CHAPTER-2

REVIEW OF LITERATURE

The study of literature is an essential step to have a clear idea of what has been done on the problem under the study. Literature review helps to discover what is already known, what methods had been hopeful and what disappointing, and what remains to be explored. A serious attempt has been made to go through the related literature and concise review of the studies related to the present problem has been described in this chapter.

The term ‘Ischaemic Heart Disease’ (IHD) encompasses a spectrum of patients who present with chest discomfort or other symptoms caused by myocardial ischaemia. The unification of these manifestations of coronary artery disease under a single term reflects the understanding that these are caused by a similar pathophysiology, characterized by erosion, fissuring, or rupture of a pre-existing plaque, leading to intravascular thrombosis and impaired myocardial blood supply (Theroux et al., 1998).

2.1 MAJOR RISK FACTORS OF CAD

Risk factor is defined as any ascertainable characteristic circumstance of a person or a group of persons that is known to be associated with an abnormal risk of having developed or being especially adversely affected by morbid process (Gorden et al., 1982). Epidemiological studies have clearly demonstrated a link between certain risk factors and coronary artery disease (Yusuf et al., 2001). These risk factors have been divided into different categories (Boudi et al., 2012) as given below:

2.1.1 Classification of Risk Factors

A. Potential or partially reversible risk factors

1. Hyperlipidemias
2. Low levels of high density lipoproteins
3. Hyperglycemia and Diabetes mellitus
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4. Hyperinsulinemia
5. Lipoprotein (a)
6. Apolipoprotein A-I
7. Apolipoprotein B
8. Homocysteine

B. Reversible risk factors
1. Cigarette smoking
2. Hypertension
3. Obesity

2.2 Partially Reversible Potential Risk Factors

2.2.1 Lipoproteins

Epidemiological studies have revealed a positive relationship between total cholesterol concentrations and mortality from coronary heart disease (CHD). Total cholesterol does not precisely predict the risk of CHD in many patients, however, because it is the sum of all cholesterol carried not only by atherogenic lipoproteins.

Total cholesterol does not predict, because it is the sum of all cholesterol and these are of five major types: very low-density lipoproteins (VLDL); low density lipoproteins (LDL); high density lipoproteins (HDL) and Intermediary lipoproteins (IDL). Of these four are atherogenic while HDL is antiatherogenic. No epidemiological data is available to assess the risk associated with chylomicrons and IDL. In general population, the three most important cholesterol carrying lipoprotein particle systems are LDL, VLDL and HDL. LDL fraction is a high predictor for IHD in younger subjects (Navab et al., 1996).

The VLDL carries most of the plasma triacylglycerol and cholesterol in the fasting state. However, it has not shown an independent impact as a risk factor for IHD. About one quarter of cholesterol found in blood is normally linked to HDL. Higher levels of HDL fraction lower the risk of IHD. HDL retards atherosclerotic process by competing with LDL for binding in tissues, thus interfering with the cellular uptake of LDL. In addition,
HDL plays important role in eliminating cholesterol from the body. A direct relationship has been reported between total plasma cholesterol and LDL-cholesterol and the risk of coronary artery disease (Castelli, 1984; Stamler et al., 1986). The risk of IHD was found to be significantly increased in men who had high LDL-Cholesterol (Lamarche et al., 1998). The prospective study suggests that the measurement of fasting LDL particle size may offer information on risk of IHD.

**Lipoprotein (a)**

Over the last decade lipoprotein (a) has been developed as a risk factor for atherosclerosis (Rosengen et al., 1990; Sigrudson et al., 1992; Danesh et al., 2000; Von Eckardstein et al., 2001; Geethanjali et al., 2002). The unique characteristic of this risk factor is its strong genetic control by the apolipoprotein (a) gene. Lp(a) was first described by (Berg, 1963) to be a dominantly inherited low-density lipoprotein (LDL)-risk particle in human plasma. It differs in structure from LDL by the highly polymorphic glycoprotein, Apo (a) which is covalently linked to Apo B moiety of LDL by a single disulphide bridge (Mchean et al., 1987). Protein and cDNA sequencing of Apo (a) have discovered a high degree of homology to plasminogen (Kratzin et al., 1987). Lp(a) is synthesized primarily in the liver (Kraft et al., 1996). The rate of Lp(a) catabolism does not correlate with Lp(a) plasma concentrations, which suggests, that Lp(a) plasma levels are controlled by synthesis rather than by catabolism. The distribution of Lp(a) in the general population is extremely broad (Uttermann et al., 1987).

There are no significant differences in Lp(a) concentrations between men and women. In healthy individuals the concentrations remain approximately unchanged during life, except in later life when Lp(a) reportedly increases in post menopausal women (Farish et al., 1993). The genetic disorders can influence Lp(a) plasma concentrations. The plasma of patients with betalipoproteinemia shows very low concentrations of Lp(a) (Menzel et al., 1990). Patients with lipoprotein, lipase deficiency (Sandholzer et al., 1992) have markedly reduced Lp(a) levels. The effect of familial hyper-cholesterolemia on Lp(a) levels is controversial. Data from family studies suggest the LDL receptor mutations have no effect on Lp(a) levels, but studies of unrelated patients have consistently revealed an association of familial hypercholesterolemia with high Lp(a) levels. The nature of this
association is presently unclear (Uttermann et al., 1995). There is clear evidence that Lp(a) is elevated in patients with nephrotic syndrome (Wanner et al., 1995). Since Lp (a) is synthesized in the liver, decrease of Lp(a) in liver diseases has been noticed (Feely et al., 1992; Gregory et al., 1994). Alcohol consumption, sex hormones and anabolic steroid hormones decrease Lp(a) level (Crooke et al., 1992; Frazer et al., 1995). During pregnancy (Zechner et al., 1996), in postmenopausal women (Schriewer et al., 1994) and in patients with primary gout Lp (a) was found to be elevated (Takahashi et al., 1995). Studies in cancer patients revealed elevated Lp(a) values as compared to controls (Wright et al., 1989; Werseh et al., 1994). An association between Lp(a) and coronary heart disease was first described by (Dahlen, 1974). It has been estimated from case control data that normolipidemic patients with Lp(a) plasma concentrations higher than 30 mg/dl have a 1.75 fold elevated risk of suffering a myocardial infarction. There has been a significant increase reported for Lp(a) levels in patients with myocardial infarction (Armstrong et al., 1986; Dahlen, 1986; Sandkump et al., 1990; Genest et al., 1991; Sandholzer et al., 1992).

