2. Review of Literature

The literature pertaining to the study on "Baseline risk factors for coronary heart diseases in Kochi" is reviewed under the following heads.

2.1. Cardiovascular Diseases and coronary heart diseases

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2.1. Cardiovascular Diseases and coronary heart diseases

Cardiovascular problems have emerged as a major health burden worldwide. The diseases encompassing cardiovascular system are generally referred as Cardio Vascular Diseases (CVD). Cardiovascular disease is a general term used to classify numerous conditions affecting heart, heart valves, blood, and vasculature of the body, which interfere with the simple purpose of cardiovascular system that is to circulate blood through out the body (John and Bhatt, 2007).

CVD is a leading cause of mortality and is responsible for one third of all global deaths, with developing countries particularly low income and middle income countries accounting for 86 percent of the Disability Adjusted Life Years (DALYs) lost to CVD world wide in 1998 (WHO, 2005).
As per WHO (2002) report, out of 16.6 million deaths attributed to cardiovascular disease world wide, 80 percent is in developing countries. WHO (2005) has also emphasized the vulnerability of developing countries to CVD. According to this report CVD contributed to 15.3 million deaths in 1996, of which 5.5 million was from developed countries and 9.77 million from developing countries.

It has been predicted that by 2020 there would be a 111 percent increase in cardiovascular death in India. This increase is much more than the 77 percent for China, 106 percent for other Asian countries and 15 percent for economically developed countries (Gupta, 2005).

A rise in the prevalence of cardiovascular disease in the early half of the twentieth century and a subsequent decline in the latter half have been well documented in industrialized countries (Mohan and Deepa, 2004). However, the scenario in developing countries, especially India, is a steady escalation in prevalence of CVD (Goyal and Yusuf, 2006 and Reddy and Yusuf, 1998). In Western countries where CVD is considered a disease of the aged, 23 percent of CVD deaths occur below the age of 70; compared to 52 percent of CVD deaths occurring among people under 70 years of age in India (Gupta, 2005 and Ghaffar et al., 2004). As a result the Indian subcontinent suffers from a tremendous loss of productive working years due to CVD deaths: an estimated 9.2 million productive years were lost in India in 2000, with an expected increase to 17.9 million years in 2030 (Goyal and Yusuf,
The health and economic implications of this staggering rise in early CVD deaths are profound.

2.1.1 Coronary heart disease and Clinical manifestations

Coronary heart disease (CHD), stroke, congestive heart failure, hypertension, cardiomyopathy, arrhythmias, aortic stenosis and aneurysm are the major manifestations of cardiovascular diseases (Kern, 2005). Of the various cardiovascular diseases, coronary heart disease (CHD) is the most prevalent cause of death, followed by stroke (Puska, 2002). Mathers (2002) also opined that of the estimated 32 million heart attacks and strokes that occur globally each year, about 12.5 million are fatal.

Coronary heart disease (CHD) or coronary artery disease (CAD), results from impeded flow to the network of blood vessels surrounding the heart and serving the myocardium (Krummel, 2004). He further stated that the major underlying cause of CHD is atherosclerosis, which involves structural and compositional changes in the inner most layer of the arteries as shown in Figure 1. These changes produce impaired or inadequate blood flow.

Kumar et al. (2005) also observed that coronary heart disease is commonly due to obstruction of the coronary arteries by atheromatous plaque. O'Leary (1999) too considered that carotid thickening is a valid indicator of generalised atherosclerosis.
Natural progression of atherosclerosis
(Ref. Krummel, 2004)

Atherosclerosis in the coronary arteries causes Myocardial Infarction (MI) and Unstable Angina (UA). A common symptom of its presence is angina pectoris, or chest pain, usually radiating down the arm and sometimes brought on by excitement or physical effort (Nix, 2005).

According to Kumar et al. (2005) no uniform syndrome and signs are initially seen in patients with CHD. Chest discomfort is usually the predominant symptom in unstable angina and acute myocardial infarction. However syndromes of CHD also occur in which ischemic chest discomfort is absent or not prominent such as asymptomatic myocardial ischemia, especially among the elderly and those with diabetes mellitus.
White (2002) describes unstable angina as a syndrome that is intermediate between chronic stable angina and myocardial infarction. It is a clinical diagnosis based on a history of chest pain and exclusion of the diagnosis of myocardial infarction (MI) by electrocardiography (ECG) or cardiac enzyme testing.

Unstable angina is the most commonly used term and has been defined by Cannon and Braunwald (2005) as the clinical presentation of chest pain that is believed to be of ischemic origin and has one of the three characteristics:

- Rest angina (pain that comes on with minimum exertion) and usually lasting more than 20 minutes (if not interrupted by nitroglycerin intake).
- New on set severe angina (that is within one month).
- Previously diagnosed angina that is distinctly increasing in frequency or occurring at a lower degree of exertion.

According to them same patients with this pattern of ischemic discomfort, especially those with prolonged chest pain, develop evidence of myocardial necrosis on the basis of cardiac serum markers (such as Creatin Kinase Muscle-Brain Function (CK-MB) or Troponin or both ) and thus have a diagnosis of non ST elevation myocardial infarction

Ischemia has been defined as tissue anemia (lack of RBC) due to obstruction of arterial inflow. Myocardial ischaemia is characterised by an
imbalance between myocardial oxygen supply and demand. Myocardial ischemia may also be caused by hypoxia when oxygen supply is reduced despite adequate blood flow and tissue perforation (Guram and Topol, 2005).

The Joint American College of Cardiology and European Society of Cardiology committee proposed an updated definition of acute, evolving, or recent myocardial infarction (American Heart Association, 2002). Typical rise and gradual fall (troponin) or more rapid rise and fall (CK- MB) of biochemical markers of myocardial necrosis with at least one of the following:

- Ischaemic symptoms
- Electrocardiographic changes such as Q waves and ST abnormalities indicative of myocardial infarction.
- Enzyme elevation indicating acute myocardial infarction.

The classic symptoms of myocardial infarction are severe, crushing substernal chest pain described as squeezing or constricting sensation with frequent radiation to the left arm, often associated with impending sense of doom. The discomfort is similar to that of angina pectoris, but it is typically more severe, of long duration (usually more than 20 minutes), and is not relieved with rest or nitroglycerin intake. Associated symptoms may include diaphoresis, dyspnea, fatigue, light-headedness, palpitation, acute confusion, indigestion, nausea, or vomiting (Deepak et al., 2004).
The pathological diagnosis of myocardial infarction requires evidence of myocyte cell death as a consequence of prolonged ischemia (Antman and Braunwald, 2005).

2.2. Prevalence of coronary heart diseases

Incidence of CHD is increasing in Asian countries and 15 to 16 percent of global mortality due to CHD is attributed by India (Pal et al., 2005). The Study of Health Assessment and Risk in Ethnic Groups (SHARE) showed a CHD prevalence of 10.7 percent among South Asians compared to 4.6 percent in Europeans (Anand et al., 2000).

Earlier studies on migrant Indians in the UK, USA, Canada and Trinidad also showed that migrant Indians had higher rates of CAD compared to the indigenous population. Mortality from CHD in men and women of Indian descent settled in overseas is higher than in other groups (Joshi et al., 2007). Thus it is consistently observed that Indians have premature CHD and higher risk for CHD (Goel et al., 2003; Palaniappan et al., 2002 Chambers et al.2000 and Enas et al., 1992).

The study by Global Burden of Diseases (GBD) showed that out of a total 9.4 million deaths in India in 1990, cardiovascular diseases caused 2.3 million deaths (25%) and 1.2 million deaths were due to CHD (Murray and Lopez, 1997). In the year 2000 they (Gupta, 2005) reported the estimated mortality from CHD in India as 1.6 million. Extrapolation of these numbers estimates the burden of CHD in India to be more than 32 million patients.
Epidemiological studies show a sizeable burden of CHD in adult rural (3-5%) and urban (7-10%) populations. Thus, there could be 30 million patients with CHD in India of whom 14 million are in urban and 16 million in rural areas. Disability Adjusted Life Years (DALYs) lost in India due to CHD according to the World Health Report, 2002 would be about 14.61 millions (WHO, 2002).

Within the Indian subcontinent also, there has been a rapid rise in CHD prevalence (Rajeshwari et al., 2005.). In 1959, Padmavati reported the prevalence of CHD to be one percent and this rose to 4.5 percent in the year 1975 (Gupta and Malhotra) and 7.9 percent in the year 1996 in subjects aged 20 years and above (Gupta and Gupta, 1996). The Chennai Urban Population Study (CUPS) carried out among 1262 individuals more than 40 years of age showed that the crude prevalence of CHD to be 11 percent while the age adjusted prevalence of CHD appears to be ten times higher in India compared to that of 40 years ago and the prevalence of CHD in urban Indians is fast approaching the figures reported in migrant Indians (Mohan et al., 2001).

A higher prevalence of CHD in urban Indians was initially reported in 1950’s by Vakil (1954). Pooled data from the states of Assam, Madhya Pradesh, Punjab, Kerala and Karnataka revealed that proportion of all cardiac admissions to various government hospitals, and incidence of CHD increased from 14 percent in 1970 to 19 percent in 1985. At Vellore (South India), admissions due to CHD in 1960 to 33 percent in 1989 indicating increasing burden (Krishnaswami et al., 1991). In a single medical college hospital in
Kerala there has been a more than 20 fold increase in admissions for acute myocardial infarction from 1966 to 1988 (Mammi et al., 1991). In Orissa, proportion of admissions due to CHD increased from 19.90 percent in 1981-1990 to 28.00 percent in 1991-2000 (Mishra et al., 2003). There are substantial regional variations in cardiovascular mortality in different parts of the country (Gupta et al., 2005), but all these studies report an increasing burden from CHD on healthcare system, especially urban hospitals, in all regions of India.

The CHD rates appeared to be higher in South India with highest in Kerala, 14 percent in urban and seven percent in rural population compared to three percent in rural north India (Enas et al. 1996). In the urban population the prevalence increased from 1.05 percent (Agra, 1960) reported by Mathur et al. and 1.04 percent (Delhi, 1962) reported by Padmavati to 6.6 percent (Chandigarh, 1968) reported by Sarvotham and Berry.

In recent years a consistent high prevalence of CHD has been reported from Delhi (9.67%, 1990) by Chadha et al. Jaipur (7.8%, 1995) by Beegom and Singh, Chennai (9.0%, 2001) by Mohan et al. Jaipur (8.1%, 2002) by Gupta et al. and Panajim (13.2%, 2004) by Pinto et al. In semi urban populations of Haryana and Kerala the prevalence has increased from 3.6 percent (Gupta and Malhotra, 1975) to 7.4 percent (Kutty et al., 1993).

