profile, lowering blood pressure, increasing insulin sensitivity, and improving hemostasis regulation. The biologic mechanisms whereby fruits and vegetables may exert their beneficial effects are multiple. Many nutrients, antioxidants, and phytochemicals in fruits and vegetables, including fiber, potassium, magnesium, and folate, could be independently or jointly responsible for the apparent reduction in CVD risk. The antioxidant value of 100 g of apple is equivalent to 1500 mg of vitamin C. A similar inverse association between intake of vegetables and AMI has been reported by a case-control study in Indian population. Consumption of fruit and vegetables is inversely related to LDL in men and women. The Dietary
factors that may contribute to a high IHD risk in India include low intakes of vitamin B-6 and folate. In South Asian households, prolonged cooking of vegetables is a common practice, which may destroy 90% of the folate content. In numerous epidemiological studies, increasing fiber intake has been associated with a lower risk of heart disease. These foods can lower LDL levels and improve insulin sensitivity.

We considered the fish and meat consumption. A major number (77.2%) of the test subjects were consuming one or more servings of fish daily. 18.5% of patients were eating fried fish daily. In present study, a major number of test subjects (74.3%) were coconut oil users, while 25.7% were using other oil also. In fish and other seafood it is present several healthy constituents, including specific proteins, unsaturated fats, vitamin D, selenium, and long-chain omega-3 polyunsaturated fatty acids (PUFAs), which include eicosapentaenoic acid (EPA; 20:5 omega-3) and docosahexaenoic acid (DHA; 22:6 omega-3). These are cardio protective agents. In humans, EPA and especially DHA are synthesized in low amounts (<5%) from their plant-derived precursor, α-linolenic acid (18:3 omega-3). Thus, tissue levels of EPA plus DHA are strongly influenced by their direct dietary consumption. More over in human trials, fish oil lowers triglyceride levels, systolic and diastolic blood pressure, and resting heart rate. Consistent with these physiological benefits, habitual fish consumption is associated with lower incidence of CHD and ischemic stroke, especially risk
of cardiac death, among generally healthy populations.\textsuperscript{288} Compared with no fish consumption, consumption of approximately 250 mg/day EPA plus DHA from fish is associated with 36% lower CHD mortality.\textsuperscript{190}

Whereas diets high in saturated fats raise the low-density lipoprotein (LDL). Saturated fats are generally solid or waxy at room temperature and are found primarily in animal products and tropical oils such as coconut oil, palm oil etc. Some red meats are high in saturated fat, which raises blood cholesterol, especially levels of LDL cholesterol, which increase the risk of IHD. In our study 24.9% of patients were consuming meat weekly once, while 11.1% were consuming more than once and the remaining 64% consuming less than once in a week. 9.5% of patients were consuming fried meat at least once in a week. But further study needed to find out the tolerable limit of these food items in our population.

Trans fatty acids raise the LDL, and lower the HDL. Trans fatty acids are formed when a liquid fat is converted to solid fat through a process called hydrogenation. Many manufacturers use hydrogenated fats in their ingredients because it creates a product with an extended shelf life and improved consistency. There are currently no safe levels of trans fat to consume each day. High intakes of trans fatty acids, which have been associated with IHD risk.\textsuperscript{289} Some patients of our study were using, trans fats from hydrogenated vegetable oils in the form of vanaspati in greater quantity, and from bakery
and fast food items. In Kerala now a day the use of trans fats are much more
and the cardioprotective effect of the fish consumption may be masked by
the use of these trans fats in high quantity. But further studies required to
quantitate the exact picture.

We considered the alcohol consumption in our study and found 50.9 %
of the patients were alcoholic or ex-alcoholic. Many researchers reported
moderate alcohol consumption is cardio protective. Helmut Schroder et al\textsuperscript{291}
reported that a total alcohol consumption of up to 30 g was inversely related
to MI, independent of other lifestyle variables or cardiovascular risk factors.
And, moderate wine, beer and spirit drinking significantly reduced the risk of
MI in their study population. The cardio protective effect of alcoholic
beverages is related to their biologically active antioxidant compounds,
ethanol and phenolics, which are able to prevent oxidation of LDL
cholesterol. Among alcoholic beverages red wine appears to be the best
choice. In contrast, excessive alcohol intake and binge drinking are toxic to
both the heart and overall health and are the third leading cause of premature
death. In present study we could not asses the exact amount of alcohol
consumption per day by the patient since we were merely depending on their
versions, which need not be reliable all the time.

We ought to be provide important information about the effects of a
unique dietary pattern that emphasizes fruits, vegetables and cereals, fish, and
α-linolenic acid in a diet. A report of Hannah Gardener et al\textsuperscript{292} shows higher consumption of a Mediterranean-style diet was associated with decreased risk of vascular events. Various studies pointed out the role of a diet rich in fruit, vegetables, whole grains, fish, and olive oil in the promotion of ideal cardiovascular health. Researchers in Finland\textsuperscript{293} tracked the diet and health habits of 1622 children for 27 years. Those who eat higher amounts of fruits and vegetables have a lower risk of stiff arteries in adulthood. Low consumption of fruits and vegetables has also been related to arterial stiffness in young adulthood, a potential indicator of high blood pressure and CVD. We suggest People who consume more fruits and vegetables often have lower prevalence of important risk factors for CVD, including high blood pressure, obesity, diabetes and low levels of homocysteine.\textsuperscript{294} But there might be a number of additional risk factors interplaying in acute myocardial infarction patients, which have not been adequately protected against by the higher vitamin intake.\textsuperscript{295} The recommendation to eat fruits and vegetables to prevent chronic diseases is mainly based on observational epidemiological studies, which leaves much uncertainty regarding the causal mechanism of this association.

