EFFECT OF DIET, TOBACCO AND HEREDITY ON LIPID METABOLISM AND HYPERTENSION

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CERTIFICATE

This is to certify that thesis entitled "Effect of Diet, Tobacoo & Heredity on Lipid Metabolism and Hypertension" has been carried out by **Ms.Siji Mathew**, *M.Sc. (Biochem.) at the Department of Biochemistry, M. P. Shah Medical College, Jamnagar under my guidance, supervision and to my satisfaction.*

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ABBREVIATIONS

Sr. No.	Abbreviations	
1.	Acute Myocardial Infarction	AMI
2.	Arachidonic Acid	AA
3.	American Heart Association	AHA
4.	ATP Binding Cassette Protein 1	ABC 1
5.	Anti-Oxidants	AO
6.	Adults Treatment Panel III	ATP III
7.	Angiotensin I Converting Enzyme	ACE
8.	Angiotensinogen	AGT
9.	Blood Pressure	BP
10.	Body Mass Index	BMI
11.	Coronary Heart Disease	CHD
12.	Cardiovascular Disease	CVD
13.	Coronary Artery Disease	CAD
14.	Central Nervous System	CNS
15.	Chylomicrons	CM
16.	Cholesteryl Esterase	CE
17.	Cholesteryl Ester Transfer Protein	CETP
18.	Chronic Energy Deficiency	CED
19.	Carbon monoxide	CO
20.	C-Reactive Protein	CRP
21.	Chennai Urban Rural Epidemiology Study	CURES
22.	Disability Adjusted Life Years	DALY
23.	Diabetes Mellitus	DM
24.	Diastolic Blood Pressure	DSH
25.	Dietary Approaches to Stop Hypertension	DASH
26.	Diet And Infarction Trial	DART
27.	Docasohexaenoic Acid	DHA
28.	Eicosapentaenoic Acid	EPA
29.	Environmental Tobacco Smoke	ETS
30.	Free Fatty Acid	FFA
31.	Free Radicals	FR
32.	Fatty Acid	FA
33.	Fraction catabolic Rate	FCR
34.	Familial Hypercholesterolemia	FH
35.	Hypertension	HT
36.	High Density Lipoprotein-Cholesterol	HDL-C
37.	Hip Circumference	HC
38.	Isolated Systolic Hyperstension	ISH
39.	Ischaemic Heart Disease	IHD
40.	Intermediate Density Lipoprotein-Cholesterol	IDL-C

Sr. No.	Abbreviations	
41.	Interleukin	IL
42.	International Study of Electrolytes and BP	INTERSALT
43.	Joint National Committee on prevention, detection, evaluation and treatment of high blood pressure	JNC
44.	Low Density Lipoprotein-Cholesterol	LDL-C
45.	Lipoprotein	Lp
46.	Lipoprotein (A)	Lp(A)
47.	Lipoprotein Lipase	LPL
48.	Lecithin Cholesteryl Acyl Transferase	LCAT
49.	Lipids Research Clinics	LRC
50.	Multiple Risk Factor Intervention Trial	MRFIT
51.	Myocardial Infarction	MI
52.	Monounsaturated Fatty Acid	MUFA
53.	Macrophage Colony Stimulating factor	M-CSF
54.	Medical Research Council Trial	MRC
55.	National Health And Nutrition Examination Survey	NHANES
56.	Nitric Oxide	NO
57.	National Cholesterol Education Program	NCEP
58.	Nicotine Replacement Therapies	NRT
59.	Oxidized Low Density Lipoprotein	Ox-LDL
60.	Pulse Pressure	PP
61.	Polyunsaturated Fatty Acid	PUFA
62.	Prostaglandins	PG
63.	Reactive Oxygen Species	ROS
64.	Recommended Dietary Allowances	RDA
65.	Renin Angiotensin System	RAS
66.	Systolic Blood Pressure	SBP
67.	Systolic Hyertension in the Elderly Program	SHEP
68.	Sympathetic Nervous System	SNS
69.	Scavenger Receptors of Class B	SRCBI
70.	Saturated Fatty Acid	SFA
71.	Single Nucleotide Polymorphism	SNP
72.	Saturated Fat	SF
73.	Total Cholesterol	TC
74.	Triglyceride	TG
75.	Therapeutic Lifestyle Changes	TLC
76.	Thomboxane A2	TXA2
77.	Very Low Density Lipoprotein-Cholesterol	VLDL-C
78.	Waist Circumference	WC
79.	Waist-Hip Circumference	WHR

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INTRODUCTION & REVIEW OF LITERATURE

INTRODUCTION & REVIEW OF LITERATURE

Hypertension (HT) affects approximately 40million individuals in India [1] and approximately 1 billion worldwide. [2] It is estimated that 30-50% of the world population above 20 years of age is afflicted with HT. [1] As the population ages, the prevalence of HT will increase even further unless broad and effective preventive measures are implemented.

Recent data from the Framingham Heart Study suggest that individuals who are normotensive at age 55 have a 90% lifetime risk for developing HT. [3] HT is a major health problem both in developed as well as in developing countries with a common end result of elevated blood pressure (BP) i.e. an epidemiological shift in the prevalence of HT in developing countries as compared to developed countries. [2,4] This is obvious from several Indian urban and rural studies. [5-9] The various studies estimated a prevalence rate of HT among urban population ranging from 1.24% in 1949 to 36.4% in 2003 and for rural people from 1.99% in 1958 to 21.2% in 1994. [4]

Elevated BP is an important direct cause of cardiovascular morbidity and mortality in general and coronary heart disease (CHD) in particular. It is also a major risk factor for the development of cardiovascular disease (CVD). The higher the level of BP, the greater is the chance of various cardiovascular diseases like heart attack, heart failure, stroke and kidney disease to develop prematurely through acceleration of atherosclerosis, the pathological hallmark of uncontrolled hypertension. The relationship between blood pressure (BP) & risk of CVD events is continuous, consistent and independent of other risk factors.

CVDs are the commonest cause of death globally and account for approximately 12 million deaths annually. The disability adjusted life years (DALY) attributed to CVD will rise to about 140-160 million with about 80% of this burden in developing countries. [10] This unexpected increase in CVD reflects the demographic economic and health transitions in these countries. In India, CVD is also the major contributor to the burden of premature mortality and morbidity and accounted for 85 million DALY'S in 1990. By the year 2020, CVD will still remain the leading cause of mortality and disability in India. [10]

HT has also been shown to be a major risk factor for cognitive impairment and dementia. [11] Also BP acts synergistically with other risk factors such as diabetes mellitus (DM), hypercholesterolemia and smoking and increases the risk

for CVD especially in the elderly. Apart from vascular risk factors, genetic factors are also known to play a role in the etiology of the CVD. [12]

Tracing the history of this malady it is interesting to note that HT has been described in Ayurvedic facts dating back to 1000 BC as Sira Kanchan and Rakta Poornta, where the tension of the blood rises from within due to the provocation and constriction of arterioles and venules.The role of mental affliction is provoking cardiac disorders and deaths is also highlighted in the Ayurvedic system of medicine. [1]

Till recent past control and prevention of communicable diseases was emphasized in India. Recently attention has shifted to control and prevention of non communicable diseases including stroke, HT, coronary artery disease (CAD) at the national level in view of the rising trend. Various hypothesis has been put forward to explain this rising trend and among these, consequences of urbanization such as changes in life style pattern, diet and stress has been implicated. The current urbanization rate in India is 35% as compared to 15% in the 1950. [13] With growing urbanization socio-developmental changes having taken place over last 40-50 years. Dramatic changes in lifestyle from traditional to modern have lead to physical inactivity due to technological advances. Rising affluence has modified the dietary pattern characterized by increased consumption of diets rich in fat, sugar and calories.

Thus seeing the rising trend of hypertensives there is an urgent need for primary prevention of HT. So in order to successfully treat a disease it is necessary to remove or reduce its cause rather than its manifestations or markers.

I. Hypertension:

The recommendation of the Seventh Joint National Committee (JNC) on the Definition and Classification of HTN are shown in table 1.1. [2]

A new category designated prehypertension has been introduced in the JNC VII criteria. Patients with prehypertension are at increased risk for progression to HT; those in the 130-139/80-89 mmHg BP range are at twice the risk to develop HT as those with lower values. [14] Recent data from the Framingham Heart Study suggest that individuals who are normotensive at age

55 have a 90% life time risk for developing HT. [3] For individuals 40-70 years of age, each increment of 20mmHg in systolic BP (SBP) or 10mmHg in diastolic BP (DBP) doubles the risk of CVD across the entire BP range from 115/75 to 185/115mmHg. [15]

Table 1.1
Definitions and Classification of Hypertension

BP classification	SBP mmHg	DBP mmHg
Normal	< 120	and < 80
Prehypertension	120-139	or 80- 89
Stage I Hypertension	140-159	or 90- 99
Stage II Hypertension	≥ 160	or ≥100

Health dangers from BP may vary among different age groups and depending on whether systolic or diastolic (or both) is elevated. A third measurement, pulse pressure is becoming important as an indicator of severity.

● High systolic BP appears to be a significant indicator for heart complications including death in all ages, but especially in middle aged and elderly people. Infact, elevated SBP may pose a significant danger for heart events and stroke events even when diastolic is normal, a condition called isolated systolic hypertension (ISH).The wider the spread between the systolic and diastolic measurements the greater the danger. ISH is the most common form of HT in people older than fifty.

● High diastolic pressure is a strong predictor of heart attack and stroke in young adults and in people of any age with essential hypertension.

● Pulse pressure is the difference between the systolic and diastolic numbers. It appears to be an indicator of stiffness and inflammation in the blood vessel walls. The greater the difference between systolic and diastolic numbers, the stiffer and more injured the vessels are thought to be. Although not yet used by physician to

determine treatment, evidence is suggesting that it may prove to be a strong predictor of heart problems, particularly in older adults. Some studies suggest that in people over 45 years old, every 10mmHg increase in pulse pressure, the risk for stroke increases by 11%, cardiovascular disease by 10% and overall mortality by 16%.

1. Hypertension Categories:

● Primary Hypertension: Primary HT is also known as essential or idiopathic HT. The causes of essential HT are unknown. The primary determinant of essential HT, which represents 95% of the hypertensive population, have not been elucidated in spite of numerous investigations undertaken to clarify the various mechanisms involved in the regulation of BP, but yet it is believed to be a result from the interplay of multiple genetic and environmental determinants. [16] Essential HT is being increasingly recognized as part of a complex multifaceted disorder which may include other abnormalities including dyslipidaemia, central obesity, glucose intolerance and hyperinsulinaemia, all of which may increase the risk of coronary heat disease (CHD). [17] Essential HT tends to cluster in families and represents a collection of genetically based disease and/or syndromes with a number of underlying inherited biomechanical abnormalities. [18,19]

● Secondary Hypertension: Secondary hypertension comprises about 5% of high BP cases; wherein the cause of this HT is identified. It is important to recognize these because they can often be improved or cured by surgery or specific medical therapy. Certain clues related to age, history, physical examination and laboratory results point to the possibility of secondary HT. For e.g.: when HT develops before 30 or after age 50, a secondary cause should be considered. Younger patients might have renal artery stenosis or coarctation of the aorta. In an older patient, the most likely cause is renovascular disease associated with atherosclerosis. Unexplained hypokalemia, hypercalcemia or hyperglycaemia may be the cause associated with secondary HT.

● Isolated Systolic HT: Systolic HT is a particular problem in the elderly and contributes significantly to cardiovascular and cerebrovascular risk. Isolated systolic HT (ISH) is defined as a sustained SBP above 140mmHg with normal DBP of less than 90mmHg.HT occurs in 50% of those over 60 years of age regardless of race.

Increased rates of ISH (>160/<90mmHg) among older individuals were observed in the 1970s. [20] Both the third National Health and Nutrition Examination Survey (NHANES III) and Framingham data have shown that SBP rises with age, contrasting a seemingly age-related decline in DBP beginning between the age of 50 -60 years. [21,22]

Systolic hypertension has been recognized as a risk factor for CVD for more than 30 yrs. [23] Garland *et al.* [24] observed an increased risk of stroke related mortality in association with an ISH of ≥160/90 mm Hg. In Finland, ISH of 165/95 mmHg in men and women aged 30 to 59 yrs was associated with increased risk of acute myocardial infarction (MI), stroke and death. [25] The Framingham studies provided the earliest data suggesting that SBP affects risk more than DBP. [26,27] Among the men screened for inclusion in the Multiple Risk Factor Intervention Trial (MRFIT) SBP was a better predictor of CHD and all cause mortality than DBP. [28] Data from the National High Blood Pressure Education Programme revealed that for all levels of DBP, SBP confers increased cardiovascular risk and reduced life expectancy. [29]

ISH in the elderly contributes to the following cardiovascular and cerebrovascular risk.

1. Three-fold increase of stroke
2. Increased risk of overall mortality
3. Increased risk of cardiovascular mortality
4. Increased risk of congestive heart failure

As the pendulum of interest once swung from DBP to SBP, today there is increasing interest in pulse pressure (PP), the difference between SBP & DBP. PP has been associated with risk of congestive heart failure, [30] coronary artery disease, [31] and stroke. [32] In a meta-analysis of data from 3 trials enrolling patients older than 60 years with systolic HT (the European Working Party on High Blood Pressure in the Elderly trial, the Systolic Hypertension in Europe [Syst-Eur] trial, and the Systolic Hypertension in China [syst-China] trial), each 10-mmHg increment in PP conferred a 20% increased risk of cardiovascular mortality. [33] More importantly, analysis from the Systolic Hypertension in the Elderly Programme (SHEP) [32] and the Established Populations for the Epidemiologic study of the Elderly [34] established PP as a risk factor for all cause mortality. Numerous studies have documented the importance of PP as a risk factor for adverse clinical outcomes in the general population [30,35] and in various selected cohorts with or without prevalent CVD. [32,36]

In patients > 60 yrs old, DBP is inversely related to adverse coronary events because increasing PP, which conveys increased risk is associated with

both higher SBP and lower DBP. [37] Also as demonstrated in the Systolic Hypertension in the Elderly Programme (SHEP) Study, the benefits of treating SBP in this high risk group are substantial, with, marked reductions in the rates of stroke, myocardial infarction, and heart failure. [37] Since SHEP, two other large studies have demonstrated that treatment of SBP leads to reductions in cardiovascular events. [38,39] Domanski *et al* [40] concluded, "Any combination of 2 of the 3 BP measures (i.e., SBP, DBP, PP) provided more information about CVD risk than any single measure." Each component of BP obtained by routine measurement has potential clinical utility in the aging vasculature, risk prediction progresses such that DBP is supplanted by SBP, which subsequently is eclipsed by PP. [41]

2. PATHOPHYSIOLOGICAL MECHANISMS OF HYPERTENSION

The cause of HT is unknown in most cases, but it seems that multifactorial events participate in the development of this pathology. The pathophysiological hallmark of HT is a rise in peripheral vascular resistance but no single or specific cause of essential HT has been firmly established. Haemodynamic studies revealed that while the cardiac output may be elevated during the developmental phases of HT, ultimately it declines progressively. Thus in the basic equation, BP= cardiac output x peripheral vascular resistance, the establishment of HT is frequently associated with a normal cardiac output and elevated vascular resistance. What causes the resistance to go up is not fully understood. [42]

Excessive sodium retention by the kidney may play a major initial role. A resetting of the pressure-natriuresis relationship wherein a rise in systemic BP evokes further sodium retention has been proposed as a possible renal mechanism. [42] Prostaglandins are important in maintaining renal and other regional circulations regulating sodium and water excretion, suppressing cardiovascular responses to pressure stimuli and potentiating the responses to kinins and other vasodepressor substances. [43] The products of prostaglandins namely PGE_2 and PGI_2 along with the kinins form the main axis of vasodilatory influence and their deficiency; particularly in kidney was considered a contributing factor in the causation of HT.

Kidney plays an important role in maintaining intravascular volume and BP. [44] In essential HT the kidney requires a higher than normal blood pressure

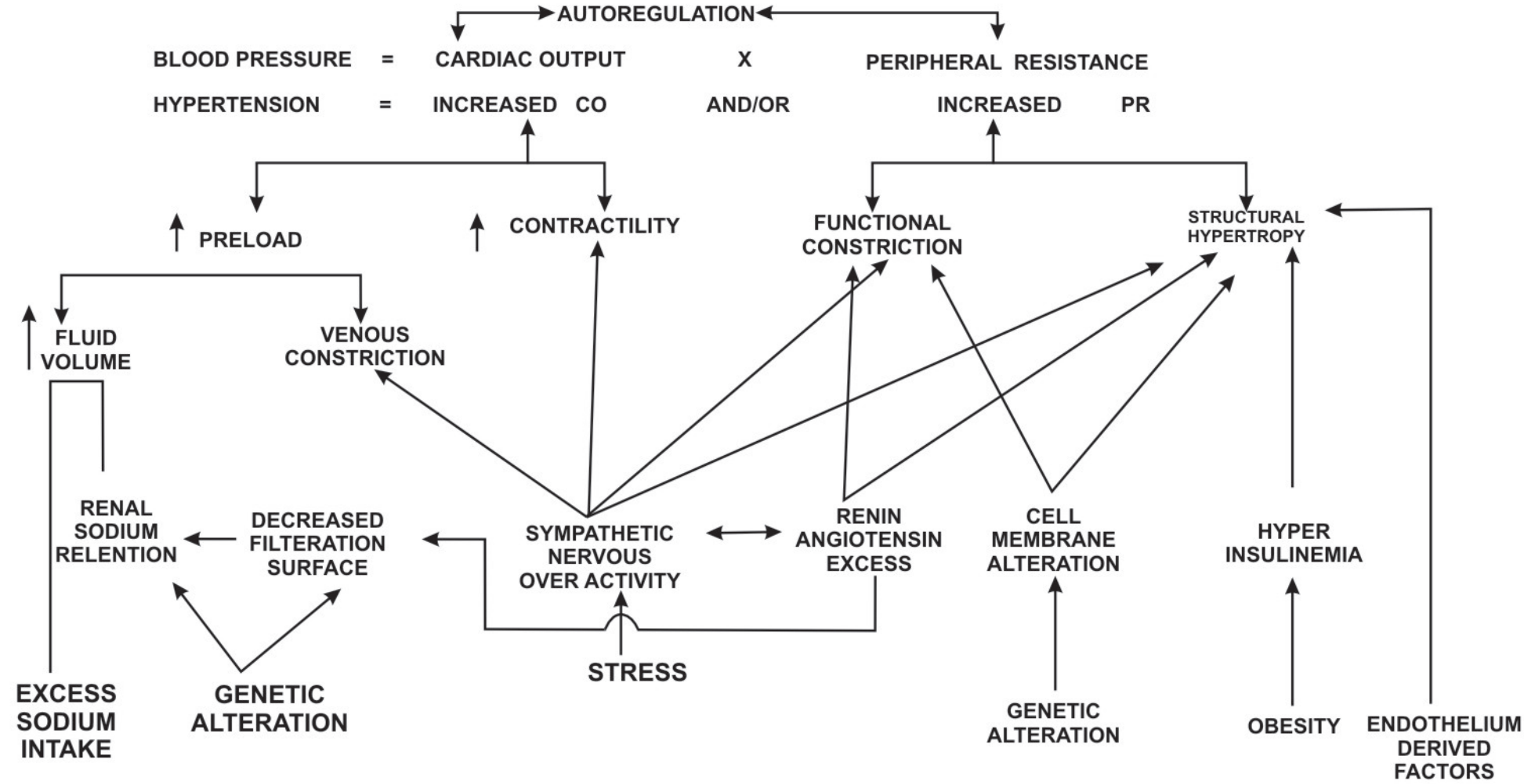
to maintain normal extra cellular fluid volume. Robert [45] reviewed the evidence that essential HT results from an inherited renal tendency towards excess vasoconstriction or an inability to appropriately increase renal blood flow. This would be especially important in certain environmental situations involving a high dietary intake of NaCl or stress with central nervous system (CNS), sympathetic nervous system (SNS) and renal vascular consequences. In addition, kidneys subjected to elevated blood pressure, over time, develop structural changes due to arteriosclerosis that limit its ability to excrete sodium and water in response to increase in pressure. Thus, defect in excretion of salt and water may play a central role in pathogenesis of essential HT. [45]

In some hypertensive patient, it has been suggested that hyperfunction of the cardiac sympathetic nerves leads to increased cardiac output and systolic hypertension. Eventually, protective peripheral arteriolar constriction i.e. auto regulation results in diastolic hypertension. [46] The SNS directly or indirectly dictates the state of cardiac output and systemic vascular resistance. Thus, inappropriate or excessive activity of SNS may increase the BP (Fig 1.1). Stero Julius [47] also showed strong evidence for increased sympathetic drive in the early phase of hypertensive process in prehypertensive and stage 1 i.e. these subjects have increase cardiac beta adrenergic and vascular alpha adrenergic drive. In addition to high plasma nor epinephrine values, their cardiac output and heart rate are also elevated. This hyperkinetic state is a stage in the evolution of established HT. Tecumsch-Michigen population based study showed that hyperkinetic state is very frequent and is seen in 37% of all prehypertensive middle aged men. The hyperkinetic subjects show higher BP readings since childhood and have strong background of parental HT. [47]

Salt dependent rat model of essential HT showed that provision of increased intake of the amino acid arginine prevents HT and nephrosclerosis on high salt intake. Arginine is the substrate for the enzyme nitric oxide synthetase which produces nitric oxide (NO) one of the potent endothelium derived vasodilators. NO also functions as a physiological regulator of basal vasomotor tone, this regulation may be abnormal in essential HT. NO also inhibits smooth muscle cell and mesangial cell mitogenesis. [45] Endothelial dysfunctions characterized by reduced production of NO and/or by increased generation of endothelien-1 may play a pathogenetic role. [42]

Specific molecular defects in cell membrane system such as Na^+/ K^+ ATPase co-transport have been described in hypertensive subject and related to the pathogenesis of hypertension. Several abnormalities like excessive passive entry of Na^+, increased maximal rate of Na^+/ Li^+ exchange, and decreased apparent affinity of the Na^+/K^+ pump for internal Na^+ have been found in red blood cells of human hypertensive. The consequence of these abnormal alterations in cellular handling of Na^+ is an increase in intracellular Na^+

FIGURE : 1.1 : ROLE OF AUTHOREGULATION IN THE PATHOLOGENESIS AND PROGRESSION OF HYPERTENSION



concentration which results in an increased intracellular free Ca^{++} concentration. [44]

Inappropriate release of renin culminating in the formation of angiotensin II which causes vasoconstriction is also a possible mechanism (Fig 1.2) Sympathetic overactivity may also augment renin release. [42] The inherited abnormalities in renin-angiotensin aldosterone system, perhaps including alterations in sympathetic nervous drive to renin release and/or an intrinsic defect in the ability of the kidney to handle volume overload, may contribute to the pathogenesis of essential hypertension.

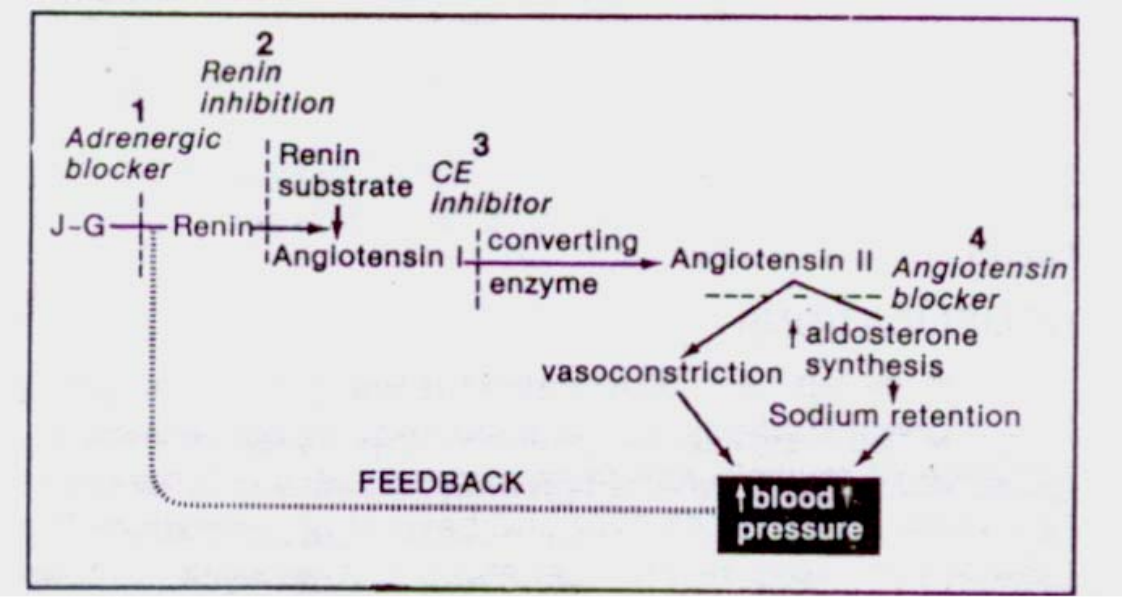


Fig 1.2 Role of renin-angiotensin system in the pathogenesis of hypertension. Note the effect of drugs at various steps in the pathway

Insulin resistance and hyperinsulinaemia are associated with hypertension. While the cause of insulin resistance is not known, it results in a failure of vasodilation, thus ensuring a rise in systematic blood pressure. [42] Many yet undetermined local hormones may participate in the pathogenesis of hypertension by causing vasoconstriction or by preventing vasodilation.

Thus in short pathophysiological factors for HT include increased sympathetic activity, overproduction of unidentified sodium retaining hormones,

chronic high sodium intake, inadequate dietary intakes of K^+ and Ca^{++}, increased or inappropriate renin secretion, deficiencies of vasodilators such as prostaglandins, congenital abnormalities of the resistance vessels, diabetes mellitus, insulin resistance, obesity, increased activity of vascular growth factors and altered cellular ion transport. [44]

3. Management:

The ultimate public health goal of antihypertensive therapy is the reduction of cardiovascular and renal morbidity and mortality. In clinical trials, antihypertensive therapy has been associated with reductions in stroke incidence averaging 35-40%; myocardial infarction 20-25% and heart failure, more than 50%. [48] In a recent Cochrane review examining long term use of antihypertensive medication in the elderly, cardiovascular morbidity and mortality was reduced by 29%, from 177 to 126 events per 1000 people. [49] It is estimated that in patients with stage1 hypertension (SBP 140-159mmHg and or DBP 90-99mmHg) and additional cardiovascular risk factors achieving a sustained 12mmHg reduction in SBP over 10 years will prevent 1 death for every 11 patient treated. In the presence of CVD or target organ damage only 9 patients would require such BP reduction to prevent a death. [50] Since most persons with HT, especially those age >50 years, will reach the DBP goal once SBP is at goal, the primary focus should be on achieving the SBP goal. Treating SBP and DBP to targets that are <140/90mmHg is associated with a decrease in CVD complications [2]

4. Lifestyle Modifications:

Adoption of healthy lifestyles by all persons is critical for the prevention of high BP and is an independent part of the management of those with hypertension. Major lifestyle modifications shown to lower BP include weight reduction in those individuals who are overweight or obese [51], adoption of the dietary approaches to stop hypertension (DASH) eating plan [52] which is rich in potassium and calcium [53], physical activity [54] and moderation of alcohol consumption. [55] (Table 1.8) Lifestyle modification reduces BP, enhance

antihypertensive drug efficacy and decrease cardiovascular risk. Combinations of two or more lifestyle modifications can achieve even better results.

Table 1.2
Lifestyle modifications to manage hypertension

Modification	Recommendation	Approximate SBP Reduction (Range)
Weight reduction	Maintain normal body weight (body mass index 18.5–24.9 kg/m^2).	5–20 mmHg/10 kg weight loss[23,24]
Adopt DASH eating plan	Consume a diet rich in fruits, vegetables, and lowfat dairy products with a reduced content of saturated and total fat.	8–14 mmHg[25,26]
Dietary sodium reduction	Reduce dietary sodium intake to no more than 100 mmol per day (2.4 g sodium or 6 g sodium chloride).	2–8 mmHg[25–27]
Physical activity	Engage in regular aerobic physical activity such as brisk walking (at least 30 min per day, most days of the week).	4–9 mmHg[28,29]
Moderation of alcohol consumption	Limit consumption to no more than 2 drinks (1 oz or 30 mL ethanol; e.g., 24 oz beer, 10 oz wine, or 3 oz 80-proof whiskey) per day in most men and to no more than 1 drink per day in women and lighter weight persons.	2–4 mmHg[30]

DASH, Dietary Approaches to Stop Hypertension.
* For overall cardiovascular risk reduction, stop smoking.
† The effects of implementing these modifications are dose and time dependent, and could be greater for some individuals.

Despite the clear benefits of pharmacological managing HT ,only approx 31% of all hypertension patients have their BP under effective control (<140/90mmHg) [56] Furthermore, only 10% of hypertensive men aged 18 to 74 years have their BP under control. [57] Although awareness and treatment of BP have increased over the past several decades, levels of control of BP especially systolic BP (SBP), have plateaued or even fallen in recent years [2,58] Also, most poor control is because of failure to attain SBP targets. There is an epidemic of uncontrolled systolic hypertension which may stem in part, from prior beliefs that elevated SBP is a normal accompaniment of aging that is tolerable so long as DBP is controlled. Recent studies on the importance of elevated SBP and especially PP have clearly shown that this approach is no longer tenable. [32]

In the traditional view of HT case, the major barrier to BP control is patient non adherence to prescribed therapies. For example the 1988 report of the JNC on Detection, Evaluation and treatment of high blood pressure states that poor adherence is the “major reason for inadequate control of high blood pressure” and physicians cite failure to make lifestyle changes and take medications as instructed as the two most common factors impeding effective treatment. [59,60] Rates of BP control in the US are consistent with world wide rates, which range from 6% to 40%. [58] Abundant evidence shows that effective BP control lowers the risk of CVD. [49,61,62] Therefore achieving adequate BP control is important for reducing the burden of HT related CVD.

HT is a cardinal risk factor for coronary artery disease and the risk of CAD further increases in presence of dyslipidemia. [63] Both HT and dyslipidemia coexist more often than by a chance alone. [64-66] Although a common metabolic abnormality may underlie both disorders another possibility is that one may be implicated in the development of the other. A few studies in Western populations have established the relationship between HT and hyperlipidaemia. [66,67]

Indian data on the co-existence of this risk factor is scanty. Epidemiologic studies in India have found more on the prevalence of either HT or CHD in various communities [68,69] the correlations of various risk factors with CHD. [70] Recently two studies have been published which show a high prevalence of lipid and glucose abnormalities in Indian hypertensive patients. [71,72] Another study [17] showed that with increasing severity of HT there was a steady and significant rise in the proportion of patients having borderline or high TC, LDL-C and low HDL-C. Various epidemiological studies in the world have shown a positive relationship between plasma cholesterol, LDL, VLDL, TG and the incidence of CHD. [73-75] In some countries as in India, the role of TC in the occurrence of MI have been found to be not significant. [76] The controversy regarding the lipid hypothesis for antherogenesis and the role of cholesterol in CHD continues.

In tropical countries [77] like India and Africa the last 2 to 3 decades have seen a marked increase in the incidences of cardiac diseases. The socio-economic development of under privileged and the rapid sophistication of life style have made diseases such as Ischemic Heart disease (IHD) and HT common in these countries. Deaths due to cardiac diseases in under developed countries like Mexico, Philippines are 17.6 and 14.8% respectively. In Asia and Africa, CHD accounts for 8 to 20% of all medical admissions to hospitals. [77]

In India, HT and atheromatosis are the most important CVD entities which have caused stroke, renal diseases, cardiac hypertrophy (due to HT) and CAD due to atheromatosis in this century. There has been progressive increase in the reported incidence of mortality due to CHD and this trend has yet not leveled off. [78]

A prospective autopsy study [79] showed a linear correlation between the concentration of plasma cholesterol and severity of atherosclerosis. This conclusion was further strengthened by the predominance of cholesterol as cholesteryl ester among the lipids in the atherosclerotic plaques and the fact that experimental manipulation of the serum cholesterol content induces or diminishes lesions [80]. The findings of Coronary Drug Project [79] strongly and significantly related serum cholesterol to focus end points viz mortality from all causes, mortality from CHD, sudden death due to CHD and incidence of nonfatal myocardial infarction. Simons [81] analyzed epidemiological data from 19 countries and found that in men 45% of inter population difference in CAD mortality could be accounted for by the variation in serum cholesterol level. Peto [82] also noted that in societies in which average TC levels are under 150mg/dl and LDL-C levels are low the risk for atherosclerosis and CAD were greatly reduced.

Thus hypercholesterolemia is a major risk factor in the development of CHD and in the progression of atherosclerosis. [83] CHD morbidity and mortality is positively related to LDL-C concentration and inversely related to HDL-C concentration. [84] Not only does lowering TC and LDL-C in asymptomatic individuals with hypercholesterolemia reduce CHD death and nonfatal coronary events [85] but lowering TC reduces risk of subsequent CHD events in people with established CHD [86] and may actually slow the progression of CHD. [87]

During the past decade, there has been tremendous progress in identifying novel risk factors and precisely delineating the role of traditional risk factors associated with CHD, with substantial research advances related to the role of lipoproteins (Lps) and lipid metabolism. Before dealing with the role of lipids and lipid metabolism, a study of lipids, lipoproteins and lipid metabolism is necessary.

II. LIPIDS:

'Lipid' is the term used to describe a number of substances of diverse chemical structure which bear little functional relationship to each other but which have in common the property of being (1) relatively **insoluble in water** and (2) **soluble in nonpolar solvents**. They can be broadly classified as fatty acids, triglycerides, cholesterol and phospholipids.

As lipids are not water-soluble they are transported in the plasma in association with proteins. Albumin is the principal carrier of free fatty acids (FFA) while the other lipids circulate in complexes known as lipoproteins. [88]

1. Lipoproteins:

The lipoproteins are macromolecular complexes of lipid (cholesterol, triglyceride, phospholipids) and protein(apolipoproteins, enzymes). All have the same basic structure, triglycerides and cholesteryl esters form a hydrophobic core surrounded by a layer of amphipathic phospholipids and protein known as apolipoproteins fig.[2.1]. [88] A small proportion of lipoprotein cholesterol is unesterified and located on the surface. The latter (apolipoprotein) are important both structurally and in the metabolism of lipoproteins. {fig. [2.2]} [88] The apolipoprotein governs the lipoprotein interaction with enzymes, lipid transport proteins and cell surface receptors.

a) Classification of lipoproteins:

Lipoproteins are classified on the basis of their densities as demonstrated by their ultracentrifugal separation. Density increases from chylomicrons (CM), of lowest density through lipoproteins of very low density (VLDL), intermediate density (IDL), low density (LDL), to high density lipoproteins (HDL). HDL can be separated, on the basis of density, into two metabolically

distinct subtypes, HDL 2 (density1.064-1.125) and HDL 3(density 1.126-1.210). Distinct subtypes of LDL are also recognized. IDL are normally present in the blood stream in only small amounts but can accumulate in pathological disturbances of lipoprotein metabolism. This approximate lipid and apo content is illustrated in fig.2.2 and the classification in table 2.2. However it is important to appreciate that the composition of the circulatory lipoproteins is not static. They are in dynamic state with continous exchange of components between the various types. The principal functions of these lipoproteins are summarized in table 2.2.