Apo lipoprotein (a) gene locus determines the risk for coronary artery disease through its allelic control of plasma Lp(a) concentration. A 2.7 fold higher risk for coronary artery disease has been reported in patients with Lp(a) plasma concentration higher than 30 mg/dl compared to patients with Lp(a) lesser than 5 mg/dl. The combination of high Lp(a) with LDL cholesterol levels amplified the risk to six fold (Armstrong et al., 1986). Several prospective studies have pointed out high Lp(a) levels as an independent risk factors for coronary artery disease (Rosengen et al., 1990; Wald et al., 1994). Higher Lp(a) values have been observed in patients with recurrent stenosis than in patients without stenosis (Desmarain et al., 1995).

Nicotinic acid and its derivative niceritrol revealed a reduction in Lp(a) levels in patients with Lp(a) levels greater than 30 mg/dl in the study conducted by (Nakahama et al., 1993). Lp(a) lowering steroid hormones are not indicated because of their side effects (Frazer et al., 1995). A promising specific Lp(a) lowering effect of the antiestrogen tamoxifen has been described (Love et al., 1994; Shewmon et al., 1994). Lipoprotein (a) measurement is very tricky; therefore, various laboratories can have very divergent and hardly comparable results. The reasons for this are different assay methodologies.
(ELISA, RIA, Radial immunodiffusion, Nephelometry etc.) and the use of different antibodies and standards. Some of these antibodies may recognize the different Apo (a) isoforms in different mode. The test system must be considered to prevent overestimating or underestimating Lp(a) related risks.

There are contrarian reports on the significance of lipoprotein(a) as CAD risk factor. (Govindraju et al., 2003) found no significant role of lipoprotein (a) levels as a risk factor in CAD in Indian patients. The mean plasma lipoprotein (a) levels in patients with CAD was 32.18 +/- 1.37 mg/dl. The value was not considerably higher than that of the mean of 29.94 +/- 2.59 mg/dl of lipoprotein (a) in the control group. (Florvall et al., 2006) found significant correlations between the apolipoproteins and other known risk markers for cardiovascular disease such as triglycerides, high-sensitivity C-reactive protein (hsCRP), and cystatin C. Serum Apo A1 is a better risk marker than are Apo B, Apo B/ApoA1 ratio, HDL-C, and LDL-C for cardiovascular disease and mortality in elderly men. Racial/ethnic differences have been reported in Lp(a) levels. African Americans have higher Lp(a) levels than the Whites (Guyton et al., 1985). Asian Indians have higher Lp(a) levels than Chinese (Low et al., 1996; Anand et al., 2000). (Rajasekhar et al., 2004) have suggested a Lp(a) cut-off level of 25mg/dl for determination of risk of CHD among Indians.

2.2.2 APOLIPOPROTEIN B

Apolipoproteins play an important role in lipoprotein metabolism. There are six types of lipoproteins found of which Apo A and Apo B have been clinically identified as the most important types due to their direct correlation with ischaemic heart disease. Apolipoprotein A-I and A-II are the major constituents of HDL. There occurs an inverse relationship between HDL-Cholesterol and Apo A-I levels and the risk of ischaemic heart disease in the general population. Apolipoprotein B is a protein cap for the LDL particle and serves the function of soluabilising cholesterol within the LDL complex. Apo B is a convenient marker for assessing the cholesterol depositing capacity of the blood; it is a better discriminator of angiographically documented coronary artery disease than LDL Cholesterol (Sniderman, 2002).
Apo B found in human plasma as two isoforms, Apo B-48 and Apo B-100. Apo B-100 is the major physiological ligand for the LDL-receptor. It is the largest monomeric protein sequenced, containing 4536 amino acids residues. Its gene has been mapped on the short arm of chromosome 2, with an approximate length of 43 kilobases and 29 exons. The LDL-binding domain of the molecule is projected to be located between the residues 3129 and 3532. Apo B-100 is synthesized in the liver and is compulsory for the assembly of VLDL. It does not interchange between lipoprotein particles, as do the other lipoproteins, and it is found in IDL and LDL particles after the removal of the Apolipoproteins A, E and C. Apo B-48 is present in chylomicrons and chylomicron remnants. It plays the essential role in the intestinal absorption of the dietary fats. Apo B-48 is synthesized in the small intestine. Apo B is a better marker of the risk of coronary artery disease than LDL cholesterol (Sniderman, 2002).

The Apolipoprotein Related Mortality Risk Study is the largest study and is regarded as definitive on the issue of the merits of Apo B versus LDL-Cholesterol. In this study, 175,553 Sweeds were followed for an average of 5.5 years. The clinical event was fatal myocardial infarction. Apo B was below the age of 70 years, whereas predictive only in those around 70 years; fatal myocardial infarction in men and Cholesterol was predictive only in men. (Contois et al., 1996; Connelly et al., 1999)

Apo B can be calculated with the same accuracy as lipoprotein lipids in routine clinical laboratories. The population surveys have been established and a level of 120 mg/dl represents the 75th percentile. Any value above 120 mg/dl is elevated (Contois et al., 1996; Connelly et al., 1999). The combination of elevated Apo B and conventional risk factors other than LDL-Cholesterol generates greater risk than the combination of elevated LDL-Cholesterol with the same other V conventional risk factors (Williams et al., 2003). The estimations of Apo B, Apo B/Apo A-I are regarded ‘as highly predictive in evaluation of cardiac risk (Waaldius et al., 2001). There is a physiological and pathophysiological reason why Apo B is a stronger predictor of risk than LDL-Cholesterol is that Apo B is present not only in LDL but also in VLDL, IDL and Lp(a) – (Wood et al., 1998). The sum of Apo B concentrations in all atherogenic particles is a better risk marker than all fractions of cholesterol (Rader et al., 1994; Sniderman et al., 2001).
Plasma Apo B concentration reflects the number of atherogenic lipoprotein molecules (Sniderman et al., 1996) quantification of apolipoprotein moieties of LDL particles provides additional information in coronary patients with normal levels of total cholesterol and LDL-Cholesterol. The recommendations of the National Cholesterol Education Program have focused on total cholesterol and LDL-Cholesterol as a basis for screening and treatment of IHD. Serum concentration of Apo B has been reported as the best discerning factor to predict the presence or absence of atherosclerosis in Iranian normolipidemic individuals and young patients undergoing coronary angiography (Haidari et al., 2001). Hyperapobetalipoproteinemia (hyperapo B) was first described by (Sniderman et al., 1980) on study of 100 consecutive patients undergoing elective coronary angiography and is characterized by an increased number of small, dense LDL particles, elevated Apo B, and normal or border line LDL-Cholesterol levels. Patients with hyper Apo B may be normal triglyceridemic or hypertriglyceridemic. It has been revealed that the two clearly atherogenic Apo B-containing lipoprotein particles make up 90% of the total number of Apo B containing particles present in plasma at any time, and plasma Apo B concentration reflects the number of these atherogenic particles (Sniderman et al., 1997). Each of these particles contains one molecule of Apo B as a constant structural moiety whereas the amount of Triglyceride and Cholesterol per particle varies, and with it, the atherogenicity of the particles varies as well. The role of Apo B as an important risk factor is biologically plausible (Sniderman, 1997) and several possible mechanisms for this can be considered. Specifically, it has been shown that small, dense LDL particles are less likely to be cleared from circulation by the high affinity LDL receptors and are more likely to have prolonged plasma residence time, increased susceptibility to oxidation and to be more avidly taken up by macrophages in the atheroma (Dejager et al., 1993). A three-fold enlarge of risk for normolipidemic patients has been reported with increased Apo B concentration (Dejager et al., 1993). (Champeau et al., 1984) found on the origin of 10 year follow up study after aortocoronary artery bypass surgery that an increase in Apo B levels was the strongest indicator of progression of coronary atherosclerosis. Apo B concentration is associated with the severity of coronary artery disease expressed as the number of vessels and extent of stenosis in each vessel that has been reported to predict cardiovascular mortality (Sullivan et al., 1997).
2.2.3 APOLIPOPROTEIN A-I