The prevalence of CHD has increased from 40 per 1000 in 1968 to nearly 110 per 1000 in 2001 (Mohan et al., 2001). According to Reddy et al. (1997) urban population has a higher prevalence of CHD and its risk factors.
than rural population. The CHD prevalence in rural India is two fold higher than over all US rates (Enas, 1992) A higher prevalence of CHD in urban than in rural areas has been observed in studies carried out by ICMR during 1965-75 (ICMR, 1992). Epidemiological studies in Agra, Delhi and Chandigarh in 1960s confirmed the high prevalence of CHD in urban subjects (Gupta and Gupta, 1996). Where as, when Mathur et al. (1968) and Wig et al. (1962) determined prevalence of coronary atherosclerosis and reported lesions of similar nature and severity in urban and rural subjects.

Meta- analysis showed that coronary heart disease prevalence in urban subjects increased from one percent in 1960 to nine percent in 1995 and in rural subjects from two percent in 1974 to 3.7 percent in 1995 (Gupta and Gupta, 1996). Gupta et al. (1996) performed comparison of CHD and risk factor prevalence in urban rural populations of Haryana and reported that CHD prevalence in urban subject was twice that of the rural.

2.3. Risk factors of coronary heart diseases

The term risk factor in relation to cardiovascular disease and specifically CHD was used for the first time in 1961 in a paper on the Framingham study (Kannel, 1961). According to McGill and McMahan (2005) risk factor is any measurable character of an individual that predicts that individual's probability of experiencing the development of a clinically manifest disease. The characters may be exposure to an environmental agent (tobacco smoke), or an intervening variable (increased serum cholesterol) resulting from an environmental agent (dietary lipids), or a genetic variant (low density
lipoprotein [LDL] receptor defect), another disease (hypertension or diabetes) or an early or preclinical manifestation of CHD (electrocardiographic abnormality).

However, since the ultimate objective is to prevent the disease, much effort has been devoted to ascertaining whether the risk factor particularly those that can be modified, are truly the causes of CHD, and by implication, whether modification of risk factor will reduce the risk for disease. Although a risk factor such as male sex cannot be modified, knowledge of why it predicts the occurrence of CHD may suggest other preventive strategies.

CHD has a multi-factorial etiology, with many of the risk factors being influenced by life style. Rapid change in dietary habits coupled with decreased physical activity as a consequence of urbanization may partly explain the escalation of CHD. India is at present experiencing an epidemiological transition with high rates of urbanization. This has led to economic improvement the consequence of which is increased fast food consumption and tobacco usage and decreased physical activity (Siscovick, 2005 and Mohan and Deepa, 2004).

2.3.1. Epidemiologic studies identifying the coronary heart disease risk factors

Between 1930 and 1950, a number of reports indicated that patients with CHD had greater levels of serum cholesterol and greater blood pressure
than other patients and were predominantly male (Steiner and Domanski, 1941 and Master et al., 1939).

To support a casual relation, it was necessary to measure the suspected variables in healthy subjects to measure the subsequent incidence of CHD, and to relate the occurrence of disease to the previously measured variables. Such a study was initiated by the Division of Chronic Disease of the United States Public Health Service among the residents of Framingham, in 1948; and the project was latter transferred to the National Heart Institute in 1949 (Dawber, 1980). The study enrolled and examined about 5000 adults, 30-59 years of age free of cardiovascular disease.

In 1957, when 90 percent of the subjects had been followed for four years, about one to 20 subjects had experienced a new episode of CHD (Dawber et al., 1957). Men with hypertension, obesity or increased serum cholesterol concentration at the initial examination had two fold to six fold greater rates of new CHD events. The effect of obesity was largely accounted for by its association with hypertension. CHD was more frequent in heavy smokers, but the association was not statistically significant. Two years later, a six-year follow up report added smoking as a predictor of CHD (Dawber et al., 1959).

In one such study at the National Heart Institute in Delhi, on over 5000 patients, have shown that the risk factors to be hypertension, smoking, diabetes in that order; 10 percent of patients had no obvious risk factors while another 10 percent were cases below the age of 40 years. Multiple risk
factors occurred in about 60 percent of patients. Other risk factors have not yet been addressed (Vashist et al., 1990). In a study at the All India Institute of Medical Sciences, New Delhi, among patients below 40 years of age, smoking was the most important risk factor (Krishnaswamy, 1998).

The epidemiological studies beginning primarily in the US in the 1950’s and latter in the Europe and elsewhere have identified several risk factors that are associated with evolution of CAD and its manifestations. These risk factors are classified as non modifiable (e.g.: sex, age, genetics and positive family history) and modifiable behavioral factors (e.g.: diet, physical inactivity, smoking, alcohol consumption); biological factors (e.g.:dyslipidemia, diabetes, hypertension, obesity) and finally societal factors, which include a complex mixture of interacting socio-economic, cultural and other environmental parameters (WHO, 2005 ; Fey, 2005; Metha and Orbach, 1999 and Kahn et al. ,1997).

Risk factors of CHD have been categorised under two major heads:

- Non modifiable risk factors
- Modifiable risk factors

2.3.2. Non- modifiable risk factors

**Age :**

Age is a non- modifiable risk factor for coronary heart disease. With increasing age, higher mortality rates from CHD are seen in both genders
According to American Heart Association (1999) about four out of five people die of CHD are age 65 or older. As per the report of World Health Organisation (2002) approximately 53 percent of CHD deaths are in people younger than seventy years of age. In Asian Indians as Rajmohan et al. (2000) reported that CHD occurs prematurely i.e. at least a decade or two earlier than that seen in Europeans.

The average prevalence of CHD was 96 per 1000 persons aged 25 years and above in urban areas and 27 per 1000 of the same age Group in rural areas (ICMR, 1992).

The age of presentation of acute coronary syndrome is about five to ten years earlier in Indian patients (Gupta, 2005). An Indian multicenter study that analysed data from 4081 subjects reported that acute coronary syndrome occurred at a mean age of 56.60 ± 12 years in men and 61.80+10 years in women (Praveen et al., 2002). In developed countries the average age of presentation is higher and the US National Registry of Myocardial Infarction reported an average age of 66.00 ± 0.05 years (Peterson et al., 2003).

At older ages, women who have heart attack are twice as likely as men, to die within a few weeks. Comorbidity is often cited as a reason for high rates of mortality and complications. Age related changes in the cardiovascular system and other organs make it reasonable to assume that ageing per se constitutes a major reason for increased morbidity and mortality in older persons. These age related changes include diastolic dysfunction,
degenerative changes in the conduction system, reduced responses to catecholamine and sympathetic stimuli and major alterations in the pharmacokinetics and pharmacodynamics of drugs. Such age related changes have major implications for the response of older patients to the disease and its treatment (Friesinger and Hurst, 1998). Kasliwal et al. (2005) in a study of patients undergoing coronary angio-bypass graft surgery (CABG) at New Delhi, reported that CHD at young age was found to be significantly associated with family history and dyslipidemia as compared to hypertension and diabetes which were common in older individuals.

**Gender:**

Male sex is one of the best-documented and strongest risk factor for CHD. Men have a greater risk of heart attack than women, and they have attacks earlier in life. The incidence of premature disease in men 35 to 44 years of age is three times as high as the incidence in women of the same age. Therefore, being older than 45 years of age is considered a risk factor for men (NCEP, 2001 and McGill and Stern, 1979).

Women tend to develop atherosclerotic CHD approximately ten years later than men (AHA, 2002), and compared with premenopausal women, postmenopausal women experience a threefold increase in risk for CHD (Kannel and Wilson, 1995). The rate of CHD events in men was about twice that in women (Dawber et al., 1959).
For women, the increased risk comes after the age of 55 years, which is after menopause for most women (Krummel, 2004). But, this gap in death rate from heart disease diminishes with aging (AHA, 2001). Eighty two percent of coronary events in women are attributable to lack of a healthy lifestyle: unhealthy dietary habits, lack of activity, cigarette use, and over weight (Stampfer et al., 2000). However, since the disease occurs on an average of ten years later in women and because women have a higher incidence of other risk factors and comorbid features (particularly hypertension, obesity and diabetes) it is difficult to assess the effect of female gender per se stated Friesinger and Hurst (1998). According to them atherosclerotic coronary heart disease manifested as angina, infarct, and sudden death is as common in women after the age of 60 years as it is in men. So the overall, the risk of CHD increases markedly as one ages (McGill and McMahan, 2005).

**Family history and Genetics:**

A family history of premature disease is a strong risk factor, even when other risk factors are considered (Goel et al., 2003; Srinivasan and Sathyamoorthy, 2002; Scheuner, 2001 and Zodpey et al., 1998). A family history is considered to be positive when myocardial infarction (MI) or sudden death occurs before the age of 55 years in a male first degree relative or the age of 65 in a female first degree relative (parents, siblings, offspring) (Krummel, 2004). This risk is further increased if the age of the affected family member is under the age of 45, or the number of affected family members is two or more first degree relatives, in which case the relative risk is three to
five (Sadikot, 2006). Numerous hyperlipidemias are inheritable and lead to premature atherosclerosis and CHD (Mahan and Stump, 2004). A positive family history makes a woman, a ten-year coronary risk of the order of seven per 100 with an affected parent. An affected sibling conveys a relative risk of 2.5 at any age (Srinivasn and Sathyamoorthy, 2002).

A positive family history of either hypertension or CHD increases the risk for future disease onset in unaffected family members. Family history is more predictive when multiple family members are affected or if they are affected at young ages (Hopkins, 1992).

Investigators have found many genes and genetic variants associated with lipid and lipoprotein abnormalities and with risk for CHD. These variants include polymorphisms in genes affecting lipoproteins. Such as genes affecting homeostasis (Franco and Reitsma, 2001); genes affecting tissues of arterial wall and the inflammatory response (Buono et al., 2002); and genes affecting the responses of plasma lipoproteins on diet (Mahajan and Bermingham, 2004 and Krauss, 2001). Familial hypercholesterolemia is a genetic disorder in which the concentration of serum cholesterol is elevated from birth and leads to premature CHD. Familial hypercholesterolemia exhibits marked phenotypic variability due to genetic, metabolic and environmental factors (Bhatnagar and Deepak, 2006). Mohan et al. (2003) have demonstrated that genetic factors are stronger in Indians compared to Europeans. The application of molecular and population genetic methods combined with progress in mapping the human genome ensure that many
more genetic variants contributing to atherothrombosis and CHD will have to be discovered. The emerging knowledge of the molecular and cellular metabolism of the atherothrombotic lesion may lead to new candidate genes.

2.3.3. Modifiable risk factors

Socio- economic factors:

For many decades (Pocock et al., 1987 and Rose and Marmot, 1981) and across multiple nation (Capewell et al., 2001), differences in socio-economic status have been consistently associated with variations in CHD and mortality and rates (Rosengren et al., 2004; Capewell et al., 2001; Wolfson et al., 1999 and Zodpey et al., 1998).