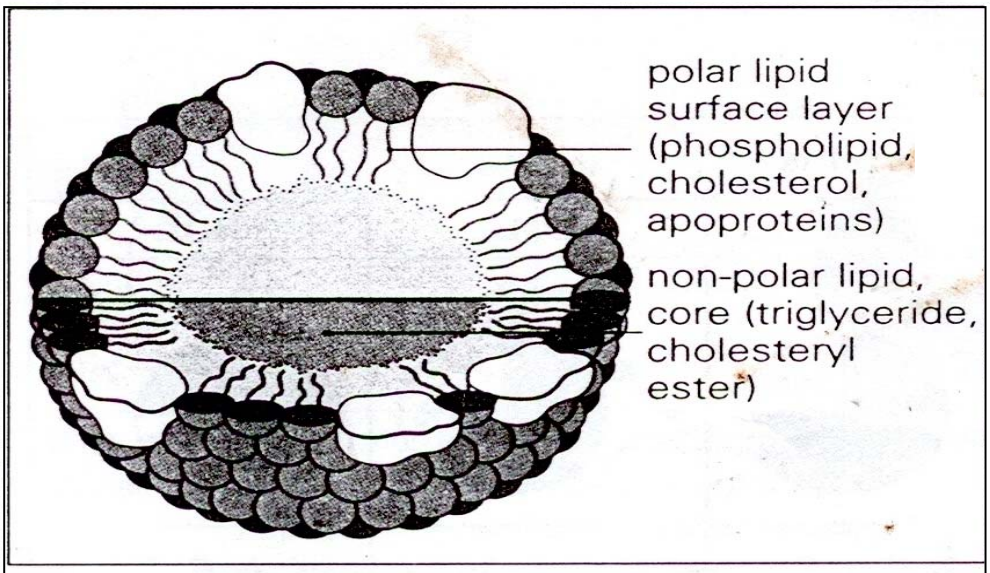


Fig. 2.1 Diagram showing the composition of a lipoprotein particle. A segment has been removed to reveal the non-polar core of cholesteryl ester and triglyceride surrounded by phospholipids and apoprotein.

Apolipoprotein	Function
A-I	cofactor for LCAT structural (in HDL)
A-II	activator of hepatic lipase structural (in HDL)
B-100	structural (in LDL and VLDL) receptor binding
B-48	structural (in chylomicrons)
C-I	cofactor for LCAT?
C-II	activator of LPL
C-III	inhibitor of LPL?
E	receptor binding

Table 2.1 Functions of the major apolipoproteins.

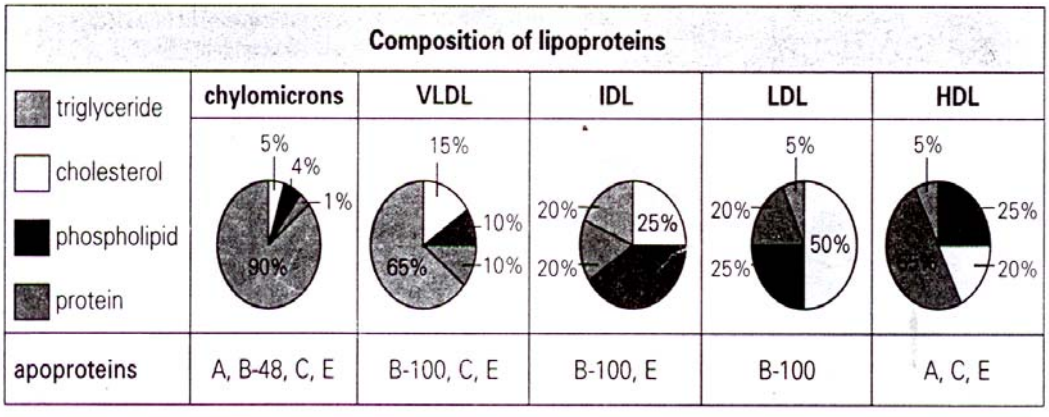


Fig 2.2

Composition of lipoproteins although composition in each class is similar, the particles are heterogeneous so the percentage given are approximate. Figure shown for HDL are for HDL3; HDL2 contains protein and more lipid. Only the principal apoproteins are shown

Classification and characteristics of lipoproteins					
lipoprotein	**density (g/mL)**	**mean diameter (nm)**	**electrophoretic mobility**	**source**	**principal function**
CM	<0.95	500	remains at origin	intestine	transport of exogenous triglyceride
VLDL	0.96–1.006	43	pre-β	liver	transport of endogenous triglyceride
IDL	1.007–1.019	27	'broad β'	catabolism of VLDL	precursor of LDL
LDL	1.02–1.063	22	β	catabolism of VLDL, via IDL	cholesterol transport
HDL	1.064–1.21	8	α	liver, intestine; catabolism of CM & VLDL	reverse cholesterol transport

Table 2.2
Classification and Characteristics of Lipoproteins

b) Lipoprotein Metabolism:

- Chylomicrons (CM):

CM (fig 2.3) is formed from dietary fat (principally triglyceride but also cholesterol) in enterocytes; they enter the lymphatics and reach the systemic circulation via the thoracic duct. CMs are the major transport form of exogenous (dietary) fat. TGs contribute about 90% of the lipid.

Fig 2.3

Chylomicrons (CM)

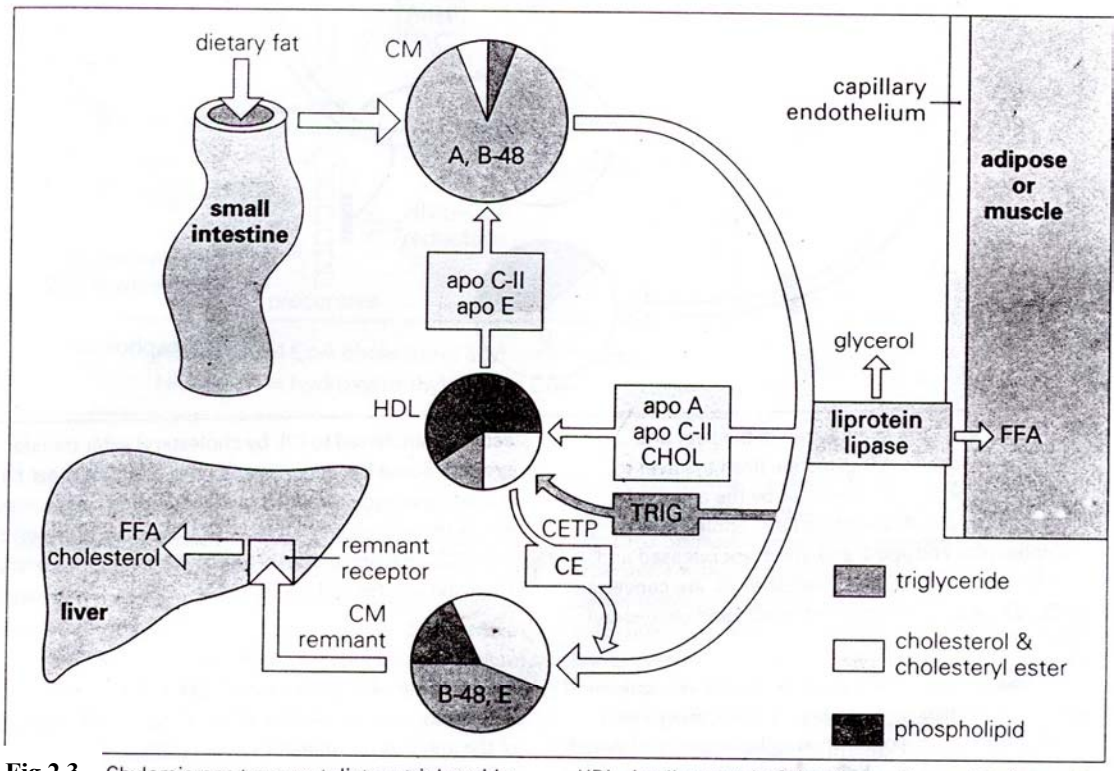


Fig 2.3 Chylomicrons transport dietary triglyceride to tissue where it is removed by the action of lipoprotein lipase. The resulting remnant particles are removed by the liver. They bind to remnant receptors (which recognize apo E) on hepatic cells, are internalized and catabolized. Apolipoproteins A and B-48 are synthesized in intestinal cells; apo C and apo E are acquired, together with cholesteryl esters (CE), from HDL. Apolipoprotein C-II activates lipoprotein lipase. As triglyceride is removed from chylomicrons, apo A, apo C, cholesterol and phospholipids are released from their surfaces and transferred to HDL where the cholesterol is esterified. Cholesteryl ester is transferred back to the remnant particles in exchange for triglyceride by cholesteryl ester transport protein (CETP).

- Very low density lipoprotein (VLDL):

VLDL (fig 2.4) are formed from triglyceride synthesized in the liver either denovo or by the reesterification of FFA. VLDL also contain some cholesterol, apoB, apoC and apoE, the apoE and some of the apoC is transferred from circulating HDL. VLDL are the principal transport form of endogenous TG and initially share a similar fate to chylomicrons triglyceride being stripped of by the action of LDL.

Fig 2.4
Very low density lipoproteins

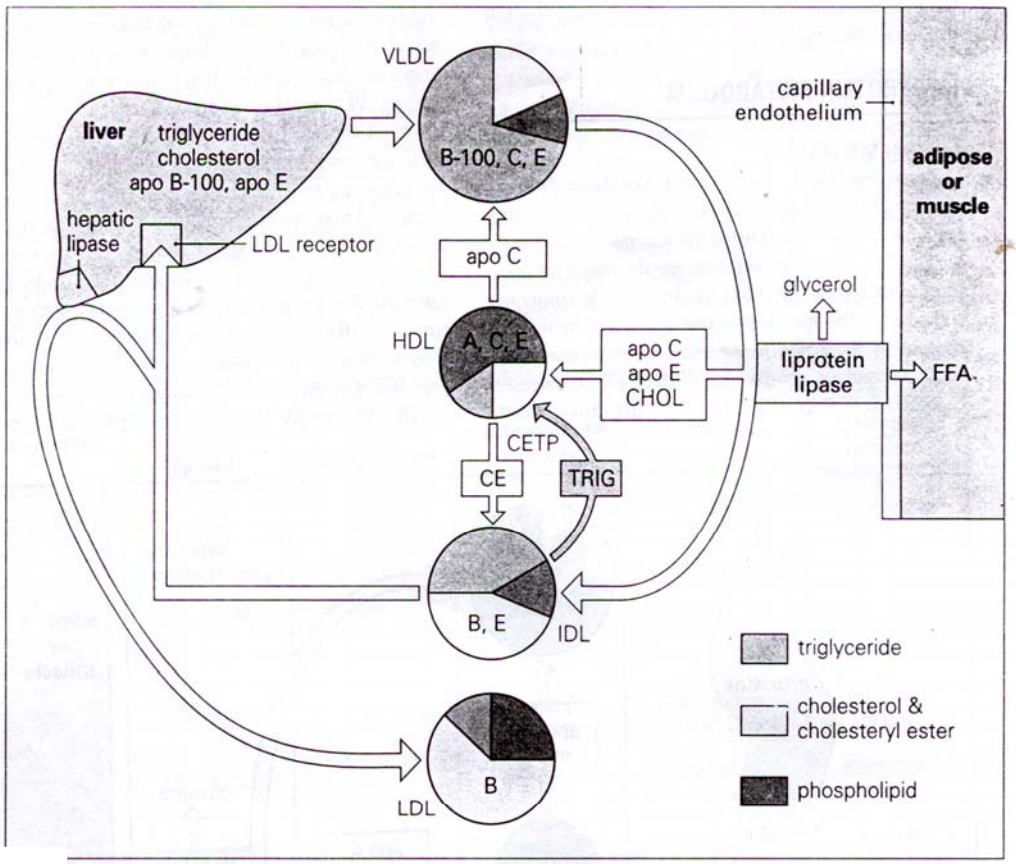


Fig 2.4 .6 VLDL are synthesized in the liver and transport endogenous triglyceride from the liver to other tissues where it is removed by the action of lipoprotein lipase. At the same time, cholesterol, phospholipids and apo C and apo E are released and transferred to HDL. By this process VLDL are converted to IDL. Cholesterol is esterified in HDL and cholesteryl ester is transferred to IDL by cholesteryl ester transfer protein. Some IDL is removed by the liver but most has more triglyceride removed by hepatic triglyceride lipase and is thereby converted into LDL. Thus the triglyceride-rich VLDL are precursors of LDL, which comprise mainly cholesteryl ester and apo B-100.

- Low density lipoprotein (LDL):

LDL is the principal carrier of cholesterol, mainly in the form of cholesteryl ester. They are formed from VLDL via IDL (fig 2.5). LDL can pass through the junctions between capillary endothelial cells and attach to LDL receptors on cell membranes that recognize apoB100. LDL receptors are saturable and subject to down regulation by an increase in intracellular cholesterol. Macrophages derived from circulating monocytes can take up LDL via scavenger receptors. This process occurs at normal LDL concentration but is enhanced when LDL concentrations are increased and by modification, e.g. oxidation of LDL. LDL concentration increases during childhood and reach adult levels after puberty.

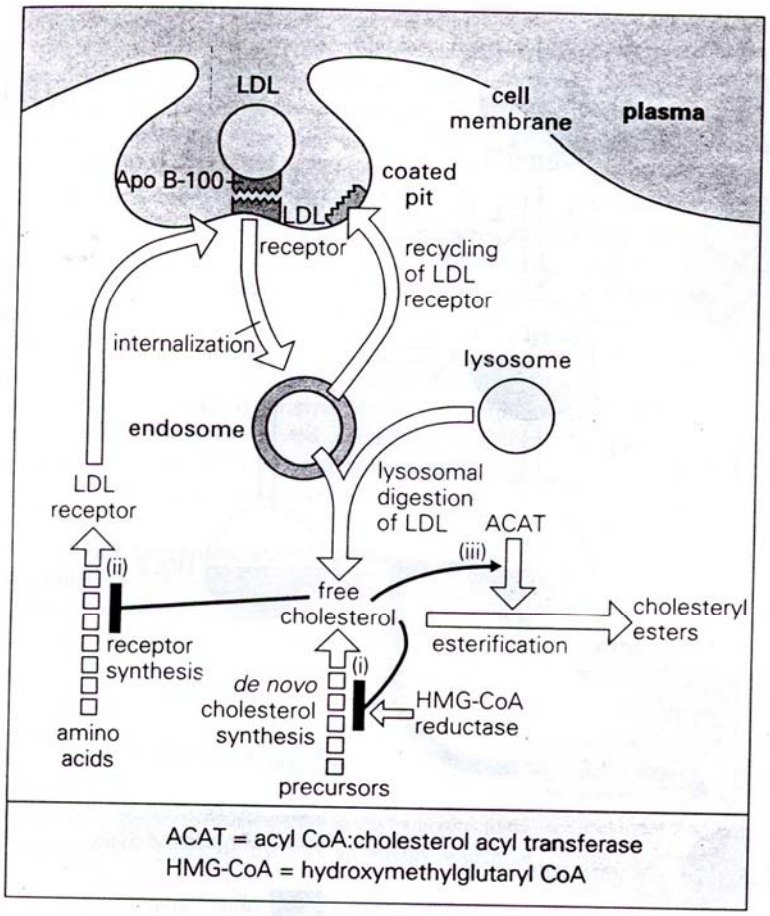


Fig 2.5 LDL metabolism. LDL are derived from VLDL, via IDL. They are removed by the liver and other tissues by a receptor-dependent process involving the recognition of apo B-100 by the LDL receptor. The LDL particles are hydrolyzed by lysosomal enzymes, releasing free cholesterol which (i) inhibits HMG-CoA reductase, the rate-limiting step in cholesterol synthesis, (ii) inhibits LDL receptor synthesis and (iii) stimulates cholesterol esterification by augmenting the activity of the enzyme, acyl-CoA: cholesterol acyl transferase (ACAT).

Fig 2.5
Low Density Lipoprotein Metabolism

- High density lipoproteins (HDL):

HDL is the smallest lipoprotein and contains the least lipid. It has a core of CE and TG and a PL coat containing apoAI and apoII. [89] HDL (fig 2.6) is synthesized primarily in the liver and to a lesser extent in small intestinal cells as a precursor (nascent HDL) comprising PL, cholesterol, apoE and apoA. Apo A1 like HDL is produced by both the liver and intestine while Apo AII is synthesized by the liver only. [90]

Fig 2.6
High Density Lipoprotein Metabolism

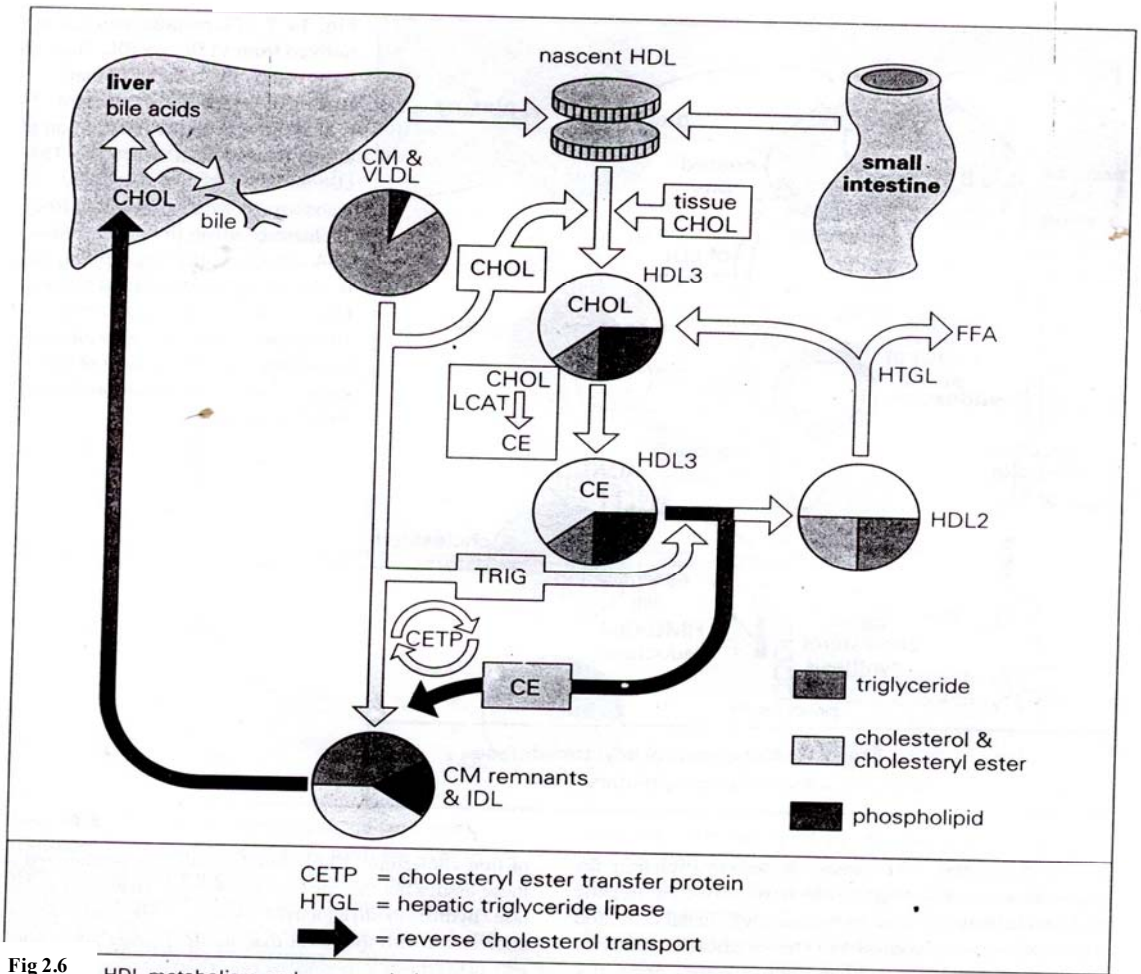


Fig 2.6 HDL metabolism and reverse cholesterol transport. Nascent HDL acquires free cholesterol from extra-hepatic cells, chylomicrons and VLDL and is thereby converted to HDL3. The cholesterol is esterified by the enzyme LCAT and cholesteryl ester is transferred to remnant lipoproteins by CETP in exchange for triglyceride. Remnant particles are removed from the circulation by the liver whence the cholesterol is excreted in bile both *per se* and as bile acids. Much HDL is recycled although some is probably taken up by the liver and catabolized. Apoprotein transfers have been omitted for clarity.

Thus HDL has two important functions: it is a source of apoproteins for CMs and VLDL and it mediates reverse cholesterol transport taking up cholesterol from senescent cells and other lipoproteins and transferring it to remnant particles which are taken up by the liver. Cholesterol is excreted by the liver in the bile, both as cholesterol and after metabolism to bile acids.

2. Disorders of lipid metabolism:

There are several rare, inherited metabolic diseases associated with the accumulation of lipids in tissues and others in which plasma lipoprotein concentration are reduced. By far, the commonest disorders however are the Dyslipidaemias. [88]

Dyslipidaemia has numerous forms mainly hypercholesterolemia, hypoalphalipoproteinemia and hypertriglyceridemia. The term itself simply refers to an abnormal metabolism of plasma lipids which can be caused by genetic, dietary and secondary disease factors. For the safe cholesterol transport, cholesterol concentration in plasma must be kept sufficiently low and its tendency to escape from the bloodstream must be controlled. [91]

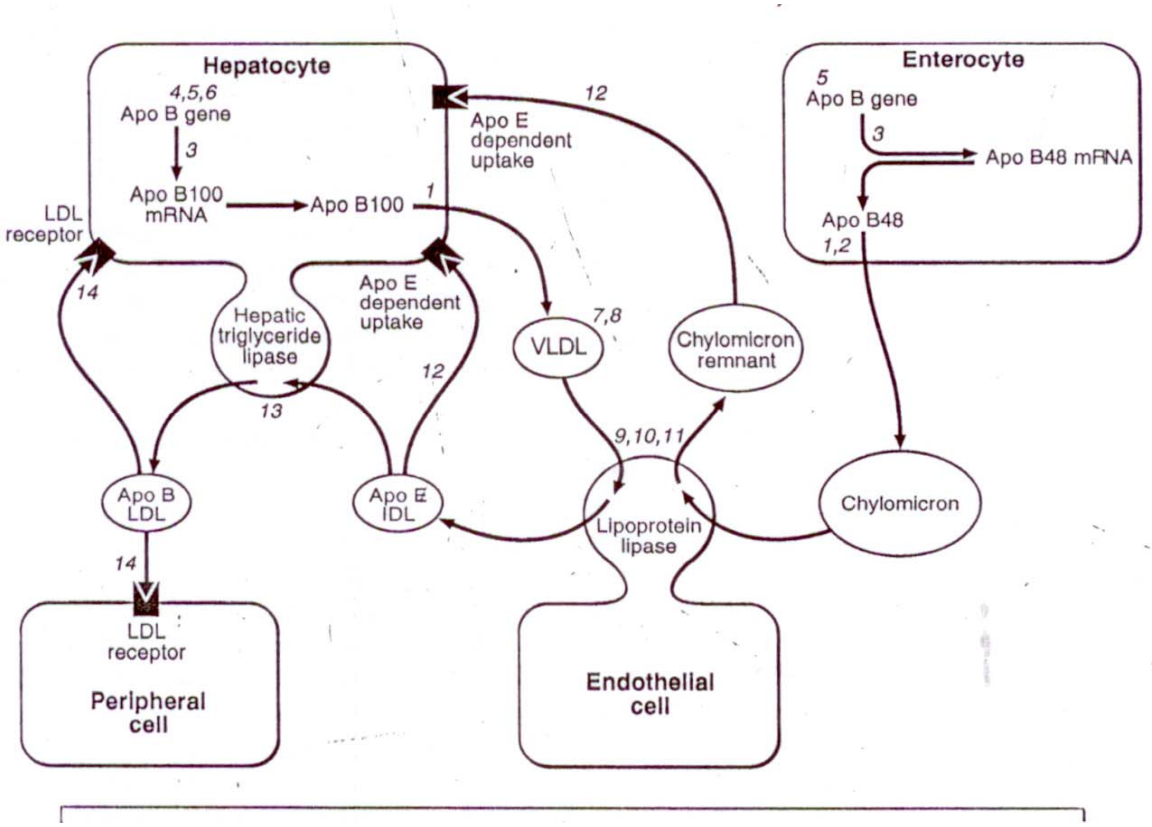
Hyperlipidaemia refers to an increased concentration of either cholesterol or TG or both these lipids in serum and results from an increase in one or other class of plasma lipoproteins. The terms hyperlipidaemia or hyperlipoproteinemia imply an increase above a defined upper limit. When hyperlipidaemia is defined in terms of a class or classes of elevated plasma lipoproteins the term hyperlipoproteinemia is used.

Three categories of causation, however has been identified viz (1) genetic (2) secondary to other diseases and (3) dietary. A deficiency of an enzyme on a single gene defect may result in an abnormal lipoprotein. However in many cases the underlying mechanism or the basic defect is not known or fully understood. Thus hyperlipoproteinemia due to genetic defect or due to unidentified cause or due to imbalance in dietary practice is known as primary hyperlipoproteinemia.

A primary dyslipoprotenemia is an inherited disorder of lipoprotein metabolism which may manifest as hyperlipidaemia, hypolipidaemia or normolipidaemia associated with lipoproteins of abnormal composition or an abnormal distribution of the normal lipoprotein classes. [92] Finally, a significant

increase in production or an increase in removal of lipoproteins can lead to a marked reduction in lipid and lipoprotein concentrations [93] (fig 2.9). [92]

Fig 2.7
The primary dysbetalipoproteinemia: sites of defects in metabolism.



Key 1.Abetalipoproteinemia
2.Chylomicronemia retention disease
3.Familial hypobetalipoproteinaemia
4.Normotriglyceridemic abetalipoproteinemia
5.Hypobetalipoproteinemia with truncated apo B100
6.Familial defecative apo B100
7.Familial combined hyperlipidemia/hyperapobetalipoproteinemia
8.Familial hypertriglyceridemia
9.Lipoprotein lipase deficiency
10.Apolipoprotein CII deficiency
11.Familial lipoprotein lipase inhibitor
12.Remnant Hyperlipoproteinemia
13.Hepatic TG lipase deficiency
14.Familial hypercholesterolemia

On diagnosing hyperlipidaemia in a given patient the hyperlipidaemic status should be evaluated to determine whether it is primary lipoprotein disorder or secondary to any of a variety of metabolic diseases. The diagnosis of primary hyperlipidaemia is made after secondary causes have been ruled out. The causes of secondary hyperlipoproteinemia are listed in table 2.3. [94]

Table 2.3
Causes of Secondary Hyperlipidaemia and Dyslipoproteinemia

Disorder	Cause
Exogenous	Drugs: corticosteroids, isotretinoin (Accutane), thiazides, anticonvulsants, β blockers, anabolic steroids, certain oral contraceptives
	Alcohol
	Obesity
Endocrine and metabolic	Acute intermittent porphyria
	Diabetes mellitus
	Hypopituitarism
	Hypothyroidism
	Lipodystrophy
	Pregnancy
Storage disease	Cystine storage disease
	Gaucher disease
	Glycogen storage disease
	Juvenile Tay-Sachs disease
	Niemann-Pick disease
	Tay-Sachs disease
Renal	Chronic renal failure
	Hemolytic–uremic syndrome
	Nephrotic syndrome
Hepatic	Benign recurrent intrahepatic cholestasis
	Congenital biliary atresia
Acute and transient	Burns
	Hepatitis
	Acute trauma (surgery)
	Myocardial infarction
	Bacterial and viral infections
Others	Anorexia nervosa
	Starvation
	Idiopathic hypercalcemia
	Klinefelter syndrome
	Progeria (Hutchinson-Gilford syndrome)
	Systemic lupus erythematosus
	Werner syndrome

The acquired hyperlipidaemia or secondary dyslipoproteinemia results from some under lying disorder that leads to alternations in plasma lipid and lipoprotein metabolism. They manifest as an increase in plasma TC and plasma TG levels, or both cholesterol and TG with or without a decrease in the circulating levels of HDL. Treatment of underlying disorder, when possible or discontinuation of the offending drug usually results in improvement in the hyperlipidaemia. [95]

The major atherogenic lipoprotein, the LDL acts for 60% to 70% of the total cholesterol while HDL usually represents some 20 to 30% of the TC and their levels are ½ correlated with the risk for CHD. The VLDL which are largely composed of TG accounts for 10 to 15% of the TC. [96]

a) Hypertriglyceridaemia:

Epidemiologically prospective and case controlled studies have shown that serum TG levels associated positively with the risks for CAD. [97,98] Semi quantitative techniques of meta-analysis on some population based prospective studies [99-102] of TG and CVD showed a relative risk of 1.32 in men and 1.76 in women indicating a 32% and 76% increase in disease risk associated with increased TG. Also, there is growing evidence that hypertriglyceridaemia is a marker for increased risk for CAD; in fact it can serve as a marker for several atherogenic factors. [103] The association between a high TG level and other atherogenic factors theoretically could exist at three levels:

- First, a high TG level would be a marker for raised concentration of atherogenic TG rich lipoproteins (Lps). TG rich lipoproteins include several species of Lps belonging to the classes of CMs and VLDL. Both classes include newly secreted Lps as well as Lps modified in the circulation. Modified and partially catabolized TG rich Lps are called remnants. Remnant Lp are product through the interaction of newly secreted Lps with several factors, most notably Lp lipase. During the catabolism of TG rich Lps they are increased in size and modified in composition. The concentration of TG rich Lps are diminished in TG content but have a gain in cholesteryl esters. Apolipoprotein composition also changes, in rare instances, when the primary structure of apolipoproptein E is genetically abnormal, catabolism and clearance of remnants is severely impaired. [104] Because of their delayed clearance, remnants become highly enriched with cholesteryl ester and apolipoprotein E. These cholesterol enriched remnants are named β-VLDL. Normal remnants contain more TG and less cholesterol than β-VLDL. All CM remnants are removed by the liver. In contrast, VLDL remnant can have 2 fates; about half normally are removed directly by the

liver, whereas the other half are converted to LDL. [103] Animal studies show that the atherogenecity of TG rich LPs increases as LP particles become more enriched in cholesteryl esters. [105]

- Second, an elevated serum TG could be a marker for other Lp abnormalities with which they frequently coexist, namely abnormally small particles of LDL and low concentration of HDL. The combination of high TG level, small LDL particles and decrease HDL chol levels has been named the atherogenic Lp phenotype [106] or simply the Lipid Triad.

Lipid Triad i.e. raised TG levels, small LDL particles and low HDL chol, the latter two abnormalities frequently occurs because of an increase in the TG component of TG rich Lps. [107] Exchange of TG in TG rich Lp for cholesteryl ester in LDL and HDL decreases the cholesteryl ester content of the latter, hydrolysis of the newly acquired TG in LDL and HDL in turn decrease the size of HDL and LDL particles. These changes manifest clinically as smaller LDL particles and low HDL cholesterol levels. Also recent prospective epidemiologic studies [86,108] have also shown that plasma TG and LDL particle size predict subsequent CAD in Caucasian populations. These small LDL particles are more atherogenic than normal sized LDL. Small LDL particles filter more rapidly into the arterial wall than do normal sized LDL, also they could be unusually susceptible to retention in the extra cellular matrix. Both properties would promote atherogenesis, moreover small LDL appears to be more particularly susceptible to oxidation [109]; this too could enhance their atherogenecity. Also an elevated serum TG may increase the risk for CAD by inducing a pro coagulant state. [110] Although an elevation in serum TG commonly causes small LDL particles and low HDL-C levels, there are other causes too.

- Third, since increased TG levels also commonly associate with HT, insulin resistance (with or without glucose intolerance) and a pro thrombotic state, they could be a marker for these non lipid risk factors. The clustering of these non lipid risk factors along with the lipid triad has been called the metabolic syndrome. [111]

The metabolic syndrome is defined as the presence of three or more of the following: [112]

1) Central obesity [waist circumference more than 40 inch in men and more than 35 inch in women]
2) A fasting TG levels of 150mg/dl or more
3) An HDL-C level of less than 40mg/dl in men or less than 50mg/dl in women
4) Blood pressure of 130/85 or higher and
5) A fasting glucose level of more than 110mg/dl

Multiple factors, which are common in our society, combine to cause the metabolic syndrome. These factors are obesity, physical inactivity, certain nutrient excesses and genetics. The syndrome also occurs more frequently with advancing age and it is more common in men than women. The higher frequency in men may be associated with truncal obesity, which seems to enhance the severity of the syndrome.

b) LDL modification and its consequences:

Because most of the cholesterol in the serum is found in the LDL (60to 70%) [96], the concentration of total cholesterol is closely correlated with the concentration of LDL-C. In clinical lipidology the concentration of LDL-C is the time-honored "gold standard" for estimating the plasma Lp-related risk of individuals for complications of atherosclerotic vascular disease. In several animal models, high levels of serum LDL rapidly induce atherosclerosis. [113] Likewise in patients who have high LDL levels on a genetic basis, premature CAD frequently occurs even in the absence of other risk factors. [114] Several studies have convincingly demonstrated that lowering of raised plasma cholesterol can retard progression, even induce regression and reduce the risk of coronary events in patients with atherosclerotic coronary artery disease. The fact that there is a wide diversity in the expression of clinical disease even in subjects with marked hypercholesterolemia reflects a complex multifactorial chronology of events and shows that factors other than raised LDL concentrations are involved in the process of atherogenesis and its clinical sequelae. One of the factors that go "beyond cholesterol" [115] is the "oxidation hypothesis".

The so-called "oxidation hypothesis" [116] states that the oxidative modification of LDL is important and possibly obligatory in the pathogenesis of the atherosclerotic lesion. It was shown that LDL would be taken up faster by macrophages as it is oxidized by the endothelial cells [117] All major types within the atherosclerotic lesions- endothelial cells, smooth muscle cells, macrophages and lymphocyte can oxidize LDL [118], but macrophages appear to be the most active.