6.6. Fasting Lipid Profile

In this study we have observed that serum total cholesterol, triglyceride and LDL cholesterol were increased significantly in MI patients when
compared with that of control subjects. In the case of HDL cholesterol, the condition was reversed. Serum cholesterol was an independent risk factor for acute myocardial infarction.\textsuperscript{4} Moreover, there was a multiplicative effect between cholesterol and other major risk factors on the relative risk of acute myocardial infarction.\textsuperscript{296}

In our study the mean value of total cholesterol were $205 \pm 1.86$ mg/dL for test group and $174 \pm 0.74$ mg/dL for the control group (P<0.0001). Similarly, the mean value of LDL cholesterol were $137 \pm 1.68$ mg/dL for test group and $108 \pm 0.69$ mg/dL for control group(P<0.0001). High total cholesterol, high LDL cholesterol, high triglycerides, low HDL-cholesterol playing important role in CAD causation, and importance has been shown in the oxidized fraction of LDL as one of the risk factors. The main mechanisms by which LDL particles act as a risk factor have been shown by Brown and Goldstein.\textsuperscript{297} They showed a receptor mediated uptake of LDL-cholesterol by cells subsequent to incorporation of cholesterol in cells. A study of Holvoet \textit{et al} have shown that CAD patients had a higher level of circulating oxidised LDL as compared to controls and the sensitivity of this circulating oxidised LDL was 76\% for cases of CAD.\textsuperscript{298} Many researchers reported that the prevalence of CAD among South Indians is increasing rapidly. Urgent steps are needed to modify lifestyle by increasing physical activity, modifying diet and perhaps making aggressive use of statins as part of the preventive strategy to reduce risk factors and thus, the burden of CAD in this population.\textsuperscript{299}
In present study the mean value of serum triglyceride were increased in test group when compared to the control group. The mean values were 132 ± 3.31 mg/dL for test group and 109 ± 1.20 mg/dL for the control group. A major number of our study group were diabetic or alcohol users or habituated with unhealthy diet. Diabetes, unhealthy diet, excess alcohol consumption etc. are certain reasons for hypertriglyceridemia. In our study we observed 30.2% of patients with abnormal serum triglyceride level. Austin et al have shown high risk of CAD in patients with increased serum triglyceride levels. In a meta-analysis of 17 population-based prospective studies, increased plasma triglyceride levels were associated with increased coronary disease risk in both men and women, after adjustment for HDL cholesterol and other risk factors. Hiroyasu Iso et al reported that serum triglycerides predict the risk of coronary heart disease, independent of total cholesterol and HDL cholesterol, among Japanese men and women who possess low mean values of total cholesterol by Western standards.

In present study the mean values of serum HDL cholesterol were decreased in test group when compared to the control group (P<0.030). The HDL particles induce the removal of cholesterol from cells, including those in atherosclerotic plaques, and carry them to the liver, by reverse cholesterol transport. The association between reduced HDL cholesterol levels and increased risk of heart disease is, well established; independently of triglyceride level and other risk factors. But the mechanisms by which
HDL confer protection from atherosclerosis include more than just reverse cholesterol transport. HDL particles seem to have anti-inflammatory and antioxidant properties, inhibiting the oxidation of LDL cholesterol and the expression of cellular adhesion molecules and monocyte recruitment. The HDL may also reduce the risk of thrombosis by inhibiting platelet activation and aggregation.

Roe et al\textsuperscript{304} reported that almost one-fifth of patients with acute coronary syndromes (ACS) have very low HDL levels (10-29 mg/dL), a finding that adds incrementally to a greater burden of atherosclerosis and a higher risk of mortality; 35% had low HDL levels (30-39 mg/dL), 39% had normal HDL levels (40-59 mg/dL), and 9.0% had high HDL levels (60-100 mg/dL). Consequently, strategies for mitigating the adverse prognosis associated with very low HDL levels warrant further exploration in patients with ACS. Watkins et al\textsuperscript{305} has shown a decrease in the risk of CAD by 2.3% with every 1 mg/dl rise in serum HDL-cholesterol. A study conducted by American Medical Association\textsuperscript{306} had shown increased risk of CAD in patients with total cholesterol - HDL cholesterol ratio $> 4$. Similar evidence was given by Ladeia et al.\textsuperscript{307}

However, in our study the value of fasting Lipid Profile of majority of the test subject were normal while comparing with that of western population. According to the western standards serum total cholesterol level of 36.1% of
our test subjects were within normal limit. LDL cholesterol level of 55.9% MI patients, serum triglyceride level of 69.8% MI patients and HDL cholesterol level of 92.1% MI patients in this study were normal when compared to western population. From the present study we pointed out the importance to develop the reference range in Indian scenario. Many physicians still follow the reference range according to the western standards.