Socio-economic status is defined by occupational position, education and income (John and Bhatt, 2007). A lower status is associated with smoking atherogenic diet, obesity, physical inactivity, poor living conditions and increased financial strain, which are felt to be analogous to chronic stress (Strike and Steptoe, 2004). Friesinger and Hurst (1998) stated that there are abundant data indicating the increase in death rate from any cause, in both genders, and in white and black Americans related to a variety of socio-economic features, particularly education and income. There has been the perception that conventional risk factors cluster in the lower socio-economic groups and that, this phenomenon can explain the increased incidence of atherosclerotic coronary heart disease (Kaplan and Keil, 1993). The socio-
economic status proved to be independent predictors in patients with established atherosclerotic coronary heart disease (Davey, 1997 and Williams et al., 1992). Studies of longer duration, with adjustment for multiple known risk factors, demonstrated an increased relative risk for study participants of lower socio-economic status (Liu et al., 1982). Studies conducted in United States and Europe also had similar results (Doornbos and Kromhout, 1990 and Rose and Marmot, 1981).

An instructive study involving 17,530 British civil servants demonstrated a coronary mortality rate 3.6 times higher in the group with the lowest socio-economic status (Friesinger and Hurst, 1998). Those living in disadvantageous conditions with social deprivation are particularly prone to CHD and this is now increasingly seen not only dietary based but also dependent on the way in which the poverty and social exclusion of these groups limits their capacity to cope and alters their metabolic and hormonal responses to their already inappropriate diets (John and Bhatt, 2007 and WHO, 1999).

At the same time Singh et al. (1998) reported that among rural North Indians, the prevalence of CHD and coronary risk factors such as hypercholesterolemia, hypertension, diabetes were significantly more among high and middle socio-economic group in both sexes compared to lower social classes. Reddy et al. (2002) also reported that the higher socio-economic group had a greater prevalence of CHD than lower socio-economic group. The epidemiological survey carried out by Padmavati in 1962 among
adults over 20 years of age in general population of Delhi showed a prevalence rate of CHD of 55 per 1000 in the high income group and 3.3 per 1000 in the low income group.

**Serum Lipids and Lipoproteins:**

A number of epidemiologic surveys, including those carried out between populations in seven countries and within countries (Framingham), and conducted also in migrating populations (UK), by Keys *et al.* (1986) and Kagan *et al.* (1974). Anderson *et al.* (1987) further revealed a positive association between cholesterol and rates of atherosclerotic CHD.

Although serum total cholesterol correlates with CHD risk, serum cholesterol is not homogeneous. Because cholesterol is completely insoluble in aqueous solution. This is accomplished by combining it as a complex with other lipids and other proteins. These complexes are called lipoproteins. The categories of lipids are distinguished by their densities. They include low density lipoproteins (LDL), high density lipoproteins (HDL), very low density lipoproteins (VLDL) (Grundy, 2005).

Most of the international studies like the MRFIT (Multiple Risk Factor Intervention Trial) Study group (Neaton and Wentworth, 1992); Seven Countries Study (Keys *et al.*, 1986) and Framingham Study (Castelli, 1984) emphasized the importance of elevated LDL and total cholesterol in the development of CHD. They also considered these factors as more important
than the other risk factors studied such as hypertension, smoking and diabetes.

Sharett et al. (2001) also found that, increased LDL or reduced High Density Lipoproteins (HDL) are important in the initiation and propagation of atherosclerotic plaques. According to Ghafoorunissa and Krishnaswamy (2000), elevated blood lipid levels (cholesterol and triglycerides) are the major risk factors of heart disease. Although elevated total cholesterol is strongly associated with increased risk of CHD, a more precise indicator of CHD risk is an atherogenic lipid profile characterised by high levels of LDL (Grundy, 2005 and Lehto et al., 1997). Consequently, the NCEP (2002) has identified LDL as the primary target of cholesterol lowering therapy.

Factors that influence the LDL increase are excess dietary cholesterol and saturated fatty acids, aging (Miller, 1984) and loss of oestrogen (in postmenopausal women) all seemingly decrease the activity of LDL c receptor (Erikson et al., 1989).

The link of low HDL to CHD was reinforced by the recognition that the physiologic function of HDL was reversal cholesterol transport (McGill and McMahan, 2005). Low HDL is currently recognized as a common and powerful risk factor for CHD (Sharrett et al., 2001 and Lehto et al., 1997).

Achari and Thakur (2004), reported that on a large retrospective study on CHD cases and healthy controls that the serum cholesterol levels, LDL cholesterol levels and total cholesterol to HDL cholesterol ratio were higher
among the CHD subjects compared to normal. They also observed that there is a lack of association of the serum triglycerides levels with CHD. In the case – control study by Burman et al. (2004) again LDL cholesterol levels and total cholesterol to HDL cholesterol ratio were higher among the CHD subjects compared to controls but there was no significant difference in serum triglyceride levels. In CUPS (Chennai Urban Population Study Chennai Urban Population Study), Mohan et al. (2001) noted that LDL cholesterol and age were risk factors for CHD but serum triglyceride did not come out as an independent variable. On the contrary, a study by Pais et al (1996) in survivors of acute myocardial infarction showed no association of lipid abnormalities with CHD.

There appears to be differences in lipid associations with CHD between native and migrant Indians. In-migrant Indians, serum triglyceride levels have been consistently found to be associated with CHD (McKeigue et al., 1989). However in native Indians, LDL cholesterol levels and total cholesterol to HDL cholesterol ratio appears to be more important. One factor which is common to all Indians is low HDL cholesterol (McKeigue et al., 1989). In the face of low HDL cholesterol levels, even small elevation of LDL cholesterol appears to be sufficient to produce an atherogenic profile (Mohan and Deepa, 2004).

**Obesity:**

Obesity has emerged as a major disorder associated with many metabolic diseases in both developed and developing countries. Although
obesity has a genetic etiology, the major precipitating factor is environmental, mostly related to sedentary lifestyle and causing conservation of energy as body fat (Snehaletha et al., 2003).

Obesity is associated with an atherogenic lipid profile, which is similar to that observed in subjects with the metabolic syndrome, and is more prominent in individuals with abdominal obesity. The most common lipid alteration in obese individuals is the reduction of HDL (Eckel et al., 2002 and NIH, 1998).

Epidemiological studies have shown that the ideal Body Mass Index (BMI) may differ for different populations. In Asian subjects, the risk association with diabetes and cardiovascular diseases occur at lower levels of BMI when compared with the western population (Banerji et al., 1999). This is attributed to body fat distribution; Asian Indians tend to have more visceral adipose tissue, causing higher insulin resistance, despite having lean BMI.

The clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults published by the National Institutes of Health (NIH) in 1998, operationally defined overweight as a BMI of 25 to 29.9 and obesity as a BMI of at least 30 (NIH, 1998). A waist circumference of at least 88 cm (35 inches) in woman or 102 cm (40 inches) in men has been associated with increased health risk (NIH, 1998).

On the basis of the fact that increase in health related risk factors and comorbidities associated with obesity occur at a lower BMI in Asian population than in other ethnic groups, World Health Organisation also advocated a
lower limit of normal BMI in Asian Indians (WHO, 2000). The lower cut off points for over weight and obesity are BMI greater than 23 and obesity BMI greater than 25 respectively.

Waist circumference and waist to hip circumference ratio are the most widely used indices of regional adipose tissue distribution and are similarly correlated with risk factors for CHD (Hans \textit{et al.}, 1995).

Lemieux \textit{et al.} (2000) reported that identification of men with a waist circumference of more than 90 cm and triglyceride levels of more than 2 mmol per litre may allow detection of as many as 80 percent of the subjects with the insulin resistance syndrome, which is associated with a cluster of risk factor for CHD. Obesity has an association with CHD presumably through its impact on risk factors, including hypertension, dyslipidemia, impaired glucose tolerance, and type 2 diabetes mellitus (Eckel, 1997). However, obesity independently predicts coronary atherothrombosis (McGill \textit{et al.}, 2002) and coronary events (Calle \textit{et al.}, 1999).

Overweight and obesity are strikingly related to total and LDL cholesterol. There is graded increase in cholesterol with increasing BMI (Keys, 1980). Citing the well-established contribution of obesity to the development of CHD, the American Heart Association added obesity to its list of major risk factors of CHD (Yusaf \textit{et al.}, 2004; Eckel and Krauss, 1998; Strohl \textit{et al.}, 1998 and Eikel, 1997).
There is also evidence from long-term observational studies that overweight is a predictor of cardiovascular atherosclerosis independent of its effects on traditional risk factors. The increase in relative risk occurs at levels of overweight frequently considered clinically insignificant by some (eg 72% increased risk for fatal or nonfatal CHD in middle aged men with a BMI of 25 to 29 compared with men having a BMI of <23). The relationship between degree of overweight and the development of CHD may be modified by age, sex, body fat distribution, degree of fitness and ethnicity (Lee et al., 1999).

Obesity also contributes to the development of congestive heart failure through its relationship to systemic and in normotensive and hypertensive obese patients, through increases in stroke volume and cardiac output along with diastolic dysfunction (Mahajan and Bermingham, 2004 and Sower, 1995). In patients with severe obesity, dialated cardio myopathy may lead to sudden death through predisposition to arrhythmias (Eckel, 1997).

The third edition of the Dietary Guidelines for Americans published in 1990 used an age-adjusted BMI cut off for overweight with a lower limit of 27 in adults aged 35 years or older. This adjustment was based on life insurance data showing that the BMI associated with minimum mortality rate increased with increasing age (Bray, 1998). Evidences indicated that dyslipidemia, smoking, obesity, and hyperglycemia are closely related to fatty streaks in the second decade of life and the same risk factors, along with hypertension, are associated with plaques in the third decade of life (McGill et al., 2000).
Ample evidences suggested that the presence of excess fat in the abdomen in proportion to total body fat is an independent predictor of CHD (Rexrode et al., 1998). Only recently, however has prospective evidence been provided that shows the abdominal obesity is associated with the accelerated progression of carotid atherosclerosis in men, independent of overall obesity and other risk factors and after only four years of follow up (Lakka et al., 2001).

The modifiable factors that were associated with changes in android obesity include generalized obesity, physical activity and cigarette smoking (Kahn et al., 1997). Android obesity is a risk factor for the development of type 2 diabetes, stroke, CHD and total mortality, independent of and additive to total obesity (Montague and O’Rahilly 2000 and Ward et al., 1994).

This relationship is significant in subjects with abdominal obesity and LDL cholesterol levels of more than or equal to 3.8 mmol per liter or serum apolipoprotein B levels of more than or equal to 1.01 gm per liter (Lakka et al., 2001). The abdominal distribution of body fat is associated with increased plasma levels of fibrinogen and factor VII, greater factor VIII C coagulant activities, in elevated tissue plasminogen activator antigen levels, and higher plasminogen activator inhibitor–1 antigen levels and activity (Svendsen et al., 1996). This hyper coagulable state that accompanies excessive central fat deposition may also be associated with left ventricular diastolic function and impaired endothelial function (Hashimoto et al., 1998).
The lower cut off waist circumference recommended by WHO (2000) for Asians was less than 90 cm for men and less than 80 cm for women and waist to hip ratio (WHR) as suggested by Willett *et al.* (1999) as less than 0.95 in males and less than 0.80 in females.