- Susceptibility of LDL to oxidation:

Oxidative modification of LDL is believed to be caused by free radicals (FR), substances with unpaired electrons which tend to be highly reactive. The nature of these free radicals and their sources within the cells are controversial. It is still not known whether cells oxidize LDL by releasing simple oxidizing agents such as super oxide or hydrogen peroxide which then attack LDL, or by releasing lipid peroxidation products formed by the oxidation of the cells own lipids. Lipid

peroxidation presumably starts in the polyunsaturated fatty acids (PUFA) in LDL-surface, resulting in oxidation modification not only of the PUFA, but also of the cholesterol moiety itself and of phospholipids. [119] The oxidized PUFA in LDL is converted into lipid hydroperoxide. These fragment into aldehyde which are believed to combine covalently with lysine and may be other as in apoB-100 the protein moiety of LDL. [115] The modified apoB-100 then becomes recognized by scavenger receptors on macrophages.

- Oxidized LDL and Atherosclerosis:

There are several mechanisms by which oxidatively modified LDL promotes atherosclerosis:

1) Chemotactic activity which facilitates the recruitment of blood monocytes.
2) Inhibition of migration of macrophages from the arterial wall back to plasma.
3) Enhanced uptake of LDL by macrophages via scavenger receptors, resulting in the formation of foam cells.
4) Direct cytotoxicity to endothelial cells which may facilitate the entry of LDL and monocytes in the arterial wall in the early stages of the disease process. [117]

Oxidized LDL (Ox-LDL) may contribute to the atherogenesis process above and beyond that of simple deposition of cholesterol within the arterial wall. It leads to enhanced uptake by macrophages and yields many modified molecules with diverse effects. [119] Ox-LDL or its products can profoundly impair the nitric-oxide mediated vasorelaxation of coronary arteries in response to agents such as acetylcholine. Hypercholesterolemia by generation of more Ox-LDL in the intima or by creation of a pro-oxidant environment that stimulates endothelial cells to release more superoxide anion, may contribute importantly to vasospasm even in the absence of significant lesions. Certain products of Ox-LDL as oxysterols are highly toxic to endothelial cells and could initiate breaks in endothelial integrity. Other products may stimulate tissue factor release and initiate coagulation. Irreversible damage occurs when too much Ox-LDL accumulates with resulting cell death and release of oxidized and insoluble lipid protein adducts leading to atheroma formation. Any process that interferes with uptake of Ox-LDL could be counter productive.

- Role of antioxidants in the prevention of CAD:

Formation of FR in humans in diseases like CAD is controlled by various antioxidants (AO) protective mechanisms. [120] These include primary enzymatic

defenses such as super oxide dismutase and glutathione peroxidase, which depend functionally on minerals like manganese, copper, zinc and selenium and stabilizing substances such as vitamin E, vitamin C, beta-carotene and vitamin A. When FR are present in excess they can attack DNA, disrupt the function of vital enzymes and lead to peroxidation of polyunsaturated fats in cell membranes. Therefore antioxidants nutrients which protect tissues against attack by free oxygen radicals play an important role. [117] The most abundant natural antioxidant in LDL is alpha tocopherol [121] and supplementation of the diet with vitamin E can increase the vitamin E content of LDL and lead to enhanced protection of such LDL from in vitro oxidation. β-carotene is the next common antioxidant in LDL. [122] A diet low in saturated fat and cholesterol and enriched in fruits, vegetables and natural antioxidants are recommended for antioxidants vitamins.

c) **Importance of HDL-C levels**:

Current guidelines for the prevention of coronary heart diseases (CHD) focus on lowering LDL-C as the primary target of lipid-modifying therapy. [123] However there is increasing interest in HDL-C as a secondary target of therapy. Raising HDL-C levels with therapeutic lifestyle changes & pharmacologic intervention might afford opportunities to further reduce the risk of CHD beyond LDL-C lowering. Although lowering LDL-C remains the primary target of lipid modifying therapy, dyslipidaemia therapies that are efficacious for both LDL-C reduction and causing HDL-C might offer further improvements in CHD risk reduction. In observational studies, plasma levels of HDL-C and its major protein, apo A-1, have been shown consistently to be inversely correlated with CHD risk. [124] Thus person with low HDL-C levels are at increased risk of CHD, [125] restenosis after angioplasty [126] and death from cardiovascular causes, especially if such persons are male [127] or have diabetes. [128] Also often persons with low HDL-C levels have other CV risk factors such as diabetes, HT or both which further increase risk. [129] Epidemiologic studies and studies in animals suggest that raising the levels of HDL-C may retard the development of atherosclerosis. [129] Studies in animals have shown that over expression of the apo AI gene prevents the development of progression of atherosclerosis. [130]

Recently a working group reporting on low levels of HDL-C as a risk factor for CHD concluded that HDL-C is a national target for cardiovascular therapy. [131] In regard to HDL-C, strong evidence from the Framingham Heart Study [132] supports the premise that low level of HDL-C predicts an increased incidence of CAD, independent of other CAD risk factors, including LDL-C levels. Infact, across all levels of LDL-C e.g. 100-200mg/dl, the level of HDL-C influence the risk of developing CAD. [132] Two primary prevention trials of LDL lowering – the Lipid Research Clinics Primary Prevention Trial using cholestyramine [133] and

the Helsinki Heart Study [134] using gemfibrozil - both demonstrated that increasing HDL-C levels lowered CAD events, independent of the effect of LDL lowering. In recent years, there has been more interest in non-pharmacological approaches to increased HDL-C levels. This has been prompted by the recognition of HDL-C as an independent risk factor for CHD [135], the difficulty in manipulating HDL-C levels through pharmacological means [136] and the recent change in the American (ATP III) definition of low HDL-C from < 35 mg/dl to 40 mg/ dl. [123] Whereas LDL and VLDL are considered atherogenic, HDL and HDL-C have been shown to be protective factors against atherosclerosis resulting in decreased occurrence of CHD. HDL-C has also been found to be the single most important lipid risk factor having an inverse association with the incidence of CHD in the Framingham study. [137] In humans, each increase in baseline HDL-C of 1 mg/dl is associated with a 6% decrease in the risk of death from coronary disease or of MI. [138] National Cholesterol Education Program (NCEP) guidelines do not identify HDL-C as a treatment target but do, nevertheless, state that a level of HDL-C < 40 gm/dl constitutes a risk factor for CHD, whereas level ≥60 mg/dl is considered protective. [123] Thus persons with HDL-C levels below 35 mg/ dl have a CHD incidence rate of more than 8 times, compared to persons with HDL-C levels greater than 65 mg/dl or above. [137]

The publication of a paper be Miller & Miller, [139] postulating that the reduction of plasma HDL-C may accelerate the development of atherosclerosis by impairing the clearance of cholesterol from peripheral tissue including the arterial wall to the liver, has created a lot of interest in the study of the role of HDL and HDL-C in CHD and other forms of atherosclerotic disease. [137,139]

- Role of HDL-C

i. Reverse Cholesterol Transport:

The main mechanism by which HDL is thought to be antiatherogenic is in the transport of cholesterol from peripheral tissues to the liver in the process of increased cholesterol transport. [140] Nascent HDL is able to facilitate removal of free cholesterol from peripheral cells, such as macrophages, thus the action of ATP binding cassette protein 1 (ABC 1). [141] Mature HDL particles form the esterification of cholesterol by lecithin cholesteryl acyl transferase (LCAT) which is activated by Apo A1, CE can be selectively taken up by the scavenger receptors of class B, type II (SRCBI) on the liver. [142] The CE can be excreted as bile acids or free cholesterol in the bile. Alternatively the CE of mature HDL can be transferred to Apo B containing lipoproteins, such as VLDL and LDL, by cholesteryl ester transfer protein (CETP) [143] with eventual uptake of LDL by the liver and excretion via the bile. [144]

ii. HDL-C and atherogenesis**:**

There are several mechanisms through which HDL-C may attenuate the formation and progression of atherosclerotic lesions, including its role in mediating reverse cholesterol transport. Additional HDL-C properties demonstrated that might protect against atherosclerosis include AO effects, attenuation of endothelial dysfunction and anti-inflammatory effects. [145] Particles of HDL like apo AI, platelet activating factor acetylhydrolase and paraoxanase provide AO protection to LDL particles by scavenging ROS (reactive oxygen species). [146] Plasma from transgenic mice that are led to express the human apo AI gene increase the oxidation of LDL in vitro to a significantly greater extent than plasma from control mice. Platelet activating factor acetyl hydrolase prevents oxidative modification of LDL and paraoxanase also increase LDL oxidation. [147] Oxidized LDL contributes to the development of atherosclerotic lesions in several ways, including accumulation in macrophages to form foam cells and modulation of various pro-inflammatory pathways. [146] HDL abolishes the transmigration of monocyte induced by modified LDL in co-culture of human aortic wall cells. [148] By preventing LDL oxidation, HDL-C may also prevent the associated increase of endothelial nitric oxide synthase. [149] Additionally HDL-C may improve endothelial function by stimulating the release of prostacyclin, a vasoactive prostaglandin synthesized by vascular endothelial and smooth muscle cells. [150] In terms of antinflammatory effects, HDL-C might reduce cytokine-mediated upregulation of cell adhesion molecules and block the nuclear factors-KB signaling cascade. [151] Thus the postulated role of HDL in attenuating formation of oxidized LDL may promote endothelial vasodilation; HDL may also stimulate fibrinolysis [152] effects that would tend to retard the evolution of atherosclerotic CAD.

- Interventions to raise HDL-C:

A number of interventions are currently available for improving HDL-C profiles and thereby potentially reducing cardiac risk (Table 2.4) (Summary of the effects of lifestyle on HDL-C).

These include lifestyles changes and pharmacologic intervention with statins or fibrates as monotherapy or statins in combination with niacin. Lifestyle changes recommended to reduce the likelihood of CHD include smoking cessation, weight loss, exercise and diet, some of which have an effect on HDL-C levels. [123] Elevated HDL-C levels are associated with other factors including estrogens, which may explain why women tend to have higher levels than men and exhibit lower incidence of CAD before the age of 50; a diet high in saturated fat which also elevates LDL-C in; regular exercise (≥ 4, 200 KJ/ week); alcohol

consumption and cessation of cigarette smoking which can lead to a 3-4 mg/dl increase in HDL-C. [153] Smoking ≥ 20 cigarettes/day was shown to decrease

Table 2.4
Summary of the effects of Lifestyle on HDL- C

Intervention	Study reference	Details	Effects on HDL-C
Alcohol intake	Rimm et al 1999	Meta analysis of 36 data records including 886 adults from 25 studies(duration 1 week to 3months)	Increase of 8.3% in an average individual consuming 30 g alcohol per day
	Hata & Nakajima 2000	Meta- analysis of 24 publication including 26 712 men(all Japanese)	Increase of 0.06 mmoL/L (3.9-9.5%) for every 23 g alcohol per day
Exercise	Leon & Sanchez 2001a and2001b	Meta- analysis of 51 (including 28 randomized controlled trail)moderate intensity exercise training trials(>12-weeks duration)including 4700 participants	Average increase 4.6 %
	Halbert et al 1999	Meta-analysis of 31 studies including 1833 normo-and hyperlipidemic subjects	Increase of 0.05mmol/L (3.3-6%) with aerobic and resistance exercise
Weight loss	Datillo et al 1992	Meta analysis of 70 studies involving diet-induced weight loss and lipid parameters	For every 1 kg decrease in body weight HDL increases by 0.009mmol/L (0.58-1.08%)
	Yu-Poth et al 1999	Meta-analysis of 37 dietary intervention studies (9276 subjects in intervention groups and 2310 subjects in control groups)	For every 1 kg decrease in body weight HDL-C increased by-1%
Smoking cessation	Maeda et al 2003	Meta-analysis of 29 cohorts from 24 studies (4476 patients)	Increase of 3.0-5.6% following smoking cessation
	Craig et al 1989	Meta-analysis of 54 published cross-sectional studies.	HDL-C levels are 5.7% higher in non smokers compared with smokers.

HDL-C levels by 11-14% in a dose dependent manner. [154] Heredity also appears to play a role. A gene condition termed familial hypoalphalipoproteinemia is expressed primarily by low levels of HDL-C. The fundamental defect in most patients with hypoalphalipoproteinemia is not known. In the other hand in hyperalphalipoproteinemia, another genetic condition, levels of apo AI and HDL-C are quite high. The prevalence of CAD is higher in hypo alpha and lower in hyper alpha, compared with those who have average levels of HDL-C. Humans who consume high-fat diets often have increased HDL-C levels. One possibility is that a high fat diet suppresses LDL receptors in the liver,

increasing LDL-C production (by decreasing VLDL remnant uptake by LDL receptors and converting more VLDL remnants into LDL) leading to more LDL-C uptake by the extra hepatic tissues. [155] A study also reported an inverse relationship between BMI and HDL-C with levels of patients in the 10th percentile for BMI being 6-7 mg/dl higher than for those in the 90th percentile [156], and a direct relationship between exercise and HDL-C was also observed. [157] Multiple regression analysis demonstrated an increase in HDL-C of approximately 2 mg/dl of every 4.5 kg weight reduction. [158]

3. Management of dyslipoproteinemia:

CVD is the major cause of death in our society. The ability to prevent the development of atherosclerosis or alternatively, to decrease established atherosclerotic plaques, often referred to as regression, has major implication for public health. Whereas the incidence of CAD was halved in the past 30 yrs, the rates doubled in India with no signs of downturn. It appears that the CAD epidemic would explode in parallel with affluence and urbanization in rural villages unless the gravity and magnitude of the problem is recognized and immediate action is taken. [159] Research from experimental animals, laboratory investigation, epidemiology and genetic forms of hypercholesterolemia indicate that the elevated LDL-C is a major cause of CHD. In addition, recent clinical trials robust show that LDL-lowering therapy reduces risk for CHD. For these reasons the Third report of the Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adults Treatment Panel III or ATP III) [160] continues to identify elevated LDL-C as the primary goals of therapy. As a result the primary goals of therapy and the cut points for initiating treatment are stated in terms of LDL. [123] The features of ATP III are shown in (Table 2.5). [123]

a) Risk-Assessment: First step in Risk Management

A basic principle of preventions that the intensity of risk-reduction therapy should be adjusted to a person's absolute risk. Hence the first step in selection of LDL-lowering therapy is to assess a person risk status. Risk assessment requires measurement of LDL-C as part of the lipoprotein analysis and identification of accompanying risk determinants. In all adults aged 20 yrs or older fasting lipid profile (TC, HDL-C, LDL-C and TG) should be obtained once every 5 years. The relationship between LDL-C levels and CHD risk continues over a broad range of

Table 2.5
New features of ATP III

❖ Focus on Multiple Risk factors

● Raises person with diabetes without CHD, most of whom have multiple risk factors, to the risk levels of CHD risk equivalent

● Uses Framingham projections of 10-year absolute CHD risk (i.e., the percent of probability of having a CHD event in 10 years) to identify certain patients with multiple (2+) risk factors for more intensive treatment

● Identifies persons with multiple metabolic risk factors(metabolic syndrome) as candidates for intensified therapeutic lifestyle changes

❖ Modifications of Lipid and Lipoprotein Classification

● Identifies LDL cholesterol < 100 mg/dl as optimal

● Raises categorical low HDL cholesterol from < 35 mg/dL to < 40 mg/ dL because the latter is a better measure of a depressed HDL

● Lowers the triglyceride classification cut points to give more attention to moderate elevations

❖ Support for Implementation

● Recommends a complete lipoprotein profile (total, LDL and HDL cholesterol and triglyceride) as the preferred initial test, rather than screening for total cholesterol and HDL alone.

●Encourages use of plant stanols/sterols and viscous (soluble) fiber as therapeutic dietary options to enhance lowering of LDL cholesterol.

● Presents strategies for promoting adherence to therapeutic lifestyle changes and drug therapies

● Recommends treatment beyond LDL lowering for persons with triglycerides ≥ 200 mg/dL

LDL levels from low to high. Therefore, ATP III adopts the classification of LDL-C levels shown in Table 2.6 [123], which also shows the classification of total HDL cholesterol and TG levels.

Risk determinants in addition to LDL-C include the presence or absence of CHD, other clinical forms of atherosclerotic disease, and the major risk factors other than LDL (table 2.7). [123] Based on these other risk determinants, ATP III identifies three categories of risk that modify the goals and modalities of LDL lowering therapy. Table 2.8 [123] defines these categories of risk and shows corresponding LDL-C goal.

Table – 2.6
ATP III Classification of LDL, TG, Total and HDL Cholesterol (mg/ dl)

LDL Cholesterol	
<100	Optimal
100- 129	Near or above optimal
130-159	Borderline high
190	Very High
Total Cholesterol	
<200	Desirable
200-239	Borderline High
≥ 240	High
HDL Cholesterol	
< 40	Low
≥60	High
Triglyceride (TG)	
< 150	Normal
150- 199	Borderline high
200- 499	High
≥ 500	Very High

The category of highest risk consists of CHD and CHD risk equivalents .The later carry a risk for major coronary events equal to that of established CHD, i.e.>20% per 10 years(i.e. more than 20 of 100 such individuals will develop CHD event within 10 years). CHD risk equivalents comprise:

1) Other clinical forms of atherosclerotic disease (peripheral arterial disease, abdominal aortic aneurysm and symptomatic carotid artery disease.

2) Diabetes
3) Multiple risk factors that confer a 10 years risk for CHD >20%

Persons with CHD or CHD risk equivalents have the lowest LDL-C goal (<100 mg/dl).

Table – 2.7
Major Risk Factors (Exclusive of LDL Cholesterol) that Modify LDL Goals*

● Cigarette smoking
● Hypertension (blood pressure ≥140/ 90 mm Hg or on antihypertensive medication)
● Low HDL cholesterol (<40 mg/dl)
● Family history of premature CHD (CHD in male) first degree relative first degree relative < 65 years ● Age (men- 45 years; women; > 55 years
* **Diabetes is regarded as a coronary heart disease (CHD) risk equivalent. LDL indicates low-density lipoprotein;** **HDL, high density lipoprotein.** **HDL cholesterol ≥ 60 mg/dl counts as a "negative" risk factor; its presence removes 1 risk factor from the total count**.

Table – 2.8
Three Categories of Risk that modify LDL Cholesterol Goals

Risk category	**LDL Goal (mg/dL)**
CHD and CHD risk equivalents	<100
Multiple (2+) risk factors*	
0-1 risk factor	<160

The second category consists of persons with multiple (2+) risk factors in which 10 years risk for CHD is ≤20%. Risk is estimated from Framingham risk scores. [123] The major risk factors, exclusive of elevated LDL-C are used to define the presence of multiple risk factors that modify the goals and cutpoints for LDL lowering treatment and these are listed in Table 2.7.The LDL-C goal for persons with multiple (2+) risk factors is <130mg/dl.

The third category consists of persons having 0-1 risk factors with few exceptions, persons in this category have a 10 year risk <10%.Their LDL-C goal is 160mg/dl.

b) Primary prevention with LDL lowering therapy:

The clinical approach to primary prevention is founded on the public health approach that calls for life style changes including (1) reduced intakes of saturated fat and cholesterol (2) increased physical activity and (3) weight control to lower population cholesterol levels and reduce CHD risk, but the clinical approach intensifies preventive strategies for higher risk persons. One aim of primary prevention is to reduce long term risk (>10 years) as well as short term risk (≤10 years). LDL goals is primary prevention depend on a persons absolute risk for CHD (i.e. the probability of having a CHD event in the shot term or the long term) - the higher the risk, the lower the goal. Therapeutic lifestyle changes are the foundation of clinical primary prevention. Nonetheless, some persons at higher risk because of high or very high LDL-C levels or because of multiple risk factors are candidates for LDL lowering drugs. Recent primary prevention trials show that LDL-lowering drugs reduce risk for major coronary events and coronary death even in the short term.

- LDL lowering therapy in three risk categories:

The two major modalities of LDL lowering therapy are therapeutic lifestyle changes (TLC) and drug therapy. The cut points for initiating lifestyle and drug therapies are shown in table 2.9. [123]

Table – 2.9

LDL Cholesterol Goals and Cut points for Therapeutic Lifestyle Changes (TLC) and Drug Therapy in Different Risk Categories*

Risk Category	LDL Goal (mg/ dl)	LDL Level at which to initiate Therapeutic Lifestyle Changes (mg/dl)	LDL Level at which to consider Drug Therapy (mg/dl)
CHD or CHD risk equivalents (10 year risk < 20 %	< 100	> 100	≥ 130 (100- 129; drug optional)
2+ Risk factors (10 year risk ≤ 20 %)	< 130	≥ 130	10 year risk 10% - 20% : ≥130
0-1 Risk factor	< 160	> 160	> 190 (160- 189: LDL lowering drug optional)

1) CHD and CHD risk equivalents:

If baseline LDL-C is ≥130mg/dl intensive lifestyle therapy and maximal control of other risk factors should be started. Moreover for more patients an LDL lowering drug will be regarded to achieve an LDL-C level of <100mg/dl thus an LDL-C lowering drug can be started simultaneously with TLC to attain the goal of therapy.

If LDL-C levels are 100-129mgldl, either the baseline or an LDL lowering therapy several therapeutic approaches are available:

● Initiate or intensify lifestyle and/or drug therapy specifically to lower LDL.
● Emphasize weight reduction and increased physical activity in person with the metabolic syndrome.
● Delay use or intensification of LDL lowering therapies and institute treatment of other lipid or non lipid risk factors.

If baseline LDL-C is <100mgldl further LDL lowering therapy is not regarded. Patients should nonetheless be advised to follow the TLC on their own to help keep the LDL level optimal.

2) Multiple (2+) risk factors and 10 year risk of ≤20% :

For persons with multiple (2+) risk factors and 10 year risk ≤20% intensity of therapy is adjusted according to 10 year risk and LDL-C levels

3) 0-1 risk factor :

Most persons with 0-1 risk factor have a 10 year <10%. They are managed according to Table-2.9.The goal for LDL-C in this risk category is <160mgldl. The primary aim of therapy is to reduce long term risk. First-line therapy is TLC. If after 3 months of TLC the LDL-C is <160mgldl, TLC is continued. However if LDL-C is 160-169mgldl, after an adequate trial of TLC, drug therapy is optional depending on clinical judgment.

❖ Therapeutic lifestyle changes in LDL lowering therapy:

ATP III recommends multifaceted lifestyle approach to reduce risk for CHD. This approach is designated therapeutic lifestyle changes (TLC). Its essential features are:

● Reduced intake of saturated fat (<7% of total calories) and cholesterol (<200mgldl) see table 2.10 [123] for overall composition of the TLC diet.
● Therapeutic options for enhancing LDL lowering such as plant stanols/sterols (2g/d) and increased viscous (soluble) fiber (10-25g/d)
● Weight reduction
● Increased physical activity

❖ Benefit beyond LDL lowering:

The Metabolic Syndrome as a Secondary Target of Therapy:

Evidence is accumulating that risk for CAD can be reduced beyond LDL lowering therapy by modification of other risk factors. The potential secondary target of therapy is the metabolic syndrome which represents the constellation of lipid and

non lipid risk factors of metabolic origin. This syndrome is closely linked to generalized metabolic disorder called insulin resistance in which the normal action of insulin are impaired. Excess body fat (particularly abdominal obesity) and physical inactivity promote the development of insulin resistance but some individuals also are genetically predisposed to insulin resistance

Table – 2.10
Nutrient Composition of the Therapeutic Lifestyle Changes (TLC) Diet

Nutrient	Recommended Intake
Saturated fat	< 7% of total intake
Polyunsaturated fat	Up to 10% of total calories
Monounsaturated fat	Up to 20% of total calories
Total fat	25%-35% of total calories
Carbohydrates	50%- 60% of total calories
Fiber	20-30 g/d
Cholesterol	<200 mg/d
Total calories	Balance energy intake and expenditure to maintain desirable body weight /prevent weight gain

- **Trans fatty acids are another LDL raising fat that should be kept at a low intake**
- **Carbohydrates should be derived predominantly from foods rich in carbohydrates including grains, especially whole grams, fruits and vegetables.**
- **Daily energy expenditure should include at least moderate physical activity(contributing approximately 200 kcal/d)**

The risk factors of the metabolic syndrome are highly concordant; in aggregate they enhance the risk of CHD at any given LDL-C level. For purpose of ATP III the diagnosis of the metabolic syndrome is made when three or more of the risk determinants shown in Table 2.11 are present. These determinants include a combination of categorical and borderline risk factors that can be readily measured in clinical practice.

Management of the metabolic syndrome has a 2 fold objective, (1) to reduce underlying causes (i.e. obesity and physical inactivity) and (2) to treat associated non lipid and lipid risk factors.

There is no doubt that abnormal BP and cholesterol levels cause major morbidity and mortality and that aggressive treatment saves lives. Careful management of hypertension and lipid disorders in adults with or at risk for CHD is an essential component of quality cardiovascular cause. Thus it is very clear that to prevent, manage or reduce the rate of hypertension and lipid disorders, the factors that influence these have to be dealt with. It is shown earlier that factor like smoking, diet, obesity, physical inactivity, DM acts synergistically with BP and lipid disorders. [123,129,153,154,156-158] Apart from vascular factors genetic factors are also known to play a role in the etiology of these disorders. [161]

Fig 2.11
Clinical Identification of the Metabolic Syndrome

	Risk factor	Defining Level
❖	Abdominal obesity* (waist circumference)#	
	Men	> 102 cm (>40 in)
	Women	> 88 cm (> 35 in)
❖	Triglycerides	≥ 150 mg/dL
❖	High-density lipoprotein Cholesterol	
	Men	<40 mg/dL
	Women	< 50 mg/dL
❖	Blood pressure	≥ 130/≥85 mm Hg
❖	Fasting glucose	≥ 110 mg/dL

* Overweight and obesity are associated with insulin resistance and the metabolic syndrome. However, the presence of abdominal obesity is more highly correlated with the metabolic risk factor than is an elevated body mass index (BMI). Therefore, the simple measure of waist circumference is recommended to identify the body weight component of the metabolic syndrome.

\# Some male patients can develop multiple metabolic risk factors when the waist circumference is only marginally increased, eg. 94-102 cm (34-40 in). Such patients may have strong genetic contribution to insulin resistance and they should benefit from changes in life habits, similarly to men with categorical increases in waist circumference.

DIET

CVD is one of the leading causes of death in the Western world and is the third cause of mortality in developing countries, accounting for ≈25% of all deaths. [162] Many risk factors for CVD, including high blood cholesterol, HT, obesity, and diabetes are substantially influenced by dietary factors. Because these risk factors are modifiable, primary preventive efforts hold much promise. [163] Despite the documented decrease in LDL-C and TC universally as a result of many preventive efforts, obesity and diabetes have continued to increase progressively, primarily because of a marked decrease in physical activity and exercise as well as an increase in caloric intake in the population. Nutritional status within a given population is subject to great variation, based on affluence, habit, religion and geography, compared to various CHD risk factors like behaviors or traits, diet appears to have a pivotal role. [164] In diet especially fat plays an important role in the development of heart diseases. It also influences serum TC, TG and Lps. [165] Current dietary advice aimed at reducing the incidence of CHD encourages reduction in the proportion of daily energy intake derived from fat. [168] Thus modification in the dietary practices can significantly improve the Lp profile and ameliorate hyperlipidaemia to some extent.

Several population studies [167,168] correlated severity of atherosclerosis, serum cholesterol level and dietary fats. Countries like Finland, Netherlands and US had the highest intake of saturated fats when compared to South European countries and Japan. The Finns were actually the least sedentary of the group studied but they were also the most hypercholesterolemic and had the highest rates of CHD. [167] In Ni-Hon-San study [169] of Japanese with the same genetic background residing in Japan, San Francisco and Hawaii had high degree of variation in their dietary habits. An increased rate of CHD seen in the above group residing in Hawaii and San Francisco paralleled the increases seen in dietary saturated fat and serum TC. The dietary composition leading to hypercholesterolemia rather than genetic make up seemed to play a key role in the increase in CHD.

A significant reduction of 28% in coronary events but no improvement in the survival was reported in the Oslo trial [170] through dietary modification. In another trial- the diet and infarction trial (DART) - it was only when intake of n-3 fatty acids (fish oil) was increased that mortality was reduced. [171] Except for the DART trial no other previous dietary secondary prevention trials were successful. [170,172] Even in primary prevention, the only trial successful in preventing coronary death was the Hjerman trial. [173] Several insights have been gained from observing vegetarians, consuming a high carbohydrate and low fat diet, had

low serum cholesterol, LDL-C and LDL/HDL cholesterol when compared to non-vegetarians. Even lacto-ovo vegetarians had 24% higher LDL-C and 7% higher HDL-C than that of strict vegetarian. Serum cholesterol levels in lacto-ovo vegetarian, vegetarian and normal American omnivorous group were 6.62, 5.33, and 7.53 mmols/lit, respectively as reported by Hardinge and Stare *et al.* [164]

In Seventh-Day Adventists study [174] it was observed that meat, eggs and dairy products were the major sources of saturated FFA and cholesterol and the same are the generally recognized risk factor of CHD. Dietary cholesterol is entirely derived from animal food like beef, pork, sea foods eggs and milk products. In people who ingest considerable amount of meat, eggs, and dairy products, dietary cholesterol can be as high as 1000 mg/day, whereas strict vegetarian can ingest almost none. [164]

The Seven Countries Study by Keys *et al* in the 1960s showed a relation between saturated fat intake, fasting blood cholesterol concentration and CHD mortality in various populations [175], which suggests the protective effect of traditional Mediterranean – type diets. A Mediterranean α-linolenic acid – rich diet had a markedly reduced rate of recurrence, other cardiac events and overall mortality. Even more recently some cohort studies in Spain and Greece have provided data supporting a cardiovascular protective effect of Mediterranean diets. [176,177] These studies, together with other reliable epidemiologic studies [178] provide the basis for the well known traditional Mediterranean diet pyramid and healthy eating model. [178] Moreover the Indo-Mediterranean Diet Heart Study [179] showed that a Mediterranean type diet (rich in α-linolenic acid from fruit, vegetables and nuts) was also of benefit for secondary prevention of CHD in non-Mediterranean populations. The Medi-RIVAGE intervention study [180] provides support to early [175] or recent [176] observation studies linking adherence to the traditional Mediterranean diet and reduced CVD mortality and reinforces the notion of its efficacy in primary as well as secondary prevention.

1. FATS:

Quality and Quantity of dietary fat have greater effect on blood cholesterol and predominant type of fatty acids present in diet play a key role in the control of serum lipids. [182] Current dietary guidelines from the American Heart Association (AHA) [183] and NCEP [184] recommend restricting consumption of fat to an upper limit of 30% of daily caloric intake. This limit translates into 67g of fat for small or sedentary individuals who need 2000 cal/day and 100g of fat for large or more

active individuals who need 3000 cal/day. Step I diet [containing 28.1% cal as fat (8.7% saturated, 11.5% monounsaturated, 7.9% polyunsaturated and 76mg/1000kcal cholesterol), 13.9% protein and 58.0% carbohydrate] and Step II diet [containing 23.7% cal as fat (6.2% saturated, 9.7% monounsaturated, 7.8% polyunsaturated and 63mg/1000kcal cholesterol), 14.4% protein and 61.8% carbohydrate] are effective in lowering blood cholesterol levels [185] and consequently are advocated as the primary dietary strategy for reducing cardiovascular risk. [186]

Population studies show that low fat diets are associated with lower LDL-C levels but also lower HDL-C levels. Similarly clinical studies involving low fat diets also showed equal percent of reduction in both HDL-C and LDL-C. Low fat diets alone do not appear to reduce CAD events. [187] Changes in fat composition, rather than quantity appear to be key to reduction in CAD events. For e.g. in the Lyon Heart Study the experiment group that experienced less CAD events consumed less lipid, saturated fat, linoleic acid and cholesterol but more oleic and linolenic acids. [188] Replacing saturated fat with monounsaturated is as efficient on LDL-C reduction as reducing total fat intakes with a smaller reduction in HDL-C levels. [187]

Dietary saturated fatty acids (SFAs) have been implicated as an important factor in the production of high levels of plasma cholesterol in populations at high risk for CHD. [189] SFAs are found typically in animal products such as beef, pork fats and lamb, dairy products such as milk, ghee, butter and cheese. Vegetable oil sources like coconut oil, palm oil, palm-kernel oil, hydrogenated oil and lard also contain saturated fats. [190] Although these FAs vary in chain length from 4 to 18 carbon (C) atoms, they are generally all considered plasma-cholesterol raising FAs. This may not be justified. For e.g. FAs with chain lengths of 4 to 10 C atoms have been claimed not to increase the cholesterol levels. [191] Likewise, stearic acid (18 C atoms, no double bonds [18:0]) has been reported not to raise plasma cholesterol levels. [192-194] The principal piece of evidence supporting this latter claim is that cocoa butter, which is rich in stearic acid, apparently does not increase cholesterol concentration as much as do fats that are high in lauric acid (12:0), myristic acid (14:0) or palmitic acid (16:0). [193] Later Keys and coworkers [194] confirmed these finding and proposed that stearic acid does not raise the plasma cholesterol levels. At the same time Hegsted *et al* [193] obtained similar results and also concluded that stearic acid does not increase cholesterol levels. Finally data obtained in studies in laboratory animals were consistent with this conclusion. [195,196] This all SFAs do not have the same cholesterol-raising potential. Margarines and shortenings high in stearic acid would provide texture in foods (as saturated fats do), without raising plasma-cholesterol levels.

PUFA are those, containing omega-3 and omega-6 fatty acids. Oils such as corn oil, safflower oil, rapeseed oil, soybean oil are rich sources of omega-6

PUFA. Marine products like seal, salmon, shellfish etc are rich sources of omega 3- FA like eicosapentaenoic acids, docosahexanoic acids and linolenic acids. The ratio of PUFA and SFA in a given fat or oil is designated as P/S value. Fats with a high P/S value of 2.1 and above are generally recognized to be hypocholesterolemic. A dietary P/S value of more than 1, even if association with a decrease in plasma cholesterol, enhanced platelet aggregation to adenine diphosphate. [197] High platelet aggregation is associated with MI [198] and closely predicts coronary events. [199] In addition a high concentration of linoleic acid could be associated with increased lipid peroxidation [200] and platelet induced aggregation. [197] The Cretan Mediterranean diet induced a high intake of α-linolenic acid (the precursor of n-3 long chain FAs), known for its beneficial effect on platelet reactivity. [201] Being rich in vegetable and fruits, the diet also supplies a high intake of antioxidants.