Apolipoprotein A-I is the major constituent of HDL. It is clearly demonstrated that there occurs an inverse relationship between HDL-Cholesterol and Apo A-I levels and the risk of ischaemic heart disease (Srivastva, 2000; Sharp et al., 2000; Tailleux et al., 2002).

The major Apolipoprotein A-I containing lipoproteins are HDL and 3 major ultracentrifugal subfractions of HDL: HDL2b HDL2a and HDL3. Apo A-I is the key Apolipoprotein and phospholipids are the key lipid class of HDL and its key subfractions. HDL2a and HDL2b are larger than HDL3 and contain more cholesterol esters in the cores. The major role of HDL and its subclass is to transport cholesterol from peripheral cells back to liver, a process referred to as Reverse Cholesterol Transport (Reader, 2002). The subclasses of these lipoproteins have been determined using analytical Ultra-centrifugation and NMR spectroscopy.

Both the liver and the intestine secrete a nascent, disc-shaped HDL particle that contains Apo A-I, phospholipids and a very small amount of cholesterol. The Apo A-I on the nascent HDL interacts with the ATP-binding cassette (ABC) protein, ABC A-I is found on the exterior of peripheral cells including the macrophages. The free cholesterol is removed from the cell by means of ABC A-I transporter onto the nascent HDL particle in plasma from within the cell into the blood compartment. Here, the cholesterol is esterified by Lecithin-cholesterol acyl transferase (LCAT) and its cofactor Apo A-I. The nascent HDL particle is transformed into a mature, spherical HDL3 particle which contains cholesterol ester and its core. As more cholesterol is incorporated by LCAT into the core of the smaller HDL3 particles, larger HDL2 subclass particles of the liver and other cells, cholesterol ester is selectively delivered from HDL into the cell.

As (Reader, 2002) pointed out, although macrophages themselves are the cell type most affected by ABC A-I deficiency with regards to cholesterols accumulation, macrophages, themselves contribute little to the bulk lipidation of plasma Apo A-I and HDL-Cholesterol levels. Liver ABC A-I may by the most vital contributor to lipidation of lipid poor A-I and therefore to HDL-Cholesterol levels. Patients with VLDL overproduction often have low HDL cholesterol levels, as well as small, dense LDL (Kwiterovich, 2002; Grundy, 2002). The low HDL is not primarily the result of decreased synthesis of Apo A-
I, faulty elimination of cholesterol through ABC A-I, or deficient activity of LCAT. Rather, the triglycerides in the core of the largest VLDL subclass are exchanged for cholesterol esters an HDL. As the triglycerides are hydrolyzed, smaller HDL subclasses are produced that contain less cholesteryl ester. The Apo A-I on these smaller HDL particles seems to be removed and degraded by the kidney more avidly than normal HDL particles, thus dropping the number of HDL particles in the blood of patients with VLDL overproduction.

There is confirmation to suggest that oxidative modification of LDL trapped in the vessel wall is critical for the stimulation of pro-inflammatory genes which are critical for inflammatory cell recruitment and the initiation and progression of atherosclerosis. Therefore, the ability to reduce LDL oxidation in the vessel wall may translate into an anti-inflammatory and anti-atherogenic effect. The antioxidant effects of HDL have been accredited to the bindings of transition metals by HDL and to the presence of paraoxygenase carried predominantly by ApoA-I containing HDL, which has powerful antioxidant effect (Navab et al., 1996).

It has been observed that Apo A-I can better identify patients with severe vessel damage than HDL-Cholesterol in a population with recent acute myocardial infarction (Garfagnini et al., 1995). The role of HDL sub fractions and apolipoproteins in the risk determination of myocardial infarction was evaluated (Buring et al., 1992). It was found that Apo A-I amplified level of prediction of myocardial infarction over the information provided by the lipids and other coronary risk factors. (Woo et al., 1993) evaluated 89 Chinese men 3 months after acute myocardial infarction and found them to have low Apo A-I as compared to the controls. He documented that low Apo A-I is a risk factor for myocardial infarction of a comparable magnitude to smoking, hypertension and obesity. The importance of measuring Apo A-I as a risk predictor for myocardial infarction was further confirmed by (Franzen et al., 1982). The levels of Apo A-I among myocardial infarction were found to be low despite having normal levels of HDL-Cholesterol. (Brewer et al., 2004) stressed on the focus on high density lipoproteins and on the inverse relationship which exists between Apo A-I and the risk to develop CAD thereby, mounting strategies to increase the function of HDL or Apo A-I and reducing the
atherosclerotic progression. The levels of Apo A-I in children were measured (Freedman et al., 1986).

It was found that children whose fathers had an infarction had a lower mean level of Apo A-I as compared to children whose fathers did not have any myocardial infarction. (Skinner et al., 1999) evaluated prospectively the outcome of a consecutive group, of unselected patients five years after coronary artery bypass graft surgery, and examined the association with coronary risk factors. They found a direct, independent association between Apolipoprotein A-I concentration and all cause mortality and late cardiac events. In a study conducted in China, Apo A-I levels were estimated among 100 coronary artery disease patients who underwent coronary angiography and compared with 144 non coronary artery disease controls. It was shown that Apo A-I is more sensitive and specific than the ordinary indices (He, 1990).