The waist to hip ratio (WHR) is often used as an indicator of abdominal fat mass; this ratio is difficult to interpret biologically because the waist and hip circumference measures are reflective of different anatomical entities. The waist circumference measures both visceral and subcutaneous fat, whereas the hip circumference includes fat mass, lean muscle mass and skeletal frame. The waist circumference contributes less error than does the WHR because the former is a single measurement (Molarius and Seidel, 1998). However, long term follow up studies have shown that high WHR (>1.0 in men and >0.8 in women) is associated with increased morbidity and mortality for several chronic diseases such as myocardial infarction, stroke, diabetes and cancer in both genders (Mahajan and Bermingham, 2004 and Lapidus *et al.*, 1984).

Visceral adiposity increases the risk for hyperinsulinemia and glucose intolerance at a given BMI (Despres, 2001). However, the waist circumference cut off loses predictive power in patients with a BMI of more than or equal to 35 Kg/m2 (Lemieux *et al.*, 2000).
Hypertension:

Hypertension is a common risk factor of coronary artery disease (Kasliwal et al., 2006; Goel et al., 2003; Srinivasan and Satyamurthy, 2002 and Jha et al., 1993). A general definition of hypertension is a systolic blood pressure of 140 mm Hg or higher or a diastolic blood pressure of 90 mm Hg or higher or both (Sadikot, 2006; Sharma et al., 2006; Krummel, 2004; Zodpey et al., 1998 and JNC VI, 1997).

Blood pressure is a function of cardiac output multiplied by the peripheral resistance (the resistance in the blood vessels to the flow of blood). The diameter of the blood vessel markedly affects blood flow. When the diameter is decreased (as in atherosclerosis), resistance and blood pressure increase (Krummel, 2004).

Cardiovascular disease may develop from direct effects of hypertension independent of the effects of atherothrombosis. Chronic increase of blood pressure is known to induce structural alterations in vasculature and in other organs. Thus, increasing levels of blood pressure or greater duration of hypertension can lead progressively to atherosclerosis with increased stress on the myocardium caused by lack of aortic compliance (Hopkins, 1992). Hypertension is a strong risk factor for cardiac and blood vessel damage and is associated with high morbidity and mortality (Gafoorunissa and Krishnaswamy, 2000). About 50 percent of first myocardial infarction patients have blood pressure higher than 160/90 mm of Hg (AHA, 2001).
Dietary salt intake also plays a critical role in regulating blood pressure and population with low salt intake, all other things being equal, have a lower average blood pressure level. In countries such as Lithuania, over 40 percent of adult men in rural areas are hypertensive warrants further studies on salt intake in the region and renewed emphasis on controlling hypertension by lowering salt intake to less than 5 g/day (Papas, 1998).

High blood pressure is estimated to cause 7.1 million deaths annually accounting for 13 percent of all deaths globally (WHO, 2002). About 15 to 37 percent of the adult population worldwide is afflicted with hypertension in the year 2000, a figure that is projected to increase to 29.20 percent by the year 2025 (Keamey et al., 2005). African Americans have a higher prevalence of hypertension in the world (37% of men; 37% of women) compared to non-Hispanic whites (25% of men; 21% of women).

Based on the available data, it is estimated that there are nearly 20 million hypertensives and 15 million cases of CHD in India (ICMR, 1992). Prevalence of hypertension is increasing in urban population, as compared to rural population (Gupta, 2004). Though the prevalence of hypertension in India has been reported to vary regionally, recent pooled analysis of several epidemiological studies in India suggest that hypertension is present in 25 percent adults in the urban areas, and ten percent of the individuals in rural areas (Gupta, 2004). The same study estimated that there were about 66 million hypertensives in India (32 million rural and 34 million urban). In
metropolitan cities the prevalence is as high as 11 percent to 27 percent (Gupta, 1997).

Gupta (2004) reported that hypertension is directly responsible for 24 percent of all CHD deaths in India. Gupta (2000) also reported a high prevalence of hypertension among urban adults including 36 percent of men and 37 percent women in Jaipur, 44 percent men and 45 percent women in Mumbai, 31 percent men, 36 percent women in Thiruvananthapuram.

These findings are in contrast to earlier studies conducted about 50 to 60 years ago, in which prevalence was one to four percent using older definitions (Gupta, 1997). Studies by Sharma et al. (2006) and Thankappan et al. (2006) negate the impact of affluence and family size and suggest that hypertension is equally prevalent in rich and poor.

In India the state Kerala is in an advanced stage of epidemiological transition compared to other states (Kutty, 2003). In a five city comparative study evaluating hypertension prevalence among women in the age group of 20 to 64 years, prevalence was reported to be the highest in Thiruananthapuram, the capital city of Kerala state (Singh et al., 1998). A study by Zacharia et al. (2003) also showed that the middle aged population in Thiruvananthapuram city had a very high prevalence of hypertension (54.2%). Another study of the elderly populations in Kerala and Maharashtra states of India, and Dhaka of Bangladesh reported a very high prevalence (55%) of hypertension both in urban and rural Kerala (WHO, 2001). With aging, the prevalence of high blood pressure increases (Krummel, 2004 and
Srinivasan and Satyamurthy, 2002). Before the age of 55, more men than women have high blood pressure. After age 65, the rates of high blood pressure in women in each racial group surpasses those of the men in their group. As the prevalence of hypertension rises with increasing age, more than half the older adult population (65 years of age and older) in any racial group has hypertension (Krummel, 2004).

A multicentric study covering five cities in India showed only age, obesity, BMI, and high socio-economic status to be the significant predictors of hypertension (Singh et al., 1997). A study conducted in a large town of eastern India, reported that old age, high BMI, and vegetarian diet are important predictors of hypertension (Das et al., 2005). But in a south Indian city, Shanthirini et al. (2003) found only the age and BMI as predictors of hypertension.

Even in early days, MacMohan et al. (1990) found that CHD is strongly and positively associated with blood pressure in a graded, independent, and consistent pattern, as shown in a meta analysis of nine major prospective studies. The Antihypertensive and Lipid – Lowering Treatment to Prevent Heart Attack Trial (ALLHAT, 2002) study clearly showed the benefit of antihypertensive treatment in subjects with other CHD risk factors. Their results established hypertension as a major, casual risk factor for CHD. In the Multiple Risk factor Intervention Trial (MRFIT), a six year follow up of 356,222 middle aged men showed that 32 percent of all CHD deaths could be attributed to diastolic blood pressure greater than 80 mmHg and 42 percent
could be attributed to systolic blood pressure greater than 120 mmHg (Stamler, 1993).

**Diabetes:**

According to Franz (2004), diabetes mellitus is a group of diseases characterised by high blood glucose concentrations resulting from defects in insulin secretion, insulin action or both. Diabetes prevalence increases with increasing age, affecting 18.4 percent of those in 65 years of age or older (ADA, 2001). According to American Diabetic Association (2002) and WHO (1999) the criterion for diagnosis of diabetes mellitus is fasting plasma glucose equal to or greater than 126 mg per dl. or the two hour blood sugar as 200 mg per dl. Prolonged exposure to hyperglycemia is currently recognized as the primary casual factor in the pathogenesis of diabetic complications (Grundy *et al.*, 1999). Both type I and type 2 diabetes are powerful and independent risk factors for CHD (Aronson and Rayfield, 2005).

Type 1 diabetes accounts for five percent to ten percent of all diagnosed cases of diabetes. Persons with type 1 diabetes are dependent on exogenous insulin to prevent ketoacidosis and death. Type 2 diabetes may account for 90 percent to 95 percent of all diagnosed cases of diabetes and is a progressive disease that, in many cases, is present long before it is diagnosed. Although undiagnosed, these individuals are at increased risk of developing macro vascular and micro vascular complications (Franz, 2004).
In individuals who are genetically prone to the development of type 2 diabetes, insulin resistance is the earliest detectable metabolic defect and can occur 15 to 25 years or more before the clinical onset of diabetes. It has been demonstrated that hyperinsulinaemia is associated with abdominal obesity, hyper triglyceridemia, reduced concentrations of HDL cholesterol and hypertension. This constellation of features is described as “syndrome X or metabolic syndrome ”(Misra, 2003; Misra, 1998; Zodpey et al., 1998 and Reaven and Laws, 1994). 'Atherogenic dyslipidemia’ is associated with metabolic syndrome and may be responsible for accelerated atherosclerosis (Grundy, 1998).

Current estimates of WHO indicated that about 150 million people have type 2 diabetes globally and this figure is expected to double by 2025 (Campbell, 2002 and Zimmet et al., 2001 and King et al., 1998). According to WHO by the year 2010 there are likely to be 25 million individuals in India with type 2 diabetes and by the year 2025 India will harbor the largest population of diabetic individuals in the world (King et al., 1998). The prevalence of diabetes mellitus as stated by Enas et al. (1998) is about 20 percent in the middle age and additional 20 percent may be having impaired glucose tolerance, even moderate elevation of glucose in Indians is associated with increased risk of CHD. The primary importance of the metabolic syndrome (diabetes) as highlighted by Isomaa et al.(2001) was that each of its components is an established risk factor for CHD. Alone, each component of the cluster conveys increased CHD risk; but as a combination, they become even more powerful.
The relative risk of CHD is three to four folds in diabetics (Stamler et al., 1993). Impaired glucose tolerance doubles the occurrence of CAD in men and triples or quadruples the risk in women particularly prior to age of 50 years (Wasir et al., 1991). According to Kleinman (1988) about 75 percent of mortality among diabetic men, and 57 percent among diabetic women, is attributable to cardiovascular disease deaths. The increase in coronary risk associated with diabetes is much greater for woman than for men (Huxley et al., 2007; Gu et al., 1999 and Connor et al., 1991). It is now clear that, in addition to being associated with an increased prevalence of hypertension and dyslipidemia, the elevated blood sugar levels characteristic of diabetes is itself associated with an increased risk for cardiovascular disease (Goel et al., 2003 and Grundy, 1999).

Where as Singh et al. (1997) observed that hypertension and CHD were significantly more frequent among subjects with diabetes compared to non-diabetes. Pacheco et al. (2002) reported that the prevalence of hypertension in the diabetic population is 1.5 to three times greater than that of non-diabetic age matched group. Serious cardiovascular events as reported by Stamler et al. (1993) are more than twice as likely in patients with both diabetes and hypertension than in patients with either disease alone. Excess body weight and obesity, central obesity, sedentary life style, higher visible fat intake (>25g/day) and social class 1-3 (higher and middle) were significantly associated with diabetes (Singh et al., 1997).
**Dietary Pattern:**

Diet plays an important role in maintaining ideal body weight, body fat and normal levels of lipids. The control of these parameters helps in the prevention of obesity, hypertension, hyperlipidemia, which in turn are independent diet related risk factor for thrombosis. Improper dietary practices can also trigger underlying genetic tendencies towards thrombosis (Ghafoorunnissa, 1996).

The role of diet in promoting health and preventing disease is difficult to elucidate, due to its complex network of foods and nutrients. Besides total energy intake, dietary composition is probably the most important discriminator within and between populations. Dietary composition is reflected in dietary patterns (Michels et al., 2005). The association between diet and cardiovascular diseases has been indisputably shown in numerous studies (WHO, 2005). Dietary pattern analysis may prove an informative addition in that it more fully captures the effect of total dietary behaviour in disease etiology (Jacobs and Steffen, 2003).