In a recent trial [188], a reduction in coronary events and cardiac deaths of close to 70% was achieved without a reduction of serum cholesterol, TG or an increase in HDL compared to controls using the α-rich linolenic Mediterranean diet. Compared with the DART trial [171] the protective effect observed was associated with dietary supply of the n-3 long chain FA precursors (α linolenic acid) instead eicosapentaenoic acid and extended to non fatal MI. The two populations with the lower CHD mortality in the world have a high intake of α linolenic acid; the Japanese in the form of canola and soybean oils, the Cretans, possibly through the consumption of purslanc [202] and walnuts. The increase in intake of oleic acid less susceptible to peroxidation [200] and in natural antioxidants, probably also play a protective part. Recent observations, of a lower risk of CHD with a high intake of Vit E [203] and higher concentration of β-carotene in adipose tissue [204] is observed. Also a low fat vegetarian diet containing nuts (some rich in α linolenic acid) reduced the rate of coronary events within 6 weeks was observed in a study. [205]

2. CALORIE:

Excessive calorie intake from sources like fats, carbohydrates, proteins or alchohol promotes hyperlipidaemia. Recommendations for energy intake have been reduced in recent years. This is because of the undoubted reduction in physical activity arising from the increasing mechanization of industry and also to the more widespread use of mechanical transport. Energy output has been determined for people undertaking various activities. Sedentary work requires about 2000 to 2500 kcal/day, light work 2500 to 3000 kcal, while heavy work such as felling trees, may need 4000 kcal or even more. Carbohydrate rich diet increases serum lipids in persons having higher baseline serum lipid levels than

in those with low or normal serum lipids. In a high carbohydrate, low fat low calorie diet: 1200 to 1500 kcal/day for women and 1500 to 1800 kcal/day for men, with approximately 60% of calories from carbohydrate, 25% from fat, and 15% from protein were present. [206] High sucrose diet provides empty calories and increases serum lipids in type III, type IV, type V than for type II HLP patients. The age and sex of the subjects may influence the response to changes in diet. [164] With increase in age, a reduction in the intake of cereals, pulses and legumes were observed in both the genders. This could be attributed to dental problems and also digestive problems commonly associated with aging. The energy intakes tended to decrease with increase in age in both the sexes, which is attributable to the decreased cereals intake. It is mentioned that the RDA for energy among the elderly are based on the actual body weights, physical activity and sex. The median intake of all the nutrients was relatively low among the elderly of both the genders compared to their adult counterparts. The prevalence of chronic energy deficiency (CED) (BMI<18.5) was marginally higher among males (53.5%) than the female (49.4%).

The use of large quantities of PUFA in vegetable oil in diet causes serious problems because fat is the most calorically dense food. Body responds to an excessive consumption of calories by converting food stuffs to fat and by depositing fat in adipose tissue which in turn stimulates the liver to synthesize more triglycerides and to secrete increased amounts of VLDL and increased fasting triglyceride concentration. Enlarged adipose tissue cells may have a reduced capacity to remove circulating TG from the plasma, and also because of their decreased sensitivity to circulating insulin which activates LPL. [207] Breads, cereals, pasta, rice, dried peas and beans are rich in carbohydrate and proteins and most have low fat content. Therefore they can be increased in the diet as substitutes for fatty foods. However they too contain calories and cannot be eaten in excess.

3. **DIET AND BLOOD PRESSURE**:

Diet has an important role in the primary prevention of HT. [208] Several epidemiologic studies have reported reduced BP linked to Mediterranean dietary pattern (a-linolenic acid rich diet). [209,210] Also vegetarians have relatively low BP levels and consume less protein than do non-vegetarians and there have been suggestions that certain proteins may raise BP.

Omega-3FAs viz eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) administered in low doses (<3g/d) has shown a BP lowering effect in

subjects with type 2 DM. [211] There are few studies showing similar results of ω-3FA therapy in patients of essential HT at a higher dose (>5g/d) of omega 3FA [212,213], attributable to platelet enrichment with EPA, which competes with arachidonic acid (AA)[an omega-6FA] as a potential substrate for the enzyme cyclooxygenase. While the predominant product of AA in the platelets thromboxane A_2 (TXA_2) is a potent vasoconstrictor the corresponding product of EPA is thromboxane A_3, which is virtually biologically inert. In contrast both prostaglandins I_3 (PGI3) derived from AA and PGI_3 derived from EPA; are potent vasodilators. Thus alterations of the ω-6FA/ω-3FA ratio in diet to near normal (8:1) with dietary modification and supplementation of ω-3FA, results in a shift of the net balance between PGI_2/PGI_3 and TXA_2/TXA_3 in the body to a more vasodilator state. [214] Beneficial effects of ω-3FA even in low doses have been seen on serum lipid profile of 935 NIDDM/IGT patients with hypertriglyceridaemia. A study by Wander *et al* [215] using better technique of measuring oxidized LDL and low dose of omega-3FA have shown decreased oxidative susceptibility.

Omega-3FA substitution result in reduction of SBP by 16.4% and DBP by 25%; which is probably attributable to reduction in insulin levels as well as production of vasodilatory eicosanoids from ω-3FA in platelet membranes by cyclooxygenase. In a study by Singer *et al* [216] on 12 patients with mild essential HT, substitution of ω-3FA in the dose of 5g/day for 8 week resulted in lowering of SBP by 9 mmHg and DBP by 11mmHg. When the patients were followed up with 1.2g/d for 8 months (period 8), the BP still remained significantly lower. A study showed beneficial role of ω-3FA on TC, serumTG, LDL and HDL also. [217] These beneficial effects of ω-3FA on serum lipid profile of hypertensive patients are probably due to blunting of the stimulating action of insulin on hepatic lipogenesis. [218] Thus any dose of ω-3FA, as long as omega6:omega3FA ratio in diet is maintained at 8:1. Omega-3-FA substitution in low dose and normalization of ratio of omega6:omega3-FA in diet to 8:1 resulted not only in improvement of BP (SBP and DBP) in patients with mild to moderate essential HT, but also in a significant decline in plasma insulin levels and favorable alterations in serum lipid profile of the patients, which are desirable for comprehensive management of essential HT. Thus it may be concluded that low dose of ω-3FA substitution along with dietary curtailment of ω-6FA may be used as an adjunctive measure in patients with essential HT.

The Dietary Approaches to Stop HT(DASH) trial has shown that a dietary pattern rich in fruit, vegetables and low fat dairy products and with reduced total and saturated fat (the DASH diet) can be effective in the prevention of HT. [52,219] This pattern was more effective than a diet rich in fruit and vegetables in which diary consumption was low. Substantial epidemiologic and clinical data exist that show that a long term high consumption of fruit and vegetable, one of the main components of the DASH diet, is inversely associated with BP levels, independent of other dietary factor. [210,220] Some prospective studies have found

a beneficial relation between diary consumption and the incidence of HT or a change in BP, but this association was only evidenced in young adults [221] and in children. [222] On the other hand dairy consumption has been associated with a higher CVD mortality risk in postmenopausal women [223], whereas the nutritional intervention in the Oslo study which was mainly focused on reducing whole fat dairy consumption was associated with a lower risk of coronary events. [224]

In the Mediterranean Cohort, low fat dairy intake was associated with a lower risk of incidence of HT, even after control for several potential confounders such as age, sex physical activity, BMI and major dietary factors related to HT. The observed risk reduction was high. Two reasons however support that a substantial protective association actually exists. First, the reported results are consistent with the findings of the coronary artery risk development in young adults study [221] and with the findings of clinical trials that included low fat dairy products in the intervention diet. [219] For instance in the DASH trial [[219], SBP and DBP reduction were -5.5 and -3.0mmHg respectively, for the combination (DASH) diet, whereas respective decrease of only -2.8 and -1.1mmHg were observed with the fruit and vegetable diet. These results also represent an important difference in the magnitude of the effect of each diet , which had clear cut difference in the amount of low fat dairy products provided. (2.0 servings/day in the combination diet compared with 0 serving/day in the fruit and vegetable diet). This is the first study that showed an inverse association between the consumption of low fat dairy products and incident HT independent of other dietary factors in a perspective follow-up population, which included subjects aged > 40 years. Thus some cross sectional studies have shown a beneficial association between dairy consumption and BP. [210,225] Calcium could partly account for the observed inverse association between dairy consumption and the risk of HT. Also it could be that other components that occur in low fat dairy products or an interaction between some different nutrients may have caused the observed reduction in the risk of HT. For e.g.:- milk proteins- both caseins and whey proteins are a rich source of angiotensin converting enzyme inhibitory peptides. In animal models, these proteins (casokinins and lactokinins) have been shown to significantly reduce BP. [226] It is plausible that SF in whole fat dairy products somehow neutralize the beneficial effect of dairy consumption. The capacity of Ca to form soaps is much higher when fat intake is increased. Therefore foods that are high in fat such as whole fat dairy foods might hinder Ca absorption, thereby reducing the bioavailability of calcium. [227] Also more recently, the WELL trial found that a diet rich in low fat dairy products resulted in a greater decrease in BP than did a low fat comparison diet, which supports the beneficial effect of low fat dairy consumption for the prevention of HT.

4. DIET AND LIPID METABOLISM:

A number of studies have revealed the central role of elevated blood cholesterol [especially increased LDL-C] in the pathogenesis of CAD, it is clear that one of the biggest challenges facing public health authorities and medical practitioners is the control of the blood cholesterol in individual patients and at the population level. [228] A low fat diet is generally recommended for patients with CHD. [229] Numerous studies have shown that a low fat diet decreases plasma total, HDL and LDL cholesterol, apoA-I and apoB concentration and also increase triglyceride concentration. [230,231] An important health concern of consuming unrestricted amounts of SF is the potential to increase the LDL-C concentration, which is an established risk factor for CHD. Plasma LDL-C and HDL-C levels decline with reductions in the intake of dietary fat. The recomitant decrease of LDL-C that occurs with a diet low in SF may override the effects associated with the decline in HDL-C. [232] Reducing the fat content of the diet from 35 to 40% of energy to 15% to 20% of energy reduces total cholesterol and LDL-C levels by 10 to 20%. [233,234] Thus response is likely attributable primarily to decrease in the SF content of the diet rather than the increase in CHD content. [235]

In a recent study the co-administration of garlic pearls with fish oil was found to be more effective than placebo in the management of dyslipidaemia. Studies with fish oil supplementation [n-3 fatty acid containing eicosapentenoic acid (EPA) and docosahexaenoic acid (DHA)] in hypocholesterolemic subjects have shown significant reductions in the serum TG and VLDL concentrations, whereas there was a significant increase in the serum LDL concentration which plays a major role in the development of atherosclerotic CAD. [236,237] Griffin [238] has reported that n-3 fatty acid shift LDL away from harmful small dense particles to larger, lighter less pathogenic ones. The Framingham Heart study and the 4-S study have reported that TG levels >100 mg/dl and HDL-C <40 are indicators of the presence of harmful small dense LDL-C particles. [239] Garlic or (allium sativum) has been used as both food and medicine in many parts of the world. [240] Garlic contains an active substance called 'allicin' and sulphur compounds like diallyl disulphide and allyl propyl disulphide which are responsible for the therapeutic properties of garlic. [241] Supplementation with garlic alone has been found to significantly lower LDL and TC concentrations. [240] Also TG levels consistently increase in response to short term consumption of a very low fat diet. [242,243] A very low fat diet is defined as one in which ≤ 15% of total calories are derived from fat (33 gm for a 2000 calories diet, 50 gm for a 3000 calorie diet) with fat calories distributed approximately equally, among saturated MUFAs and PUFAs. Also approximately 15% of total daily calories consumed should be derived from protein and ≥ 70% from carbohydrates. Higher TGs levels are frequently accompanied by lower HDL-C levels and higher TC/HDL-C ratios [243,244] as well as increased levels of small dense LDL particles. [245] Very low fat

diets increase TG levels regardless of whether the diet is high in simple or complex carbohydrates [235] but the increase may be attenuated by higher dietary fiber intake or weight loss. [244] Weight loss attenuates the HDL-C lowering effect of very low fat diets and is related in part to blunting the increase in TG levels. [243,244]

Epidemiological studies have shown that the majority of heart attacks occur in normolipidaemic individuals with low HDL-C (≤ 40 mg/dl). [125,246] Among normolipidaemic subjects HDL-C vary greatly. [247] About 15-20% of the male population has low HDL-C (≤40mg/dl). Data from the Framingham study [246] as well as data by Assmann *et al* [248] showed that the incidence of CHD increased in subjects with low HDL-C despite normal TC(<200mg/dl) or LDL-C (<135mg/dl). The major protein constituent of HDL is apoA-I. ApoA-I concentration can be influenced by genetic and environmental factors, diet and exercise. [249] A high fat diet increases apoA-I concentration by increasing production rate and decreasing fraction catabolic rate (FCR) without altering apoA-I mRNA levels; [250] the major regulations of apoA-I levels occur post transcriptionally.

HDL is not homogenous; they contain several subpopulations. [251] The largest size (alpha1) is an apoA-I only particle corresponding approximately to the HDL_2 fraction. [252] Smaller $alpha_2$ and $alpha_3$ particles correspond to HDL_3. On an average American diet (AAD), healthy normolipidaemic low HDL-C subjects have different concentration of HDL sub populations compared to normal HDL-C individuals. It was observed in a recent study that the HDL $alpha_1$ subpopulation is lower and HDL $alpha_3$ is higher in low HDL-C subjects compared to normal HDL-C individuals. [253] Also increased CETP activity has been shown in subjects with low HDL-C. [254] In a particular study the response to low fat diets of subjects with low and normal HDL-C were compared. Low fat diets resulted in a significant decrease in HDL-C both on step1 and step2 diets in subjects with normal HDL-C. The atherosclerotic index LDL-C/HDL-C did not change in individuals with normal HDL-C; while in low HDL-C subjects, it decreased significantly from 3.92 to 3.49 (11%). Also in an earlier study, [255],HDL-C levels in school boys who consumed different habitual diets were compared wherein; HDL-C levels were strongly and inversely related to carbohydrate intake. Diets rich in n-3 PUFAs have high HDL-C levels. [256] Although diet high in MUFA does not elicit a significant change in HDL-C levels, [257] the dietary glycemic load (which represents the equivalent elevating effect on BP levels of 1 gm of pure glucose or white bread) is negatively correlated with HDL-C levels. [258] Thus a diet rich in n-3 PUFA sources include oils (olive, canola, soya, flaxseed), nuts (almonds, peanuts, walnuts, pecans), coldwater fish (salmon, mackerel) and shellfish with limited carbohydrates that contribute a high glycemic load (such as those found in ready to eat cereals, potatoes, white bread and snack foods) can be recommended to increase serum HDL-C levels.

Clinical trials and epidemiological studies suggest an increase of 1mgldl HDL-C results in a 2-3% decrease in coronary risk while an increase of 1mgl/dl LDL-C results in a 1% increase in the risk of CHD. Thus every mg/dl change in HDL-C concentration provides a 3 fold greater contribution to the production of CHD than does a 1mg/dl change of LDL-C. [125,229]

The result of a controlled metabolic study have suggested that dietary fatty acids containing at least 1 double bond in the transconfiguration (transFAs) have a detrimental effect on serum lipid levels relative to FAs containing only double bonds in the cis configuration or in some cases SFAs. [259] Adverse effects of dietary transFAs on the risk of the development of CVD have also been reported in some studies of large cohorts. [260,261] TransFAs are naturally present at low levels in meat and dairy products as a result of bacterial fermentation in ruminant animals. They are also formed in varying amounts during the hydrogenation of oil, a process used to transform oil from a liquid to a semisolid or solid state. Recent studies consistently demonstrate a positive relation between the level of intake of trans fatty acids and LDL-C levels. [262,263] Soybean oil and semi liquid margarine has the lowest levels of transFAs of the various fats that are studied and they are also low in saturated fat. In the use of soyabean oil or semi liquid margarine results in the most FAV total and LDL-C levels and ratios of TC/HDL-C, whereas the use of stick margarine or butter results in the opposite effects. The fats with intermediate levels of trans and SFAs resulted in intermediate values. In addition, from a practical perspective they provide a sound basis on which to make strong recommendation to the general public and food manufacturers to emphasize the use of vegetable oils in their natural state and minimal hydrogenation.

It is known that unrestricted amount of saturated fats have the potential to increase the LDL-C concentration, but in a particular study it was shown that the diet high in stearic acid significantly reduced plasma levels of TC and LDL-C, as compared with the diet rich in palmitic acid. [264] The high stearic acid diet reduced both the total and LDL-C levels as much as the high oleic acid diet. Also neither the high stearic acid nor the high oleic acid diet increased plasma TGs or reduced HDL-C, as compared with the high palmitic acid diet. Stearic acid is a saturated FA and we may speculate about why it does not increase plasma cholesterol levels as much as palmitic acid does. One possible mechanism for the cholesterol lowering action of stearic acid, as compared with palmitic acid, may be that stearic acid but not palmitic acid, is rapidly converted to oleic acid.

The Mediterranean and α-linolenic Enriched Groningen Dietary intervention (margarine) study, [265] a primary prevention study in hypocholesterolemic subjects showed the benefit of the alpha-linolenic acid contained in a Mediterranean diet. Also the Lyon Heart Study for secondary prevention of CHD [188] showed that the positive effect of a Mediterranean type

diet enriched with alpha-linolenic acid (mainly in the form of margarine), the survival rate after a first MI increasing markedly compared with that for the control group [low fat diet]. The Mediterranean diet provides greater intakes of soluble fibres (from fruit, vegetable, legumes and cereals) and MUFA (oleic acid from olive oil) which are known independently to have cholesterol and LDL-C lowering effects. [231,266] Fibre rich diets [266] and a high consumption of fruit and vegetable have been related to a reduced occurrence of CHD. [176,177] The reduction in plasma TG (mainly in the form of TRLs) observed only in the Mediterranean group may have been due mainly to a high intake of fish and long chain of n-3 FAs. [267] In line with most recent theories on optimal eating patterns for prevention of CHD [268] and according to Law's concept, [269] the observed lowering in plasma cholesterol actually indicates a reduction in CV risk of 19% with the low fat diet and 15% with the Mediterranean diet.

5. CURRENT GUIDELINE FOR DIET:

Current American Heart Association (AHA) recommendations regarding diet and related lifestyle practices for the general population are based on evidence indicating that modification of specific risk factors will decrease incidence of CHD. [229] These risk factors include cigarette smoking; elevated levels of plasma cholesterol, particularly LDL-C, low levels of HDL-C; increased BP; DM; obesity especially visceral adiposity and physical inactivity. To reduce the impact of these risk factors on the occurrence of CHD in the general population, in 1996, the AHA recommended the following population wide dietary and lifestyle goals.

a) Eat a variety of foods:

Dietary recommendations should enable individuals to adopt eating patterns consistent with their own lifestyles and that will supply the calories, proteins, EPAs, carbohydrate, vitamins, minerals and fiber needed for good health. This is achieved by eating foods from all the food groups including fruits and vegetables; non fat and low fat diary products; whole grain bread, cereals, pasta, starchy vegetable and beans; and lean meat, skinless poultry and fish. The AHA recommends that healthy individuals obtain an adequate nutrient intake from foods eaten in variety, balance and moderation. Excessive intake of calories, sugar and salt should be avoided.

b) **Balance food intake with physical activity and maintain or reduce weight**:

Loss of excess weight and long term maintenance of a healthy weight can improve blood lipid levels and blood pressure and reduce risk for heart disease, the most common form of diabetes, stroke and certain cancers. [270] In many individuals with increased abdominal or visceral fat, even modest weight reduction may result in improvement in many metabolic CHD risk factors, particularly those associated with insulin resistance, including low HDL level, elevated TG levels and small dense LDL. [271] Successful long term maintenance of a healthy body weight can be promoted by regular physical activity in conjunction with a diet that is limited in calories particularly those derived from fat and relatively rich in complex carbohydrates and fiber. [272]

c) Choose a diet low in fat, saturated fatty acids and cholesterol:

The AHA's population wide recommendation to consume no more than 30% of total calories as fat is aimed at reducing saturated fatty acid intake and maintaining a healthy body weight. The AHA emphasizes restriction of saturated fatty acid intake because this is the strongest dietary determinant of plasma LDL-C levels. [193] Total plasma and LDL-C levels are mainly affected by lauric (12 C atoms), myristic (14) and palmitic (16) acids. Reduced intake of these C raising saturated fatty acids has resulted in a reduction in plasma LDL-C levels in well controlled dietary studies. Short chain (less than 10 carbon atoms) fatty acids and stearic acid (18) have little effect on cholesterol levels. [273]

Currently AHA recommendation is less than 10% of total calories come from saturated fatty acids. Controlled clinical studies indicate that reducing saturated fat intake from the current average intake of 12% to 14% [194,274] of calories can lead to an average reduction of 3% to 5% in CHD risk in the population as a whole. There is, however, inter individual variation in plasma LDL-C response to reduced intake of saturated fatty acids, partially influenced by genetic factors. [275]

To reduce lipid and lipoprotein levels while maintaining caloric intake, SFAs in the diet can be replaced by either PUFAs or MUFAs, carbohydrates [276] or protein, [277] all of which have differing effects on plasma serum lipids and lipoproteins. The AHA currently recommends that intake of Ω-6 fatty acids be no more than 10% of total calories.Ω-3 PUFA, derived primarily from fish, can also

be substituted for dietary saturated fatty acids and may have beneficial effects beyond those associated with lowering LDL-C levels. [278]

MUFA suitable replacement for SFAs, although, net effect on serum lipids and lipoproteins is not much different from that of PUFAs, they may have some advantages. Unlike polyunsaturates, monounsaturates are not as susceptible to oxidation, which may play a role in atherogenesis. The AHA therefore recommends a MUFA intake in the range of 10 to 15% of total calories. [279] Dietary cholesterol [280] can increase plasma and an LDL-C level in epidemiological studies [281,282] has been shown to be related to CHD risk independent of its effects on blood cholesterol levels. Currently the AHA recommends that dietary cholesterol intake be less than 300mg /day.

d) Choose a diet with plenty of vegetables, fruits and whole grain products:

These foods should contribute the majority of daily energy intake between 55 and 60% of total calories. Fruits, vegetables, whole grains and legumes provide important vitamins, minerals, fiber and complex carbohydrates as part of a diet moderate in total fat and low in saturated fat content. Diets high in unrefined carbohydrates also tend to be high in both soluble and insoluble fiber. Foods rich in soluble fiber, including oats, barley, beans, Soya products, guar gum and protein found in apples, cranberries, currants and goose berries can help maximize a reduction in plasma total and LDL-C levels as part of a fat modified diet. [283] Total dietary fiber intake of 25 to 30 g/d from foods, not supplements, will help ensure an eating pattern high in complex carbohydrates and low in fat.

e) Choose a diet moderate in sugar:

Sugar intake has not been directly related to risk for CVD, but diets high in refined carbohydrates are often high in calories and low in complex carbohydrates, fiber and essential vitamins and minerals.

f) Use salt and sodium in moderation:

The AHA recommends that the general public consumes no more than 6 gms of sodium chloride (NaCl) per day. This recommendation is based on the evidence for an association between dietary NaCl intake and BP derived from a couple of epidemiological observations [284,285] and clinical trials of salt restriction. Results of therapeutic trials of NaCl restriction in hypertensive individuals also documents modest but significant reductions in BP. [286,287] The AHA has elected to limit NaCl intake to 6g/day. However slightly higher intake (6 to 7.5g/ day) have not been demonstrated to increase CV risk or raise BP in normotensive persons without other CV risk factors.

III. TOBACCO AND SMOKING

Smoking and tobacco habits have a more firmly established pernicious influence on cardiovascular mortality and morbidity. More than 1.1 million individuals are affected by myocardial infarction (MI) each year in North America and >20% of these individuals are habitual smokers. [288] Cigarette smoking promotes atherosclerosis & is associated with an increased risk of sudden death, angina, MI, peripheral vascular disease and stroke. [289,290] It is observed that men who smoke cut their lives short by 13.2 years while women who smoke lose 14.5 years of life. In 1934, Howard first proposed such an association after observing that the increased incidence of CAD in Europe after World War I coincided with a sharp rise in the number of smokers during the war. In 1964 the US Surgeon General's report noted that the causative role of smoking was not proved but was strongly enough suspected to warrant counter measure. In 1979, the Surgeon General's report contained much stronger, wording referring to a definite association between smoking and CAD, with the report of an increase of 2 to 3 fold risk of CAD with smoking [291]

In the Framingham study the relative risk of sudden coronary death was about 10 times higher in men and 4.5 times higher in women when compared to their non-smoking counter parts. [292] Also a multiple regression analysis of the Framingham offspring study showed that smoking was significantly associated with lower HDL-C levels of 4mg/dl in men and 6mg/dl in women. [293] Other studies have shown a 7-20% reduction in HDL-C levels in smokers. [294,295] Thus there is a linear dose dependent effect between the number of cigarettes smoked per year and HDL-C levels. Continuous smoking of large number of cigarettes disturbs the lipid metabolic balance and liver functions. It was observed that effect of smoking on lipid metabolism and liver functions depend on the number and regularity of smoking. Pooling project research group study [296] and Key's Minnesota business and professional men study [297] showed that an increase in CHD risk is associated with an increase in the number of cigarettes smoked.

1. Increased risk of CHD:

Cigarette smoking increases the risk of CHD by itself. When it acts with other factors, it generally increases the risk.

Smoking:

I) increases blood pressure

ii) Decreases exercise tolerance and
iii) Increases the tendency for blood to clot

Smoking also increases the risk of recurrent CHD after bypass surgery. Cigarette smoking is the most important risk factor for young men and women. It produces a greater relative risk in persons under age 50 than in those over 50. Cigarette smoking combined with a family history of heart disease also seems to greatly increase the risk. In subjects, smoking 10 to 15 cigarettes daily a tendency of high TC and TG and low HDL-C is found but no change in LDL and VLDL is seen.

2. Pathophysiology:

Cigarette smoking has a major impact on the cardiovascular system. Smoking is a leading contributing factor to aortic aneurysm, atherosclerosis, IHD, MI, peripheral vascular disease and stroke. [289,290] There are four principal mechanisms that contribute to acute cardiac events that are due to smoking: induction of a hypercoagulable state, reduction of oxygen delivery because of carbon monoxide (CO), coronary vasoconstriction and nicotine mediated heamodynamic effects.

a) Induction hypercoagulable state:

Smoking affects both coagulation factors and platelet function. Smoking increases factor VII, which is involved in the initiation of coagulation and contributes to blood coagulability. [298] Changes in red cell deformability and plasma viscosity associated with smoking, increases the thrombus formation. After cigarette smoking there is reduced platelet survival time [299] and increased circulating platelet aggregates release of platelet specific proteins. [298] Platelet aggregation is increased due to the reduction in production of endothelial cell prostacyclin, an inhibitor of platelet aggregation, by tobacco smoke. Short ended platelet survival is found in smokers and is considered an indirect indicator of platelet activation. This could explain the increase in thrombus formation in vivo. Smoking causes acute and chronic inhibition of cyclooxygenase which inhibits prostacyclin and increases the biosynthesis of the thromboxane A_2, an eicosanoid releases by activated platelets, which supports the notion that smoking activates platelets. [298] It is also a potent vasoconstrictor and platelet

agonist with a half life of approx 30 seconds at physiological pH. Smokers have higher levels of fibrinogen and factor VII and are decreased after smoking cessation, although this decrease may take several years. Increased levels of factor VII and fibrinogen are associated with an increased risk for CAD. [298]

b) Reduction of oxygen delivery because of CO:

Smokers inhale CO and their carboxy hemoglobin levels average approximately 5% per packs smoked per day. These levels compare with levels of 1% to 3% in non smokers. [300] Smoking acutely increases myocardial O_2 demand by raising peripheral resistance, blood pressure, heart rate and possibly coronary artery flow and reduce O_2 carrying capacity of hemoglobin due to CO. CO binds to hemoglobin available to carry oxygen and allostericaly inhibiting hemoglobin mediated oxygen release. [300] Cardiac patients exposed to CO during exercise experience an increase in both ventricular dysfunction and number and complexity of ventricular arrhythmias. [289] Thus a reduction in oxygen delivery because of CO inhalation can lead to events such as arrhythmia and MI.

c) Coronary vasoconstriction:

Smoking causes constriction of the coronary arteries and has been observed to produce acute vasospasm during angiography. [301] Coronary vasoconstriction is a result of α-adrenergicallly mediated increases in coronary artery tone. [302] Intracoronary Doppler measurements have demonstrated that cigarette smoking conducts both epicardial arteries and coronary resistance vessels and also increases total coronary vascular resistance. [301] In smoking with CAD, vasoconstriction decreases coronary blood flow despite the increase in O_2 demand associated with smoking. [301] The resulting reduction in myocardial blood supply can produce arrhythmias, ischemia and MI.

d) Nicotine mediated heamodynamic effects:

Rapid absorption of the nicotine in cigarette smoke leads to arterial plasma concentration in body organs 6 to 10 times higher than venous plasma conc. [289]

This rapid delivery of high conc. of nicotine can lead to intense immediate cardiovascular effects because there is minimal time for development of tolerance. [289] The nicotine mediated heamodynamic effects of smoking include an increase in heart rate and BP, which increases myocardial work. Nicotine also increases O_2 demand and causes arterial constriction, which impairs blood flow to the heart. [301] Furthermore nicotine increases both heart rate and myocardial hypoperfusion in cardiac patients. [289] The introduction of nicotine into healthy non smokers has been shown to blunt the increase in coronary blood flow that occurs with a nicotine-induced increase in heart rate. This finding suggests that low doses of nicotine are capable of constricting coronary arteries. [289] For high risk cardiac patients, eliminating nicotine induced coronary constriction is important in the prevention of MI.

3. Atherosclerosis:

Smoking accelerates endothelial atherosclerosis through damage to the endothelium and increased fibrinogen levels. [303] Over time inhaled CO from cigarette smoke damages the endothelium and accelerates the process of atherosclerosis. [304] Approx 25% to 50% of the relation of cigarette smoking to the occurrence of CAD is attributable to the effect of smoking on increased fibrinogen levels in the blood. [303] High fibrinogen levels enhance the tendency for thrombosis, leading to occlusive clinical events. [303]

4. Metabolic Effect of tobacco Use:

Nicotine administration and cigarette can lead to an increase in fatty acids in serum as first observed by Kershbaum *et al*. [305] The increase is mediated by catecholamine release. There is no change in concentration of serum total cholesterol and phospholipids. Smoking has an additional indirect effect on lipid metabolism by affecting LPL which is an important enzyme in the metabolism of cholesterol and triglycerides. Smoking elevates VLDL-C and reduces HDL-C and thus increases atherogenic property. Cigarette smoking is also associated with reduced LCAT activity, [306] CETP activity [307] and HDL-C. [128] The combination of these metabolic effects may promote endothelial cell injury and reduce efficacy of vascular repair mechanisms. Smoking affects cardiovascular system adversely by increasing plasma free fatty acids, growth hormone, ADH, cortisol and

glucose. Cigarette smoking in women is associated with earlier menopause, which is considered an important risk factor of CVD. Smoking increases metabolic clearance rate of estradiol in liver [308] and is responsible for lower level of estrogen. In postmenopausal women, smoking increases bone loss.

5. Pro inflammatory and Pro coagulant markers in CAD:

Experimental studies have shown that tobacco glucoprotein products, induce the release of interleukin (IL)-6 and macrophage colony stimulating factor (M-CSF) from alveolar epithelial cells [309] and from pulmonary macrophages. [310] Smoking renders LDL more susceptible to per oxidative modification by macrophages and smooth muscle cells. [311] Oxidized LDL can induce expression of M-CSF by endothelial cells. [312] In circulation, M-CSF released by vascular macrophages and injured endothelium [410] induces monocyte/macrophages activation, [313] facilitates platelet monocyte adhesion and activation [313] and this leads to release of platelet thromboxane A2 (TXA_2). [314] M-CSF also promotes tissue factor expression [315] and release of IL-6 by vascular cells [316] leading to c-reactive protein (CRP) production. [317] Smoking status has been also associated with enhanced TXA_2 released by platelets, [314] elevated IL-6 and CRP plasma levels in healthy [318] and increased tissue factor expression in human atherosclerotic plaques. [319] Cigarette smoking appears to be a triggering factor for M-CSF and CRP production in patients with coronary atherosclerosis. Rohde et al have also shown a relation between smoking status, increased CRP levels and risk to develop CAD in apparently healthy subjects. [318] And alternative pathway for CRP production by liver involves the generation of oxidized LDL [320] which may be significantly enhanced by smoking. M-CSF increases cholesterol uptake by macrophages [321] and mediates the monocyte induced apoptosis of the vascular smooth muscle cells [322] resulting in foam cell formation, [323] the hall- mark of atherogenesis.

In a prospective study of patients with chronic CAD, cigarette smokers had approximately three fold levels of M-CSF and two fold CRP levels compared with non smokers and healthy control. Also a two fold levels of 11 – dehydro TXB_2 in smokers than non smokers and healthy control in agreement with another study in healthy volunteers was seen. Thus this prospective study links cigarette smoking to the circulatory levels of a major atherogenic cytokine namely, M-CSF of a pro-coagulant and inflammatory protein namely, CRP in addition to thromoboxane A_2 production in patients with chronic CAD. [324]

6. Nicotine dependence:

Tobacco dependence is driven by nicotine addiction which perpetuates itself by controlling the release of several neuro transmitters (dopamine, γ amino butyric acid, nor epinephrine, serotonin). [325] The immediate release of neurotransmitter produces sensation of stimulation and pleasure with prolonged exposure to nicotine, tolerance to these effects develops and the presence of nicotine in the brain becomes necessary to maintain normal function. When tobacco use ceases, there are subnormal levels of dopamine, norepinephrine and serotonin in the brain, with associated withdrawal symptoms. [290] Although motivated patients may have high initial quit rates (up to 60 % within the first six months), the relapse rates at one year increase dramatically because of patients' strong addiction to nicotine. [289] In addition, a large no of individuals who initially stops smoking but relapse after one year do so because of the withdrawal symptoms. Withdrawal symptoms range from anxiety, depressive symptoms or dysphoria to intense cravings and hunger. [290]

7. Smoking cessation:

Smokes from cigarettes contains from .5 to 3 mg of nicotine depending on different brands when smoke is inhaled, practically all the nicotine is absorbed and the plasma nicotine levels may increase up to 40 to 50 mg per ml of the plasma. CO also constitutes 3 to 6 % of cigarette smoke. COs high affinity for binding to hemoglobin elevates carboxy hemoglobin level and reduce the oxygen carrying capacity of the blood. Thus more than 500,000 people each year die of smoking in North America, making smoking the leading preventable cause of premature death. [326] Approximately 70% of the 50 million North American smokers want to quit smoking but only 2.5% per year actually succeed in quitting. Both pharmacological and behavioral smoking cessation aids have been developed to improve the chances of overcoming nicotine dependence. These aids can be classified into two groups: Nicotine Replacement Therapies (NRTs) and non –NRTs. NRTs including the nicotine patches, gum and inhalers supply the user with nicotine while avoiding the toxic chemicals ingested from cigarettes. The two non NRTs are bupropion and behavioral therapy.