The Atherosclerosis Risk in communities study conducted, showed that although Apo A-I was strongly predictive of coronary artery disease when considered alone, it did not add to risk prediction when considered together with LDL-Cholesterol, HDL-cholesterol and Triglycerides (Sharrett et al., 2001).

(Christie et al., 2003) suggested that instead of measuring the cholesterol in HDL or LDL, measuring their respective apolipoproteins i.e. Apo A-I and Apo B and thereby calculating the ratio of Apo B/Apo A-I is more helpful in predicting the risk for IHD. Workers on the Northwick Park Heart Study emphasized at risk over a 6 years period in 2508 middle aged men who did not have coronary disease at baseline. The main findings of the study revealed that the ratio of Apo B/Apo A-I was related with the strongest effect on risk for CAD. The apolipoproteins can be of help in improving the capabilities of classifying subjects regarding their risk, because the diversity of roles played by apolipoproteins in lipid metabolism. Studies suggest that the metabolic fate of a lipoprotein is regulated by its protein rather than its lipid content (Forte et al., 1994). To assess comparability between different methods, the IFCC Committee on Apolipoprotein Standardization has made available to manufacturers and reference laboratories the WHOIFCC. First International Reference Materials for Apo A-I and Apo B (Albers et al., 1992) demonstrated that Apo A-I and Apo B can be measured by a variety of
immunochemical methods with the degree of accuracy and precision required for assessing the risk for coronary artery disease. These studies present critical cut points that can be used to assess the risk of coronary heart disease and may compose the basis for wide spread clinical use of Apo A-I and Apo B measurements. There are a large number of studies reporting that the serum concentration of Apo A-I discriminates patients with the highest coronary risk (Sigurdson et al., 1992; Garfagnini et al., 1995).

Measurement of Lp (a), Apo B and Apo A-I can be performed using analytic Ultracentrifugation, NMR spectroscopy and Immunoturbidimetric methods (Otvos, 2000). These methods have been automated and standardized, and the results obtained thereby have been found to be accurate and reproducible.

Although many studies are available to correlate between IHD and various risk factors but there are a very few reports on the exact role of these parameters in coronary artery disease. In Indian population where IHD quite prevalent, the estimation of Apo B, Apo A-I, Lp (a) and thereby the ratio of Apo B/Apo A-I can be very helpful for diagnosis, prognosis and its correlation with IHD.

2.3. Reversible Risk Factors

2.3.1 Obesity and Overweight

Overweight and obesity are defined as atypical or unnecessary fat accumulation in the body that may damage health. The Obesity Epidemic: Nowadays entire world is facing the outburst of obesity. Changes in diet together with progressively more inactive lifestyles have sparked off epidemics of obesity in several Asian countries. Several surveys of risk factors conducted across South Asian countries have exposed high and rising rates of overweight, central obesity, diabetes, high blood pressure and dyslipidaemia in urban populations. World Health Organization (WHO, 2005) latest projections indicate: that globally in 2005 around 1.6 billion adults (age 15+) were overweight; at least 400 million adults were overweight. WHO further projects that by 2015, approximately 2.3 billion adults will be overweight and more than 700 million will be obese. At least 20 million children under the age of 5 years are overweight worldwide in 2005. Some time ago, it was considered a problem only in high-income countries, now
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Overweight and obesity are noticeably on the rise in low and middle-income countries, mainly in urban settings. Studies have also pointed out that India, in its phase of economical transition, is very much in the grip of this epidemic. But this epidemic of ‘obesity’ in India is not appreciated because most commonly used indicator of obesity i.e. Body Mass Index (BMI) underestimates the adiposity of Indians. Reports also suggest that for any given BMI, Indians tend to have a higher magnitude of adiposity.

Definition of Obesity and applicability of International criteria to Indians: Classically BMI is used as a simple index to classify overweight and obesity in adult populations and individuals. It is defined as the weight in kilograms divided by the square of the height in meters (kg/m²) (WHO, 2005).

Table 2.1. Classification of BMI by different criteria

<table>
<thead>
<tr>
<th>Body Mass Index Kg/m²</th>
<th>Under Weight</th>
<th>Normal Weight</th>
<th>Over Weight</th>
<th>Obesity-I</th>
<th>Obesity-II</th>
<th>Obesity-III</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHLBI (1998) The Obesity Task Force of the National Heart, Lung and Blood Institute:</td>
<td>&lt;18.5</td>
<td>18.5-24.9</td>
<td>25-29.9</td>
<td>30,34.9</td>
<td>35-39.9</td>
<td>&gt;40</td>
</tr>
<tr>
<td>WHO (2000) Geneva</td>
<td>&lt;18.5</td>
<td>18.5-24.9</td>
<td>25-29.9</td>
<td>30,34.9</td>
<td>35-39.9</td>
<td>&gt;40</td>
</tr>
<tr>
<td>WPRO-for Asian (2000) Erdembileg et al., 2000</td>
<td>&lt;18.5</td>
<td>18.5-22.9</td>
<td>23,24.9</td>
<td>25-29.9</td>
<td>&gt;30</td>
<td>---</td>
</tr>
<tr>
<td>Who (Public health action points) Asian (2004) Lancet</td>
<td>&lt;18.5</td>
<td>18.5-22.9</td>
<td>23,27.4</td>
<td>&gt;27.5</td>
<td>&gt;32.5</td>
<td>&gt;37.5</td>
</tr>
</tbody>
</table>
In the year 2004, WHO expert consultation concluded that Asians normally have a higher percentage of body fat than white people of the same age, sex, and BMI. They were at a higher risk of type 2 diabetes and cardiovascular disease below the existing WHO BMI cut-off point of 25 kg/m². For many Asian populations, added trigger points for public health action were identified as 23 kg/m² or higher, representing increased risk, and 27.5 kg/m² or higher as representing high risk. The consultation further identified the potential public health action points (23.0, 27.5, 32.5, and 37.5 kg/m²). With this in mind, the International Diabetes Federation had accepted the BMI value of >25 kg/m² and 23 kg/m² as the cut-off for obesity for Asian men and women respectively. Several studies from India had suggested cutoffs for BMI ranging from 19-22 kg/m² while that of waist circumference from 72-85 cm in men and 65.5 - 80 cm in women (Lancet, 2004).