Many prospective cohort studies have examined the association between intake of individual nutrients or foods and risk of CHD, but few have evaluated the relation of overall dietary patterns, to the risk. Conceptually, examination of overall dietary patterns would more closely parallel the real world, where people do not eat isolated nutrients but rather meals consisting of a variety of foods with complex combinations of nutrients that may be interactive or synergistic. Studies of individual foods or nutrients can be
difficult to interpret because of strong correlations among them. In dietary pattern analysis, the overall 26.4 percent (972 million) of the adult world population collinearity of nutrients or foods can be used to advantage, because patterns are characterized on the basis of habitual food use (Wirfalt et al., 2001). Dietary pattern analysis according to Appel et al. (1997) is potentially useful in making dietary recommendations because overall dietary patterns might be easy for the public to interpret or translate into diets. It was also observed in clinical studies that changes in dietary pattern appeared to be more effective in lowering blood pressure than was supplementation with single nutrients. Dietary patterns are likely to vary by sex, socio-economic status, ethnic group and culture (Hu et al., 1999). Many risk factors for CHD, including high blood cholesterol, hypertension, obesity and diabetes are substantially influenced by dietary factors. Because these risk factors are modifiable, primary preventive efforts hold much promise (Rajaram, 2003).

Vegetarian dietary practices have been associated with a reduction in many chronic diseases, including cardiovascular disease. (Thorogood et al., 1990). A healthy vegetarian diet is characterised by more frequent consumption of fruits and vegetables, whole grains, legumes, and nuts, resulting in higher intakes of dietary fibre, antioxidants, and phytochemicals. Compared with non vegetarian diets, plant based diets are generally low in fat. So these plant foods and nutrients influence IHD (Ischemic Heart Disease) risk factors such as blood lipids, lipoproteins, blood pressure, and lipid per-oxidation, thereby reducing the overall mortality from IHD (Rajaram, 2003).
Frequent consumption of foods rich in phytochemicals such as allicin, polyphenols, isoflavones, and anthocyanins is associated with reduced incidence of CHD (Wan et al., 2001). Some foods that contain significant amounts of these phytochemicals and have been investigated in human studies included garlic (allicin), cocoa (polyphenols), soy (isoflavones), red wine and grape juice (anthocyanins). These foods are known to favorably alter some cardiovascular risk factors and thereby decrease the incidence of CHD.

➢ Dietary Fat

Ninety years of consistent scientific research indicated that the dietary fat is the most crucial factor in the causation of CHD. Diet has an important role in maintaining ideal body weight; body fat and normal levels of lipids (Krauss, 2005; WHO, 2005 and Ghafoorunnissa and Krishnaswamy, 2000).

Previous studies clearly indicated that nutritional factors appear to be important in the pathogenesis of CHD. The role of dietary fat in causing higher body fat content and also increased prevalence of CHD have been described in Indians (Heller et al., 1998). Prevalence of diabetes mellitus and dislipidemia in various subsets of Indian patients correlates with omega six to omega three ratio in dietary lipids (Wahlquist and Dalais, 1997). Correction of faulty fat intake reverses the disease process (Singh et al., 1999). Ghafoorunnissa and Krishnaswamy (2000) also emphasized that an opportune modification in dietary fat and fatty acids can bring about regression of pathological process.
Several factors determine fat intake by the Indian population. First, fat intake is income dependent and there are regional preferences in both the quality and type of fat consumed (Vinodini et al., 1993).

Cost and advertisements claiming cholesterol lowering potential of oils influence the choice of oil in the urban middle and high-income groups. Vanaspathi consumption is more common in Northern States. It is widely used in confectionary, bakery and in ready to eat foods (Katan, 2000). Purchased ghee as well as that made at home from milk contributes to its high consumption in urban middle and high-income groups (Gujarat Co-operative Milk Marketing Federation, 1993).

Vegetable oil used in cooking constitutes about 80 percent of visible fat consumption; vanaspathi and ghee are the other sources. Three major factors determine the quantity of visible fat intake by the Indian populations: (1) state wise culinary habits (2) income and (3) living in metropolitan cities, which leads to higher consumption. The vegetable oil chosen for cooking is generally single oil especially in rural areas and the choice varies region wise (Singh and Mulukuntia, 1996).

The invisible fats present in the foodstuffs also need to be accounted. Two thirds of the fat present in cereals and millets are in the bound and structural forms (Ghafoorunissa, 1989). Studies in rats, however have demonstrated that bound and structural fat in rice are biologically available (Ghafoorunissa, 1990).
Several studies were conducted on the fat intake on the incidence of CHD. In the early 1990s, a study by Browner (1991) in United States suggested that reducing fat consumption from 37 percent of energy intake to 30 percent would prevent two percent deaths from CVD primarily among people older than 65 years. Later Willett (2000) suggested that replacing saturated and trans-fatty acids in the diet with monounsaturated fat could be more important for preventing CHD than reducing the total amount of fat consumed. For example, replacing six percent of energy intake from predominantly animal fat with monounsaturated fat could potentially reduce CHD by six to eight percent.

Literature also reveals that there has been an increasing trend of replacing traditional cooking fats condemned to be atherogenic with refined vegetable oils promoted as “Heart-friendly” because of their PUFA content. Inspite of the use of such fats, the prevalence of the diseases is steadily increasing to almost epidemic proportions (Mehta, 2004).

Compelling evidences from epidemiological and clinical studies also indicated that types of fat are more important than total amount of fat in the diet in determining risk of CAD. Using fourteen year follow up data from the Nurses Health study, Hu et al. (1997) found a weak positive association between saturated fat intake and risk of CAD but a significant and strong positive association with intake of trans fatty acids. In the Nurses Health study, (Hu et al., 1997) after other fats were adjusted for monounsaturated fat intake, it was inversely associated with risk of CHD, although the association
was weaker than that for polyunsaturated fat. In metabolic studies, replacing carbohydrates with mono unsaturated fat raised HDL without affecting LDL (Mensink et al., 1992). This replacement also improved glucose tolerance and insulin sensitivity among patients with diabetes mellitus. In addition, monounsaturated fat is resistant to oxidative modification (Parthasarathy et al., 1990).

In this context the controversy pointed out by Bhatnagar et al. (1995) regarding the role of dietary fat intake and serum cholesterol level in the etiology of CAD in Indians is of interest. In India saturated fat intake may be associated with CHD in higher social class (Singh et al., 1995). It seems that the amount of total and saturated fat and dietary cholesterol consumed by Indian urbans is much lower than that reported for developed countries. However, the serum cholesterol of Indian urbans is not proportionately lower compared to serum cholesterol level in these countries (Kamath et al., 1999). Similar disparity in dietary intake and serum cholesterol levels has been observed in Hong Kong, among Chinese children, which may be due to possible genetic difference in the efficiency of handling dietary fat. Such genetic difference in handling of nutrients may be manifestation of the thrifty phenotype, which may be developed due to genetic and metabolic adaptations during scarcity or during poor nutrition in foetal life and infancy (Berenson et al., 1998).
Several studies have illustrated how diet alters serum cholesterol levels. In the seven country study, mean concentrations of cholesterol of each group were highly correlated with percentage of energy derived from saturated fatty acids, and even more strikingly related to a formula which also took into account the intake of PUFA’S (Keys, 1980).

The saturated fatty acids in the diet and not the dietary cholesterol are the primary inducers of increases in LDL cholesterol in the blood. These saturated fatty acids vary markedly in their effects. Myristic acid, largely derived from milk fat, is the major stimulus for the increased serum levels of LDL. Lauric acid, present in fat and oil from tropical plants and in milk in moderate amounts and palmitic acid, present in animal fat and tropical plant fat and oil are strong stimulators of raising LDL levels. A major saturated fat, stearic acid, present in beef and lard does not increase serum LDL cholesterol levels (Muller, 2001). A relationship between intake of milk fat and the prevalence of CHD in European countries has been shown repeatedly the powerful effect of myristic acid in milk fat. The studies showed that the substantial fall in CHD rates is predominantly explained by a fifteen percent fall in average serum cholesterol levels as the consumption of milk fat-in milk, butter and milk products-drops (Renauds and Lanzmann, 2002 and WHO, 1999). The WHO’s population nutrient goals recommends to restrict the intake of saturated fatty acids to less than ten percent, of daily energy intake and less than seven percent for high risk groups. Within these limits, the intake of
foods rich in myristic and palmitic acids should be replaced by fats with a lower content of these particular fatty acids. The amount and quality of fat supply has to be considered keeping in mind the need to meet energy requirements (WHO, 2005).

The new chemical species of trans- fatty acids produced by hydrogenation have multiple, unusual structures and have been shown to induce deleterious increases in LDL cholesterol levels and decreases in HDL cholesterol levels (Krummel, 2004). Trans fatty acids are geometrical isomers of cis-unsaturated fatty acids that adapt a saturated fatty acid like configuration. Partial hydrogenation, the process used to increase the shelf life of polyunsaturated fatty acids (PUFAs) creates trans fatty acids and also removes the critical double bonds in essential fatty acids necessary for the action (WHO, 2005). Metabolic studies have demonstrated that trans fatty acids render the plasma lipid profile even more atherogenic than saturated fatty acids, by not only elevating LDL cholesterol to similar levels but also by decreasing HDL cholesterol (Katan, 2000). Garcia et al. (2005) also observed a positive relationship between the consumption of trans fat and the development of endothelial dysfunction, a precursor of atherosclerosis. The epidemic of CHD over the last 70 to 80 years can be attributed to increased intake of both saturated and trans-fatty acids, so WHO (2005) recommends that these fatty acids constitute less than one percent of total energy intake.

Poly unsaturated fatty acid (PUFA) is important for several diversified physiological functions (Vinodini et al., 1993). Linoleic (LA) and alpha
Linolenic (ALNA) are metabolised by the same enzymes to long chain n6 PUFA. The conversion of ALNA to long chain n-3PUFA is slow due to competitive interactions in the metabolism of LA and ALNA (Simopoulos, 1988). Diet should provide an adequate intake of PUFA’s, i.e. in the range six to ten percent of daily energy intake. There should also be an optimal balance between intake of n-6 PUFA’s and n-3 PUFA’s, i.e. five to eight percent and one to two percent of daily energy intake, respectively (WHO, 2005).

In addition omega-3 polyunsaturated fats reduce the clotting tendency of blood and further minimize the thrombotic processes that are part of mechanisms underlying the development of CHD (Yochum et al., 1999). Low intake of polyunsaturated fat is linked to a much higher rate of sudden cardiac death. Various careful placebo-controlled randomized trails have shown a major reduction in the likelihood of sudden death from CHD when intakes of these fatty acids are increased, either by consumption of fatty fish twice weekly, the provision of fish oils or the inclusion of Mediterranean-type diet rich in nuts and fish (Toobert et al., 2003).