Cessation of smoking is related to a marked decrease in CVD, including reduced cardiac arrest, coronary death and MI. A substantial decrease in CHD, mortality for former smokers compared with continuing smokers. This decrease

in risk occurs relatively soon after cessation of smoking and increasing interval since the last cigarette smoked are associated with progressively lower mortality rates from CHD. Gordon and Kannel, [327] reported 20- 60% reduction in risk of heart attacks in moderate (20 cigarettes per day) and heavy (40 cigarettes per day) smokers, two years after cessation of smoking. Rosenberg [328] in his study of 3285 women, showed that within 4 years of stopping smoking, the risk of CHD decline to a level approximately that for women who had never smoked. HDL-C level will rise to the levels of non smokers after smoking cessation for 30 to 60 days with the elevation sustained at one year. [294] Its elevation by a mean of 4 mg/dl is more so in women than in men and in persons with elevated baseline HDL-C levels (47 mg/dl). [329] Also person with diagnosed CHD experience as much as a 50% reduction in risk of re-infarction, sudden cardiac death and total mortality if they quit smoking after the initial infarction. Smoking cessation results in decreased fibrinogen level, reduces oxidative damage from CO and also increases the ratio of HDL/LDL-C. [303] These changes help reduce the risk of CAD and MI caused by arthrosclerosis. [330] Smoking cessation decreases mortality caused by atherosclerotic diseases by 50% within five years in both men and women. [331] Thus there is overwhelming evidence demonstrating both the cardiovascular hazards of smoking and the prompt benefit that occurs with smoking cessation.

But it is no longer enough simply not to smoke. Non smokers have to be alert to the presence of environmental smoke produced by others. Environmental tobacco smoke (ETS) is a mixture of more than 4000 compounds over 50 of which are known to cause cancer. ETS consists of two different kinds of smoke. Approximately 85% is side stream smoke, the smoke emitted from the burning of cigarettes, cigar or pipe between puffs. The remainder is the main stream smoke exhaled by the smoker. Although both smoke are chemically very similar, undiluted side stream smoke burns at a lower temperature and therefore contains high concentration many of the toxic elements in tobacco smoke including nicotine, CO, Benzene, ammonia, 4-amino-biphenyl and benzo [a] pyrene. ETS also affects heart diseases. Byrd et al [332] concluded that 37,000 CHD deaths occur per year in USA due to ETS exposure accounting for seventy percent of all deaths due to the same. Passive smoking has also been shown to lower HDL-C level with a significant relationship between the HDL-C level of children and adolescents and passive smoking by adult smokers in the home. [333] Therefore passive smoking is an important risk factor for heart disease morbidity and mortality.

Cigarette smoking is as widespread and significant as a risk factor and is the leading preventable cause of disease and death worldwide. A comprehensive approach to smoking cessation involving pharmacotherapy, nicotine replacement therapy and counseling should be recommended. [334]

IV. HERIDITARY

Over the past few years research in HT and CVD has focused on different biochemical variables such as positive family history, lipid levels, smoking, alcohol etc. However all these are useful only when the patient is in the advanced stage of the disease. One would definitely like to prevent the occurrence of these diseases much earlier than this and in an individualized manner. The advances in the field of genetics and genomics have enabled us to understand the role of genes and its minor variations in the pathogenesis of different diseases. With the “Human Genome Project” completed and the rapid technological advances in the field of biotechnology and molecular biology, new candidate genes are continuously emerging for various aspects of cell biology, for modulating HT and CVDs .Also the human gene sequence would give us a better correlation between genotype-phenotype and may also help us identify individuals at an increased risk for the above mentioned diseases. Medical genetics is predicted on the concept of genetic variation resulting in disease and has traditionally focused on diseases that can be tracked through families. Classical genetics uses pedigree analysis of families and is able to use statistical methods to couple genes with disease through what is termed linkage analysis. The reason for the strength of linkage analysis is that individuals are well matched for genetic background. The most common variations in the human genome are single base changes called single nucleotide polymorphisms (SNPs). Although human beings are 99% genetically identical that 0.1% of the 3 billion base pairs in the human genome has 3 million base pairs of difference between individuals. One of the major advances from studying various polymorphisms including SNPs of multitude of genes which are involved in the pathogenesis of HT and CVD is the possibility of predicting the development of these diseases and their probable outcomes.

Since the discovery of DNA in 1950s and elucidation of this molecule as the information keeper of the cell, explosive knowledge and development of technologies have taken place in the field of molecular biology. Various techniques like cell transformation, gene transduction, reverse copying of mRNA to cDNA, cutting DNA at desired places using restriction enzymes, ability to join the desired fragments with multitude of DNA and RNA ligating enzymes, discovery of PCR technology etc have resulted in understanding the detailed mechanisms of gene control by environmental factors, the process of cell division, apoptosis, angiogenesis, vasculogenesis and several other cellular events within our body. In order to understand better how different genes ultimately translate into differences in various disease conditions and survival, it is essential to be able to read the whole human genome. These considerations led to “Human Genome Project” in 1990s which has now been completed

successfully and thus are in a position to look ahead and see how this knowledge can be helpful in understanding and managing CVD and HT.

1. Facts in relation to Heredity:

Although a positive family history is widely accepted as an independent risk factor for CHD there is little published evidence to support this view. It is also observed that a positive family history is not an independent primary risk factor of the same magnitude as HT, hyperlipidaemia, DM, obesity or smoking but showed that in younger patients the positive family history of premature CHD is consistent with an inherited susceptibility to the action of coronary risk factors. [335] Asian Indians who have settled overseas and those in urban India have increased CHD mortality rates as compared to most other ethnic groups. [336] Numerous studies in the last four decades have confirmed this observation. [337,338] Reasons for this increased risk are thought to be genetic but are yet unclear.

2. Heredity and Blood Pressure:

Activation of the renin angiotensin system (RAS) that regulates cardiovascular homeostasis has been proposed a very important step in the pathogenesis of HT and atherosclerosis. In the Angiotensin I converting enzyme (ACE), the effective molecule of RAS system which convert angiotensin I to angiotensin II, a 287bp deletion(D) polymorphism was identified with increased ACE level, [339] and as a potential risk factor for myocardial infarction. [340] In Indian population, the D allele of the ACE gene conferred no appreciable increase in the risk of CHD, MI [341] or in HT. [342] However D allele was significantly associated with an early onset of HT rather than late onset of HT and although non-significant the D allele form was highest in subjects with family history of CHD. [342]

Also Angiotensin II carries out its action through angiotensin II type receptor (AGTRI).The AGTRI geneA/C166 polymorphism was very first identified by Bonnardeaux *et al* [343] and was shown to be significantly associated with essential HT. Again a strong linkage was demonstrated between the primary substrate of this system angiotensinogen (AGT) gene and essential hypertension

in Utah and French Caucasians and also associations of two molecular variants in exon 2, M235T and T174M with BP. [344]

Previously the role of apoE polymorphism in causing atherosclerotic events have been reported. [345,346] ApoE is an exchangeable protein which acts as an ligand for LDL receptors. It also has a repair function in response to tissue injury. It plays an essential role in lipid metabolism specially in the removal of atherogenic remnants of TG-rich lipoproteins [347] and by reversing cholesterol transport in plasma and intercellular lipid transport within tissues. These common isoforms of apo E including E2, E3, E4 [348] have been identified. It is well known that the E4 isoform is associated with increased levels of TC and β-lipoprotein [349] and increased susceptibility to CVD. [350] Some studies have suggested that high BP may be associated with the presence of the E4 allele [351,352] while others have found its association with E2 allele. [353] Mechanisms of apoE such as increased rigidity and decreased elasticity of the aorta and other large vessels [354] may contribute to the development of HBP and thus explain the lack of association in the elderly subject.

There is convincing evidence that the relationship between apo E genotype and plasma Lp lipid levels is context dependent being significantly influenced by age [355] and sex. [356] Recent evidence [357] also indicated that the responses of plasma lipoprotein lipid levels to different lipid lowering interventions may be affected by an individual apoE genotype indicating the significance of gene environment interactions. These changes in lipid parameter indicate a delayed degradation of the administered fatty load. The most significant changes were evident in the subgroup of apoE4 carriers reflecting their higher fasting lipid levels. This abnormal lipid metabolism is similar in character as observed in patients with confirmed IHD and is another manifestation of an increased atherogenic risk of HT patients.

Thus significant association of E4 allele is observed with HT in addition to other well known risk factors and positive family history. These observations emphasize the need to monitor HT and lipid metabolism especially in middle aged males and those with a positive family history to reduce the susceptibility to CAD.

3. Heredity and Lipid Metabolism:

It is pronounced that “In India approximately four people die of heart attack every minute because Indians are genetically predisposed to the disease. One

of the best understood inborn error of metabolism determining elevated levels of plasma cholesterol and LDL-C is the autosomal dominant disorder of familial hypercholesterolemia (FH). FH is caused by mutations in the LDL receptor gene located on chromosome 19 and containing 18 exons. Though certain isolated populations show the presence of common mutations due to founder gene effect, [358] there exists mutational heterogeneity in the LDL-R gene with over 800 mutation identified across the entire length of the gene. No common mutation has been yet identified in FH cases from India. [359] A few point mutations, however have been reported in Indian families residing in South Africa, which suggest a high frequency of FH in the Indian subcontinent. [360] Recently a missense mutation in exon 9(E387K) and a polymorphism (C1617T) in exon 11 in a Gujarati family from Mumbai have been observed. [361] The E387K mutation of exon 9 has been previously identified in an Asian Indian of Gujarat origin residing in the UK, French and in America. [358] Considering the fact that there exist various distinct communities in India which has remained segregated from each other for over centuries, due to various religions, cultural or geographical reasons, it is likely that there might exist some common community based mutations. The E387K mutation identified could be one such mutation among Gujarati community in India.

In recent times new markers like the apo E polymorphism (seen above in case of BP regulation) have been found associated with CHD and are being extensively studied. [347] The apoE4 isoform is associated with increased cholesterol level and thus an increased risk of CHD. [362] A small study from the Southern parts of rural India in tribal communities suggested that the low frequency of the apo E4 allele was a contributing factor for the low prevalence of CHD in this community. [363]

Apo C3 (chromosome 11q23), important in the regulation of plasma TG concentration is major component of TG rich Lps-CM and VLDL and as minor component of HDL. It is a noncompetitive inhibitor of lipoprotein lipase (LPL) and thereby plays a role in reducing hydrolysis of TRL. Ito *et al* [364] have reported that over expression of apo C3 resulted in hyperglyceridemia with positive linear relation between apoC3, TG, and reduce HDL-C levels. This action of apo C3 is prevented by insulin. [365] Several forms of hypertriglyceridemia in humans originate from genetic abnormalities. In human hypertriglyceridemia, the composition and particle size of TG rich Lps appears to determine their atherogenecity. For e.g., with genetic deficiency of LPL, newly secreted CMs accumulate in serum, these CM are large TG enriched Lps. Patients having chylomicronemia because of genetic difference of LPL rarely develop CAD, [366] presumably CM are not atherogenic. Another disorder, familial hypertriglyceridemia is characterized by large TG enriched VLDL. The incidence of CAD in patients with familial hypertriglyceridemia likewise appears to be relatively low. [367] In yet another condition, familial combined hyperlipidaemia, VLDL are smaller and more enriched in cholesterol than in familial

hypertriglyceridemia. [367] Finally, patients with familial dysbetalipoproteinemia have elevated to β-VLDL, this disorder definitely predisposes to premature CAD. [368] Genetic forms of hypertriglyceridemia thus strongly imply that TG rich Lps are potentially atherogenic and that atherogenecity of TG rich lipoproteins increases Lps become smaller and more enriched in cholesterol.

Faster [369] found significantly shortened platelet survival half life of 89+/-1.98 hours in patients having symptomatic CAD, when compared with the platelet survival half life in the controls (3103+/-2.8 hours). Increased platelet consumption at the sites of lesion of coronary atherosclerosis and the same in young persons indicates accelerated atherosclerotic process. The normal healthy people with strong positive family history of CAD also showed shortened platelet survival time which might represent sub clinical disease.

In a study of coronary artery disease among Indians showed that only 14% of Asian Indian men and 5% of women had optimal HDL-C level. [370] Thus decreased HDL-C is one of the common feature observed among Asian Indians. Also patients with positive family history of CAD showed raised serum apo B levels than those having negative family history. A positive coefficient of correlation was observed between serum apo B and LDL levels suggesting that more the number of apo B particles more will be the synthesis of atherogenic LDL particles. Thus elevated serum apo B levels turn out be a genetic factor responsible for causation of CAD. [371]

Recently a condition termed SyndromeX that predisposes Indians to a whole repertoire of biochemical bullets blasting the heart is increasingly seen by experts as the prime culprit for the alarming rise in heart disease in the country. The understanding of its potential for mischief came from a recently concluded 10 year study of 4500 patients by the Coronary Artery Disease Institute (CADI) in Lisle, Illinois, that found the Indian Community had much higher levels of a deadly genetic factor called Lp(A) than other ethnic groups. It is 10 times deadlier in causing clogged arteries that lead to heart attacks than bad cholesterol LDL. [372]

4. Genetic Aspects of CVDs:

Despite high contribution of factors such as hypercholesterolemia, systemic HT, smoking, and diabetes in development of CAD, evidence from family studies show that genetic factors also contribute significantly to the

predisposition to CAD. Knowledge of genetic risk factors will help define the mechanisms of the disease and could ultimately assist in the rational design of selective prophylaxis or therapy. Many single genes have been identified as the basis for different CVDs. However unlike other genetic disorders, CVDs are not solely due to to a single gene mutation/polymorphism. It has a multifunctional etiology and is termed as a complex disease caused by variety of genes as well as environmental factors.

The major genetic causes for CVDs are (i) chromosomal disorders and single gene disorders (8%), (ii) environmental teratogens (2%) and (iii) multifactorial disorders, which means both genetic and environmental factors interact (90%). Arterial HT, glucose intolerance and mild forms of hyperlipoproteinemia are likely to have polygenic inheritability influence and each could be solely responsible for most of the observed aggregation of CAD. [373] Thus three ways in which a positive family, history might be related to the development of CHD are (i) as an index of the inheritance of risk factors (elevated BP, serum total cholesterol, smoking, obesity, impaired glucose intolerance) which tend to cluster within families, (ii) as a truly independent risk factor and (iii)as a vulnerability factor potentiating the action of risk factors. [335] Clinical studies have shown that CVDs are associated with strong genetic components with difference types of inheritance. [374,375] Apart from possible therapeutic developments, once the abnormalities in the gene leading to disease in family is identified, it may be possible to assign the risk to the other members of the family who have not yet developed the disease or to offer prenatal diagnosis.

5. Shared genes in blood relatives:

It is acknowledged that family history is an important risk factor for CVDs and HT. The following is the information to determine whether or not a person is at higher risk of CVDs and HT due to genetics i.e. family history or not.

- First degree relatives are person's children, parents or brothers and sisters. The subject shares 50% of the genes with these family members.
- Second degree relatives are the subject's aunt, uncle, grandparents, half siblings, nieces and nephews. The subject share 25% of the genes with these family members.

- Third degree relatives are cousins and great grandparents. They share 12.5% genes with these family members.

Obviously, the subject's risk of genetically linked illness is four times higher if that illness is in a first degree family member, as it is in a third degree family member as the subject share four times more genes with the first degree relative as you do with the third degree relative.

Once it is known that a person is at a higher risk to develop an illness on basis of his family history, the subject should concentrate on the lifestyle. Genes alone don't explain the sudden spurt in heart disease among the young. The answer is lifestyle- smoking, obesity, physical inactivity, high serum cholesterol, diabetes. Through genetics or nature genes are present in a subject, but these genes are nurtured by unhealthy lifestyle associated with rising affluence, rapid urbanization and mechanization. In a nutshell **"Genetics load the gun, lifestyle pulls the trigger".**

V. OVERWEIGHT & OBESITY

Hippocrates wrote “Corpulence is not a disease itself, but the harbinger of others”, recognizing that obesity is a medical disorder that also leads to many comorbidities. Overweight is associated with a host of adverse health outcomes and places severe burden on the world health care system. [376] WHO [377] describes obesity as one of the most blatantly visible, yet most neglected, public-health problems that threatens to overburden both, more and less developed countries. The risk increases with increasing adiposity and there is excess mortality at any age. The problems of overweight and obesity have achieved global recognition only during the past 10 years, in contrast to underweight, malnutrition and infectious disease which have always dominated thinking.

Excess bodyweight is the sixth most important risk factor contributing to the overall burden of disease worldwide. [378] The International Obesity Task Force estimates that at present at least 1.1 billion adults are overweight, including 312 million who are obese. Also 10% of these are children classified as overweight or obese.

In males at 18 years of age, approximately 15 to 18% of body weight is fat, while in women it is 20 to 25%. This percentage tends to increase with age which may not be desirable. Obesity has been defined as a body fat content greater than 25% of total body weight for men and more than 30% for women. [379] On the otherhand, overweight has been defined as a relative weight greater than 120% of what is ideal. Relative weight itself involves dividing a patient’s weight by a standard weight that is based on the patient’s height. [380]

Risk from overweight and obesity predispose to many disease conditions like diabetes, HT, coronary and vascular disease. The importance of overweight and obesity in association with CAD has been well known. Obesity at an early age is thought to have a greater influence on CVD than late onset obesity. The excess body fat associated with obesity is considered a risk factor for many chronic diseases and predisposes to premature CVD. Even in healthy young people who are obese, some degree of myocardial dysfunction has been demonstrated echocardiographically which tends to be reversible with weight loss. [381]

A recent report described associations between overweight and obesity and the prevalence of chronic conditions including high BP and high blood

cholesterol levels in National Health and Nutrition Examination Surveys (NHANES) III data. [382] Additional association of adiposity at baseline and incidence of HT and Dyslipidaemia have been shown in men and women and in diverse race or ethnic groups in large prospective cohort studies. [383-386] Also clinical trials have shown the effect of weight loss on lowering BPs and lowering lipid values. [158,387,388] The science base for concluding that higher levels of body mass are causally related to higher levels of BP and total cholesterol and lower levels of HDL-C is substantial and convincing.

It has been suggested that central, particularly visceral fat is a more important contributor to cardiovascular risk than total body fat. Also it has become obvious that metabolic complications of obesity are associated with upper body segment or abdominal obesity. [389] Increase risk of CVD has been found in individuals presenting with distribution of excess fat in the abdominal region. [390]

Several factors seem to participate in the pathogenesis of obesity and atherosclerosis viz: excess intake of dietary calories, over and above the daily requirement (most important factor in the development of obesity), sedentary lifestyle, addiction like smoking, heavy alcoholism and increased mental stress in day-to-day life. Inspite of continued upliftment in health consciousness, there is an upsurge in the incidence of CAD (the most devastating slow global pandemic) and obesity. [391] Primordial and secondary preventive measures like restriction of dietary calories and SFAs, [392] adoption of vegetarian diet, relaxation exercise etc has failed to prevent the increase to an appreciable extent. Thus the prevalence of overweight and obesity is increasing and obesity is now estimated to be the second leading cause of preventable death after cigarette smoking in the US. [393,394] Therefore obesity, with its array of comorbidities, necessitates careful clinical assessment to identify underlying factors and to allow coherent management.

1. Determining Obesity:

Criteria for identifying an individual as overweight or obese are now available through a number of techniques, yet anthropometry is the simplest and most practical technique. Among them body mass index (BMI), as a measure of obesity is proved useful and easily applicable clinically to give a reasonable estimation of adiposity and is also claimed to represent the degree of body fat content. BMI is a relative weight index that shows highest correlation with independent measures of body fat. It is one of the most accurate ways to determine when extra pounds translate into health risks. It is also a measure

which takes into account a person's weight and height to gauge total body fat in adults. BMI is calculated by dividing the weight in kilograms by the square of height in metres. ($kg/m^{2)}$

A recent review supports the use of BMI in clinical practice to define overweight and obesity. [387] WHO now accepts a BMI of 25 kg/m^2 or higher as abnormal; the overweight category is classified as obese when the BMI is 30 kg/m^2 or more. The risks of diabetes, HT and dyslipidaemia increase from a BMI of about 21 kg/m^2, thereby reducing life expectancy and greatly increasing the health and societal economic burden. [395] The standard criteria used to define obesity in the western literature is a BMI greater than 27.8 for men and greater than 27.3 for women. [393] But the distribution of BMI in the western population differs considerably from that of Indians. [396] Thus the desirable upper limit of BMI in Indian population is <23. [392]

Someone with a BMI of 26 to 27 is about 20% overweight, which is generally believed to carry moderate health risks. The higher the BMI, the greater the risk of developing additional health problems. There are numerous reports suggesting that BMI values greater than 2.6 for women are associated with increased risk of fatal and non-fatal CHD, NIDDM and a rise in all cause mortality rates. [384,397] Other studies also show that BMI and the pattern of body fat distribution affect morbidity and mortality from CVD. [398,399] MI, sudden death and coronary insufficiency are all associated with a high BMI. [400]

Measures of regional adiposity such as waist circumference (WC), hip circumference (HC), waist-hip ratio (WHR) and subscapular to triceps skin fold thickness correlate highly with other measures of overweight such as BMI and may be even more strongly correlated with lipoprotein cholesterol fractions. [401] Central adiposity is a predictor of CVD independently of major risk factors, including BMI. [402] Part of the relationship between central adiposity and CVD is mediated by a modification of the metabolism of insulin and lipids. [403] Dyslipidaemic individuals are more frequently "centrally obese". (E.g. with a high WHR) [404] These observations have been made in a variety of populations from developed [405,406] and less developed countries. [406]

The WHR has been found to be of value in identifying people with abnormal distribution of body fat and it is now believed that excessive body fat around the abdomen in contrast to that around the hip would be a clinical as well as epidemiological marker in predisposing, towards CAD. [398] WHR ≥0.9 for men and WHR ≥0.8 for women are coded as high WHR by gender. [407] BMI and WHR are routinely employed because they are directly related to clinical entities (i.e. peripheral overweight, central obesity, etc.) High BMI [386] and high WHR [408] are associated with higher incidence of CAD.

WC reflects the proportion of body fat located intra-abdominally and is the best indicator of changes in Intra-abdominal fat (IAF) during weight loss. [409] The WC relates closely to BMI and is also the dominant measure in the WHR. Studies by Pouliot *et al* [410] suggest that WC is superior to WHR in providing assessment of abdominal obesity and related metabolic complications. Optimum WCs are lower for Asians: 90cm for men and 80 cm for women, [411] compared with 102cm and 88cm suggested for white people. [377] Individuals, who fall into the BMI range of 25 to 34.9 and have a waist size of over 40 inch for men and 35 inch for women, are considered to be at especially high risk for health problems. Both BMI and WC can be useful measures of determining obesity and increased risk for various diseases. According to the National Institutes of Health, a high WC is associated with an increased risk for type 2 diabetes, dyslipidaemia, HT and CVD when BMI is between 25 and 34.9.

Thus these predictive associations suggest the possibility of employing 1 or more anthropometric measurements of central obesity as a first step in population screening for dyslipidaemia. [405,406] Using inexpensive and readily obtainable anthropometric measurements instead of more costly and time-consuming wet-or even dry-chemistry laboratory cholesterol measurements is relevant in developing countries where an emerging epidemic of CVD is occurring amidst rising health care costs.

2. Disease burden from excess weight in adults:

The prevalence of the high BMI according to age, and the proportion of the disease burden attributable to the excess weight are shown in the detailed estimates of the years of ill health and lives lost between the ages of 30 years and 75 years because of excess weight. [395] CVD dominates, followed by diabetes, HT and some cancers, especially in women. Again, the burden of disease is high in Eastern Europe and Latin America, but the Asian countries have a surprisingly high burden in view of their lower obesity rates. This finding relates to the higher absolute risk of diabetes and probably CVD among Asian, [395] Hispanic, [412] and perhaps African populations, partly because they are more prone to abdominal obesity with its excess risks.

Many of the comorbidities of obesity are reflected in the so-called metabolic syndrome, originally defined arbitrarily by WHO on the basis of insulin resistance with other features of obesity: [413] large WC, abnormal concentrations of TGs, HDL-C and fasting glucose and HT. The effects of obesity on

cardiovascular health and disease are many, one of the most profound of which is HT.

3. Obesity and Hypertension:

The risk of HT is up to 5 times higher among obese people than among those of normal weight, [414] the variability in response reflecting differential genetic susceptibility as well as dietary factors. Up to two-third of cases of HT are linked to excess weight, [415] and cross-sectional population surveys [416] suggest that more than 85% of HT arises in individuals with BMI values above 25kg/m^2.

In INTERSALT, an International study of electrolytes and BP, BMI was used to evaluate association with BP, [417] since BMI is highly correlated with weight or body fat while being independent of height [418] and was found to relate independently to BP. [419] Results from some studies on BP also suggest that BMI and other weight for height indices have stronger association with BP than does either weight alone or skinfold measurements. [420,421] Also in another study, when weight, directly adjusted for height was analyzed, it continued to be strongly related to systolic and diastolic pressures as was BMI. [419] The difference in systolic pressure associated with a 10 kg difference in weight was about 3.0 mm Hg. For DBP the difference in BP associated with a 10 kg difference in weight varied from 2.0 mmHg in women aged 40-59 years to 2.7 mm Hg in men aged 20-39 years. [419] All the three measure of anthropometry i.e. BMI, WC, HC showed positive correlation with DBP while HC showed positive correlation with systolic as well as DBP. [423] Rabkin *et al* [424] also showed agreement with the above reports on the correlation of BP and the measures of anthropometry.

Although different population studies have suggested HT to be directly attributed to obesity, the precise mechanism is not fully understood. Contemporary thinking concerning the link between obesity and subsequent renal failure has evolved from repeated observations of the relationship between body weight and BP. It is well documented that BP increases with weight gain and decreases with weight loss. In addition, there is increasing evidence that obesity may provide the impetus for sympathetic nervous system activation as well as for changes in renal structure and function. There is considerable evidence that renal dysfunction, characterized by increased tubular Na reabsorption and resetting of pressure natriuresis plays a key role in increasing BP in obese subjects. The increased tubular pressure reabsorbtion is closely related to the sympathetic nervous and renal angiotensin systems as are

structural changes that cause compression of the renal medulla. Renal vasodilation, glomerular hyperfilteration and increased arterial pressure are compensations that help overcome increased renal tabular reabsorbtion and maintain sodium balance in obesity. This also leads to increased glomerular capillary wall stress, which along with activation of the neurohumoral systems, increased lipids, and glucose intolerance, eventually causes glomerulosclerosis and loss of nephron function in obese subjects. [425]

The increase in BP with excess weight gain arises partly because of the release from adipocytes of angiotensinogen (a precursor of angiotensin that has well known effects on BP), an increase in blood volume associated with the greater body mass and in response to a rise in blood viscosity. The change in blood viscosity is induced by the release of profibrinogen and plasminogen activator inhibitor-1 from adipocytes with a fall in plasminogen activator. [426]

Diets conducive to weight gain independently amplify BP. Dietary fats, especially SFs; induce a rise in SBP and DBP as well as hypercholesterolemia, as shown in the Dietary Approaches to Stop HT (DASH) trials. [219] Energy dense diets rich in fats and refined sugars promote weight gain [427] and high sugar intakes also induces increases in BP of 6.9mm Hg (systolic) and 5.3 mmHg (diastolic). [428] Energy density is reduced by higher intake of fruit and veg, which the DASH trial also showed lowered BP.

4. **Obesity and Dyslipidaemia**:

Obesity has a strong effect on lipid metabolism, regardless of ethnic group. Dyslipidaemia progressively develops as BMI increases from 21 kg/m^2 with a rise in proatheromatous, dense small particle sized LDL. Increased weight is a determinant of higher level of TGs, elevated LDL-C and low HDL-C. [429] This change increases the risk of CHD by 3-6 times.

Hoffman *et al* [398] have reported a positive correlation of TC and TG with BMI. The association between obesity and LDL-C is more complex. LDL-C increases with BMI in men, but such increases are not as pronounced in women, the elderly and some ethnic groups. Increasing body mass is associated with small atherogenic LDL. Furthermore, central obesity in women is associated with elevated LDL-C conc. [425]

A negative correlation exists between HDL-C and BMI. [430] In the Framingham study [431] a clear correlation between BMI and lower HDL-C was shown with 25% men and 7% women with BMI > 30 having HDL-C < 35 mg/dl. A meta-analysis examining the effect of weight loss on HDL-C levels demonstrated that the levels increased by 0.35 mg/dl per kg of weight reduction in subjects who achieved a stabilized, reduced weight but increased by 0.27 mg/dl in subjects during active weight loss. [158] In subjects who maintained a stable diet for six weeks after weight loss, HDL-C levels, LPL levels and LCAT activity increased, these increases may contribute to enhanced cholesterol esterification and reverse cholesterol transport. [432]

Rabkin *et al* [426] in his study, has also observed a significant negative correlation between BMI and HDL-C in men and women aged 18-74 years. In another meta-analysis of 70 studies, the effect of weight loss on dieting showed a consistent linear association between weight loss and HDL-C, with an HDL-C increase of 2 mg/dl and LDL-C decrease of 4 mg/dl for every 4.5 kg weight loss maintained. [158]

Left ventricular hypertrophy occurs in 70% of women with both obesity and HT and around 14% of cases of heart failure in women (11% in men) are attributable to obesity. [433] The effect of obesity on heart function is probably due to a combination of factors including HT, dyslipidemia, DM, increased fatness and left ventricular mass, endothelial dysfunction and atherosclerosis. Extensive Cochrane analysis [434] suggest that a weight loss of 10 kg will induce a reduction in TC concentration of about 0.25 mmol/L. These epidemiological inferences are paralleled by intervention studies, which have shown that weight loss improves the lipid profile as well as HT.

5. Management of Obese Patient:

Various measures are used to grossly estimate the degree of obesity in large scale epidemioiological setting, including body weight, BMI, WC and the waist-to-hip ratio. It is essential that valid and reliable measures of dietary intake be used in studies aimed at determining the links between dietary intake and obesity. Another factor to consider is diet composition. The recommendations for dietary intake for the prevention of CVD may require modification.

Obesity is the normal physiological response to an environment in which energy intake exceeds energy output. It is an adaptive mechanism. Major environmental changes that support this adaptive mechanism are the greater

availability of foods and the increase in sedentary lifestyle. Also obesity can develop when an imbalance exists between energy intake and energy expenditure. In the context of a 3000- calorie diet, typical energy expenditure can be anywhere from 450 to 1500 calories. There is little evidence that "defective" energy expenditure exists. Efforts to increase energy expenditure by increasing physical activity are considered an important treatment for obesity. Diet and exercise strategies provide relatively equal amount of weight loss in premenopausal and postmenopausal women. In men, this combination is also a very effective means of achieving weight loss.

a) **Physical inactivity**:

Many studies have shown the relation between sedentary lifestyle and weight gain, but reliable direct measures of physical activity are only just emerging. [435] Nevertheless, the secular decline in physical activity is obvious. Morris and colleagues showed more than 50 years ago [436] that vigorous exercise was crucial to cardiovascular health, but highly sedentary adults now derive benefit from even slight exertion. [437] Exercise has many benefits, from psychosocial to physical, independent of its contribution to weight stability. A report by the US Surgeon General on physical activity and health highlighted the significant health benefits which are associated with regular physical activity. [438] They include:

1) lowered all cause mortality
2) decreased risk of CVD mortality
3) prevention or delayed development of HT
4) reduced BP in those with HT
5) decreased risk of colon cancer
6) decreased risk of developing non-insulin dependent diabetes; and
7) relief from symptoms of depression and anxiety.

Regular aerobic exercise increases the HDL-C level by 3 to 9% in healthy sedentary persons [439] by stimulating the production of pre-β HDL-C and reverse cholesterol transport. [440] There is a dose response relationship between aerobic exercise (running) and HDL-C levels in middle aged men with a HDL-C increase of 0.2 mg/dl and LDL-C reduction of 0.1 mg/dl for every kilometre run per week. [441] Also regular exercise yields greater increases in HDL in men with low HDL-C levels, elevated TG levels and abdominal obesity than in those with isolated low HDL-C levels. [442] Moderate exercise is also associated with reduction in TC, LDL-C and TG levels. [443]

However, the recent emphasis on weight maintenance has highlighted the importance of total energy output - 60-90 minutes per day of walking, [444] 10,000 steps monitored on a pedometer, or 15,000 steps in individuals attempting to maintain weight loss. Physical activity is helpful in weight loss, and essential for

limiting the progressive decline in lean tissues with age, but its main importance in body weight is in maintaining rather than increasing a 5-10% weight loss. In addition to the benefits of a lower weight, physically active obese subjects are at a lower risk of all cause and cardiovascular mortality compared to the sedentary obese independent of changes in weight.

b) Dietary Management:

National studies of BMI of different groups [445] show that intake is now the dominant determinant with lower physical activity following, rather than preceding, weight gain in some cases. [446] Thus a decline in activity was probably a particular feature of the 1960s and 1980s, but the transformation of our food habits, industry competition is now the main amplifier of the epidemic. [447]

Dietary quality is important; [448] about 20% proteins restrict the recognized inevitable loss of about 25% lean tissue that accompanies fat loss and helps in satiety. Dietary benefits are amplified by daily intake of 400-600 gm vegetable and fruits, with less than 20% fat; adequate n-3 fatty acids but the lowest possible amount of SFAs, less than 5% sugar and fiber-rich carbohydrates; such diets also have lower energy density and greater bulk, which further improves satiety. Explicit guidance on transferring to a low energy-density diet can double the quantity of food eaten and still achieve the energy deficits needed.

Lately, very strict diets such as the low-carbohydrate Atkins diet have become popular. They have been shown to have good effects on blood lipid concentration, BP and glucose control. These effects are, however generally short lived and not superior to standard approaches over the longer term. [449] The degree of weight loss strongly depends on the ability of patient to adhere to their diets, [450] and the more restricted the regimen the greater the demand for intense discipline in the face of an intense physiological desire to eat.

The increasing epidemic of obesity in the world has stimulated interest in identifying or predicting individuals who are at greatest health risk at an early age. [451] This is particularly important to allow early implementation of preventive strategies. The scientific community has not yet reached consensus on viable ways to approach the problems associated with obesity. However, several lines of attack are being investigated. Because of the complexity of the obesity problem, a multifactorial approach will undoubtedly be required.

AIMS & OBJECTIVES

AIMS & OBJECTIVES:

1) To study the effect of Age and Sex on BP, Serum lipids and Anthropometric Indices in normal healthy individuals.

2) To explore the effect of Age and Sex on BP, Serum Lipids and Anthropometric Indices in hypertensive patients.

3) To evaluate the Levels of Serum Lipids and Anthropometric Indices with regard to levels of Hypertension

4) To examine the effect of Diet on BP, Serum Lipids and Anthropometric Indices.

5) To analyze the effect of Tobacco Consumption on BP, Serum Lipids and Anthropometric Indices.

6) To scrutinize the effect of Heredity on BP, Serum Lipids and Anthropometric Indices.

METHODOLOGY

❖ Study Population:

The present study was conducted at Department of Biochemistry, M.P Shah Medical College, Jamnagar, Gujarat. The study population included subjects from Jamnagar with varied lifestyle based on their occupation. A total of 1146 person (593 women and 553 men) participated in the study. Individuals' ≥ 30 years of age were included in the study. Random subjects free of not only HT but any disease and also who were not on any particular medication were included in the study as controls. The control group consisted of 400 healthy people (217 women and 183 men) between the age group of 30 to 80 years.