The International Obesity Task Force of WHO had proposed the definition of obesity in its Technical Report Series No 894 published in the year 2000. These had been developed by western researchers based on studies in Caucasian populations, and were not designed to be applicable to all populations. Important differences exist in the form of higher/lower body fat content for a given BMI in South-east Asians and Asian Indians. To determine if WHO recommended cut-off values for BMI and WHR were appropriate for the different sub-populations, in Singapore a cross-sectional population based study was done. Data on socio-economic status, body weight, body height, waist and hip circumferences and blood pressure was measured using standardized protocols.

At low categories of BMI (BMI between 22 and 24 kg/m² and WHR (WHR between 0.80 and 0.85 for women, and between 0.90 and 0.95 for men), the absolute risks for cardiovascular diseases were found to be high, ranging from 41 to 81%. The results showed that, at relatively low BMI and WHR, Singaporean adults experienced higher risk (absolute and relative) for cardiovascular risk factors. These findings, in addition to earlier reported high percentage body fat among Singaporeans at low levels of BMI, confirmed the need to revise the WHO cut-off values for the various indices of obesity and fat distribution, viz BMI and WHR, in Singapore.
2.4 Prevalence of Obesity and overweight

Data composed by the National Center for Health Statistics indicate that the prevalence of obesity, defined as a BMI > 30 kg/m², has increased from 12.8% between 1976 and 1980 to 22.5% from 1988 to 1994 (Flegal et al., 1998). Information from a preliminary analysis of 1999 National Health and Nutrition Examination Survey (NHANES) data indicated that the prevalence of overweight had increased to 34.0% and the prevalence of obesity to 27.0%. Review of Indian studies suggests varied prevalence of obesity. In most of the studies the criteria taken is however BMI >30 Kg/m² of obesity. Prevalence of obesity in Delhi has been shown to be (Gopinath et al.,1994 BMI>25 27.8%), (Krishnanan et al.,2003 BMI>27.5 Kg/m²) 2% (NFHS-III in 2005-06) respectively. (Table 2.2).

Table 2.2: Prevalence of Obesity in India

<table>
<thead>
<tr>
<th>STUDY GROUP</th>
<th>YEAR</th>
<th>BMI Criteria</th>
<th>(%)</th>
<th>POPULATION</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Males 15-49 yrs</td>
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<td>Females 15-49 yrs</td>
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<td>Males 15-49 yrs</td>
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<td></td>
<td></td>
<td>Females 15-49 yrs</td>
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<tr>
<td>NFHS- III</td>
<td>2005-06</td>
<td>BMI&gt;25</td>
<td>9.0</td>
<td>Males 15-49 yrs</td>
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<tr>
<td></td>
<td></td>
<td>BMI&gt;30</td>
<td>13.0</td>
<td>Females 15-49 yrs</td>
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<td></td>
<td></td>
<td></td>
<td>1.0</td>
<td>Males 15-49 yrs</td>
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<td></td>
<td></td>
<td></td>
<td>3.0</td>
<td>Females 15-49 yrs</td>
</tr>
<tr>
<td>Krishnan et al.,2003 (Haryana)</td>
<td>2003</td>
<td>BMI&gt;25</td>
<td>25.4</td>
<td>Males 15-64 yrs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>BMI&gt;23-27.4</td>
<td>34.9</td>
<td>Females</td>
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<tr>
<td></td>
<td></td>
<td>BMI&gt;27.5</td>
<td>30.1</td>
<td>Males</td>
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<td></td>
<td></td>
<td></td>
<td>28.1</td>
<td>Females</td>
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<td></td>
<td></td>
<td></td>
<td>10.7</td>
<td>Males</td>
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<td></td>
<td></td>
<td></td>
<td>20.5</td>
<td>females</td>
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<tr>
<td>Mishra et al.,2001</td>
<td>2001</td>
<td>BMI&gt;25</td>
<td>65.4</td>
<td>Indian adult Urban</td>
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<tr>
<td></td>
<td></td>
<td>BMI&gt;30</td>
<td>13.9</td>
<td>Urban Females</td>
</tr>
<tr>
<td>Nutrition foundation of India (Delhi)</td>
<td>1999</td>
<td>BMI&gt;25</td>
<td>48.6</td>
<td>Overall Females</td>
</tr>
<tr>
<td></td>
<td></td>
<td>BMI&gt;30</td>
<td>14.0</td>
<td>Urban Females</td>
</tr>
<tr>
<td>Gopinath et al.,1994 (Delhi)</td>
<td>1994</td>
<td>BMI&gt;25</td>
<td>27.8</td>
<td>Overall Females</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>33.4</td>
<td>Overall Females</td>
</tr>
</tbody>
</table>

28
According to the National Family Health Survey-III report, in India, the mean BMI for women aged 15-49 in India was 20.5 and for men it was 20.2. The percentage overweight or obese was rather lower for men age (9 %) than for women age (13 %). Men are also less likely to be obese (1 percent) than women (3 percent). This was a growing problem in India, with the percentage of ever-married women age 15-49 who were overweight or obese increasing from 11 percent in NFHS-2 to 15 percent in NFHS-3. Overweight and obesity had become extensive problems among several groups of women in India, particularly older women, women living in urban areas, women who were well educated, women in households in the highest wealth quintile, and Sikhs. About one-quarter or more of women in each of these groups had a BMI of 25 or more and 5-10 percent had a BMI of 30 or more. A study in Bombay revealed that the prevalence of obesity among young adult males varied from 10.7% to 53.1%.

Mishra et al., 2001 had also compared statistics of Obesity between Indians in US and India. Their findings have been tabulated as follows.

**Table 2.3: Obesity in US Indians and Rural and Urban Indians (Mishra et al., 2001)**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Indians (US)</th>
<th>Indians (URBAN)</th>
<th>Indian (RURAL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean BMI (Kg/m²)</td>
<td>25.4</td>
<td>24.8</td>
<td>21.9</td>
</tr>
<tr>
<td>BMI &gt; 30 (Kg/m²)</td>
<td>11%</td>
<td>13%</td>
<td>2%</td>
</tr>
<tr>
<td>BMI &gt; 23 (Kg/m²)</td>
<td>73.3%</td>
<td>65.4%</td>
<td>31.8%</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>22.5%</td>
<td>38.6%</td>
<td>7.7%</td>
</tr>
<tr>
<td>Mean WHR</td>
<td>0.89</td>
<td>0.94</td>
<td>0.84</td>
</tr>
<tr>
<td>WHR &gt; 0.90</td>
<td>43.8%</td>
<td>65.7%</td>
<td>23%</td>
</tr>
</tbody>
</table>

It is clear that in addition to the extent of adiposity, regional distribution of fat storage is an important indicator of medical risk related with obesity. Much of the focus of risk measurement has been on central obesity, with measure of waist circumference used as a predictor. Mexican National Health Survey was conducted in 2000 and it was found that there was a high occurrence of abdominal obesity in normal-weight women with co-morbidities relating better to Waist circumference than to BMI in both sexes. The National Institutes of Health cut-off points for Waist circumference help to spot those at increased health risk within the normal-weight, overweight, and class I obese BMI categories were studied at Kingston, Ontario. Many of the associations remained significant after adjusting for the confounding variables (age, race, poverty-income ratio, physical activity, smoking, and alcohol intake).