Monounsaturated fatty acids, such as those found in olive oil and rapeseed oil have a neutral effect on serum cholesterol levels (WHO, 2003). An increased intake of these fatty acids raises the level of the beneficial HDL cholesterol and reduces the circulatory fatty acids in the form of triglycerides, which are an independent risk factor of CHD (Yochum et al., 1999). Intake of oleic acid, a monounsaturated fatty acid, should make up the rest of daily
energy intake from fats, to give a daily total fat intake ranging from 15 percent up to 30 percent of daily energy intake (WHO, 2005).

These goals can be met by limiting the intake of fat from dairy and meat sources, avoiding the use of hydrogenated oils and fats in cooking and manufacture of food products, using appropriate edible vegetable oils in small amounts. Preferences should be given to food preparation practices that employ non-frying methods (WHO, 2005).

Dietary cholesterol

Cholesterol in the blood is derived from two sources: diet and endogenous synthesis. Diary fat and meat are major dietary sources. Egg yolk is particularly rich in cholesterol but unlike dairy products and meat does not provide saturated fatty acids (WHO, 2005). Although dietary cholesterol raises plasma cholesterol levels (Krummel, 2004 and Hopkins, 1992), observational evidence for an association of dietary cholesterol intake with CHD is contradictory (Hu, 1999).

In addition to the effects of dietary cholesterol alone on serum lipids, dietary SFAs and cholesterol have a synergistic effect on LDL cholesterol level. Together they decrease LDL receptor synthesis and activity, increase all lipoproteins (Etherton, 1988). The intake of cholesterol has generally been positively related to the risk of CHD after adjusting for other risk factors, such as age, blood pressure, serum cholesterol level and cigarette smoking (Krummel, 2004).
Fish and fish oil

There is strong evidence that consumption of fish, especially those species with high content of omega-3 fatty acids, confers protection from ischemic heart disease (Etherton et al., 2002 and Marckmann and Gronbaek, 1999) and that this relationship is particularly strong for CHD mortality and sudden cardiac death, which has been reported to be on an average 52 percent lower in men consuming fish at least once weekly versus men consuming less (Albert et al., 1998).

Although fish have a number of important nutritive qualities, it is likely that their major cardiovascular benefit is due to their content of omega-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) (equivalent to one portion of fatty fish per week) was associated with a 50 percent lower incidence of primary cardiac arrest compared with individuals consuming no fish (Albert et al., 2002). This effect appears to be related to enrichment of membrane phospholipids with omega-3 fatty acids and a resulting reduction in risk for abnormal cardiac conductivity (Siscovick et al., 2000). Other properties of these fatty acids that may benefit risk for CHD include antiplatelet and antiinflammatory effects, as well as reduction in plasma triglycerides at higher doses (Etherton et al., 2002).

Based on these studies, as well as results of interventional trials with omega-3 fatty acids, the American Heart Association (AHA,) recommended consumption of two portions of fish per week particularly those fish rich in omega-3 fatty acids (eg. salmon, mackerel. tuna, sword fish, herring,
sardines, lake trout). Because these fish (particularly predatory fish such as sword fish and some type of tuna) can contain significant quantities of contaminants including methyl mercury, polychlorinated biphenyls, and dioxin, the U.S. Environmental Protection Agency and the U.S. Food and Drug Administration (FDA) have provided guidelines for maximal intakes, an issue of particular concern for children and women of child bearing age. In most cases, however the recommendation of two portions per week falls within the guidelines (Krauss, 2005).

Vegetables and Fruits:

The more that people consume a variety of fruits and vegetables, the stronger the protection against CHD (WHO, 2005). Many ecological studies in countries and regions of low fruits and vegetable consumption have shown higher rates of CHD than in places where the intakes of fruits and /or vegetables are high (Ness and Powles, 1996). A detailed analysis of the geographical distribution of mortality for CHD within Albania by Gjonca and Bobak (1997) indicated that it was lowest in Southwest, where most of olive oil, fruits and vegetables are produced and consumed. They also reported that diet is the most plausible explanation for this paradox of high life expectancy in a poor country; low consumption of total energy, meat, and milk products but high consumption of fruits, vegetables and complex carbohydrate decrease the risk of CHD.

The American Heart Association and other national agencies therefore recommended a diet that includes greater than five serving of fruit and
vegetable (including berries, green leafy vegetables and cruciferous vegetables and legumes) daily. These recommendations are also based primarily on the belief that fruit and vegetable intake may reduce CHD risk through the beneficial combination of micronutrients, antioxidants, phytochemicals and fibre in these foods. These beliefs have led to the investigation of individual components of fruit and vegetable as potential preventive agents against cardiovascular diseases. Several studies relating these constituents of fruit and vegetable intake to cardiovascular disease risk found that higher intake of dietary fibre, folate or antioxidants are associated with lower risk (Law and Morris, 1998).

Significant contribution of dietary essentials through fruits and vegetables have been emphasized by many authors. Fruits and vegetables according to Zantonski (1998) are rich in dietary fibre and contain 100 compounds that may be responsible for their protective effects. These include antioxidants such as vitamin C, E, carotenoids, flavonoids, folic acid, potassium, magnesium and non-nutritive bioactive constituents such as phytoestrogens and other phytochemicals. Fruits and vegetables contain fibre and micronutrients which can reduce the risk of CHD (WHO, 2005; Law and Morris, 1998 and Rimm et al., 1996) and may account for some of the health inequalities between socio-economic classes, in addition to the traditional nutritional risk factors influencing lipid metabolism and there by the risk of CHD. Brown et al. (1999) reported that a high content of soluble dietary fibre in the diet have a cholesterol lowering effect. Fruit and vegetables are rich in dietary fibre, which has been shown to decrease LDL concentrations (Stone,
2001). According to Judd and Truswell (1985) soluble fibre may act like the lipid lowering drug cholestyramine and promote sterol excretion as well as LDL receptor mediated removal. Insoluble fibre does not influence lipid metabolism to any appreciable extent.

A study of vegetarians, vegans, fish eaters (who do not eat meat) and omnivores in Britain has enabled lipid levels to be examined over a wide range of intakes within a single population, and revealed an association between total and LDL cholesterol and intakes of SFA’s. Cholesterol had an inverse association between these lipid measurements and PUFA’s and dietary fibre (Thorogood et al., 1990).

The effect of fruits and vegetable consumption on CHD was further studied. The estimates showed that a mean increase intake of 150g per day could reduce the risk of mortality from CHD by 20 to 40 percent from stroke by up to 25 percent and from CVD by six to twenty two percent; the lowest estimates account for the impact of smoking and heavy drinking (Klerk, 1998). Raising fruit and vegetable intake is known to reduce blood pressure and serum cholesterol levels, the increased plasma antioxidants possibly preventing lipid peroxidation of LDL cholesterol (Zantonski, 1998)

- **Nuts**

Several studies have indicated an association of nut consumption with reduced cardiovascular disease risk (Albert et al., 2002; Sabate, 1999 and Hu et al., 1998). Women who consumed five ounce of nuts per week had a 35
percent lower risk of nonfatal myocardial infarction compared to those eating
less than one ounce per month (Hu et al., 1998), while men who consumed
nuts twice per week or more had a 47 percent reduction in risk for sudden
cardiac death and a 30 percent reduction in total coronary heart disease
mortality compared with those who rarely or never consume nuts (Albert et
al., 2002).

Nuts are good sources of monounsaturated fatty acids, fiber, minerals
and flavonoids. Walnuts are particularly rich in polyunsaturated fatty acids
such as linoleic(LA) and alpha-linolenic(ALNA) acid. Studies of almond intake
have indicated beneficial effects on plasma lipoproteins (Jenkins et al., 2002)
but comparisons with the effects of other nuts have not been reported
(Krauss, 2005).

Carbohydrate:

Though the association between dietary fat intake and CHD is well
established, the role of dietary carbohydrate is less clear. Murray and Lopez
(1997) is also of the opinion that the role of dietary carbohydrate is less well
recognized, although the American Nurses study reported that diet with high
glycemic index increase the risk of CHD. Other studies have shown that such
diets increase the risk of NIDDM-Type 2 Diabetes (Liu et al., 1998). Generally
high carbohydrate diets, especially diets high in sugars have been associated
As stated by All India Heart Foundation (AIHF, 1999) there are certain subsets of carbohydrate, which have a higher glycemic index and are associated with low HDL cholesterol concentration. The Glycemic index (GI) is the area of the blood glucose curve produced by a certain food, expressed as a percentage of the area produced by the same amount of carbohydrates eaten as glucose or white bread. The dietary GI was positively associated with risk of CHD in a large prospective study, the Nurses Health Study. It was concluded that people whose dietary carbohydrates had a low GI had higher concentration of HDL Cholesterol than did other groups, independent of other factors (Jeppersen et al., 1998).

At the same time a study by Liu (1998) has shown that high glycemic load does not appear to affect risk of CHD among women with low BMI’s (<23). This finding may partly explain why some populations, such as those in rural China, have low rates of CHD despite high carbohydrate intakes. Traditionally, these populations consume carbohydrates in less refined forms, have high amounts of physical activity, and have a low prevalence of obesity. These factors can improve insulin sensitivity and may lead to greater tolerance of a relatively high glycemic load. High glycemic index carbohydrates are characterized by rapid absorption and increased post-prandial glucose and insulin responses reported Wolever (1990). Low insulin sensitivity, like low HDL cholesterol concentration, is associated with CHD.

However an exhaustive review published by Parks and Hellerstien (2000) on carbohydrate induced hypertriglyceredemia concluded that if the
carbohydrate content of a high carbohydrate diet is made up primarily of monosaccharides, particularly fructose, the ensuing hypertriglyceredemia is more extreme than if oligo and polysaccharides are consumed. Purified diets, whether based on starch or monosaccharides, induce hypertriglyceredemia more readily than do diets higher in fibre in which most of the carbohydrate is derived from unprocessed whole foods.

**Personal habits and lifestyle:**

**Smoking**

Tobacco smoking is “the most important of the known modifiable risk factors for CHD” (McGill and McMahan, 2005; Pradeepkumar et al., 2005; WHO, 2005; Bazzano, 2003 and Zodpey et al., 1998). Smoking accelerates atherogenesis and increases risk for manifestation of CHD. Heart disease is strongly associated with tobacco use (Rani et al., 2003; Shimkhada and Peabody, 2003 and Gupta et al., 1997).

According to the Indian Council of Medical Research (ICMR), in India each year nearly 4.5 million develop heart disease and 3.9 million develop chronic obstructive lung disease as a result of tobacco consumption (Pai, 2001; Kumar, 2000 and ICMR, 1992). In India, tobacco is smoked both as cigarettes and beedies (Pais et al., 2001). Beedi is a hand rolled tobacco leaf of 4.0-7.5 cm containing 0.15-0.25 g of tobacco (Gupta et al., 2005). Taking a conservative estimate of a two-fold risk of smokers developing CHD, the
number of cases attributable to smoking would be nearly 21 percent or 1.3 million of prevalent CHD (ICMR, 1992).