In the patient group, first time detected untreated hypertensive subjects of 30-80 years of age and a total of 746 (376 women and 370 men) individuals were enrolled. HT was considered to be present if the SBP ≥ 140 mm Hg or the DBP ≥ 90 mm Hg [2]

Control and patient volunteers were interviewed according to a specifically designed questionnaire and were thereby noted in the record forms itself which is illustrated on the next page.

❖ Methods:

• Blood Pressure Measurement:

The BP was measured by a doctor using a mercury column sphygmomanometer by a standardized protocol in the sitting posture, with feet on the floor and arm supported at heart level. Following the standardized technique, the doctor made two separate measurements after making the patient take proper rest. In some cases, where high BP was recorded for the first time, the physicians checked the BP more than twice and took the average of the two close readings.

QUESTIONNAIRE

Name of the Patient:-

Address:-

Age: - Sex:-

Occupation:-

Family Income:-

Members of the family:
0-5 yrs _____ 5-10 yrs _____ > 10 yrs_____

BP: - Systolic: _____ mm Hg Diastolic: _____ mm Hg

Weight: _____ (kg) Height: _____ (m) BMI _____kg/m^2
Waist: _____ (cm) Hip: _____ (cm) WHR _____

Whether diagnosed for any disease? If yes state:

Family History:-

DM	HT	Heart attack	Paralysis

Tobacco Consumption: - Y/N

Smoking – No of Cigarettes/ Bidi per day:
Chewing – Tobacco/ Gutkha per day:
Pan with Tobacco per day:

Dietary Intake:

Cereals	Pulses	Sugar/Gur	Oil/Ghee	Milk	Veg/Pot	Fruits	Non Veg.

Physical activity: Sedentary / Mild / Moderate / Severe

- **Anthropometric Measurements:**

The height was measured barefoot with head in horizontal plane to the nearest 0.1 cm using a graduated tape attached to the wall. The weight was measured in light clothes using a weighing machine. BMI (weight in kg/ height in m^2) was calculated. The waist and hip circumference was measured to the nearest 0.5 cm in the subjects standing barefoot and wearing light clothes. The waist circumference was measured at the level of the umbilicus and the hip at the level of the greater trochanter using a non-stretchable measuring tape. WHR was calculated from the above data.

- **Nutritional Assessment:**

The amount of an individuals daily food intake in relation to the cereals, pulses, sugars, oil, milk, vegetable, fruits, non veg, etc. were noted in the questionnaire. Through this information, an individual's daily calorie and fat intake were calculated using the "Nutritive value of Indian foods" given by the Indian Council of Medical Research. [452]

- **Collection of Samples:**

5 ml of venous blood was withdrawn after an overnight fast of 12 hrs and was allowed to clot for 25-30 minutes for proper serum extraction after centrifuging for 5 minutes. This serum was used to estimate the parameters within two hour of sample collection.

- **Biochemical Markers:**

The following biochemical markers were determined: 1) TC 2) TG 3) HDL-C using "Accucare" manual kit.

1. Total Cholesterol (TC): *Allain* et al [453]

Principle: Cholesterol esterase hydrolyses cholesterol esters into free cholesterol and fatty acids. In the second reaction cholesterol oxidase converts cholesterol to cholest-4-en-3-one and hydrogen peroxide. In presence of peroxidase, hydrogen peroxide oxidatively couples with 4-aminoantipyrine and phenol to produce red quinoneimine dye which has absorbance maximum at 510 nm. The intensity of the red colour is proportional to the amount of total cholesterol in the specimen.

2. Triglyceride (TG):

Principle: Glycerol released from hydrolysis of triglycerides by lipoprotein lipase is converted by glycerol kinase into glycerol-3-phosphate which is oxidized by glycerol phosphate oxidase to dihydroxyacetone phosphate and hydrogen peroxide. In presence of peroxidase, hydrogen peroxide oxidizes phenolic chromogen to a red coloured compound.

3. High Density Lipoprotein Cholesterol (HDL-C): *Burnstein et al* [454]

Principle: Phosphotungstate/Mg^{2+} precipitates chylomicrons, LDL and VLDL fractions. HDL fraction remains unaffected in supernatant. Cholesterol content of HDL fraction is assayed using the above stated principle of cholesterol.

LDL-C concentration was calculated using Friedwalds and Fredricksons formula [216] which assumed that VLDL-C is present in a concentration equal to 1/5 of the TG concentration. Thus

$$\text{LDL-C} = \text{TC} - \left(\frac{\text{TG}}{5} + \text{HDL-C} \right)$$

❖ Statistical Analysis:

Mean, standard deviation and standard error were calculated. Students ‘t’ test was applied. ‘p’ values were calculated to assess significance of the results.

RESULTS

1. Effect of Age on BP, Serum Lipids and Anthropometric indices in Normotensive subjects:

Systolic and diastolic blood pressures were 117.05/74.33 & 119.22/78.58 in normal healthy male individuals and 116.23/72.60 & 117.65/75.41 in normal healthy female individuals in the age groups 30-50 and 51-80 years respectively. The BP increased with age in both sexes and this rise was extremely significant in DBP ($P<0.001$) while SBP showed a minor significance ($P<0.05$). Moreover in all age groups females were having lower SBP and DBP than those of males of corresponding age groups. The difference in SBP between the gender in the age group 51-80 was found to be highly significant ($P<0.01$) whereas DBP exhibited massive significance ($P<0.001$) in both the age groups.

Total Cholesterol concentrations were 176.0 & 186.5 mg/dl for males and 171.8 & 179.4 mg/dl for females in respective age groups. In male and female subjects, TC increased with age and this increase was tremendously significant ($P<0.001$). Both the age groups 30-50 and 51-80 years showed a difference in TC concentration between the genders and this difference was greatly significant ($P<0.01$).

The genderwise triglyceride concentrations in the aforesaid two age groups were 116.5 & 125.1 mg/dl for males and 93.9 & 97.6 mg/dl for females respectively. Even though an increase in TG concentration was seen with age, this rise remained insignificant in both the genders. The TG concentration of females in both the age groups were significantly ($P<0.001$) lower than those of the males in the respective age groups.

HDL-C concentration was 46.5 & 50.0 mg/dl for females whereas males illustrated a similar concentration in both the age groups (41.6 mg/dl). Thus an increase with age in the females were observed which was immensely significant ($P<0.01$). Moreover in both the age groups females were having higher HDL-C concentration than those of males of corresponding age groups and this difference was particularly significant ($P<0.001$).

LDL-C concentrations demonstrated an increase with age in both the gender with mean value being 111.2 &119.8 mg/dl in males and 106.5 &109.9 in females respectively. In males this increase was found to be very

significant (P<0.01). In each age group the difference according to gender in LDL-C concentration was also somewhat significant (P<0.05).

Table 3: Effect of Age on BP, Serum Lipids, BMI and WHR in Normotensive cases

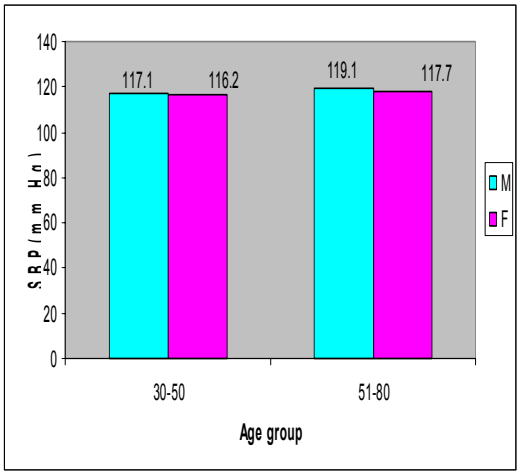
Age Group	G	N	SBP mmHg	DBP mmHg	TC mg/dl	TG mg/dl	HDL-C mg/dl	LDL-C mg/dl	VLDL-C mg/dl	TC/HDL-C	LDL-C/HDL-C	BMI	WHR
30-50 (A)	M	110	117.05 ±0.71	74.33 ±0.46	176.0 ±1.6	116.5 ±3.8	41.6 ±0.97	111.2 ±2.0	23.31 ±0.75	4.5 ±0.12	2.9 ±0.1	25.07 ±0.33	0.93 ±0.008
	F	163	116.23 ±0.71	72.66 ±0.3	171.8 ±1.5	93.9 ±2.8	46.5 ±0.83	106.5 ±1.6	18.7 ±0.57	3.88 ±0.07	2.45 ±0.06	25.39 ±0.32	0.82 ±0.005
51-80 (B)	M	73	119.12 ±0.49	78.58 ±0.84	186.5 ±2.7	125.1 ±6.3	41.6 ±1.4	119.8 ±2.8	25.0 ±1.3	4.86 ±0.2	3.18 ±0.15	24.19 ±0.63	0.95 ±0.007
	F	54	117.65 ±0.65	75.41 ±0.46	179.4 ±1.8	97.6 ±8.0	50.0 ±1.5	109.9 ±2.8	19.5 ±1.6	3.77 ±0.13	2.35 ±0.12	24.54 ±0.4	0.83 ±0.007

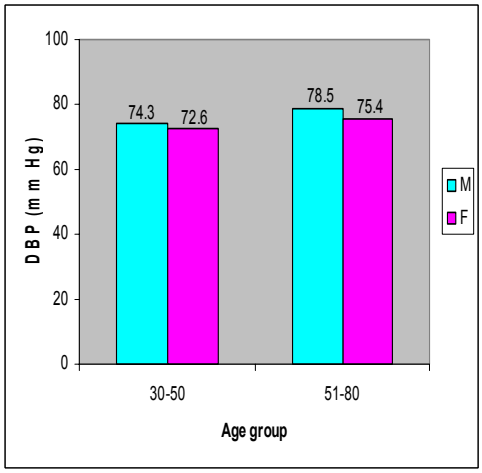
Values are Mean ± S.E. M = Male ; F = Female ; N = Number of population

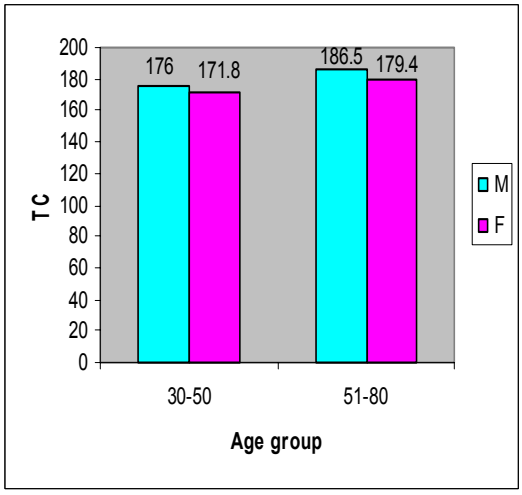
Table 3a: Statistical Analysis of Table 3

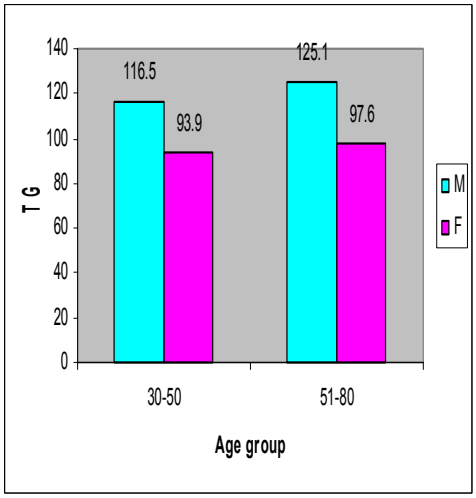
COMPARISON	SBP mmHg	DBP mmHg	TC mg/dl	TG mg/dl	HDL-C mg/dl	LDL-C mg/dl	VLDL-C mg/dl	TC/HDL-C	LDL-C/HDL-C	BMI	WHR
AM vs AF	NS	P < 0.001	P < 0.01	P < 0.001	P < 0.001	P < 0.05	P < 0.001	P < 0.001	P < 0.001	NS	P < 0.001
BM vs BF	P < 0.01	P < 0.001	P < 0.01	P < 0.001	P < 0.001	P < 0.01	P < 0.001	P < 0.001	P < 0.001	NS	P < 0.001
AM vs BM	P < 0.01	P < 0.001	P ≤ 0.001	NS	NS	P < 0.01	NS	P < 0.05	P < 0.05	NS	P < 0.05
AF vs BF	P < 0.05	P < 0.001	P < 0.001	NS	P < 0.01	NS	NS	NS	NS	P < 0.05	P < 0.05

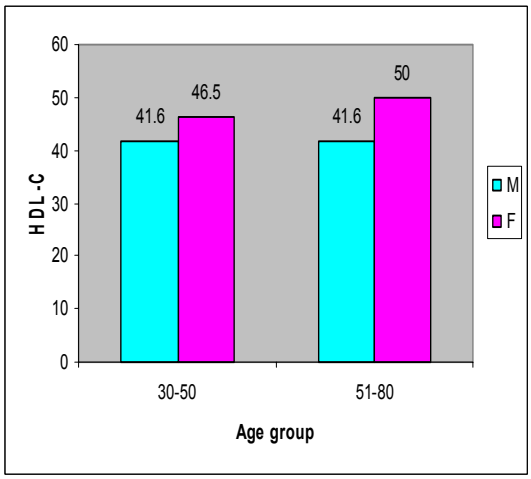
Graph 1: Effect of age on BP, Serum Lipids and Anthropometric Indices in Normotensive cases:

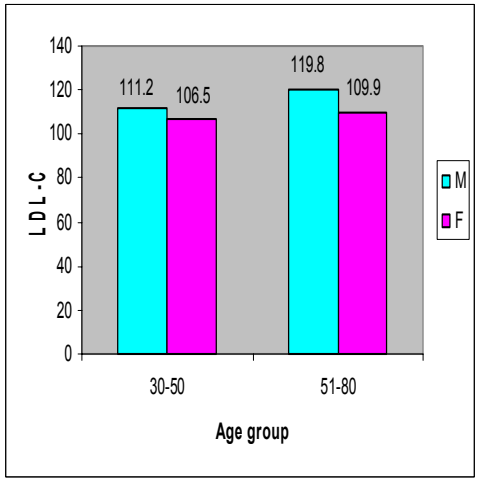


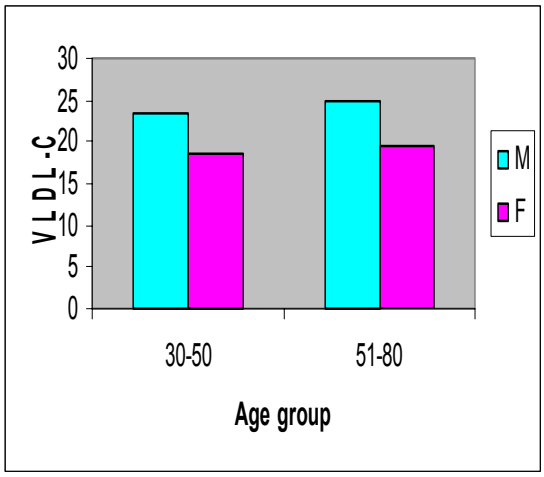


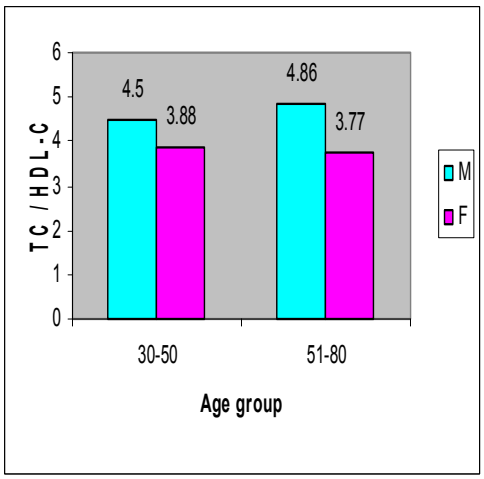


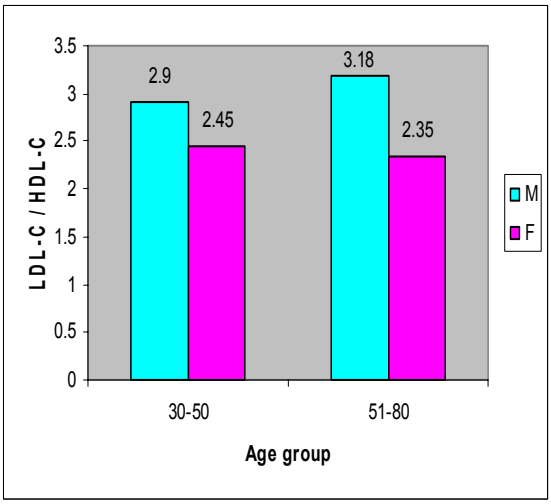


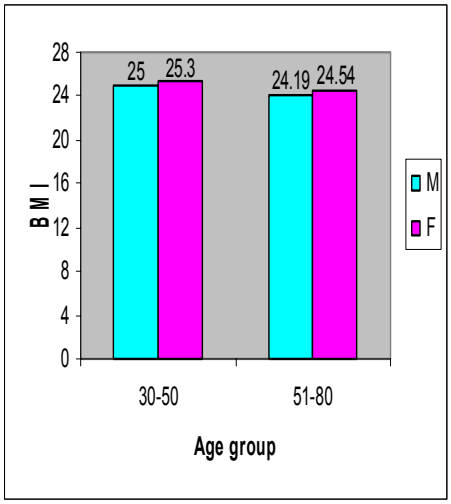


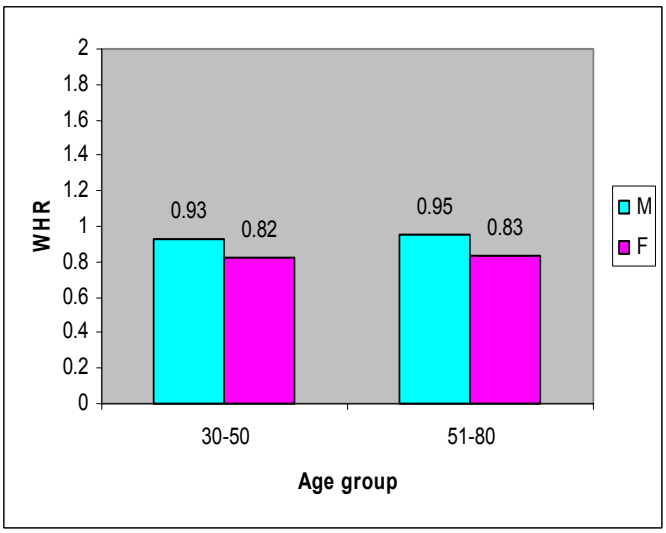



VLDL-C
30
25
20
15
10
5
0
30-50
51-80
Age group
M
F


TC / HDL-C
6
5
4
3
2
1
0
4.5
3.88
4.86
3.77
30-50
51-80
Age group
M
F


LDL-C / HDL-C
3.5
3
2.5
2
1.5
1
0.5
0
2.9
2.45
3.18
2.35
30-50
51-80
Age group
M
F


BMI
28
24
20
16
12
8
4
0
25
25.3
24.19
24.54
30-50
51-80
Age group
M
F


WHR
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
0.93
0.82
0.95
0.83
30-50
51-80
Age group
M
F

VLDL-C concentration exhibited an increase with advancement of age but with no significance in either of the gender, whereas the difference in the VLDL-C concentration according to gender in each age group was found to be enormously significant (P<0.001).

The atherogenic ratios TC/HDL-C & LDL-C/HDL-C demonstrated a similar trend of increase with age in only males with a significance of P<0.05, while the difference according to gender was found to be exceedingly significant (P<0.001) in both the corresponding age groups. Genderwise the mean values of TC/HDL-C & LDL-C/HDL-C were 4.5, 4.86, 2.9 & 3.18 in males and 3.88, 3.77, 2.45 & 2.35 in females respectively.

Among anthropometric indices the values of BMI were 25.07 & 24.19 in males and 25.39 & 24.54 in females respectively. As can be observed a decrease with age is obvious but vague significance was seen in females only (P<0.05). Also the difference between the genders in each group was not found to be significant. WHR exhibited values like 0.93 & 0.95 in males and 0.82 & 0.83 in females. Here increase with age was observed and this rise was found to be slightly significant (P<0.05). Also the difference according to gender in WHR was seen to be extremely significant (P<0.001) in each of the age groups.

2. Effect of Age on BP, Serum Lipids and Anthropometric indices in Hypertensive subjects:

In hypertensives, the SBP & DBP showed a specific pattern as observed for normal healthy individuals (Table 3). The SBPs & DBPs in hypertensive patients were 144.2/91.67 & 151.96/94.1 mmHg for males and 142.22/89.93 & 149.36/92 mmHg for females in the age groups 30-50 and 51-80 years in both genders respectively. In each age group female patients showed remarkably significant (P<0.001) lower BP values than the corresponding values of male hypertensive subjects. Also an increase with age was observed in both the genders and this rise was found to be incredibly significant (P<0.001). Moreover the BP values of the hypertensive subjects of both genders in both the age groups were much higher than those seen in control groups and were enormously significant (P<0.001).

Total cholesterol values for male hypertensives subjects were 236.7 & 245.6 mg/dl whereas for female hypertensive subjects the values were 230.7 & 238.2 mg/dl for the age groups 30-50 & 51-80 years respectively. Serum cholesterol concentration of male hypertensives was higher than those of female hypertensive in all age groups and this increase was outstandingly significant ($P<0.001$). Also the TC conc increased agewise in both sexes which were found to be exceedingly significant too ($P<0.001$). Moreover in both sexes, TC when compared with control group showed exceptionally significant difference ($P<0.001$), as hypertensives had higher cholesterol concentration in both the age groups.

A pattern analogous to the control group was seen in hypertensive patients also when TG conc were observed. TG conc values were 192.6 & 207.4 for males and 160.3 & 170.9 for females respectively. There seemed to be a greatly significant ($P<0.01$) increase with age in both the genders and also the difference between the genders in both the age groups were incredibly significant ($P<0.001$). Male and female hypertensive volunteers in the age groups 30-50 & 51-80 years had higher TG conc than their normal counterparts in the respective age groups as shown in Table 3. This difference was tremendously significant ($P<0.001$).

The two age groups 30-50 & 51-80 years showed HDL-C conc 38.75 & 39.48 mg/dl for males and 42.7 & 44.1 mg/dl for female hypertensive subjects respectively. All male hypertensive subjects had less HDL-C concentration than those of female hypertensive subjects and this difference in HDL-C concentration between two genders were exceedingly significant ($P<0.001$). Even though HDL-C concentration increased agewise in both genders, the trend was insignificant. The hypertensive patients of both genders had much lower HDL-C concentration than those of healthy individuals in both genders and their age groups. This decrease was found to be enormously significant ($P<0.001$).

LDL-C concentration in both male and female hypertensive subjects demonstrated an increase with age but among them only males exhibited any significance ($P<0.01$). In each age group females were having lower LDL-C than their male counterparts but the difference between the two genders were insignificant. Male and female hypertensive volunteers were also having higher LDL-C concentration than those found in normal healthy individuals in each age groups and their difference was incredibly significant ($P<0.001$).

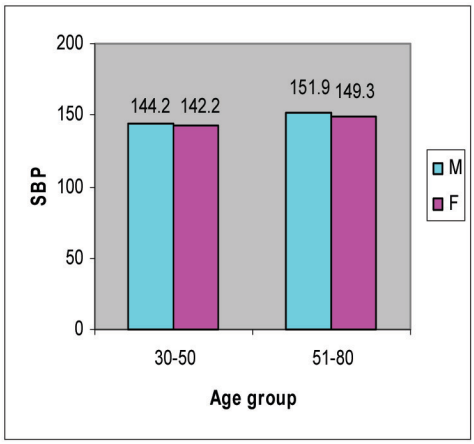
Table 4: Effect of Age on BP, Serum Lipids, BMI and WHR in Htsive cases													
Age Group	G	N	SBP mmHg	DBP mmHg	TC mg/dl	TG mg/dl	HDL-C mg/dl	LDL-C mg/dl	VLDL-C mg/dl	TC/HDL-C	LDL-C/HDL-C	BMI	WHR
30-50 (C)	M	153	144.22 ±0.34	91.67 ±0.48	236.7 ±1.3	192.6 ±2.9	38.75 ±0.79	159.4 ±1.5	38.52 ±0.59	6.46 ±0.13	4.4 ±0.1	28.05 ±0.17	0.98 ±0.007
	F	152	142.22 ±0.4	89.93 ±0.55	230.7 ±1.1	160.3 ±3.1	42.7 ±0.93	156 ±1.3	32.06 ±0.63	5.74 ±0.11	3.93 ±0.09	29.43 ±0.21	0.85 ±0.005
51-80 (D)	M	217	151.96 ±0.24	94.1 ±0.42	245.6 ±2.0	207.4 ±3.9	39.48 ±0.61	164.6 ±1.9	41.5 ±0.77	6.5 ±0.1	4.39 ±0.08	26.32 ±0.16	0.98 ±0.005
	F	224	149.36 ±0.41	92.0 ±0.3	238.2 ±2.0	170.9 ±3.5	44.1 ±0.71	159.8 ±3.3	34.2 ±0.7	5.72 ±0.12	3.89 ±0.12	28.18 ±0.29	0.86 ±0.004

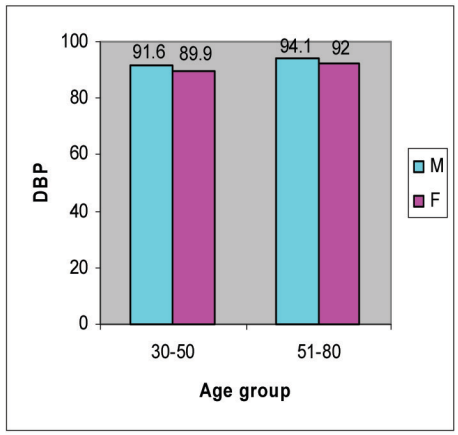
Values are Mean ± S.E.

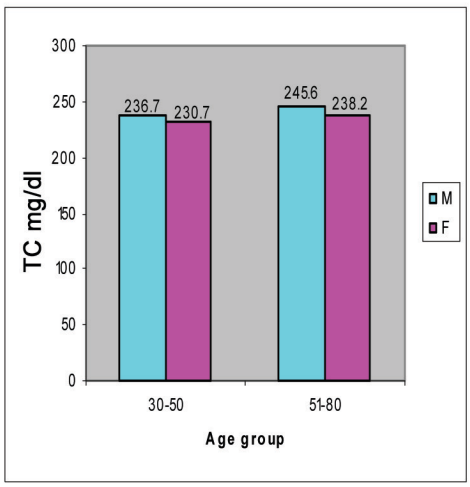
Table 4a: Statistical Analysis of Table 4											
COMPARISON	SBP mmHg	DBP mmHg	TC mg/dl	TG mg/dl	HDL-C mg/dl	LDL-C mg/dl	VLDL-C mg/dl	TC/HDL-C	LDL-C/HDL-C	BMI	WHR
CM vs CF	P < 0.001	P < 0.01	P < 0.001	P < 0.001	P < 0.001	P < 0.05	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001
DM vs DF	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001	NS	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001
CM vs DM	P ≤ 0.001	P ≤ 0.001	P ≤ 0.001	P ≤ 0.001	NS	P ≤ 0.01	P ≤ 0.001	NS	NS	P ≤ 0.001	NS
CF vs DF	P ≤ 0.001	P ≤ 0.001	P ≤ 0.001	P < 0.01	NS	NS	P < 0.01	NS	NS	P ≤ 0.001	NS

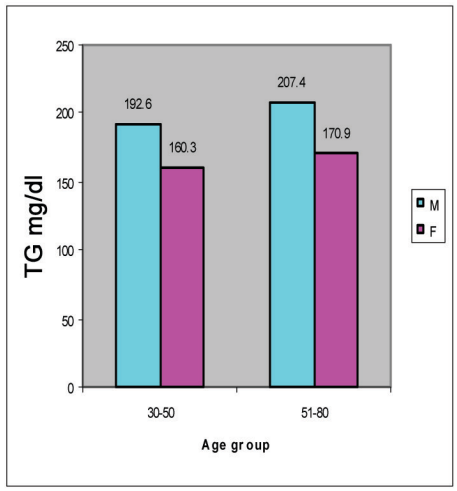
VLDL-C concentration of hypertensive subjects in both genders were in the same lines as hose of TGs. In both the genders, VLDL-C increased with the advancement of age and this rise was highly significant (P<0.01). Females in both age groups showed lower VLDL-C than their male counterparts and this difference was exceedingly significant (P<0.001). VLDL-C of hypertensives in both sexes was higher as compared to the healthy individuals of both gender and it was remarkably significant (P<0.001).

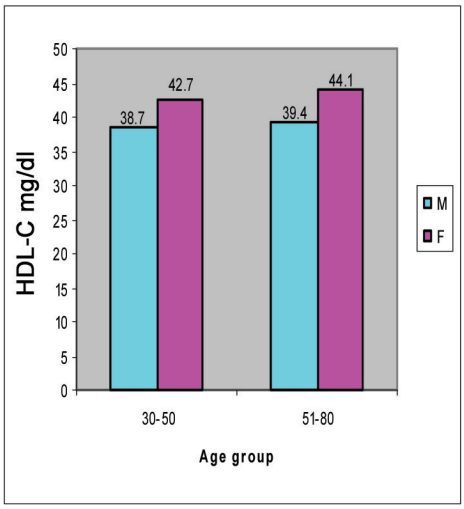
Graph 2: Effect of age on BP, Serum Lipids and Anthropometric Indices in Hypertensive cases:

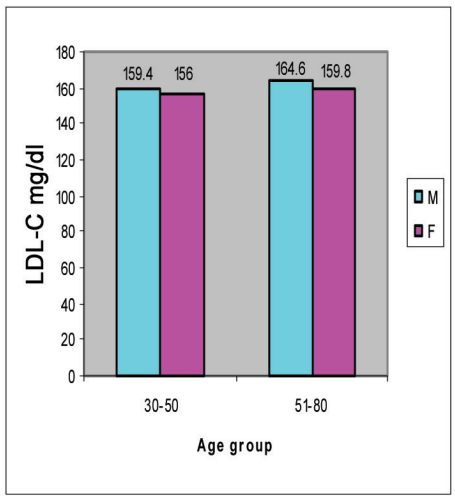


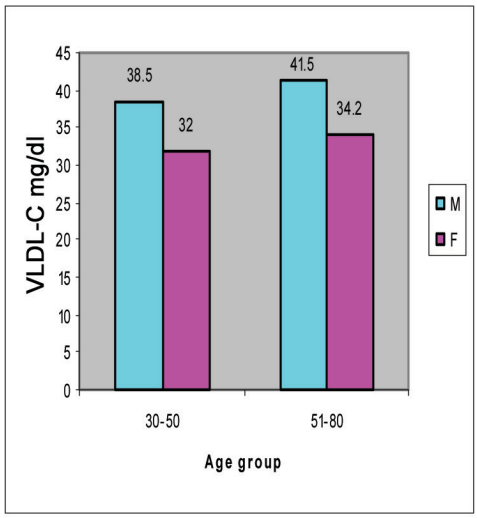


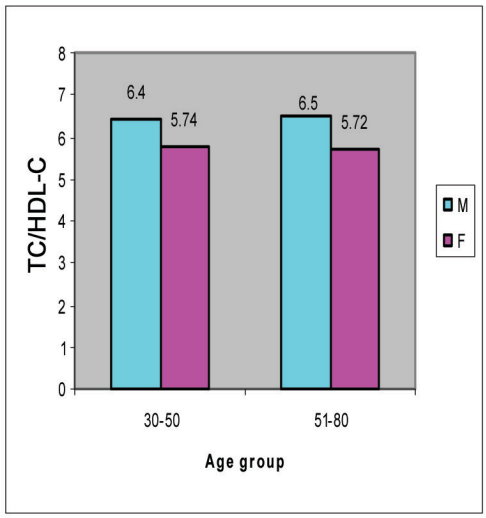


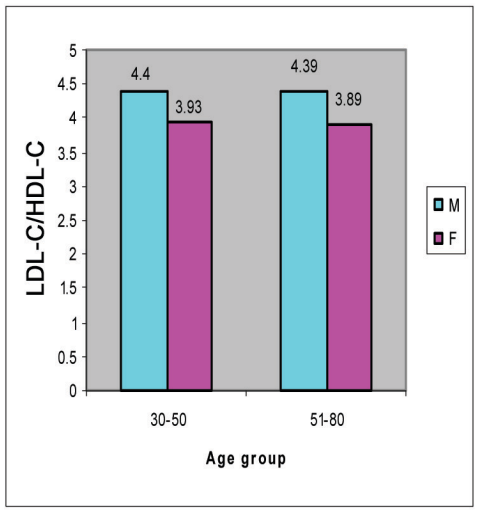







VLDL-C mg/dl
45
40
35
30
25
20
15
10
5
0
38.5
32
41.5
34.2
30-50
51-80
Age group
M
F


TC/HDL-C
8
7
6
5
4
3
2
1
0
6.4
5.74
6.5
5.72
30-50
51-80
Age group
M
F


LDL-C/HDL-C
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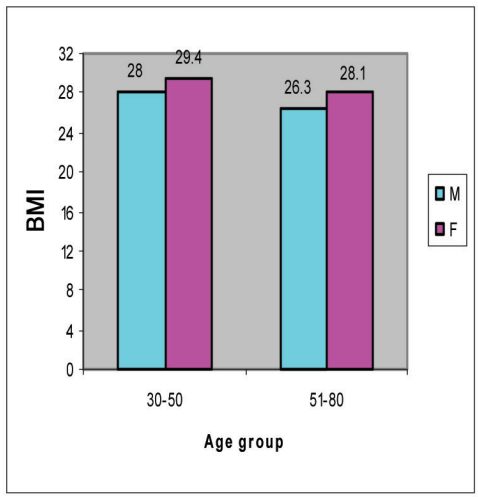
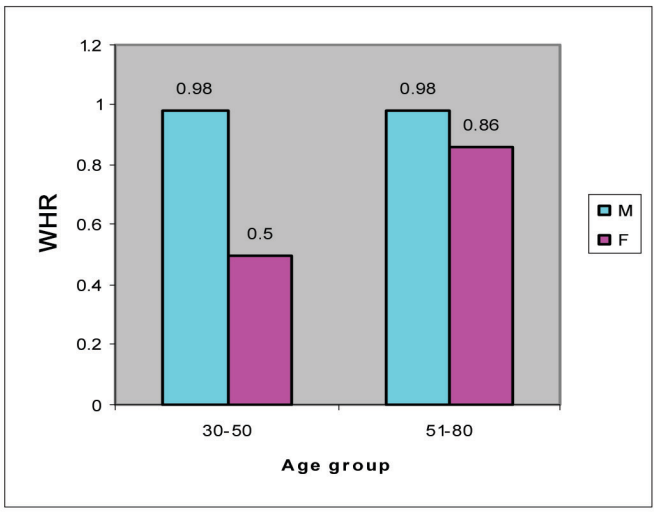
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
4.4
3.93
4.39
3.89
30-50
51-80
Age group
M
F


BMI
32
28
24
20
16
12
8
4
0
28
29.4
26.3
28.1
30-50
51-80
Age group
M
F


WHR
1.2
1
0.8
0.6
0.4
0.2
0
0.98
0.5
0.98
0.86
30-50
51-80
Age group
M
F

The atherogenic ratio TC/HDL-C in hypertensives was above 4.5 and it was considered as a potent risk factor for CHD and atherosclerosis. In both genders TC/HDL-C values did not differ much with advancement of age and thus remained insignificant while the difference between genders in both age groups was outstandingly significant ($P<0.001$). All normal healthy individuals of both genders had TC/HDL-C values less than 4.5 and these differences in genders for both age groups were exceptionally significant ($P<0.001$).