A cross sectional study in China aimed to identify the usefulness of BMI, WC and waist-to-hip ratio (WHR) in screening for obesity in an Asian population. A cross-sectional sample was chosen. Then receiver-operating characteristic analyses were used to assess the performances of the three anthropometric indices. The investigators have concluded that BMI and WC are two important predictors for obesity in Chinese, and WHR is an alternative.

2.6 Hip circumference (HC): Relationship between Hip circumference and metabolic risk factors has been studied in an urban adult population of Tehranian men by (Esmailzadeh et al., 1998) in a population-based cross-sectional study a representative sample of 4040 men aged 18-74 years was assessed in 1998. Demographic data were collected; anthropometric indices and blood pressure were measured according to standard protocol. Hypertension was defined based on Joint National Committee (JNC) Biochemical analysis was conducted on fasting blood samples. After alteration for potential confounding variables, a significant decreasing trend was observed among hip circumference quintile categories for odds of having hypercholesterolemia (odds ratios...
among quintiles: 1.00, 0.83, 0.76, 0.66, 0.51, respectively, \( P \) for trend = 0.03), diabetes (1.00, 0.74, 0.55, 0.29, 0.20, \( P \) for trend = 0.01). It was concluded that Hip circumference is independently and negatively associated with metabolic risk factors.

In another Cross-sectional study by (Han et al., 1998) in a random sample of 5887 men 7018 women aged 20-59 years, selected from the civil registries of Amsterdam, associations of waist and hip circumference with lifestyle factors was seen. It was find out that the risk of having smaller hips than expected from body mass index was times (1.1-1.4) in male and 1.2 times (1.0-1.3) in female smokers, 1.2 times (1.1-1.3) in men and 1.1 times (1.0-1.2) in women who were inactive. It was concluded that understanding the influences of lifestyle factors on size of waist and the hips is important for health promotion directed at the general public.

2.7 Skin fold thickness (SFT): Body fat percentage can be calculated indirectly by measuring the body skinfold thickness. Asians have higher insulin resistance compared to white Caucasians and this is thought be due to physiological and structural alterations in the muscle due to poor nutritional status. A lower total body muscle mass, which has an independent effect on sensitivity and glucose disposal. The risk of diseases appears to increase as meaning of the percent fat content in the body, above an upper limit of normal. It also determines the risk for developing insulin resistance. The percent of body fat that considered normal varies with the age and sex of an individual. The exact value of above which a person may be considered overweight or obese is debatable. However a value of 20% BF for defining overweight and 25% BF for defining obese has been suggested by various workers. Obesity is a serious, chronic disease that is known to reduce life span, increase disability and leads to many serious illnesses. These illnesses, including diabetes, heart disease, gallstones and stroke, are the co-morbidities of obesity. Study by The Lewin Group confirmed results from other studies in finding a direct correlation between increases in BMI and increases in the prevalence of co-morbid conditions like arthritis, breast cancer, heart disease, colorectal cancer, Type II diabetes, endometrial cancer, end stage renal disease, gallbladder disease, hypertension, liver disease, low back pain, renal cell cancer, sleep apnea, stroke and urinary incontinence. Studies have calculated the percentage of obese persons with each co-morbid condition and calculated the total costs to the U.S. health care system of treating patients with
obesity excluding the costs of treating obesity itself. Ideal body mass was associated with 6.3% to 36.1% lower annual health care expenditure in females and 3.6 to 18.2% lower health care expenditure in males. Obesity is an important risk factor for various medical conditions including definite forms of cancer, osteoarthritis, sleep apnea, gall bladder disease, and nonalcoholic fatty liver disease. In addition, excess weight predisposes to cardiovascular disease through multiple mechanisms the majority of which form part of the definition of the metabolic syndrome.

The clinical utility of the metabolic syndrome as opposed to its single components in risk stratification has been debated. In a cross sectional study done using data from the Third National Health and Nutrition Examination Survey (NHANES III), it was found out that 63% of men and 55% of women were overweight and a graded increase in the prevalence ratio (PR) was observed with increasing severity of Overweight and Obesity for all of the Health outcomes. The prevalence of having 2 or more health conditions increased with weight status category across all racial and ethnic subgroups.

2.8 Hypertension

Hypertension has been defined as Systolic blood pressure more than 120 mm Hg or Diastolic blood pressure more than 90 mm Hg by JNC-VII report. It is a composite health problem in the community. It is a risk factor for many non-communicable diseases. It is three times more common in urban areas as compared to rural areas. The prevalence reported in various Indian studies has been tabulated as follows.

Table 2.4. Prevalence of Hypertension in India

<table>
<thead>
<tr>
<th>Study Group (Year)</th>
<th>Age group (years)</th>
<th>Criteria SBP/DBP</th>
<th>Male (%)</th>
<th>Female (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gupta et al., (1995)</td>
<td>&gt;20</td>
<td>&lt;140/190</td>
<td>30</td>
<td>34</td>
</tr>
<tr>
<td>Srinath Reddy et al.,</td>
<td>10-69</td>
<td>&lt;140/90 (self reported)</td>
<td>10.6</td>
<td>11.2</td>
</tr>
<tr>
<td>(2002-03)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Krishnan et al., (2003-04)</td>
<td>15-64</td>
<td>&lt;140/90</td>
<td>23.1</td>
<td>15.7</td>
</tr>
</tbody>
</table>
Several large epidemiological studies had shown an relationship between body index and blood pressure in normal weight and overweight patients. Weight gain in life particularly seemed to be an important risk factor for the development of hypertension. Obesity and hypertension were both major public health problems in Western society. Results from the Framingham Study had shown that high blood pressure (1) and overweight (2) were both independent risk factors for cardiovascular disease. Hypertension was one of the most common obesity-related complications, and about 30% of hypertensive individuals could be classified as being obese. Obesity had been shown to be an independent risk factor for the development of hypertension. Several large epidemiological studies have documented the alliance between body weight and blood pressure. Blood pressure was clearly and strongly correlated with BMI.