Although South Asians have levels of LDL cholesterol comparable to other populations, LDL particle size tends to be smaller. Small LDL particles, through increased susceptibility to oxidation, are more atherogenic than larger particles. HDL particle size, in addition to the actual level of HDL cholesterol, also appears to be an important predictor of CHD risk. South Asians not only have lower HDL levels but also have a higher concentration of small, less-protective HDL particles. Asian Indian males have a higher prevalence of low HDL2b than non-Asian Indians, which suggests impaired reverse cholesterol transport. This finding was also observed in Asian Indian men with apparently normal HDL values. A study of Ram B Singha et al in Indian population shows that Serum cholesterol level was directly related to prevalence of coronary artery disease even in those with low cholesterol concentration (<5.18 mmol/l) and it is possible that some Indian populations may benefit by increased physical activity and decline in serum cholesterol below the range of desired serum cholesterol in developed countries.
So the major concern of our observation is that subjects who maintain desirable cholesterol concentration as per western standards also are targets for myocardial infarction. In the circumstances, further study is needed to implement an ideal normal range of serum or plasma lipid of our population. Also analysis of other risk factors that are non-conventional and newly emerging will be of immense importance in the eventual assessment of the risk status.

6.7. Lipoprotein (a)

Lp (a) is an LDL like particle which has apolipoprotein (a) attached to apolipoprotein B molecule via a disulphide bond. There are 34 different Lp (a) isoforms depending on the size of apo (a) polymorphism. Plasma Lp (a) levels are highly hereditary and a stable lifelong level is attained by age two. Ninety percent of the variation in plasma levels is accounted by the apo (a) gene and 70 % by the size of apo (a) isoforms.\textsuperscript{312}

Lp (a) may contribute to the development of not only atherosclerosis like LDL, but also thrombosis and thus MI.\textsuperscript{313} Mechanism of pathogenicity of excess Lp (a) include enhanced thrombogenesis and impaired fibrinolysis by competing with plasminogen, inhibition of transforming growth factor B, destabilization of plaque, increased smooth muscle cell proliferation and migration, formation of occlusive thrombus, impaired formation of collateral...
vessels, enhanced oxidation uptake and retention of LDL cholesterol and up regulation of expression of the plasminogen activator inhibitor.\textsuperscript{314}

In our study we observed that Lp (a) level in test group was highly significant while comparing with healthy control group (P<0.0001). Earlier studies conducted\textsuperscript{324} also observed higher Lp (a) in MI patients. Lima \textit{et al}\textsuperscript{11} determined serum levels of Lp (a) and lipid profile of a group of individuals submitted to coronary angiography, with the aim of establishing the possible correlation between these parameters and the severity of coronary artery disease. The value obtained in the test and control groups for Lp(a) indicate a progressive increase in the serum levels of this parameter according to the severity of coronary atheromatosis. Similar findings have been reported by Uusimaa \textit{et al}\textsuperscript{316} from University of Oulu, Finland that the serum Lp(a) level is associated with the angiographic severity of CAD. Atherosclerotic plaques, but not normal human arteries contain Lp (a),\textsuperscript{317} and results from in vitro and animal studies have implicated Lp (a) in foam-cell formation, smooth muscle–cell proliferation, and plaque inflammation and instability.\textsuperscript{318}

Lp (a) can cross the endothelial barrier between plasma and the arterial intima and may be trapped within the arterial intima, particularly at sites of injury. Thus, Lp (a) can deliver cholesterol to atherosclerotic plaques like LDL. Furthermore, Lp (a) promotes thrombosis partly through competitive inhibition of plasmin generation and through inactivation of
tissue factor pathway inhibitor, a potent inhibitor of the tissue factor–mediated coagulation cascade.

In present study we found that the clinicians here in north Kerala were not considering the Lp (a) value at all and they were giving importance to FLP values for the treatment of MI patients. But it is to be included in routine analysis for better management of CAD. Geethanjali et al \(^{319}\) studied the Plasma lipoprotein (a) levels in south Indian patients and reported that it is significantly elevated in patients with coronary artery disease as compared to controls.

Zorio \(^{320}\) et al reported that Lp(a) levels are markers of early MI and that Lp(a) levels >30 mg/dL are associated with severe patterns of coronary atherosclerosis. Our observations were in line with the findings of Zorio \(^{et al.}\). Pia R. Kamstrup \(^{et al.}\)\(^{321}\) observed a stepwise increase in risk of MI with increasing levels of lipoprotein(a), with no evidence of a threshold effect. Extreme lipoprotein (a) levels predict a three to four fold increase in risk of MI in the general population and absolute ten year risks of 20% and 35% in high-risk women and men. However Nascetti \(et al.\)\(^{322}\) did not observe any change in Lp (a) levels in cardiovascular disease patients and they concluded that Lp (a) should not be considered as an independent risk factor in CVD patients.
So both the prothrombic and atherogenic mechanisms of Lp (a) were providing more defined indications for the determination of Lp(a) values in clinical practice. Here, there was enough evidence to support the introduction of routine assessment of Lp(a) levels in clinical laboratories in the monitoring of patients at risk for coronary artery disease.

6.8. Cardiac Markers

In our study, increased aspartate aminotransferase (AST), creatine kinase-MB (CK-MB), cardiac troponin T (cTnT) and cardiac troponin I (cTnI) levels were found in patients with MI as compared to healthy controls. Elevated levels of CK-MB, cTnT and cTnI have been regarded as biochemical markers of myocyte necrosis. Last 50 years, there has been a progressive improvement in the tissue specificity of biomarkers of myonecrosis, and in their clinical sensitivity and specificity. In the past, the AST test was used to diagnose myocardial infarction, but more accurate blood tests have largely replaced it for cardiac purposes. In present study significant levels of AST were found in patients with MI as compared to healthy controls (p value<.0001). Vuddandi Prabodh et al conducted a study in South India, reported that the mean levels of AST and troponin I in cases of acute myocardial infarction were statistically significant.