The earliest data on tobacco use in Kerala comes from a multicentre study in 1969, which included the Ernakulam district of Kerala. Mehta et al. (1969) reported that there was a 22 percent prevalence of current smoking among men and 0.4 percent among women equal to or greater than 15 years of age. During a ten-year follow up study, a five percent increase in tobacco use was reported (Gupta et al., 1980). Another study in Thiruananthapuram district in 1995 reported a prevalence of 50.1 percent for current smoking among men and 1.7 percent among women 35 years and more of age (Sankaranarayanan et al., 2000). The fiftieth National Sample Survey (NSS, 1998) conducted in Kerala in 1993-1994 reported that the prevalence of smoking was 31.6 percent among men and 0.6 percent among women 15 years and more of age. Data from the National Family Health Survey (NFHS, 2001), a cross sectional survey done in 1998-1999 among a sample of 2834 Kerala households reported that the current smoking prevalence for men was 28 percent and for women less than one percent.

Smoking was independently associated with four-fold risk of AMI with a clear dose effect (Pais et al., 1996). A study among southern India estimates that 70 lakhs death per year in India as a result of smoking (Gajalakshmi et al., 2003). It is estimated that 60 percent of patients below 40 years of age with heart disease use tobacco (Gupta et al., 1997). Smoking is of particular concern for patients with diabetes and hypertension (Sacco et al., 1999).
Compared to men with less than 12 years of schooling, those with less than 5 years of schooling were seven times more likely to smoke (Pradeepkumar et al., 2005). Krummel, (2004) also reported that smoking prevalence is higher in persons with less than high school education (35%) compared to those with college education (12%).

Smoking is associated with lower levels of HDLc, opined Rader (2005). Clinically, smoking decreases HDL cholesterol (by an average of 6-8 mg/dl) and increases VLDL cholesterol and blood sugar levels. After quitting, CHD risk decreases by 50 percent and within 15 years the relative risk of CHD mortality approaches that of a lifetime non-smoker (AHA, 2002).

➢ Alcoholism

Alcohol results in hypertriglyceridemia by providing an increased energy intake, and also by stimulating hepatic synthesis (Banoona and Lieber, 1975). Moderate alcohol intake of one to two drinks daily protects against CHD and ischemic stroke but increase the risk of sub-arachnoid hemorrhage (Colditz, 1990). Significant alcohol use was defined as daily consumption of at least one unit (equivalent to 300ml of beer and 30 ml of other spirits such as whisky, rum, gin and vodka) (Banerji et al., 1999).

The benefit of light to moderate alcohol intake seems to be mediated largely by a decrease in the risk of coronary mortality (Thunji, 1997). However, the interactions of alcohol intake with serum cholesterol appear to be unique. The CHD events rate was highest for non-drinkers and lowest for
those taking one to six alcoholic beverages per week. High alcohol intake was not protective when serum cholesterol was greater than 249 mg/dl. Moreover for all serum cholesterol categories, alcohol had a “u” shaped relationship with CHD events, with CHD events higher for both non-drinkers and for those ingesting more than one alcoholic beverage per day.

Epidemiological studies have also supported this protective effect of moderate alcohol consumption on the risk of CHD. Several studies have demonstrated that beer as well as red wine has beneficial effects in protecting against CHD (Brenner et al., 2001).

Bobak et al. (2000) in his study of beer drinkers, also found the lowest risk of myocardial infarction among men who drank almost daily and who drank four to nine liters of beer a week. They further observed that the protective effect was lost in men who drank twice a day or more. This is similar to result of studies of other beverages.

Moderate alcohol consumption, up to two drinks per day, was significantly protective for stroke after adjustment for cardiac disease, hypertension, diabetes, current smoking, body mass index and education (Howard et al., 1998).

The association of alcohol intake to non-cardiovascular mortality is less consistent; risk possibly decrease with light to moderate intake but increases sharply in heavy drinkers because of accidents, liver disease, and certain cancers as stated by Longnecker and Enger (1996).
Reduced physical activity

An early study comparing the incidence of CHD among the London bus drivers (sedentary) and conductors (active) suggested that the physical activity protected men from CHD (Morris et al., 1953). Increased physical activity and fitness are clearly associated with reductions in the risk of cardiovascular disease, (Kraus et al., 2002; Zodpey et al., 1998; Singh et al., 1995; Blair et al., 1995., Blair et al.,1989;, Leon et al.,1987 and Paffenbarger et al.,1986)

Physical activity also contributes to maintain a lower blood pressure throughout life and to lowering the ratio of LDL to HDL cholesterol in the blood. The benefits of physical activity explain its substantial importance in limiting death and illness from CHD (WHO, 2005) Moderate physical activity favorably affects HDL cholesterol concentration, blood pressure, body weight, and insulin resistance mechanisms by which it may reduce CHD risk (McGill and McMahan, 2005 and Krummel, 2004).

Opportunities for people to be physically active exist in the four major domains of their day-to-day lives: at work; for transport (eg: walking or cycling to work); in domestic duties and in leisure time or recreational activities. Physical inactivity as defined by WHO (2002) is doing very little or no physical activity in any of these domains.

Physical inactivity, or a low level of fitness, is an independent risk factor for CHD and is estimated to cause, globally, about 22 percent of CHD (WHO,
Twelve percent of all mortality in the United States is related to sedentary people, who have twice the risk of developing CHD as do active people (Powell, 1987). Despite the public health recommendations to increase activity levels, 29 to 38 percent of adults in national surveys reported no leisure time physical activity (Schoenborn and Barnes, 2002). In addition to its possible role as a primary risk factor for the development of CHD, physical inactivity may affect the secondary association of other cardiac risk factors (Caspersen et al., 1991). The Framingham Offspring Study found that patients who participated in at least one hour of conditioning activities per week had an improved cardiac risk profile when HDL, heart rate, body mass index, and tobacco use were analysed (Daneberg et al., 1989).

Moderate physical activity favorably affects HDL cholesterol concentration, blood pressure, body weight, and insulin resistance, mechanisms by which it may reduce CHD risk (Berlin and Colditz, 1990). Physical activity may also protect one from myocardial infarction by improving the efficacy of cardiac function (McGill and McMahan, 2005). Even the beginning of moderate physical activity in the middle age was associated with less risk for CHD (Paffenbarger et al., 1993).

### Stress

According to Atwater and Duffy (1999), stress can be defined as one pattern of responses an individual makes to stimulus-events that disturb his or her equilibrium or exceeding coping abilities. A stressor is an environmental condition or psychological factor that results in stress. In modern medicine,
psychosomatic physicians have described links between stressful life events, specific personality traits and the development of CHD and hypertension (Katon et al., 1992). As early as 1940’s Kemple (1945) found that coronary patients can be characterised as aggressive, hostile, reactive, power and prestige seeking and depend on external achievement for satisfaction and security.


The harmful potential of emotional stress on the cardiovascular system has been reviewed extensively (Rozanski et al., 1999 and Singh et al., 1999). Constructs like "job strain"(Karasek and Theorell, 1996), "vital exhaustion"(Kop, 1999), and low socio-economic status, the latter actually referring to a wide range of socio-economic measures (Kaplan and Keil, 1993), have all been suggested as independent risk factors for cardiovascular disease.

A behavioural style that has received much attention as a risk factor of coronary heart disease is type A, coronary-prone behaviour, characterized by
a sense of competitiveness, time urgency, and over commitment. The primary cardiovascular risk of the type A behaviour, and of its hostility-anger complex in particular, may involve endothelial damage and presumably hemostatic activation because of pronounced hemodynamic and neuro-endocrine reactivity to environmental stressors in persons with high trait hostility and anger (Suls et al., 1993). Despite substantial research since Friedman and Rosenman (1974) originated the concept in the mid 1970’s no one has been able to identify the precise aspects of the type A behaviour pattern that engenders (provoke) the heart disease risk, and this concept is gradually losing favour among researchers (Sauter et al., 1998).

Several studies have found increased mortality from CAD and a poorer outcome in the aftermath of a coronary event among depressed individuals (Jain, 2006 and Wulsin and Singal, 2003). Recent literature also points to a possible link between anxiety disorders and cardiovascular events, with the strongest evidence for phobic anxiety (Jain, 2006 and Hemingway and Marmot, 1999).

Measures of depression, anxiety, hostility and anger have been shown to be associated with CHD in prospective studies (Jain, 2006, Wulsin and Singal, 2003; Rugulies, 2002 and Bishop and Robinson, 2000). Psychosocial factors may be related to atherosclerosis through their association with behavioural risk factors, such as smoking, physical activity and diet. Psychosocial factors may also directly affect biological process such as inflammation (Kop et al., 2002 and Suarez et al., 2002), hemostasis (Strike and
Steptoe, 2004 and Frimerman et al., 1997), cardiovascular reactivity (Finney et al., 2002 and Guyll and Contrada, 1998), endothelial injury and endothelial function (Rajagopalan et al., 2001; Ghiadoni et al., 2000 and Skantze et al., 1998), platelet activation (Shimbo et al., 2002 and Markovitz, 1998), autonomic function (Stein et al., 2000) and abdominal obesity (Björntorp, 2001), that are involved in the development of atherosclerosis.

The National Institute for Occupational Safety and Health (NIOSH, 1999) defines job stress as “the harmful physical and emotional responses that occur when the requirements of the job do not match the capabilities, resources, or needs of the worker. Considerable evidence indicated that occupational stress contributes to a wide range of health effects (NIOSH, 1999 and Sauter et al., 1998). According to Sauter et al. (1998) job stress is a leading cause of worker disability in Europe and the United States. Stress produces changes in the level of antibodies in the blood and may alter cell mediated immunity, although it is not known whether these changes are long lasting and represent an adverse health effect (Ursin, 1998 and Olff et al., 1995).

According to Schanll et al. (1994) the chronic pathophysiologic effects of stress are usually considered under the rubric of psychosomatic disorders like headache and gastritis or may encompass such diseases as cardiovascular disease, hypertension and ulcers. Studies since the mid 1970’s have shown significant associations between high-strain occupations and subsequent development of cardiovascular disease, after analytically
controlling for other potential risk factors such as age, smoking, education and obesity. Between 1981 and 1988, most of the more than 40 studies have found significant, positive associations between job strain and cardiovascular disease.

Hellerstedt and Jeffery (1997) stated that basic agreements among researchers that job stress affects behavioural outcomes such as absenteeism, substance abuse, sleep disturbances, smoking, and caffeine use. Many investigators have concluded that the most important factor ameliorating the stress response is social support. Social support includes emotional, informational, and instrumental support. A large amount of research has demonstrated that social support can reduce the adverse health effects of stress (Sauter et al., 1998).

Stress is associated with following emotional changes as given by Reber and Reber (2001):

- Anxiety – a vague, unpleasant emotional state with qualities of apprehension, dread, distress and uneasiness.

- Fatigue – The internal state or condition that results from extended effort and underlies the diminished capacity to perform; this causes a feeling of weariness or tiredness.