In the more recent INTERSALT study by (Dyer et al., 1989) the relationship between body mass index (BMI) and blood pressure was studied in over 10,000 men and women, between 20 and 59 years of age, sampled from 52 centers around the world. In this large study population, BMI was significantly associated with systolic and diastolic blood pressure and was independent of age, alcohol intake, smoking habit, and sodium and potassium excretion. Also, eventual studies had shown that obesity increased the risk of developing hypertension. Weight gain in adult life especially seemed to be an important risk factor for the development of hypertension. In a recent, updated evaluation of the Nurses’ Health Study, a long-term follow-up study of more than 80,000 female nurses, BMIs at 18 years of age and midlife were positively related with the occurrence of hypertension. Weight gain after 18 years of age significantly increased the risk for hypertension (compared with weight gain 2 kg, multivariate relative risks were 1.74 for a gain of 5.0 to 9.9 kg, and 5.21 for a gain 25.0 kg). Excess weight, and even modest adult weight gain, substantially increased risk for hypertension. Each 1-kg increase in weight after age 18 was associated with a 5% increased risk for hypertension.

2.9 Obesity, Skinfolds, Circumferences and Cardiovascular Diseases

Body composition and physique interrelationships to biomarkers of liver disease, insulin resistance, and lipid and cytokine expression have been explored (Mager et al., 2013). Such investigations examine anthropometric variables like weight, height, body mass index (BMI), waist circumference (WC), waist-height ratio (WHtR), and multiple
skinfold thickness. Beside from these, fat mass (FM) and somatotype analysis have been used in these studies.

Hudova et al., (2013) studied relationship of cardiovascular disease (CVD) in central Slovakian adults with socioeconomic and educational differences and found that population with low socioeconomic and educational background was at high risk of CVD due to high level of smoking and physical inactivity compared to population with high socioeconomic and high educational background even though the later population had high BMI and high blood pressure.

Pavlica et al., (2013) established the correlation between triceps, skinfold thickness in relation to BMI and the risk factors in premenopausal and postmenopausal women. This study shown that BMI equally correlated with risk factors as well as skinfold thickness. Pike et al.,(2013) investigated the relationships of maternal body mass index (BMI) and fat mass with childhood wheeze and examined the influences of infant weight gain and childhood obesity.

Studies conducted by Budimir et al.,(2012) disclose that body composition is weak and inverse predictor of arterial stiffness and their influence is sex-dependent. Waist circumference (WC), waist-hip ratio (WHR) and waist-height ratio (WHtR), body mass index (BMI), body fat percentage (% BF), were key predictors of arterial stiffness in the females, while BMI was the principal predictor in the males. Relationship between body mass index (BMI) obesity and blood pressure (BP) in children were studied by Zhang et al.,(2011) and found that there was a strong positive relationship between fat mass index (FMI) and BP in children.

Abdominal obesity assessed by waist or waist/hip ratio is both related to increased risk of all-cause mortality, cancer and sleep apnea. The risk is very high in younger adult compared to older adults. Obesity is also a risk factor for sleep apnoea where neck circumference appears to give the strongest association, and waist-hip ratio is a risk factor especially in severe obstructive sleep apnoea syndrome. Study confirms that (Seidell et al.,2010) the waist circumference and waist-hip ratio are better indicators of all-cause mortality than BMI. The anthropometric index change that
correlates best with cardiovascular risk factor were investigated (Toschke et al., 2008). No better anthropometric predictor for the limited prediction of cardiovascular risk changes was observed among the considered parameters. Cardiovascular risk factors should be tracked to prove a cardiovascular effect of weight change and/or intervention.

Dual emission X-ray absorptiometry (DXA) is widely used to compare adiposity by skinfolds and body mass index (BMI) and to obtain the cardiovascular risk in adolescents (Steinberger et al., 2005). Study confirms that DXA is an effective tool for predicting adverse cardiovascular risk profile and comparable with risk profile derived based on BMI and skinfolds data. Study conducted on Chinese children (Li et al., 2004) to correlate serum lipid and apolipoprotein A-I (apoA-I) and B (apoB) levels obesity in children confirms that HDLC as well as TC levels should be examined to assess coronary risk.

An association between hypercholesterolemia and nutritional status of hospitalized elderly people were investigated (Bonnefoy et al., 2002). Study propose that total cholesterol retained albumin, APO AI, APO B and RBP as predictor factors of cholesterolemia for women and APO AI, APO B and triglyceride for men. Prevalence of small dense low-density lipoprotein (SDLDL) particles in obese youths compared to youths with SDLDL and large buoyant Low-density lipoprotein LDL (LBDLDL) subclass phenotypes in total body and abdominal fatness, cardiovascular fitness, and markers of the insulin resistance syndrome (IRS) were studied (Kang et al., 2002) and observed that level of SDLDL might be a risk factor for coronary heart disease.

Effects of anthropometric parameters (body mass index, waist-to-hip circumference ratio, waist circumference, and ratio of subscapularis to triceps skinfold thickness) were investigated (Zak et al., 2002) on plasma lipoproteins, fatty acid composition and lipoperoxidation were assessed to correlate the risk factors of coronary heart disease. Subscapular is to triceps skinfold thickness ratio had the lowest discriminating ability in all data. Waist-to-hip ratio dominated in effect size value only in VLDL oxidability. Body mass index reflected most significantly plasma, LDL, and VLDL triglyceride;
HDL and VLDL cholesterol; and content of linoleic acid in LDL phosphatidylcholine.

2.10 Non-Cardiac Co-morbidities

2.10.1 Osteo-arthritis (OA)

Osteoarthritis has been currently defined by the American College of Rheumatology (ACR) as a heterogeneous group of conditions that lead to joint signs and symptoms which are linked with defective integrity of articular cartilage, in addition to related changes in the underlying bone at joint margins. The prevalence of OA is increasing; mainly due to increasing life span. Overweight people have a high prevalence of knee OA.