In 1989 Rotenberg et al concluded their work as, AST should be determined in every patient with suspected AMI because its determination
may contribute to the diagnostic yield of LD isoenzymes tests, especially in patients with AMI admitted 48-72 hours after onset of symptoms, when creatine kinase declined to near normal values. In present study we observed 33.7% of patients with normal AST level. AST level elevate in a period of 6 to 10 hours after the MI and its determination is no longer used as a marker for myocardial injury.

In our study significant levels of CK-MB were found in patients with MI as compared to healthy controls (p value < .0001). CK-MB still has a formal place in defining myocardial infarction. Observing the rise and fall of the biochemical marker creatine kinase-MB isoenzyme (CK-MB) has been termed as the “gold standard” for the diagnosis of MI. This enzyme normally exist in cellular compartment and leak out into the plasma during myocardial injury due to disintegration of contractile elements and sarcoplasmic reticulum. Similar results have been reported by many researchers and our study is in good agreement with these observations.

The creatine kinase-MB isoenzyme (CK-MB) is not specific for myocardium. So CK-MB measurement is not totally specific for MI and there are various causes for elevated CK-MB concentrations other than MI. We observed an elevated level of CK-MB only in 81.1% of the test groups. Most of the patients were admitted in the hospital within 4 hours of the symptoms of MI or MI and often we could collect the blood sample immediately after
the admission. Serum CK-MB concentration rise in parallel following myocardial injury, starting to increase 4–6 h after injury, reaching peak serum concentrations after 12–24 h and returning to baseline after 48–72 h.76

The levels of cTnT in patients with MI were highly significant when compared to healthy controls of present study (p value < .0001.) and also significant levels of cTnI were found in patients with MI as compared to healthy controls (p value < .0001). Sustained release of troponin is a marker of permanent myocardial injury. It is released considerably longer than cytosolic CKMB.330 Troponin is a complex contractile protein that normally is not found in serum. It is released only when myocardial necrosis occurs.331 Cardiac troponin T and I are proteins of the troponin regulatory complex involved in cardiac muscle contraction. Both have very high myocardial tissue specificity and offer an improved sensitivity and specificity for MI versus a combination of ECG and traditional biochemical markers. The Cardiac-specific isoforms of troponin T and I have emerged as sensitive indicators myocardial infarction and, importantly, for risk stratification of acute coronary syndrome patients.332

Gupta et al333 reported that the cardiac-specific troponins are highly sensitive and specific markers of myocardial damage and therefore cardiac troponins are the preferred markers for the diagnosis of myocardial infarction. Serum levels increase within 3-12 hours from the onset of chest pain, peak at
24-48 hours, and return to baseline over 5-14 days.\textsuperscript{334} So, unlike CK-MB, cTnT and cTnI are released for much longer time and can be detectable in the blood following MI. In our study, 18.9\% of patients who had MI had CK-MB levels not significantly different from controls. In a study by Kliemam S \textit{et al},\textsuperscript{102} 31\% of the patients with normal CK-MB had elevated troponin-T levels. Similarly, Zurich SW \textit{et al}\textsuperscript{335} found using a single troponin T determination, that 46\% of patients with confirmed MI had an abnormal cTnT and normal CKMB initially.

In present study both troponins (T&I) were highly significant. Both troponins are almost equally good markers and it is difficult to explain which is better because both have some positive and negative points. cTnI is 100\% cardiospecific, but cTnT is elevated in chronic renal disease, trauma and skeletal muscle disease also. The overall diagnostic specificity and efficiency of cTnI is better than cTnT.\textsuperscript{336} However, the third generation cTnT assays don’t allow the skeletal TnT interference. Both cTns undergo posttranslational modifications such as phosphorylation, oxidation, reduction, proteolysis and form complex with other troponins. cTnI is more prone to these modifications and these modifications may prevent some antibodies used in the assay system from binding to the molecules and thereby diminishing the signal. There are some discrepancies in the standardization of cTnI assays.\textsuperscript{337}
The life-time of cTnT in blood (5-14 days) is somewhat more than that of cTnI (4-10 days). Although cardiac troponins are extremely specific for myocardial necrosis, they do not discriminate between ischaemic and non-ischaemic etiologies of myocardial injury. Combining troponin with other cardiac biomarkers may offer complimentary information on the underlying pathobiology and prognosis in an individual patient. 92.2% patients of our study were shown elevated level of cTnI, while 89.8% of test groups were presented with increased level of cTnT. So the failure to show a rise in cTnT or cTnI does not exclude the diagnosis of ischaemic heart disease.

None of the markers available so far meets all the criteria required for an ideal biochemical marker of myocardial injury. However, among the currently available markers cTns appear to be the most promising as far as their sensitivity, specificity, turnaround time and cost is concerned. The improved sensitivity and specificity of cTns has almost eliminated the place of LD and CK and even CKMB in the diagnosis of cardiac injury. Between cTnT and cTnI, the latter seems to be better considering its cardiospecificity and efficiency. However, the discrepancies in its standardization limit it from being the best and much is needed to be done to harmonize the test results.