- Conflict – an extremity broad term used to refer to any situation in which there are mutually antagonistic events, motives, purposes, behaviours and impulses.
➢ Depression – a mood or state characterised by a sense of inadequacy, a feeling of despondency, a decrease in activity, pessimism, sadness, and related symptoms.

➢ Hostility – a long lasting emotional state characterised by enimity towards others and manifested by desire to harm or inflict pain upon those at whom it is directed.

➢ Anger as defined by Atwater and Duffy (1999) is a feeling of displeasure or resentment over mistreatment.

2.3.4. New risk factors

Recently, a number of newer cardio vascular risk factors have been identified. These factors are of great interest in native Indians where more than 60 percent of the CHD remains unexplained by conventional risk factors (Mohan and Deepa, 2004). CHD may be related to non-traditional risk factors such as C-reactive protein, fibrinogen, lipoprotein and homocystine. Comparative studies on newer risk factors illustrated that Asian Indians have higher C-reactive protein, plasminogen activator inhibitor (PAI 1), and homocystine levels (Sadikot, 2006 and Deepa et al., 2002). The current evidence is insufficient to conclusively support the additive value of these special risk factors over conventional risk factors (Hackam and Anand, 2003).
Homocysteine:

Homocysteine is a non essential amino acid that is not found in the diet. Dietary methionine is converted to homocysteine in the cellular space, where it can be metabolized by pathways that use either pyridoxine (vitamin B6) or cobalamine (vitamin B12) as co-factors (John and Bhatt, 2007).

Elevated plasma levels of homocysteine, an intermediate formed during the metabolism of methionine, are associated with a modest increase in the risk of CHD (Wald et al., 2002; Ridker et al., 1999 and Welch and Loscalzo, 1998). A ten percent increase in circulating homocysteine increases the risk of heart disease by ten to 15 percent (Boushey et al., 1995).

Possible mechanisms by which hyperhomocysteinemia plays a role in atherogenesis are endothelial damage, smooth muscle cell proliferation, alterations in arachidonic acid metabolism, promotion of pro-coagulant activity and possible interactions with or modification of the effects of other risk factors like elevated LDL fractions and low HDL. (Sadikot, 2006; Ellen, 1996; Fortin and Ernest, 1995 and Hajjer, 1993). Clarke et al. (1991) found high homocysteine levels in 42 percent of patients with cerebrovascular diseases, 28 percent of patients with peripheral vascular disease and 30 percent of cases with CVD. Others found that the mean homocysteine level of patients with coronary,
peripheral and cerebrovascular diseases was significantly higher than that of comparable controls.

In the physician’s Health study, subjects with homocysteine levels in the upper 5th percentile had an MI (Myocardial Infarction) rate three times that of the rest of cohort (Stampfer et al., 1992) In the Framingham study 40 percent of subjects were found to have increased levels of homocysteine associated with low intakes of folic acid and vitamin B6. All these individuals all demonstrated significantly increased carotid artery stenosis (Sellub et al., 1995). New evidence suggests that the deficiency of folate lead to increased risk of CVD. Inadequate levels of folates raise levels of plasma homocysteine and elevated plasma homocysteine has been associated with increased risk of CHD. This level can be reduced by extra folic acid intake (Yu et al., 1998).

**Lipoprotein(a):**

Lipoprotein (a) is a specialised form of LDL discovered by Berg (1963) more than 40 years ago. This represents a class of lipoprotein particles having a protein moiety apolipoprotein-100, linked to apolipoprotein(a), by disulfide bridges. The fourth krinkle of apolipoprotein(a) exhibits a marked degree of homology with plasminogen apo-a and represents a quantitative genetic trait transmitted in an autosomal codominant mode (Scanu ,2005 and Malhotra et al., 1997). Lipoprotein (a) levels have been consistently shown to be elevated among Asian Indians compared to other ethnic groups suggesting a genetic predisposition to CHD (Enas, 2001 and Bhatnagar et al., 1995).
The combination of high lipoprotein (a) and high homocysteine levels is very common among Indians and carries a 32 fold increased risk of CHD (Hopkins et al., 1997).

**C- reactive protein:**

Elements of a chronic inflammatory reaction in atherosclerotic lesions led to the discovery that the plasma concentration of C- reactive protein (CRP), a trace plasma protein secreted in response to inflammation, was associated with CHD (Berk, 1990). This association has been confirmed in a number of case- control studies and prospective studies (DeFrranti and Rifai, 2002). C-reactive protein is believed to be both a marker and a mediator of atherosclerosis (John and Bhatt, 2007). Increased CRP levels also are associated with obesity, but multivariate analysis indicate that the CRP association is independent of obesity and other CHD risk factors (Albert et al., 2002). In the Physicians’ Health Study the risk of MI was three times greater in people in the highest CRP quartile compared to the controls (Ridker et al., 1997).

**Foetal programming:**

A study of 1586 men born in Sheffield, UK, during 1907-1925, showed that it was particularly the people who were small at birth as a result of growth retardation, rather than those born prematurely, had an increased risk of the disease. Replication of UK findings has led to wide acceptance that low rates of foetal growth are associated with CHD in later life .For example,
confirmation of a link between low birth weight and adult CHD has come from
studies of 1200 men in Caperhilly, South Wales, and of 70297 nurses in USA
(Frankel et al., 1996). The latter study found two fold fall in the relative risk of
non-fatal CHD across the range of birth weight. Similarly, among 517 men
and women in Mysore, South India, the prevalence of CHD in men and
women aged 45 years or older fell from 15 percent in those who weighed 2.5
kg or less at birth to four percent in those who weighed 3.2 kg or more (Barker
and Godfrey, 2004). Several studies have shown the inverse association
between birth weight and prevalence and mortality of CHD in adult life
(Frankel et al., 1996). These studies therefore suggested that early life
influences may contribute to the risk of CVD later in life (Berenson et al.,
1998).

Leon et al. (1996) and Pond (1985) found that the inverse association
of birth weight with glucose tolerance and with blood pressure were most
pronounced among people with high body mass indices (BMI) in adulthood.
Frankel et al. (1996) reported an inverse association between birth weight and
CHD in a cohort from South Wales, for subjects whose information was
recorded on early life socio-economic experience, biological, behavioural and
socio-economic risk factors in middle age, and subsequent ten-year incidence
of CHD. Similarly Barker (1994) also observed the association of birth weight
with adult glucose tolerance, blood pressure and it was found a strong
indicator of risk of CHD only among obese adults.
Studies of the offspring’s whose mothers experienced severe malnutrition at the end of World War II in Netherlands, have shown that adulthood obesity was less prevalent among those exposed late in gestation and in early infancy and more prevalent among those exposed during the first two trimesters of pregnancy than in unexposed people (Pond, 1985).

Adults today may still therefore be impacted by their childhood lifestyle, including diet. Health behavior learned in childhood may also be carried over into adulthood (Kelder et al., 1994). Thus diet in childhood may play an important role in developing CVD in adulthood.

**Oxidative stress:**

Oxidative stress has been identified throughout the process of atherogenesis, beginning at the early stage when endothelial dysfunction is barely apparent. As the process of atherogenesis proceeds, inflammatory cells, as well as other constituents of the atherosclerotic plaque release large amounts of reactive oxygen species (ROS), which further facilitate atherogenesis. In general increased production of reactive oxygen species may affect three fundamental mechanisms that contribute to atherogenesis, oxidation of LDL, endothelial cells dysfunction, and monocytes migration (Berliner and Heinecke, 1996). A number of studies suggest that ROS oxidize lipids and that the oxidatively modified LDL is a more potent proatherosclerotic mediator than the native unmodified LDL. Cardiovascular diseases resulting from oxidative damage may be prevented and or mitigated by dietary antioxidants (Bowen and Omaye, 1997). In the last 20 years many basic
clinical and epidemiological research has suggested a potential protective effect of antioxidant nutrients such as β-carotene, vitamin C, vitamin E and Zinc on the risk of cancer and cardiovascular diseases (May et al., 1998; Byers et al., 1992 and Jialal et al., 1991). Vitamin A has an antioxidant activity against the thyl radical whilst its precursor, β-carotene is a multifunctional lipid soluble antioxidant capable of physiologically quenching singlet oxygen and inhibiting free radical chain reactions (Jialal et al., 1991).

The habitual intake of flavonoids from food sources such as tea may lead to a lower risk of atherosclerosis and CHD and also protect against stroke (Tijburg et al., 1997). This seems reasonable since tea pigments can reduce blood coagulability, increase fibrinolysis, prevent platelet adhesion and decrease cholesterol content in aortic walls. Green and black teas are able to protect against nitric oxide toxicity. In addition the consumption of quercetin may protect against CVD by reducing capillary fragility and inhibiting platelet aggregation (Gaby, 1998). There is a large body of evidence to suggest that high dietary intake of fruits and vegetables are associated with decreased incidence of CHD (Ness and Powles, 1996).

The consumption of nutrients from fruits and vegetables, such as dietary fibre, potassium and antioxidant vitamins, has been associated with a reduced risk of CVD in prospective studies (Iso et al., 1999). However, when the cardiovascular protective effect of some of these nutrients, for example antioxidant vitamins, was tested in clinical trials, the results were at best non-significant (Marchioli et al., 2001). In this respect, short term clinical trials have
shown that diets supplemented with fruits and vegetables are associated with a lowering of blood pressure and plasma cholesterol (Appel et al., 1997). Finally, multifactorial intervention trials including increased fruit and vegetables consumption in survivors of myocardial infarction (MI) events have demonstrated major reductions in the recurrence of cardiac events despite modest changes in cardiovascular risk factors (Singh et al., 2002).

**Fibrinogen and CHD:**

Serum fibrinogen is an independent and newer risk factor for CHD. Fibrinogen increases the blood viscosity and plays a key role in thrombosis (Rissam et al., 2001). A number of prospective studies have shown plasma fibrinogen to be a highly significant risk factor in the development of CHD. Fibrinogen is a large glycol-protein having a normal level of 1.5 to 4gm/dl. Various factors affect its level in the circulation. Fibrinogen was found to be a major independent risk factor in several population studies including Framingham (Ernest and Koenig, 1997 and Ernest, 1993).

Plasminogen activator inhibitor I (PAI-1) is a fast acting inhibitor of lipoprotien(a) and constitutes the key regulator in fibrinolytic system. Elevated PAI-1 levels are present in several conditions including those individuals who have central obesity, high levels of triglycerides and increased insulin resistance (Eirkssan, 1995). Increased PAI-1 expression has been demonstrated in smooth muscle cells and macrophages of the atherosclerotic plaques, suggesting that PAI-1 may play a role in atherogenesis as well (Loukianos, 1996).
Thrombogenic factors show a declining trend in people eating fish oil. Most commonly the bleeding time prolonged, platelet aggregation is inhibited and thromboxane production in platelets (a vaso-constrictive effect) is suppressed, PAI-1 or inhibitor of plasminogen is lowered (Tremoli, 1995).

Factors associated with an elevated fibrinogen are smoking, sedentary life style, elevated triglycerides, and genetic factors (Wood, 2001). Genes explain 30 percent to 50 percent of the variability in fibrinogen levels (deMaat, 2001).