LDL-C/HDL-C ratio of hypertensives in both the genders showed a similar trend just like TC/HDL-C wherein no significance was observed with advancement of age while females displayed lower values than males and this difference observed in each age group was tremendously significant ($P<0.001$). Unlike healthy individuals these hypertensive patients had the ratio greater than 3.0 which is also an important risk factor.

Among the anthropometric indices BMI showed values greater than 25kg/m^2 in both genders of the two age groups in hypertensive patients. An extremely significant ($P<0.001$) decrease with age was identified in both the genders while the female hypertensives demonstrated a higher BMI than the males of the corresponding age group. This difference between the genders was also exceedingly significant ($P<0.001$). Also the difference observed between hypertensive and normotensive subjects was enormously significant ($P<0.001$).

WHR also an anthropometric index did not show any significance with advancement of age in both the genders and female hypertensive subjects exhibited a lower ratio than males of corresponding age groups. This difference between the genders was remarkably significant ($P<0.001$). Apart from this the values of WHR of hypertensive patients were much higher than those observed in normotensive individuals and this rise was tremendously significant ($P<0.001$).

3. Levels of Serum Lipids and Anthropometric indices with regard to Levels of HT:

Hypertensive volunteers were regrouped according to the levels of hypertension into three subgroups viz prehypertension (80-89 mmHg), Stage-I (90-99 mm Hg) and Stage-II (≥ 100 mmHg) based on the two age groups as referred in the above instances (30-50 & 51-80 years) to study the effect of HT on serum lipids and anthropometric indices. As DBP in hypertensive subjects increased from prehypertension (80-89 mmHg) to Stage-II HT (≥ 100 mmHg), the SBP also increased from 132.49 to 164.4 mmHg in males and from 130.89 to 162.3 mmHg in females respectively. DBP and SBP in females were lower than those of males of corresponding hypertensive groups. But these differences

according to the gender were insignificant except in the DBP of Stage-I and Stage-II hypertensive subjects.

TC conc also increased with increase in DBP in hypertensive subjects. The TC conc in PreHT, Stage-I and Stage-II levels of 30-50 age group were 240.6, 245.5 & 249.2 mg/dl and of 51-80 age group the values were 249.9, 250.4 & 251.2 mg/dl. Thus increase with age in TC was observed in the corresponding hypertensive groups but it remained insignificant except in the PreHT level. In females also TC concentration increased from 230.5 mg/dl in preHT level to 237.7 mg/dl in stage-II hypertensive group of 30-50 age group and in 51-80 age group it increased from 238.4 in preHT to 241.9 in stage-II HT group. Here also increase in TC concentration with the increase in DBP was outstandingly significant ($P<0.001$) in only preHT & control group in both the genders. In each levels of HT female TC concentration was less than that in male HT volunteers and this difference was vastly significant ($P<0.01$).

The TG concentration in preHT, Stage-I and Stage-II HT increased but insignificantly with increase in BPs in both sexes. TG concentration were 200.4, 172.1 & 208.1 in 30-50 years males while it was 213.5, 191.6 & 185.4 in 51-80 years males respectively. The same in females were 159.8, 161.4 & 154.1 in 30-50 age group and 177.9. 171.3 & 152.9 in 51-80 years age group. Thus an increase with age is observed but with no significance in both the genders. Also the female TG concentration was less than that in male HT volunteers and this difference were extremely significant ($P<0.001$). These conc were higher than those seen in normotensive males and females and the difference between control and preHT TG concentration is found to be incredibly significant ($P<0.001$).

HDL-C concentration were 41.6, 41.2, 39.07 & 37.1 in 30-50 years males and 41.6, 40.0, 37.0 & 40.4 in 51-80 years males while the same in females were 46.5, 49.2, 35.6 & 39.4 in 30-50 years and 50.0, 44.4, 38.6 & 41.6 in 51-80 years of the control group and the various levels of HT respectively. The decrease in HDL-C concentration from control group to stage-I and an increase in the concentration from stage-I to stage-II was a little significant in females ($P<0.05$) but in male hypertensives this variation in the levels was insignificant in 51-80 years when preHT to stage-I and stage-I to stage-II were compared. With advancement of age each level of HT showed a decrease in HDL-C concentration in male hypertensives whereas in females a significant increase ($P<0.05$) with age was observed. Also in each levels of HT female HDL-C concentration was more than that in male hypertensive subjects and this difference was somewhat significant ($P<0.05$) except in stage-II HT level. All male and female (except 30-50 years female of preHT group) hypertensive subjects had much lower HDL-C concentration in comparison to normotensive males and females as shown in Table 5.

Table 5: Levels of Serum Lipids, BMI and WHR with regard to Levels of HT

Levels of HT	Age Group	G	N	SBP mmHg	DBP mmHg	TC mg/dl	TG mg/dl	HDL-C mg/dl	LDL-C mg/dl	TC/HDL-C	LDL-C/HDL-C	BMI	WHR
Normal < 80	30-50 (A)	M	110	117.05 ±0.71	74.33 ±0.46	176.0 ±1.6	116.5 ±3.8	41.6 ±0.97	111.2 ±2.0	4.5 ±0.12	2.9 ±0.1	25.07 ±0.33	0.93 ±0.008
		F	163	116.23 ±0.71	72.66 ±0.3	171.8 ±1.5	93.9 ±2.8	46.5 ±0.83	106.5 ±1.6	3.88 ±0.07	2.45 ±0.06	25.39 ±0.32	0.82 ±0.005
	51-80 (B)	M	73	119.12 ±0.49	78.58 ±0.84	186.5 ±2.7	125.1 ±6.3	41.6 ±1.4	119.8 ±2.8	4.86 ±0.2	3.18 ±0.15	24.19 ±0.63	0.95 ±0.007
		F	54	117.65 ±0.65	75.41 ±0.46	179.4 ±1.8	97.6 ±8.0	50.0 ±1.5	109.9 ±2.8	3.77 ±0.13	2.35 ±0.12	24.54 ±0.4	0.83 ±0.007
Prehyper-tensive 80-89	30-50 (C_1)	M	68	132.49 ±1.1	83.78 ±0.38	240.6 ±3.9	200.4 ±8.9	41.21 ±1.0	159.3 ±3.9	6.03 ±0.16	4.01 ±0.14	27.39 ±0.53	0.96 ±0.011
		F	63	130.89 ±0.97	83.97 ±0.40	230.5 ±4.3	159.8 ±8.6	49.2 ±1.6	149.3 ±3.8	4.88 ±0.13	3.18 ±0.13	28.49 ±0.74	0.86 ±0.009
	51-80 (D_1)	M	113	135.97 ±0.78	87.60 ±0.14	249.9 ±3.6	213.5 ±8.5	40.07 ±0.71	167.1 ±3.5	6.41 ±0.13	4.29 ±0.11	26.10 ±0.35	0.98 ±0.007
		F	105	137.45 ±0.83	86.19 ±0.30	238.4 ±3.5	177.9 ±6.9	44.46 ±0.81	158.4 ±4.0	5.53 ±0.12	3.69 ±0.11	28.42 ±0.51	0.87 ±0.007
Stage - I 90-99	30-50 (C_2)	M	45	144.47 ±1.3	93.8 ±0.49	245.5 ±5.8	172.1 ±10	39.07 ±1.1	172 ±5.7	6.48 ±0.22	4.56 ±0.19	28.87 ±0.78	1.005 ±0.01
		F	60	142.4 ±1.3	93.38 ±0.45	233.0 ±3.0	161.4 ±11	35.6 ±1.2	165.3 ±3.6	6.96 ±0.23	4.92 ±0.19	29.52 ±0.71	0.83 ±0.007
	51-80 (D_2)	M	69	150 ±1.5	97.93 ±0.21	250.4 ±4.4	191.6 ±9.5	37.07 ±1	175.2 ±4.8	7.11 ±0.22	4.99 ±0.19	26.81 ±0.51	0.97 ±0.007
		F	76	149.3 ±1.5	95.89 ±0.4	238.1 ±3.5	171.3 ±7.3	38.6 ±1.5	165.2 ±4.0	6.86 ±0.27	4.87 ±0.24	28.26 ±0.65	0.85 ±0.007
Stage - II ≥ 100	30-50 (C_3)	M	38	162.4 ±1.9	105.4 ±0.92	249.2 ±3.6	208.6 ±14	37.11 ±1.0	170.4 ±4	6.87 ±0.18	4.73 ±0.17	29.76 ±0.53	1.0 ±0.01
		F	27	160.1 ±1.9	103.1 ±0.89	237.9 ±5.7	154.1 ±10	39.44 ±1.0	167.7 ±7.0	6.15 ±0.24	4.36 ±0.25	32.93 ±1.1	0.88 ±0.01
	51-80 (D_3)	M	34	164.4 ±1.8	108.9 ±1.2	251.2 ±4.8	185.4 ±7.1	40.41 ±1.5	173.7 ±4.3	6.44 ±0.23	4.48 ±0.2	25.74 ±0.78	0.98 ±0.01
		F	40	162.3 ±2.0	106.1 ±0.61	241.9 ±4.6	152.9 ±11	41.68 ±0.8	169.7 ±5.2	5.88 ±0.15	4.14 ±0.16	29.70 ±0.67	0.86 ±0.008

Values are Mean ± S.E.

Table 5a: Statistical Analysis of Table 5										
Comparison	SBP mmHg	DBP mmHg	TC mg/dl	TG mg/dl	HDL-C mg/dl	LDL-C mg/dl	TC/HDL-C	LDL-C/HDL-C	BMI kg/m^2	WHR
AM Vs AF	NS	P < 0.001	P < 0.01	P < 0.001	P < 0.001	P < 0.05	P < 0.001	P < 0.001	NS	P < 0.001
BM Vs BF	P < 0.01	P < 0.001	P < 0.01	P < 0.001	P < 0.001	P < 0.01	P < 0.001	P < 0.001	NS	P < 0.001
AM Vs BM	P < 0.01	P < 0.001	P ≤ 0.001	NS	NS	P < 0.01	P < 0.05	P < 0.05	NS	P < 0.05
AF Vs BF	P < 0.05	P < 0.001	P < 0.001	NS	P < 0.01	NS	NS	NS	P < 0.05	P < 0.05
C_1M Vs C_1F	NS	NS	P < 0.05	P < 0.001	P < 0.001	P < 0.05	P < 0.001	P < 0.001	NS	P < 0.001
D_1M Vs D_1F	NS	NS	P < 0.01	P < 0.001	P < 0.005	P < 0.05	P < 0.001	P < 0.005	P < 0.001	P < 0.001
C_1M Vs D_1M	P < 0.01	P < 0.001	P < 0.05	NS	NS	NS	P < 0.05	P < 0.05	P < 0.01	NS
C_1F Vs D_1F	P < 0.001	P < 0.001	NS	P < 0.05	P < 0.005	NS	P < 0.01	P < 0.005	NS	NS
C_2M Vs C_2F	NS	NS	P < 0.05	NS	P < 0.01	NS	NS	NS	NS	P < 0.001
D_2M Vs D_2F	NS	P < 0.001	P < 0.01	P < 0.05	NS	NS	NS	NS	P < 0.05	P < 0.001
C_2M Vs D_2M	P < 0.005	P < 0.001	NS	NS	NS	NS	P < 0.05	NS	P < 0.01	P < 0.05
C_2F Vs D_2F	P < 0.001	P < 0.005	NS	NS	NS	NS	NS	NS	NS	P < 0.05
C_3M Vs C_3F	NS	P < 0.05	P < 0.05	P < 0.001	NS	NS	P < 0.01	NS	P < 0.01	P < 0.001
D_3M Vs D_3F	NS	P < 0.01	NS	P < 0.01	NS	NS	P < 0.01	NS	P < 0.001	P < 0.005
C_3M Vs D_3M	NS	P < 0.01	NS	NS	P < 0.05	NS	NS	NS	P < 0.001	NS
C_3F Vs D_3F	NS	P < 0.005	NS	NS	P < 0.05	NS	NS	NS	P < 0.01	NS

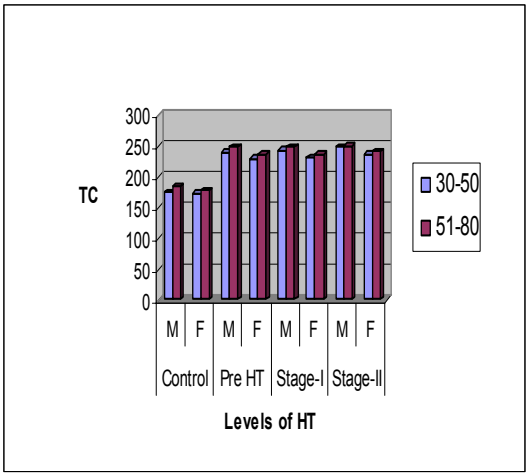
LDL-C increased from 111.2 mg/dl in control group to 172.4 mg/dl in stage-I and then decreased to stage-II with 170.4 mg/dl in 30-50 male hypertensives. Similar pattern was observed in 51-80 years male with 119.8, 167.1, 175.2 & 173.7 mg/dl conc of LDL-C correspondingly. In females an increase with increase in DBP was observed in LDL-C concentration among both the age groups. This increase from normal to stage-I was enormously significant (P<0.001) in both the genders as well both the age groups. While the increase in females from stage-I to stage-II and the decrease in male within the same levels remained insignificant. Also an insignificant increase with age was obtained in each level of HT of LDL-C concentration. Moreover, female LDL-C concentration was less than that in male HT subjects in each level of HT but significance was proclaimed in only preHT level. LDL-C concentration in all three hypertensive subgroups of both sexes among the two age groups were considerably higher than their corresponding normotensive counterparts and tremendous significance (P<0.001) was observed with preHT level.

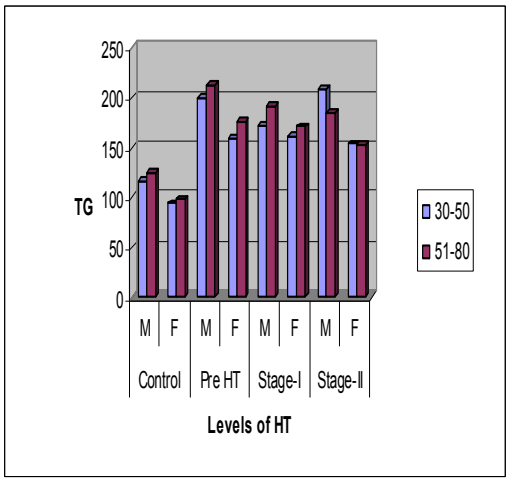
Table 5b: Statistical Analysis of Table 5(Contd)										
COMPARISON	SBP mmHg	DBP mmHg	TC mg/dl	TG mg/dl	HDL-C mg/dl	LDL-C mg/dl	TC/HDL-C	LDL-C/HDL-C	BMI kg/m^2	WHR
AM Vs C_1M	P < 0.001	P < 0.001	P < 0.001	P < 0.001	NS	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.05
AF Vs C_1F	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.05	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001
BM Vs D_1M	P < 0.001	P < 0.001	P < 0.001	P < 0.001	NS	P < 0.001	P < 0.001	P < 0.001	P < 0.01	P < 0.01
BF Vs D_1F	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001
C_1M Vs C_2M	P < 0.001	P < 0.001	NS	P < 0.01	NS	P < 0.05	P < 0.05	P < 0.01	P < 0.05	P < 0.01
C_1F Vs C_2F	P < 0.001	P < 0.001	NS	NS	P < 0.001	P < 0.001	P < 0.001	P < 0.001	NS	P < 0.05
D_1M Vs D_2M	P < 0.001	P < 0.001	NS	P < 0.05	P < 0.01	NS	P < 0.001	P < 0.001	NS	NS
D_1F Vs D_2F	P < 0.001	P < 0.001	NS	NS	P < 0.001	NS	P < 0.001	P < 0.001	NS	P < 0.05
C_2M Vs C_3M	P < 0.001	P < 0.001	NS	P < 0.01	NS	NS	NS	NS	NS	NS
C_2F Vs C_3F	P < 0.001	P < 0.001	NS	NS	P < 0.01	NS	P < 0.01	P < 0.05	P < 0.01	P < 0.005
D_2M Vs D_3M	P < 0.001	P < 0.001	NS	NS	P < 0.05	NS	P < 0.01	P < 0.05	NS	NS
D_2F Vs D_3F	P < 0.001	P < 0.001	NS	NS	P < 0.05	NS	P < 0.001	P < 0.01	P < 0.05	NS

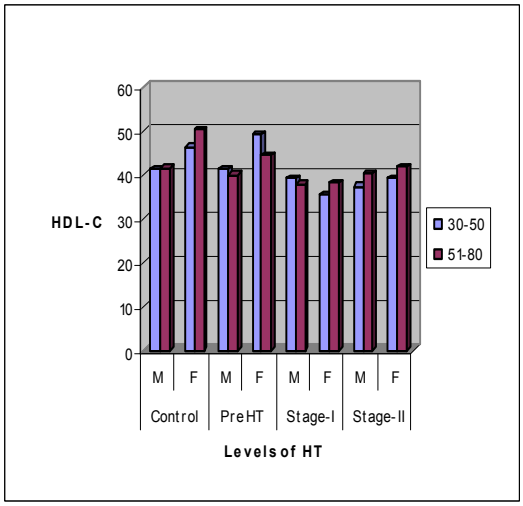
In hypertensive subjects of both genders within the two age groups, TC/HDL-C & LDL-C/HDL-C values were more than 4.5 & 3.0 respectively. These ratios increased with extreme significance (P<0.001) from normal to stage-I in both genders and age groups and decreased with a minor significance (P<0.05) from stage-I to stage-II level. Within each levels of HT an increase with age in males and a decrease with age in females were analyzed but slight significance was seen in only preHT level (P<0.05). The ratios in females were lower than those in male hypertensive subjects within the three subgroups of HT and this difference was immensely significant (P<0.01) in preHT and stage-II level.

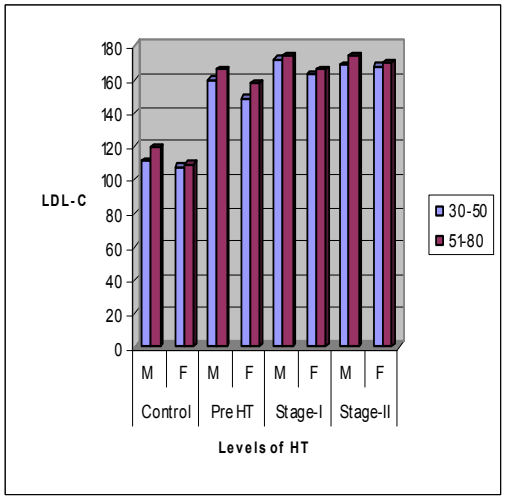
In all the three subgroups of HT, BMI was more than 25 in both the genders and age groups. In 30-50 years, with increase in DBP, BMI significantly increased (P<0.05) in both the genders while in 51-80 years BMI remained nearly alike in all the three subgroups of HT. The BMI values in each level of HT decreased with age in both genders but it was vastly significant (P<0.01) in only males. Also female BMI values was more than that of male hypertensive volunteers of corresponding groups and this difference was greatly significant (P<0.01) in only 51-80 age group. All values of BMI in each of the level of HT was considerably higher when compared to their normotensive counterparts and it was exceedingly significant (P<0.001) in preHT level.

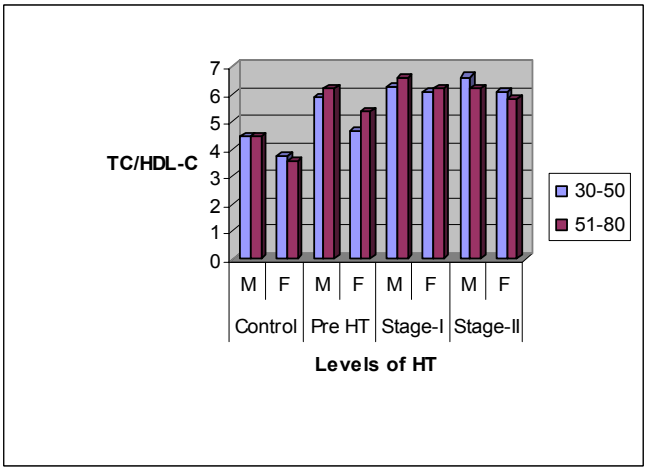
Graph 3: Levels of Serum Lipids and Anthropometric Indices with regard to Levels of HT:

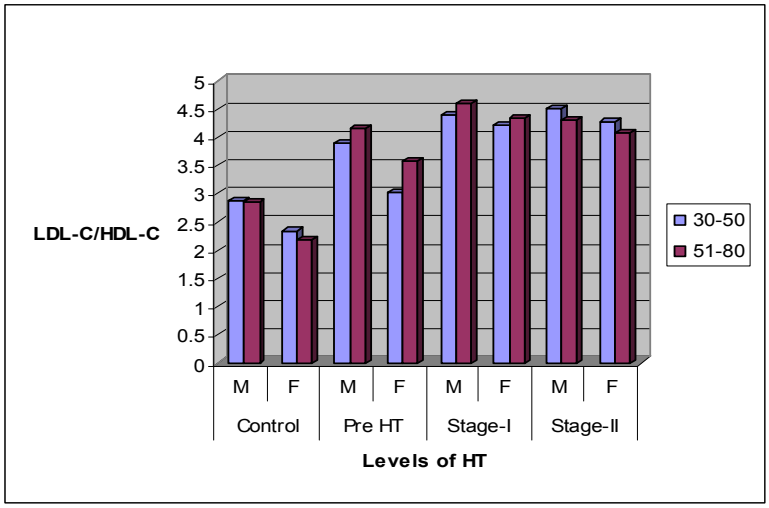


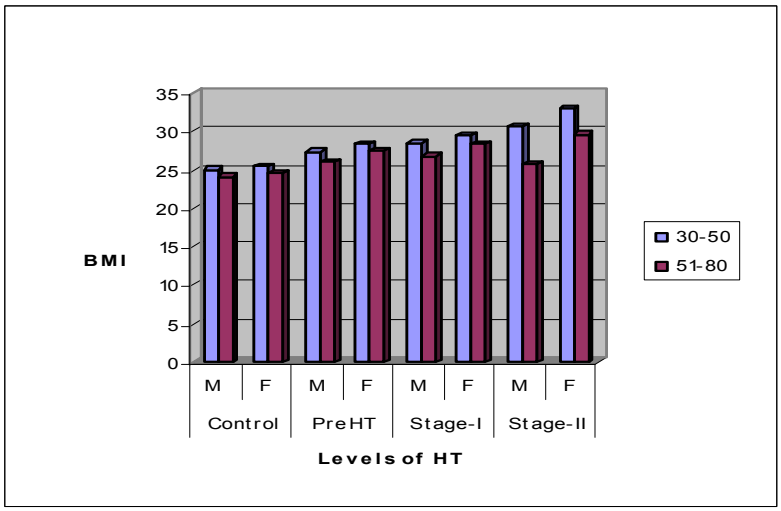









LDL-C/HDL-C
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
M F M F M F M F
Control
Pre HT
Stage-I
Stage-II
Levels of HT
30-50
51-80


BMI
35
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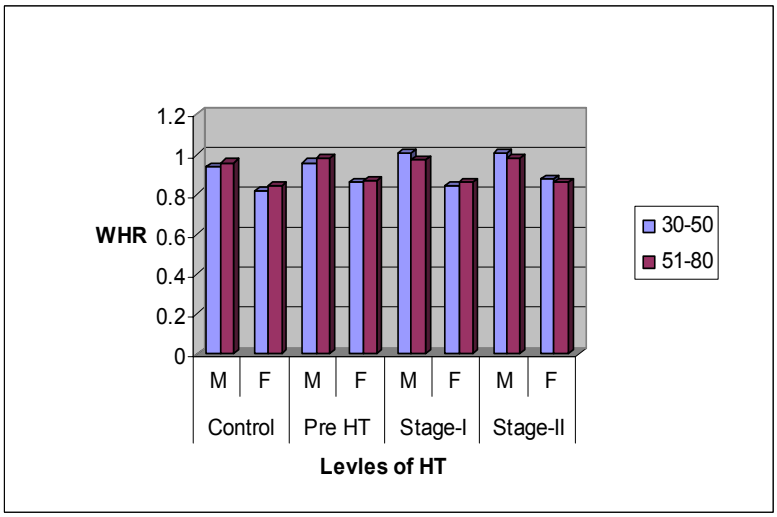
25
20
15
10
5
0
M F M F M F M F
Control
Pre HT
Stage-I
Stage-II
Levels of HT
30-50
51-80


WHR
1.2
1
0.8
0.6
0.4
0.2
0
M F M F M F M F
Control
Pre HT
Stage-I
Stage-II
Levles of HT
30-50
51-80

WHR remained similar to BMI with increase in level of HT. Both the gender of 30-50 years showed a highly significant (P<0.01) increase with level of HT while 51-80 year hypertensives remained nearly related through the levels of HT. All values of WHR were higher than their normotensive subjects in each level of HT in both the genders and age groups.

4. Effect of Diet on BP, Serum Lipids and Anthropometric indices:

(a) **Calories**: Normotensive individual and hypertensive patients were regrouped according to amount of calorie intake per day within the two age groups to see the effect of calories on BP, serum lipids and anthropometric indices.

Normotensive individuals consuming high calorie diet had significantly higher SBP & DBP (P<0.005) in both genders within the two age groups 30-50 years and 51-80 years when compared to low calorie diet consuming normotensive subjects. A parallel trend was observed in the hypertensive patients in relation to BP and the significance was found to be P<0.001. Also the BP values of the hypertensive patients consuming high calorie diet in the two age groups were much higher than those seen in normotensive subjects consuming low calorie diet and were tremendously significant (P<0.001). Thus the blood pressures in hypertensive subjects within the two age groups consuming high calorie diet were 152.1/96.1 & 156.1/101.7 in males and in females the values were 148.3/94.7 & 152.2/98.7 mmHg. While the blood pressures in normotensive subjects consuming low calorie diet were 116.2/93.49 & 119.0/75.3 mmHg in males and 115.7/70.67 & 118.0/74.48 in females respectively.

TC & TG also showed a significant difference and positive correlation with the amount of calorie consumption in both genders as well as age groups in hypertensive and normotensive subjects. Normotensive subjects consuming high calorie diet within two age groups had 178.5 & 185.1 mg/dl TC and 121.9 & 131.2 mg/dl TG concentration in males and the same in females were 174.8 & 182.9 mg/dl TC concentration and 99.9 & 114.2 mg/dl TG concentration respectively. The values in hypertensive subjects consuming high calorie diet were 245.0 & 250.6 mg/dl TC and 207.7 & 210.3 mg/dl TG concentration in males and in females they were 232.4 & 241.5 mg/dl TC and 179.8 & 181.0 mg/dl TG concentration respectively. Also both, TC & TG concentrations of the hypertensive patients consuming high calorie diet of both genders in the two age

groups were much higher than those seen in normotensive subjects consuming low calorie diet and enormously significant (P<0.001).

Table 6.1: Effect of Diet on BP, Serum Lipids, BMI and WHR in Normotensive cases

Age Group	Diet	G	N	SBP mmHg	DBP mmHg	TC mg/dl	TG mg/dl	HDL-C mg/dl	LDL-C mg/dl	TC/HDL-C	LDL-C/HDL-C	BMI	WHR
30-50	Low Calorie (A_1)	M	59	116.2 ±0.95	73.49 ±0.47	171.9 ±3.4	106.9 ±5.4	40.49 ±1.2	110.0 ±3.5	4.44 ±0.15	2.88 ±0.13	25.40 ±0.40	0.94 ±0.01
		F	60	115.7 ±0.57	70.67 ±0.28	168.8 ±2.6	88.8 ±4.3	42.70 ±1.7	108.4 ±3.2	4.35 ±0.19	2.90 ±0.17	24.25 ±0.58	0.80 ±0.007
	High Calorie (A_2)	M	50	118.1 ±1.1	75.32 ±0.49	178.5 ±4.2	121.9 ±5.5	41.9 ±1.5	112.3 ±4.0	4.55 ±0.21	2.92 ±0.18	24.70 ±0.51	0.93 ±0.01
		F	103	116.5 ±0.45	72.66 ±0.40	174.8 ±2.4	99.9 ±3.8	43.4 ±0.97	111.4 ±2.5	4.22 ±0.11	2.73 ±0.09	26.05 ±0.36	0.83 ±0.007
Above 50	Low Calorie (B_1)	M	37	119.0 ±0.69	75.3 ±0.5	174.8 ±4.5	110.3 ±8.2	41.5 ±2.0	111.2 ±4.4	4.50 ±0.21	2.94 ±0.19	24.25 ±0.58	0.80 ±0.01
		F	32	118.0 ±0.77	74.48 ±0.58	172.8 ±3.0	86.4 ±6.2	43.22 ±1.6	112.2 ±2.7	4.13 ±0.14	2.71 ±0.12	24.78 ±0.52	0.84 ±0.01
	High Calorie (B_2)	M	34	124.0 ±1.7	77.60 ±0.38	185.1 ±8.3	131.2 ±8.6	40.6 ±2.3	118.3 ±7.9	5.04 ±0.38	3.29 ±0.32	25.44 ±0.73	0.95 ±0.01
		F	22	122.5 ±2.5	76.55 ±0.48	182.9 ±5.8	114.2 ±5.4	42.5 ±2.6	117.6 ±2.7	4.62 ±0.31	3.04 ±0.28	27.64 ±1.1	0.82 ±0.008

Values are Mean ± S.E.

Table 6.1a: Statistical Analysis of Table 6.1

COMPARISON	SBP mmHg	DBP mmHg	TC mg/dl	TG mg/dl	HDL-C mg/dl	LDL-C mg/dl	TC/HDL-C	LDL-C/HDL-C	BMI kg/m^2	WHR
A_1M vs A_2M	NS	P < 0.005	NS	P < 0.05	NS	NS	NS	NS	NS	NS
A_1F vs A_2F	NS	P < 0.001	P < 0.05	P < 0.05	NS	NS	NS	NS	P < 0.01	P < 0.001
B_1M vs B_2M	P < 0.005	P < 0.001	NS	P < 0.05	NS	NS	NS	NS	P < 0.05	NS
B_1F vs B_2F	P < 0.05	P < 0.005	P < 0.05	P < 0.001	NS	NS	NS	NS	P < 0.01	NS
A_2M vs A_2F	NS	P < 0.001	NS	P < 0.001	NS	NS	NS	NS	P < 0.01	P < 0.001
B_2M vs B_2F	NS	P < 0.005	NS	P < 0.05	NS	NS	NS	NS	P < 0.05	P < 0.001
A_2M vs B_2M	P < 0.001	P < 0.001	NS	NS	NS	NS	NS	NS	NS	NS
A_2F vs B_2F	P < 0.01	P < 0.001	NS	P < 0.01	NS	NS	NS	NS	NS	NS

In normotensive subjects consuming high calorie diet, HDL-C was seen to increase in both sexes of 30-50 years while 51-80 years demonstrated a decrease when compared to subjects consuming low calorie diet. The hypertensive subjects on the contrary, illustrated an increase in females of both age groups while males did not show much change in relation to low calorie diet.

Table 6.2: Effect of Diet on BP, Serum Lipids, BMI and WHR in Normotensive cases

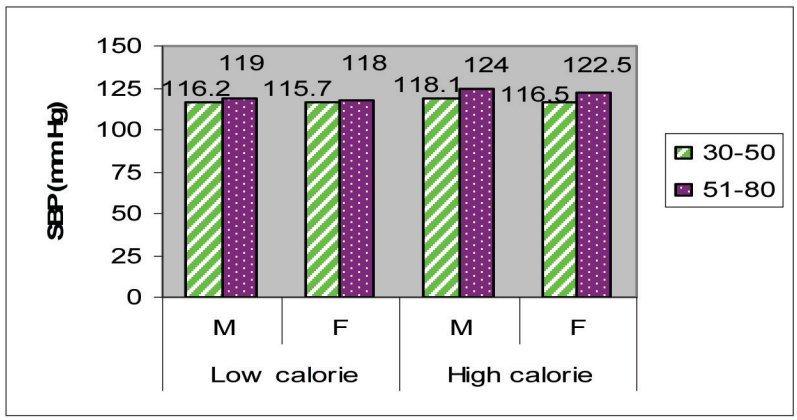
Age Group	Diet	G	N	SBP mmHg	DBP mmHg	TC mg/dl	TG mg/dl	HDL-C mg/dl	LDL-C mg/dl	TC/HDL-C	LDL-C/HDL-C	BMI	WHR
30-50	Low Fat (A_3)	M	12	116.3 ±1.8	73.33 ±1.4	167.8 ±5.7	109.3 ±13.0	40.25 ±2.5	105.7 ±7.1	4.38 ±0.33	2.83 ±0.33	24.25 ±0.97	0.98 ±0.01
		F	13	118.3 ±0.98	71.54 ±2.6	167.2 ±6.7	76.8 ±7.5	42.3 ±1.6	109.5 ±6.6	4.01 ±0.21	2.64 ±0.19	26.31 ±1.2	0.80 ±0.01
	High Fat (A_4)	M	104	119.1 ±0.99	75.04 ±0.33	186.2 ±3.0	125.8 ±4.7	41.5 ±1.0	119.5 ±3.2	4.74 ±0.13	3.09 ±0.12	25.11 ±0.34	0.93 ±0.008
		F	156	116.1 ±0.37	72.56 ±0.31	179.0 ±1.9	102.5 ±4.1	42.3 ±0.8	116.2 ±2.0	4.52 ±0.12	2.99 ±0.10	25.31 ±0.33	0.82 ±0.005
Above 50	Low Fat (B_3)	M	12	118.5 ±1.8	75.7 ±4.3	174.8 ±8.5	94.5 ±11.0	39.2 ±1.8	116.6 ±10	4.63 ±0.40	3.13 ±0.38	23.75 ±1.1	0.99 ±0.02
		F	13	118.6 ±1.7	73.8 ±3.5	167.2 ±9.3	70.9 ±10.0	39.3 ±1.6	113.7 ±7.8	4.32 ±0.28	2.95 ±0.24	21.46 ±1.0	0.86 ±0.01
	High Fat (B_4)	M	67	124.1 ±1.7	77.82 ±0.28	190.3 ±5.1	127.9 ±6.6	41.9 ±1.5	122.8 ±4.9	4.96 ±0.25	3.27 ±0.20	24.4 ±0.45	0.95 ±0.008
		F	48	120.5 ±1.6	75.17 ±0.51	184.5 ±3.8	103.8 ±8.7	43.3 ±1.9	120.5 ±4.6	4.80 ±0.3	3.25 ±0.27	24.71 ±0.42	0.83 ±0.007

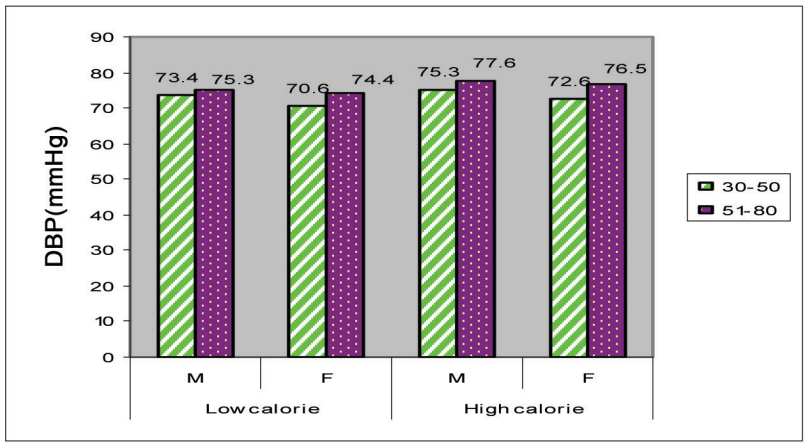
Values are Mean ± S.E.