Any way the Troponins have ushered in a new era of highly specific and sensitive cardiac markers used in various cardiovascular clinical situations. With many qualities of an ideal marker, troponins are favorably
considering in the management of the rising cardiovascular morbidity and mortality. However, historically CK-MB has proven as most useful marker for the diagnosis of MI according to WHO criteria and certain clinical situations still warrant CK-MB as the ideal choice of cardiac biomarker, especially in cases of detecting reinfarctions. More over the cost per test is much less than that of troponins.

6.9. C - reactive protein (CRP)

Many studies have suggested that C - reactive protein is one of the risk factor for cardiovascular disease. In present study we evaluated CRP level in MI patients along with other risk factors, and noticed a significant elevation of CRP level in MI patients while comparing with that of controls (p<0.001). The elevation of CRP has been linked to atherosclerosis. Atherosclerosis, or cholesterol plaguing of the arteries, is known to have an inflammatory component that is thought to cause the rise in CRP levels in the blood. The inflammatory cell types typically found in the atheroma include monocyte-derived macrophages and lymphocytes. Macrophages present in the atherogenous plaque lead to the release of mediators like cytokines and chemokines which in turn increase the plasma concentration of CRP which amplify inflammatory and procoagulant responses. Similar findings were reported by Ridker et al and they revealed the key role of Inflammation in the pathophysiology of atherosclerosis. CRP is a strong independent predictor
of risk of future myocardial infarction, stroke, peripheral arterial disease, and vascular death among people without known cardiovascular disease. In addition, among patients with acute coronary ischemia, stable angina, and myocardial infarction, levels of CRP have been associated with increased vascular event rates. Therefore CRP is an adjunct to lipid screening in the detection of people at high risk for coronary artery disease, especially in primary prevention.\textsuperscript{341}

As major number (86.7\%) of patients in this study had an elevated level of CRP, we suggest a strong association between CRP levels and MI. In this study of north Kerala population we discussed the different risk factors of myocardial infarction. The study of Festa et al\textsuperscript{156}, connecting these different risk factors of myocardial infarction with CRP ie, CRP was positively correlated with body mass index, waist circumference, blood pressure, and levels of triglycerides, cholesterol, LDL-cholesterol, plasma glucose, and fasting insulin, and inversely correlated with the high-density lipoprotein cholesterol level and the insulin sensitivity index. However Idrissia Abdelmouttaleb et al\textsuperscript{342} suggest that CRP has a strong association with acute coronary events, and do not support the hypothesis that CRP is a potent determinant of chronic stable coronary disease.

Indeed, with increasing levels of adverse cardiovascular events, baseline concentrations of CRP follow a parallel and graded rise. The addition
of CRP to traditional cholesterol screening enhances cardiovascular risk prediction independently of LDL-Cholesterol, suggesting that increased CRP concentrations may identify asymptomatic individuals with normal cholesterol concentrations at high risk for future cardiovascular events.

6.10. Homocysteine

Homocysteine is an amino acid not used in protein synthesis. Its role is to serve as an intermediate in methionine metabolism. Homocysteine itself is located at a branch-point of metabolic pathways: either it is irreversibly degraded via the transsulphuration pathway to cysteine or it is remethylated back to methionine.

The result of present study shows a significant increase of homocysteine level in MI patients. A number of case-control and cohort studies has been reported the relationship between elevated level of Homocysteine and the risk of CAD. Homocysteine has been identified as a novel risk factor for CAD in Indians. Anand et al reported that Homocysteine levels are higher among Asian Indians than Whites in several countries. A very high prevalence of hyperhomocystinemia (>15 micromol/L) in 75% of subjects in India, which was strongly correlated with cobalamin deficiency (and not folic acid deficiency, which was rare). Total cobalamin of <150 pmol/L was found in 47% of subjects. There was no difference between vegetarians and non-vegetarians. Also, about 75% of the subjects had signs of
cobalamin deficiency. Thus, impaired cobalamin status appears more important than folate deficiency among Asian Indians.\textsuperscript{176}

76.2\% of patients in this study had an elevated level of homocysteine. It is reasonable to assume that dietary deficiency of folic acid and or cobalamine in certain MI patients may increase the homocysteine level. So it is necessary to include fruits and vegetables in routine diet to ensure cardiac protection.

Hyperhomocysteinemia produced by dietary deficiency of folate and increased methionine in monkeys induces endothelial dysfunction, as shown by impaired vascular relaxation response to acetyl choline or adenosine diphosphate, decreased thrombomodulin anticoagulant activity, and increased platelet-mediated vasoconstriction to collagen infusion.\textsuperscript{346} Although a few small studies showed no relationship of homocysteine with CAD in India, no biological explanation other than small sample size has been provided. Low consumption of fruits and vegetables, however, is common throughout the world. It was estimated that inadequate consumption of fruits and vegetables could have accounted for 2.6 million deaths worldwide in the year 2000. WHO and many international organizations recommend a minimum intake of 400-500g or five servings (5 servings x 80g) of fruits and vegetables per day to reduce the risk of chronic diseases.\textsuperscript{281} Asian Indians have lower prevalence of daily fruit and vegetable intake (27\% vs. 45\% for rest of the world).\textsuperscript{347}
1 micromol/L increase in homocysteine level is associated with an increase in CAD risk of 12% in men and 16% in women. In vitro studies indicate that homocysteine may have a harmful effect on endothelial cells, increase coagulability, and have a proliferative effect on smooth muscle cells. Stamler et al reported, nitric oxide is the important mediator of endothelial, platelet, and smooth muscle function, which reacts with homocysteine to form S-nitroso-homocysteine, counteracting the adverse vascular effects of homocysteine, including endothelial dysfunction, vasoconstriction, and platelet aggregation. So we recommend the screening for homocysteine at population level or food-fortification with B vitamins (adequate consumption of fruits and vegetables) to reduce overall CVD risk. From this study we suggest to reduce the CVD risk in hyperhomocysteinemic individuals in our community by controlling “classical “risk factors such as smoking, elevated blood pressure, adverse lipid profiles and diabetes, and by promoting a healthy lifestyle.