Osteoarthritis typically develops gradually and progresses over several years. Usually, the pain gradually worsens over time, but it may stabilize in some patients. Osteoarthritis of the knee is a principal cause of disability in elderly persons. Osteoarthritis also causes millions of Americans to miss work because of back pain. However, there are not many studies in India giving the prevalence of the condition in the community. A study by Chopra et al. in rural population of western India have found out that 7.9% and 11.5% of population suffered from knee pain and lumbar pain. Another study by Pingle et al., (2009) has found out the prevalence of OA to be as high as 36.2% in a population above 15 years. In a recent study, as higher body mass index significantly correlated with an increase risk of hip replacement due to OA. OA is the leading cause of chronic disability at older ages, largely due to knee and hip involvement. More than 13% of American aged 55-64 years and more than 17% of American aged 65-74 years have pain and functional limitation related to knee OA. The cardinal symptom of OA is pain, which occurs with joint use and is reassured by rest. It is usually aching in character and poorly located. Short lasting morning stiffness is a common complaint. Crepitus, a crackling or grating sound as the joint is moved, may be due to cartilage loss and joint loss and joint surface irregularity. Joint enlargement may be due to secondary synovitis, an increase in synovial fluid, or marginal proliferative changes or bone osteophytes. Currently there is no gold standard diagnostic test for OA and although the diagnosis is frequently radiographic. The ACR has established classification criteria for hip, knee, and hand OA based on clinical, laboratory, and radio logical items. The sensitivity and specificity of
ACR set of criteria to diagnose OA-Knee has been shown to be 77% (68-84%) and 77% (68-84%) respectively in the list format. Diabetes Mellitus is a life-long disease marked by high levels of sugar in the blood. It can be caused by too little insulin (a hormone produced by the pancreas to regulate blood sugar), resistance to insulin, or both. Diabetes has rapidly become a global epidemic. WHO projects that diabetes death will increase by more than 50% worldwide in the next 10 years. The prevalence of diabetes and its adverse health effects has risen more quickly in South Asia than in any other large region of the world. India has a elevated number of people with diabetes than any other country. The number of people with diabetes is likely to rise by 195% in India during 1995-2025 to reach 57.2 million in 2025.

In study by (Misra et al., 2001) it was observed that the prevalence of diabetes in urban Indians was 13.6%.

**Table 2.5: Comparative statistics of Prediabetes and Diabetes between Indians in US and India.**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Indians (US)</th>
<th>Indians (URBAN)</th>
<th>Indians (RURAL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prediabetes</td>
<td>32.9</td>
<td>23.4</td>
<td>12.5</td>
</tr>
<tr>
<td>Diabetes</td>
<td>17.4</td>
<td>13.6</td>
<td>8.4</td>
</tr>
<tr>
<td>Overall</td>
<td>50.2</td>
<td>37</td>
<td>20.9</td>
</tr>
</tbody>
</table>

It had long been recognized that higher BMI’s were linked with a risk of incident type 2 diabetes, and a central fat allocation appears to be a stronger risk factor than overall obesity. With increasing obesity, diabetes prevalence was also on the increase, and in turn, diabetes was associated with at least a doubling of risk for cardiovascular diseases.

As for cardiovascular disease, it was only more lately that the obesity had again been brought into focus. In particular the INTERHEART study, an international case-control study of myocardial infarction had revealed that obesity and in particular central obesity,
was a potent risk factor. While cardiovascular disease had recently been on the decrease with improved treatment for hypertension and lipids and the control of smoking, the increase in obesity and diabetes were likely to reverse this trend.

In a Jaipur based study by Gupta et al., (2007) it was found that there was a major increase in prevalence of hypertension, diabetes, and metabolic syndrome with BMI in both men and women. BMI <20 kg/m² was linked with the lowest prevalence of hypertension, diabetes and metabolic syndrome and a progressive increase was seen in these risk factors groups with increasing BMI steep increase in the prevalence of hypertension, diabetes, and metabolic syndrome was observed at BMI >20 kg/m².

2.10.2 Bronchial Asthma and BMI

There is an increasing interest in the association between obesity and asthma in recent years. The relationship to an abnormal BMI has been more widely studied for asthma than chronic obstructive pulmonary diseases. Higher the BMI and higher proportions of obese subjects have been found among patients with asthma than control subjects; both in adult population. (Schachter et al., 2001) did not report on gender- BMI interactions. Normal weight has been defined as BMI 18.0 to 24.9 in this study and odds ratio are derived from the reported prevalence of asthma, and hence unadjusted. There was weak evidence of a relation of recent asthma to BMI group (p=0.06). However, there was strong confirmation of an exertion in the severely obese compared to the normal weight group. Akerman et al., (2004) sought to investigate whether obesity may be related to asthma. They undertook a retrospective medical record review of patient records at an inner-city academic asthma center. Obesity was defined as a BMI greater than 30. Asthma severity was defined by using the National Heart Lung and Blood Institute (NHLBT) 1997 guidelines. There were 113 females and 30 males involved in the study. This study found that the prevalence of obesity increases with increasing degree of asthma severity in a group of adult asthmatics followed at the centre. Patients with severe asthma had a 16 fold increase in the risk of having obesity (BMI>30) compared to patients with mild intermittent asthma.
In a cross-sectional study by Luder et al., 2000 at New York State among 5524 subjects aged 18 years and above, the alliance between BMI and asthma in men and women has been explored. This study revealed that men and women differ significantly in the association between BMI and asthma prevalence only with respect to the lowest weight category. While women had a monotonic association, men showed a U-shaped relationship, indicating that both extremes of weight are allied with higher prevalence of asthma.

2.10.3 Sleep apnea

This condition is identified by episodes of stopped breathing during sleep. Obstructive sleep apnea syndrome describes a range of upper airway obstruction during sleep from primary snoring to severe obstructive sleep apnea. This sleep-related breathing disorder is an under-diagnosed clinical entity which is reported to be affecting up to 5% of the population in Western countries. Snoring is the hallmark of obstructive sleep apnea, but it is dismissed and not brought to the notice of the doctor. Obstructive sleep apnea (OSA) occurs because of recurrent occlusion of the upper airway during sleep and obesity occurs in most patients with OSA and is considered to be a major risk factor for its expansion. However, not all patients with OSA are obese and some of these non-obese patients have obvious abnormal craniofacial configuration. Sleep-disordered breathing has been linked to chronically elevated blood pressure in cross-sectional epidemiological studies. The Berlin questionnaire is an instrument validated to use in the Western population to define the occurrence of risk factors for OSAHS namely snoring behavior, wake-time sleepiness or fatigue and the presence of obesity or hypertension.

2.11 Need for the Present Study

It is now apparent that South Asia is home to many metabolic disorders. The prevalence of these metabolic disorders varies according to region, urbanization, lifestyle patterns, socioeconomic factors, culture and genetic factors. Of the biochemical factor, lipid profile and apo-lipoproteins have shown considerable association with obesity as well as CAD and there is need to undertake such studies among different human populations living in different geographical regions.
Keeping in mind the growing trends of CAD in India, and to review the CAD and its linkage obesity and other risk factors, the present study was undertaken on the Punjabi Khatri’s adults of northern India with the objective to generate data about the association of lipid profile, obesity and Apo lipoprotein B.