6.11. Fibrinogen

Fibrinogen is considered as one of the probable risk factors of myocardial infarction. In our study group the plasma fibrinogen level was significantly higher than that of control subjects. Prospective epidemiological studies have reported positive associations between the risk of coronary heart disease (CHD) and plasma fibrinogen levels.
In our study the mean value of plasma fibrinogen in test group was higher (350.98 ± 1.26 mg/dL) than that of control group (324.03 ± 1.08 mg/dL) and found to be highly significant (p < 0.001). Fibrinogen is the major coagulation protein in blood; it is the precursor of fibrin, and an important determinant of blood viscosity and platelet aggregation. Fibrin appears to be a multi-potential component of atherogenesis, intervening at virtually all stages of lesion development. Fibrin and microthrombus deposition on normal intima is associated with endothelial disruption and intimal oedema, and oedema is a primary characteristic of early proliferative lesions. Fibrin strands on or in the intima encourage smooth muscle cell (SMC) migration and proliferation, and contribute to the growth of plaques. Fibrin also provides a continuing source of fibrin degradation products (FDP), and these have mitogenic activity which will sustain SMC proliferation in growing plaques, and act as chemoattractants for blood leucocytes. Accumulation of the lipid core in fibrous plaques may also be influenced by fibrin which appears to bind the lipoprotein Lp(a) with high affinity, thereby immobilizing its lipid moiety within the lesion. Many previous studies found fibrinogen levels can be reduced considerably by lifestyle interventions that also affect levels of established risk factors (such as regular exercise, smoking cessation, and moderate alcohol consumption), there is importance in the measurement of fibrinogen, may help in disease prediction or prevention.
Various risk factors of MI were correlated with fibrinogen, particularly smoking, diabetes, cholesterol level and CRP. Hisataka Sakakibara et al\textsuperscript{119} investigated an association between fibrinogen levels and cardiovascular risk factors in apparently healthy Japanese subjects. They showed that plasma fibrinogen levels are positively correlated with conventional cardiovascular risk factors such as age, smoking status, total cholesterol, CRP and hemoglobin A1c (HbA1c). On the other hand, high-density lipoprotein (HDL) cholesterol is negatively correlated with fibrinogen. Fibrinogen levels also tended to be associated positively with body mass index and negatively with exercise habits. It has been estimated that up to 50\% of the increase in CHD risk associated with smoking could be attributed to the effects of smoking on fibrinogen. In present study the above mentioned risk factors were significant and well correlated with the fibrinogen level in MI patients of north Kerala.

In a large, population-based, prospective study, the Atherosclerosis Risk in Communities (ARIC) Study, plasma fibrinogen was found to be an important risk factor for CHD in women.\textsuperscript{351} In an Iranian study performed in 2007, serum fibrinogen levels were significantly higher in patients with AMI with ST-change.\textsuperscript{352} The mechanisms by which plasma fibrinogen may be involved in atherothrombosis are, increased platelet aggregation tendency, increased fibrin formation, and stimulation of vascular cell proliferation and migration, with increasing plasma fibrinogen levels.\textsuperscript{353} Thus, elevated plasma
fibrinogen levels may cause a hypercoagulative state that could influence the
degree and duration of thrombus formation at the time of coronary injury.

Here we found that plasma fibrinogen level was significantly high in
northern Kerala population and it implies that high serum fibrinogen levels
are risk factor for premature MI, and which is well in agreement with the
works of Omran et al\textsuperscript{352} and Ernst et al.\textsuperscript{353} This is associated with significant
elevation of total cholesterol, prevalence rate of smoking and hemoglobin
A1c. So we project an idea about estimation of fibrinogen level in plasma that
may be useful for the prediction and better management of MI.

6.12. Diabetes

In present study we found that 45.5\% of MI patients were diabetic and
they were using hypoglycemic agents. Diabetes (Both type I and type II) are
powerful and independent risk factors for coronary artery disease (CAD),
stroke, and peripheral arterial disease.\textsuperscript{354} Atherosclerosis accounts for virtually
80\% of all deaths among North American diabetic patient compared with one
third of all deaths in the general North American population.\textsuperscript{355} More than
75\% of all hospitalisations for diabetic complications are attributable to
cardi ovascular disease.

It was found in present study that the level of fasting blood sugar in
patients with MI were highly significant when compared to control subjects.
(p value<.0001). Approximately 80\% of deaths in diabetic patients are
attributable to cardiovascular disease (CVD), which in turn is highly correlated with dyslipidemia. Nathan DM et al\textsuperscript{356} reported that atherosclerosis-induced coronary artery disease is the main cause of morbidity and mortality in diabetic patients. Diabetic dyslipidemia consists of elevated TG, low HDL, and an increased proportion of small dense LDL. Glycosylation of proteins and lipoproteins can interfere with their normal function by disrupting molecular conformations, alter enzymatic activity, reduce degradative capacity, and interfere with receptor recognition. Thus, changes in the normal physiology of proteins those are relevant to atherogenesis, may promote atherosclerosis in diabetic individuals. The mechanism of LDL glycosylation increases its atherogenicity. Advanced glycosylation of the phospholipid component of LDL is accompanied by the progressive oxidative modification of unsaturated fatty acid residues. Glycosylation of LDL apoB reduces its recognition by the LDL receptor and increases uptake through the scavenger receptor.

The endothelial dysfunction is the initial step in atherosclerosis and occurs in patients with chronic hyperglycemia. Kawano et al\textsuperscript{357} reported that in hyperglycemia patients, oral glucose loading rapidly suppresses endothelial-dependent vasodilatation through increase in the production of oxygen-derived free radicals. Many studies pointed out in patients with diabetes and Impaired Glucose Tolerance (IGT) is usually associated with
other coronary risk factors, such as dyslipidemia, hypertension, and obesity. These factors are also known to cause endothelial dysfunction.\textsuperscript{358}

Considerable epidemiological and clinical studies have established that even a prediabetic state, including IGT, is strongly associated with the occurrence of cardiovascular diseases.\textsuperscript{359,360} Postprandial acceleration of oxidative stress and inflammation has been observed in patients with type 2 diabetes.\textsuperscript{361} Mita T \textit{et al} \textsuperscript{362} reported that the reduction in carotid intima-media thickness was associated with the improvement in control of postprandial but not fasting hyperglycemia. Chiasson \textit{et al} \textsuperscript{363} also reported that postprandial hyperglycemia is an important target to prevent cardiovascular events. Therefore, treating postprandial hyperglycemia may have a positive effect on atherosclerosis progression and cardiovascular diseases. It is one of the limitations in our study, we were included only the level of fasting blood sugar in present study. Where as Stumvoll \textit{et al} \textsuperscript{364} suggested that antidiabetic agents can prevent cardiovascular events by improving the control of hyperglycemia in both preprandial and postprandial conditions, which may inhibit atherosclerosis progression caused by hyperglycemia-induced oxygen-derived free radicals. Moreover, O'Keefe \textit{et al} \textsuperscript{365} reported that postprandial hyperglycemia and hyperlipidemia is associated with increased inflammation, endothelial dysfunction, decreased fibrinolysis, plaque instability, and cardiac events, even in nondiabetic patients.
In our study we found that approximately half of the MI patients were under the treatment of diabetes. When considering the prediabetic condition, the situation is more pathetic. We could assess that the diabetic control is very essential for decreasing the severity of MI in our population. The prevalence rate of diabetes in our population is around 7% to 10%. This means the diabetic screening in our population may decrease the incidence of MI. In controlled diabetic population MI cases drastically decreased due to low intake of dietary fat, consequent low level of cholesterol, good exercise, maintenance of ideal body weight and smoking cessation. This may be targeted to the whole community, likely to reduce the social and economic burden, hence it is needed good steps to reduce events of MI. As the diabetic patients remain a high-risk group for MI, an increased awareness and appropriate delivery of established therapies to this group is essential in the face of a rising diabetic population of Kerala. We observed that only 54.5% of MI patients were non diabetic in present study, here we have to consider firmly the impaired glucose tolerance or pre-diabetic condition also, as it is associated with the occurrence of endothelial dysfunction and thus coronary artery disease. Using tracer labeled VLDL and LDL Kissebah et al 366 have found an increased LDL turnover in adult-onset diabetics, even when the fraction of total flux of VLDL converted to LDL is lower than normal. It has therefore been postulated that an increase in the turnover of LDL could be an important factor in the deposition of lipid-rich material in the arterial walls.
They have shown that improved control of diabetes results in diminished cholesterol synthesis.

6.13. Hypertension

We could find a significant association of hypertension with acute myocardial infarction. 33.7% of the MI patients in our study group were hypertensive, and were using antihypertensive agents. The “Interheart” study showed that 22% of heart attacks in Western Europe were due to a history of high blood pressure and those with hypertension had almost twice the risk of a heart attack. For adults aged 40 to 69 years, each 20 mm Hg rise in usual systolic blood pressure or 10 mm Hg rise in diastolic blood pressure doubles the risk of death from CHD.

Hypertension is a low-grade inflammatory process because high blood pressure levels are associated with increases in circulating levels of inflammation markers which can reflect vascular inflammatory processes. The vascular inflammation associated with hypertension could be the link between high blood pressure levels and the atherosclerotic process, which is the principal origin of cardiovascular disease, the leading cause of worldwide mortality. High blood pressure levels are accompanied by increases in oxidative stress due to both higher reactive oxygen species (ROS) production and reduced ROS scavenging by antioxidant defence. This situation favours endothelial function alterations which allow the expression of adhesion
molecules and initiation of fatty streak, the earliest structural change in the atherosclerotic process. At the same time, this inflammation, allows endothelial dysfunction since some inflammatory mediators can negatively affect endothelial cell function.

Inflammation, therefore, plays a critical role in development and in complications of the atherothrombotic process. Changes in mechanical stress and activation of humoral factors such as the reninangiotensin-aldosterone system can be underlying not only increases in oxidative stress (and consequently endothelial dysfunction) but also the development of the inflammatory process associated with hypertension. In a Swedish study of 7500 patients followed up for 27 years, the identified etiological factors for CHF were hypertension in 20.3%, and CAD either alone or in combination with hypertension in 58.8%. However Fox et al have reported hypertension to be the primary attributable factor for CHF in only 4.4% of incident cases of CHF examined prospectively.

From our study we found that around 1/3rd of MI patients were hypertensive. This is pointed out the importance of public awareness against hypertension. Various informations are available to prevent or control this burden and public awareness programs are still more essential in this regard. As per the recommendations of the VIIth Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure
(2003), those with a blood pressure reading of 120/80 mm Hg should be considered as having `normal' BP, while those with 120-139/ 80-89 mm Hg should be treated as those in the `pre-hypertension' stage. The `pre-hypertensive' group should be targeted in public health programmes because through proper diet, exercise and lifestyle modifications, these group of persons can be prevented from developing hypertension. Physical inactivity, excess sodium intake, incomplete medication and improper control of blood pressure can lead to resistant hypertension. So we suggest that to reduce the incidence of MI in our population by detecting the prehypertensive group and give strict instruction to normalize their blood pressure. We also suggest to improve the public awareness program in primary health care level which imparts to maintain normal blood pressure and various measures to keep it under control. In present study we showed that both systolic and diastolic blood pressure were important in MI.

6.14. Smoking

In the present study 68.8% (417) of the MI patients were smokers. Out of 417 smokers 297were (71.2%) current smokers and 120 patients (28.8%) were ex smokers. The most common avoidable cause of cardiovascular mortality is the use of Tobacco worldwide. Najem et al have found that the immediate noxious effects of smoking are related to sympathetic nervous over activity, which increases myocardial oxygen consumption through a rise
in blood pressure, heart rate, and myocardial contractility. Smoking enhances platelet aggregability, increases blood viscosity and shifts the pro- and antithrombotic balance towards increased coagulability (e.g., fibrinogen, von Willebrand factor, ICAM-1 and P-selectin). Insulin resistance is higher in smokers compared with nonsmokers, and hemoglobin A1c is dose-dependently elevated, as is homocysteine. Smoke exposure may influence the kinetics of markers with different response to transient or chronic changes in cigarette smoking behavior. Chronically, cigarette smoking induces arterial stiffness which may persist for a decade after smoking cessation.

Here we observed that the high rate of smokers among MI patients, might have been increased due to lack of awareness on the effects of smoking and its relation to coronary artery disease (CAD) in rural Kerala. Also we analysed the percentage of younger patients who were addicted to smoking and noticed that 9% of MI patients who were smokers aged less than 40 years or 64% of young MI patients (below 40 years) were smokers. Demosthenes B et al reported that cigarette smoking seems to play the most important role for having a MI in individuals under the age of 36 years. We also noticed that the risk was increased in ex-smokers at least thrice compared to those who have never smoked which also may be considered with great importance.

Kerala has one of the lowest consumption areas of tobacco as reported in the National Family Health Survey. However the Global Adult Tobacco
(GAT) survey (2011-12) shows yet another alarming fact that the state has high smoking prevalence rate than the national average; with more than one-third males in Kerala using tobacco in one form or the other. Thus, a high prevalence of tobacco use and other adverse lifestyle variables that may be the major determinants of cardiovascular diseases in north Kerala. This study pointed out the importance of prohibiting the smoking and other tobacco products, that has been intensified in India recently, since still smoking continues to be a predominant public health problem among males in rural areas of Kerala particularly among lower socio-economic population. Considering the high priority given to tackle this threat, there is a need to develop multiple approaches where measures to strengthen existing regulations against tobacco combined with cost effective interventions for tobacco cessation particularly in rural areas has to be initiated and sustained. Also Patient education and awareness programs are of great importance in the rural areas to reduce the burden of CAD.

6.15. Family history of Ischeamic Heart Disease (IHD)

In our study we noticed 29.7% of test group subjects and 14.6% of control subjects were having a positive family history of IHD. Similar findings were observed by Ciruzzi M et al. They analysed the frequency of family history of IHD in patients with acute myocardial infarction in Argentine and their study confirms that a family history of AMI is a strong
and independent risk factor for AMI. In the population from Argentina, family history accounted for 14% of all cases of AMI in men and 26% in women.

Chow CK et al\textsuperscript{377} suggested that more than one third of admissions for premature myocardial infarction (Premature CHD is that before age of 55 years in men and 60 years in women) could be prevented by screening and treating first-degree relatives. First-degree relatives of patients with premature myocardial infarction have double the risk themselves. In our study 13.4% of patients were below 40 years of age and it was found in analysis that 39% of the MI patients and 21% of Control subjects were having the positive family history of IHD for below 40 years. Family history of IHD is an independent risk factor for AMI, and intervention on modifiable risk factors may be beneficial also in those with a family history of the disease. We suggest that people with a family history of coronary artery disease need to be especially cautious about controlling all of the risk factors that they can control - such as smoking, obesity, exercise, diet, diabetes, hypertension and cholesterol. And also suggest to screen the first degree relative, may drastically decrease the incidence of MI in our community.

Azin Alizadehas et al\textsuperscript{378} studied 200 patients with AMI and positive family history of CAD (FH Pos.)- as case group and 200 AMI patients without family history of CAD -as control group (FH Neg.). Information
about first and second-degree relatives was obtained, including age, occurrence of MI, and other risk factors related to CAD. They found Subjects with a positive family history of CAD were younger and more susceptible to CAD and needed frequent interventional procedures. Several aspects of the relation between family history of ischemic heart disease (IHD) and risk of myocardial infarction need further quantification.