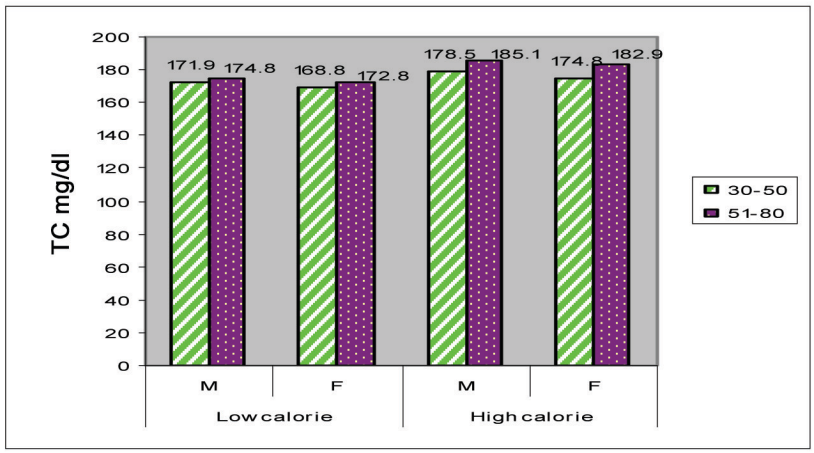
Table 6.2a: Statistical Analysis of Table 6.2

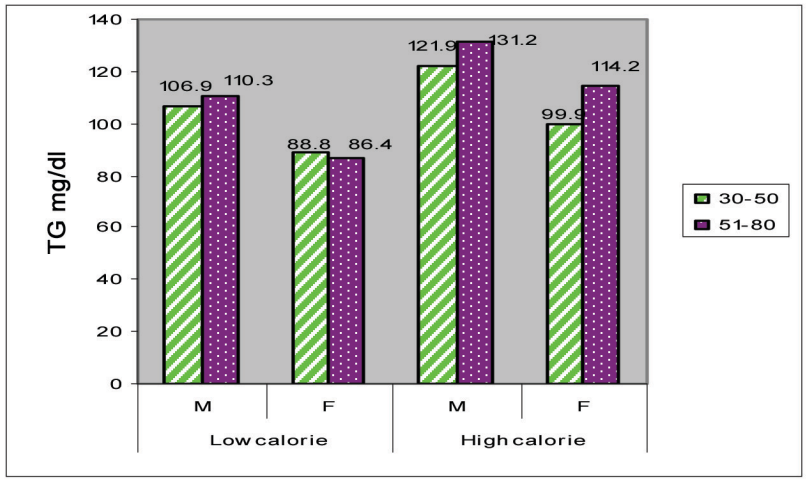
COMPARISON	SBP mmHg	DBP mmHg	TC mg/dl	TG mg/dl	HDL-C mg/dl	LDL-C mg/dl	TC/HDL-C	LDL-C/HDL-C	BMI kg/m^2	WHR
A_3M vs A_4M	NS	NS	P < 0.01	NS	NS	P < 0.05	NS	NS	NS	P < 0.01
A_3F vs A_4F	P < 0.05	NS	P < 0.05	P < 0.005	NS	NS	P < 0.05	P < 0.05	NS	NS
B_3M vs B_4M	P < 0.01	NS	P < 0.05	P < 0.01	NS	NS	NS	NS	NS	NS
B_3F vs B_4F	NS	NS	P < 0.05	P < 0.01	NS	NS	NS	NS	P < 0.005	NS
A_4M vs A_4F	P < 0.005	P < 0.001	P < 0.01	P < 0.001	NS	NS	NS	NS	NS	P < 0.001
B_4M vs B_4F	P < 0.05	P < 0.001	NS	P < 0.01	NS	NS	NS	NS	NS	P < 0.001
A_4M vs B_4M	P < 0.01	P < 0.001	NS	NS	NS	NS	NS	NS	NS	P < 0.05
A_4F vs B_4F	P < 0.01	P < 0.001	NS	NS	NS	NS	NS	NS	NS	NS

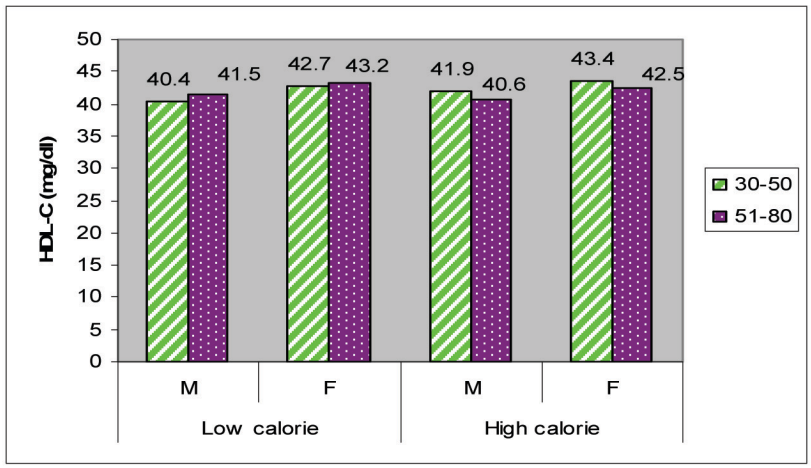
Graph 4.1: Effect of diet (calorie) on BP, Serum Lipids and Anthropometric Indices in Normotensive cases:

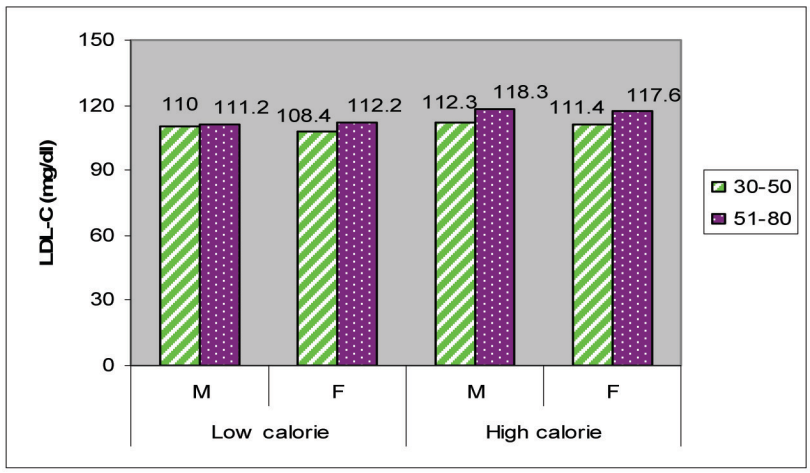


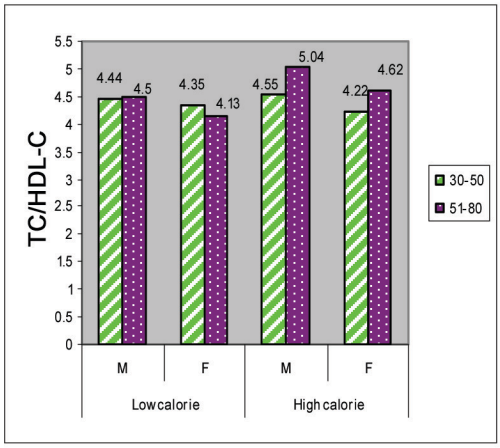


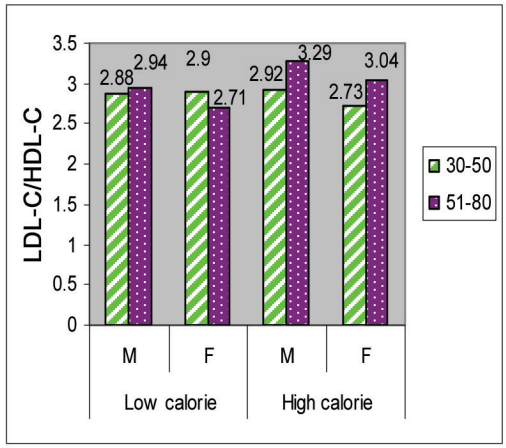


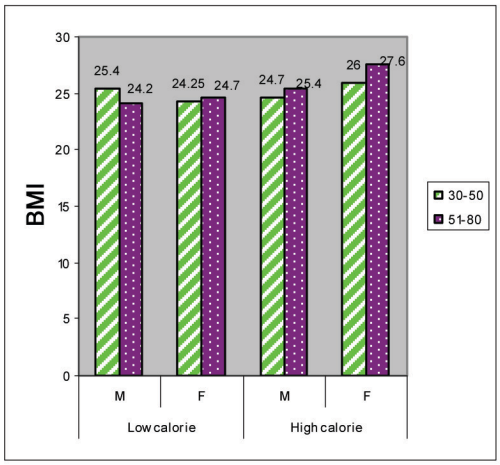

TG mg/dl
140
120
100
80
60
40
20
0
106.9
110.3
88.8
86.4
121.9
131.2
99.9
114.2
M
F
M
F
Low calorie
High calorie
30-50
51-80

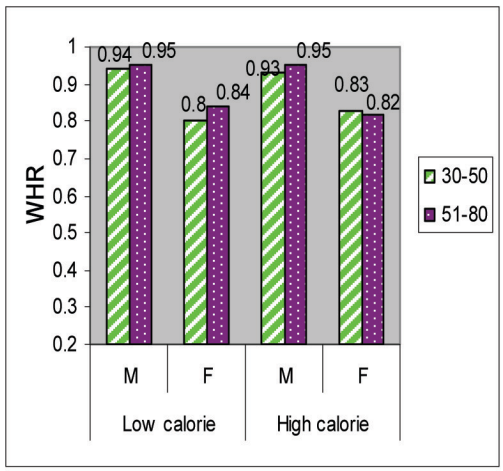

HDL-C (mg/dl)
50
45
40
35
30
25
20
15
10
5
0
40.4
41.5
42.7
43.2
41.9
40.6
43.4
42.5
M
F
M
F
Low calorie
High calorie
30-50
51-80


LDL-C (mg/dl)
150
120
90
60
30
0
110
111.2
108.4
112.2
112.3
118.3
111.4
117.6
M
F
M
F
Low calorie
High calorie
30-50
51-80

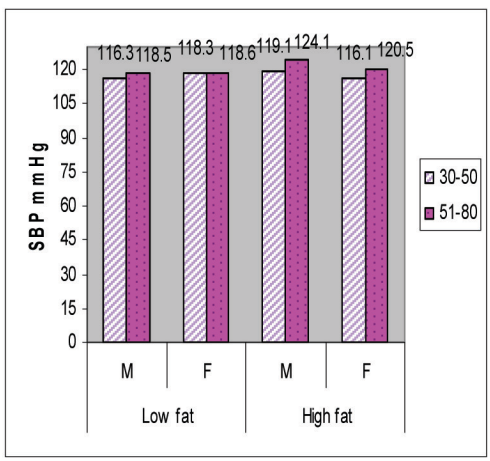


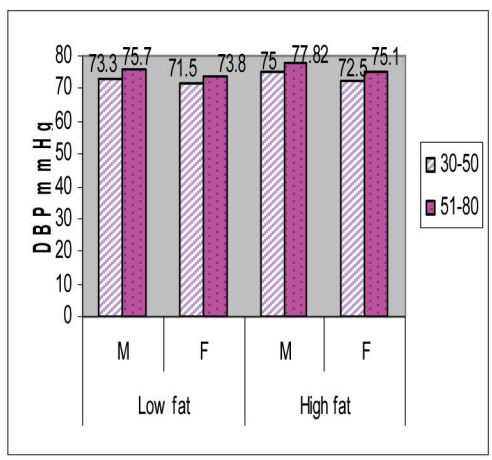


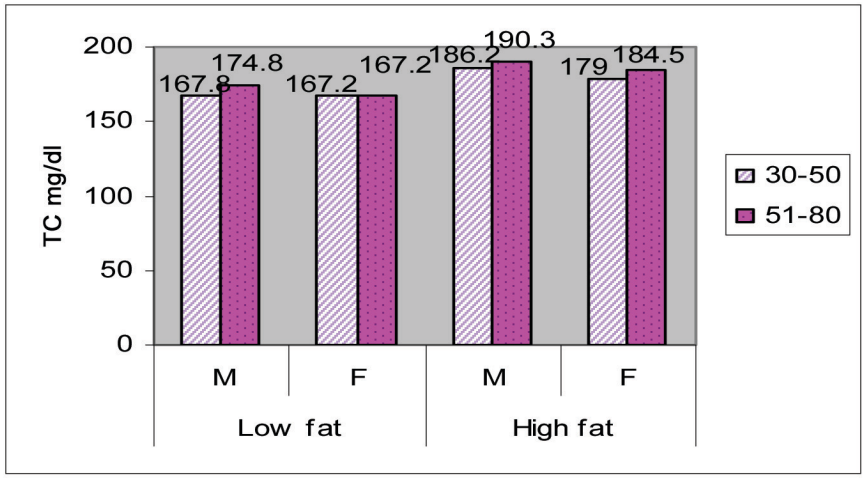


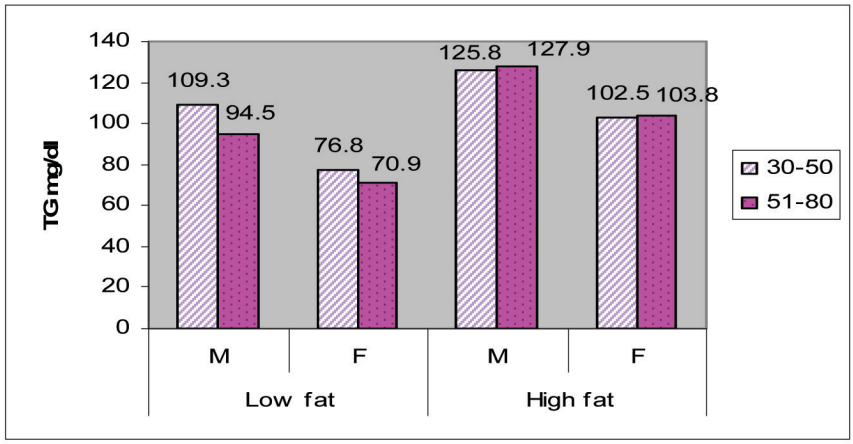


<u>Graph 4.2</u>: Effect of diet (fat) on BP, Serum Lipids and Anthropometric Indices in Normotensive cases:






TC mg/dl
200
150
100
50
0
167.8
174.8
167.2
167.2
186.2
190.3
179
184.5
M
F
M
F
Low fat
High fat
30-50
51-80


TG mg/dl
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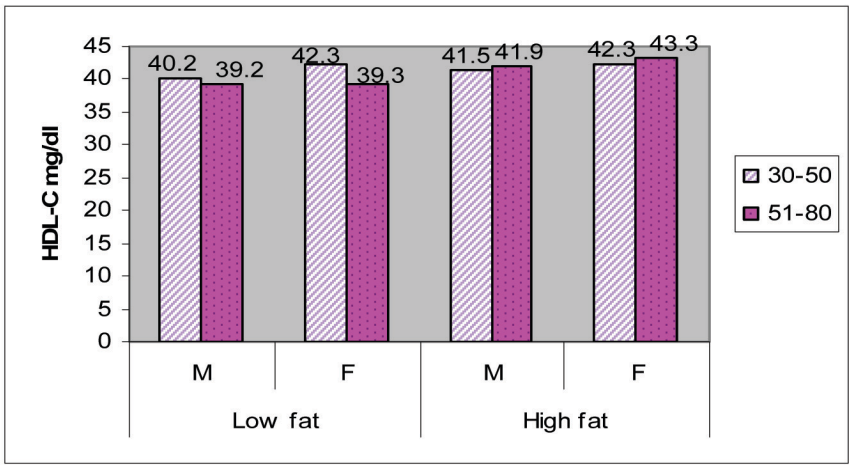
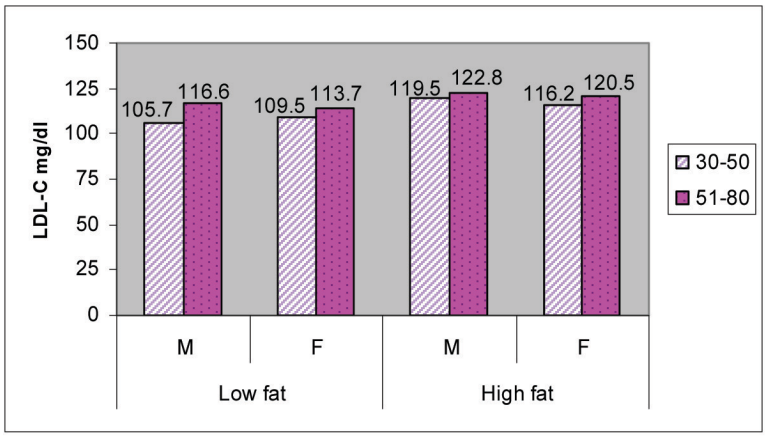
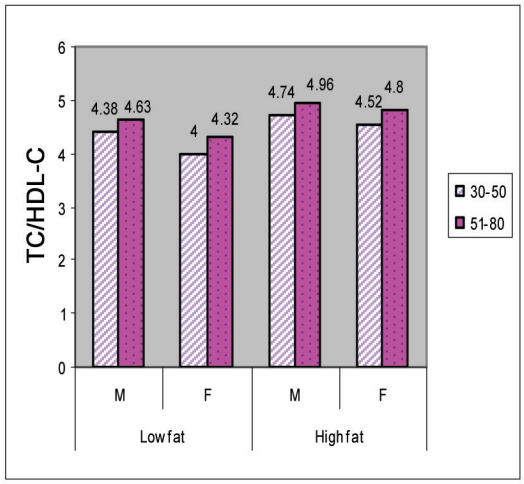
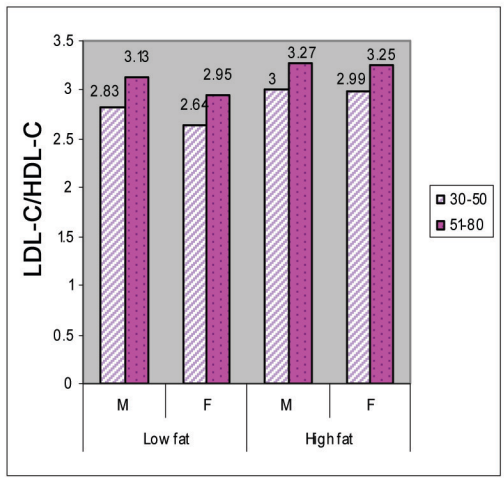
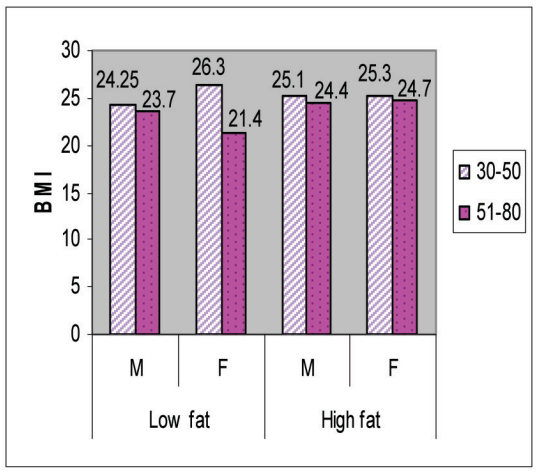
120
100
80
60
40
20
0
109.3
94.5
76.8
70.9
125.8
127.9
102.5
103.8
M
F
M
F
Low fat
High fat
30-50
51-80

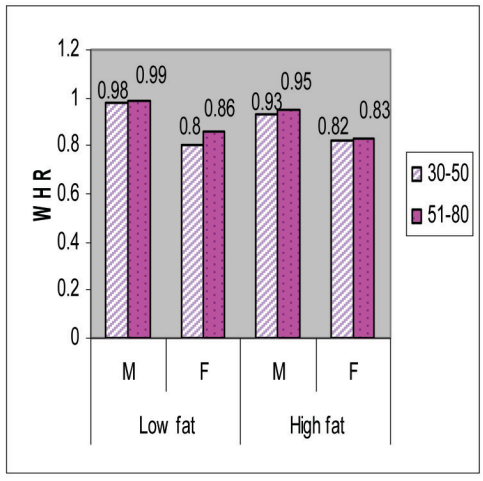

HDL-C mg/dl
45
40
35
30
25
20
15
10
5
0
40.2
39.2
42.3
39.3
41.5
41.9
42.3
43.3
M
F
M
F
Low fat
High fat
30-50
51-80


LDL-C mg/dl
150
125
100
75
50
25
0
105.7
116.6
109.5
113.7
119.5
122.8
116.2
120.5
M
F
M
F
Low fat
High fat
30-50
51-80


TC/HDL-C
6
5
4
3
2
1
0
4.38
4.63
4
4.32
4.74
4.96
4.52
4.8
M
F
M
F
Low fat
High fat
30-50
51-80


LDL-C/HDL-C
3.5
3
2.5
2
1.5
1
0.5
0
2.83
3.13
2.64
2.95
3
3.27
2.99
3.25
M
F
M
F
Low fat
High fat
30-50
51-80


BMI
30
25
20
15
10
5
0
24.25
23.7
26.3
21.4
25.1
24.4
25.3
24.7
M
F
M
F
Low fat
High fat
30-50
51-80


WHR
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1
0.8
0.6
0.4
0.2
0
0.98
0.99
0.8
0.86
0.93
0.95
0.82
0.83
M
F
M
F
Low fat
High fat
30-50
51-80

Table 6.3: Effect of Diet on BP, Serum Lipids, BMI and WHR in Hypertensive cases

Age Group	Diet	G	N	SBP mmHg	DBP mmHg	TC mg/dl	TG mg/dl	HDL-C mg/dl	LDL-C mg/dl	TC/HDL-C	LDL-C/HDL-C	BMI	WHR
30-50	Low Calorie (C_4)	M	56	149.0 ±2.2	91.1 ±1.1	219.0 ±4.1	183.1 ±10.0	39.6 ±1.5	142.8 ±4.4	5.98 ±0.26	3.96 ±0.22	27.65 ±0.61	0.95 ±0.01
		F	41	144.8 ±2.4	90.2 ±1.2	223.6 ±6.6	150.8 ±12	42.07 ±1.4	142.2 ±5.6	5.49 ±0.20	3.72 ±0.19	30.32 ±1.1	0.84 ±0.01
	High Calorie (C_5)	M	96	152.1 ±1.5	96.1 ±1.2	245.0 ±5.7	207.7 ±8.9	38.7 ±0.96	164.8 ±5.6	6.62 ±0.19	4.46 ±0.17	29.25 ±0.58	0.99 ±0.009
		F	112	148.3 ±1.3	94.7 ±1.2	232.4 ±3.6	179.8 ±6.8	42.9 ±1.2	153.6 ±3.8	5.76 ±0.15	3.84 ±0.13	28.49 ±0.49	0.86 ±0.006
Above 50	Low Calorie (D_4)	M	91	151.2 ±1.5	93.3 ±0.96	236.3 ±6.0	193.9 ±10	39.45 ±0.94	158.1 ±5.6	6.29 ±0.21	4.22 ±0.18	25.87 ±0.45	0.97 ±0.009
		F	62	144.8 ±2.1	90.2 ±1.1	223.6 ±5.6	150.8 ±8.7	42.07 ±1.3	142.8 ±6.0	5.49 ±0.22	3.72 ±0.21	30.32 ±0.51	0.84 ±0.007
	High Calorie (D_5)	M	126	156.1 ±1.6	101.7 ±1.4	250.6 ±3.9	210.3 ±7.2	39.5 ±0.84	169.0 ±3.9	6.61 ±0.16	4.47 ±0.14	27.26 ±0.39	0.98 ±0.006
		F	160	152.2 ±1.3	98.7 ±1.1	241.5 ±3.5	181.0 ±7.1	44.4 ±0.85	160.9 ±4.2	5.77 ±0.15	3.91 ±0.15	28.99 ±0.45	0.86 ±0.005

Values are Mean ± S.E.

Table 6.3a: Statistical Analysis of Table 6.3

COMPARISON	SBP mmHg	DBP mmHg	TC mg/dl	TG mg/dl	HDL-C mg/dl	LDL-C mg/dl	TC/HDL-C	LDL-C/HDL-C	BMI kg/m^2	WHR
C_4M vs C_5M	NS	P < 0.001	P < 0.001	P < 0.05	NS	P < 0.001	P < 0.05	P < 0.05	P < 0.05	P < 0.005
C_4F vs C_5F	NS	P < 0.005	NS	P < 0.01	NS	P < 0.01	NS	NS	P < 0.05	NS
D_4M vs D_5M	P < 0.01	P < 0.001	P < 0.01	NS	NS	P < 0.05	NS	NS	P < 0.01	NS
D_4F vs D_5F	P < 0.05	P < 0.001	P < 0.05	P < 0.05	NS	NS	NS	NS	P < 0.01	NS
C_5M vs C_5F	P < 0.05	NS	P < 0.05	P < 0.01	P < 0.005	P < 0.05	P < 0.001	P < 0.001	NS	P < 0.001
D_5M vs D_5F	P < 0.05	P < 0.05	P < 0.05	P < 0.001	P < 0.001	NS	P < 0.001	P < 0.005	P < 0.001	P < 0.001
C_5M vs D_5M	P < 0.05	P < 0.001	NS	NS	NS	NS	NS	NS	NS	NS
C_5F vs D_5F	P < 0.01	P < 0.01	P < 0.05	NS	NS	NS	NS	NS	NS	NS

Table 6.4: Effect of Diet on BP, Serum Lipids, BMI and WHR in Hypertensive cases

Age Group	Diet	G	N	SBP mmHg	DBP mmHg	TC mg/dl	TG mg/dl	HDL-C mg/dl	LDL-C mg/dl	TC/HDL-C	LDL-C/HDL-C	BMI	WHR
30-50	Low Fat (C_6)	M	17	141.3 ±2.5	90.7 ±2.3	206.4 ±5.4	135.1 ±16	42.1 ±4.0	137.2 ±8.4	5.74 ±0.61	3.95 ±0.52	26.35 ±1.1	0.96 ±0.03
		F	12	138.5 ±3.0	91.2 ±3.4	207.6 ±11	140.9 ±9.9	39.3 ±0.93	140.1 ±11	5.27 ±0.25	3.55 ±0.27	28.67 ±1.8	0.93 ±0.01
	High Fat (C_7)	M	134	148.2 ±1.5	96.3 ±1.0	239.1 ±4.4	196.8 ±7.5	39.01 ±0.8	160.7 ±4.3	6.41 ±0.16	4.32 ±0.14	28.91 ±0.47	0.98 ±0.007
		F	137	143.5 ±1.1	94.7 ±0.87	232.8 ±3.3	159.0 ±6.3	42.7 ±0.96	158.3 ±3.4	5.76 ±0.15	3.93 ±0.11	31.8 ±0.46	0.85 ±0.005
Above 50	Low Fat (D_6)	M	29	141.8 ±1.9	91.55 ±0.93	224.3 ±11	177.2 ±10	40.83 ±1.4	148.1 ±9.7	5.61 ±0.27	3.73 ±0.25	26.86 ±0.85	0.95 ±0.01
		F	13	140.8 ±4.3	91.8 ±1.7	212.3 ±8.0	157.8 ±11	41.23 ±2.4	139.5 ±7.9	5.29 ±0.26	3.47 ±0.21	26.31 ±0.94	0.85 ±0.01
	High Fat (D_7)	M	187	150.2 ±1.0	98.9 ±0.8	245.1 ±3.8	200.9 ±6.3	39.5 ±0.71	165.4 ±3.6	6.48 ±0.14	4.38 ±0.12	29.17 ±0.45	0.98 ±0.005
		F	110	147.0 ±1.0	96.4 ±0.73	240.4 ±3.1	169.8 ±6.1	44.5 ±0.74	161.9 ±3.5	5.73 ±0.13	3.93 ±0.13	30.13 ±0.37	0.86 ±0.004

Values are Mean ± S.E.

Table 6.4a: Statistical Analysis of Table

COMPARISON	SBP mmHg	DBP mmHg	TC mg/dl	TG mg/dl	HDL-C mg/dl	LDL-C mg/dl	TC/HDL-C	LDL-C/HDL-C	BMI kg/m^2	WHR
C_6M vs C_7M	P < 0.01	P < 0.01	P < 0.001	P < 0.001	NS	P < 0.01	NS	NS	P < 0.05	NS
C_6F vs C_7F	NS	NS	P < 0.01	P < 0.05	P < 0.01	P < 0.05	P < 0.05	NS	P < 0.05	P < 0.001
D_6M vs D_7M	P < 0.001	P < 0.001	P < 0.05	P < 0.05	NS	P < 0.05	P < 0.005	P < 0.01	P < 0.01	P < 0.01
D_6F vs D_7F	NS	P < 0.01	P < 0.005	NS	NS	P < 0.01	NS	P < 0.05	P < 0.001	NS
C_7M vs C_7F	P < 0.01	NS	NS	P < 0.001	P < 0.001	NS	P < 0.001	P < 0.01	P < 0.001	P < 0.001
D_7M vs D_7F	P < 0.01	P < 0.01	NS	P < 0.001	P < 0.001	NS	P < 0.001	P < 0.01	P < 0.05	P < 0.001
C_7M vs D_7M	NS	P < 0.01	NS	NS	NS	NS	NS	NS	NS	NS
C_7F vs D_7F	P < 0.01	NS	P < 0.05	NS	P < 0.05	NS	NS	NS	P < 0.005	P < 0.05

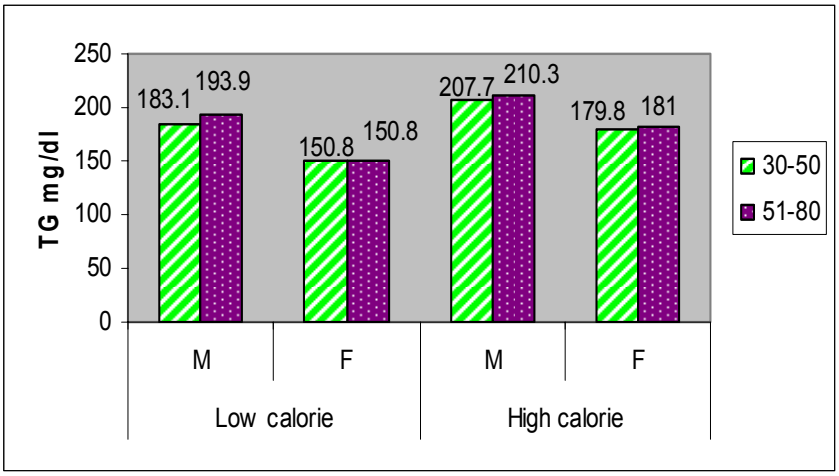
But in both normotensive and hypertensive subjects the rise or fall of HDL-C concentration with gender and age groups remained insignificant. In high calorie group, HDL-C concentration of hypertensive subjects in the two age groups were 38.7 & 39.5 mg/dl in males and 42.9 & 43.2 in females while in low calorie group the HDL-C concentration of normotensive subjects were 40.49 & 41.5 mg/dl in males and 42.7 & 43.2 in females. The difference in HDL-C concentration between the high calorie and low calorie groups in both genders and age groups were not significant.

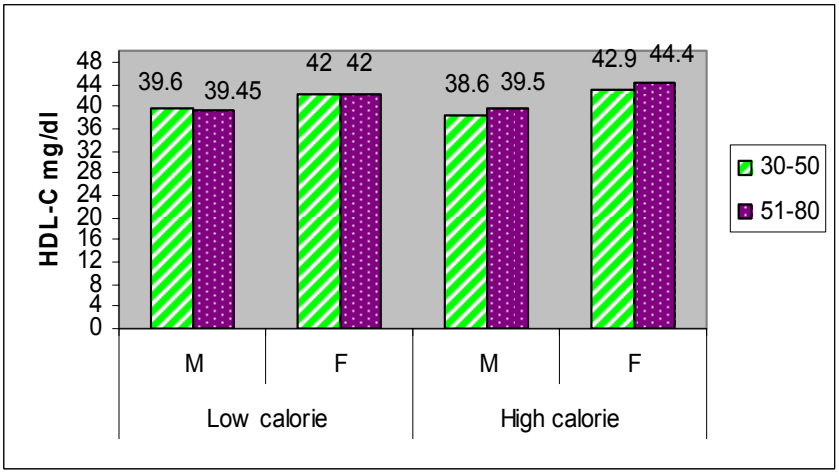
The normotensive and hypertensive subjects consuming high calorie diet showed a related pattern in increase of LDL-C concentration in both genders and age groups when compared to their respective low calorie consuming subjects. But this increase in normotensive remained insignificant while hypertensive subjects showed a greatly significant increase ($P<0.01$). The values of LDL-C concentration of hypertensive subjects consuming high calorie diet in both the age groups were 164.8 & 169.0 mg% in males and 153.6 & 160.9 mg% in females while the control group consuming low calorie group had values like 110.0 & 111.2 mg% in males and 108.4 & 112.7 mg% in females respectively. Thus the difference in LDL-C concentration between these diet groups in both the genders and age groups were remarkably significant ($P<0.001$).

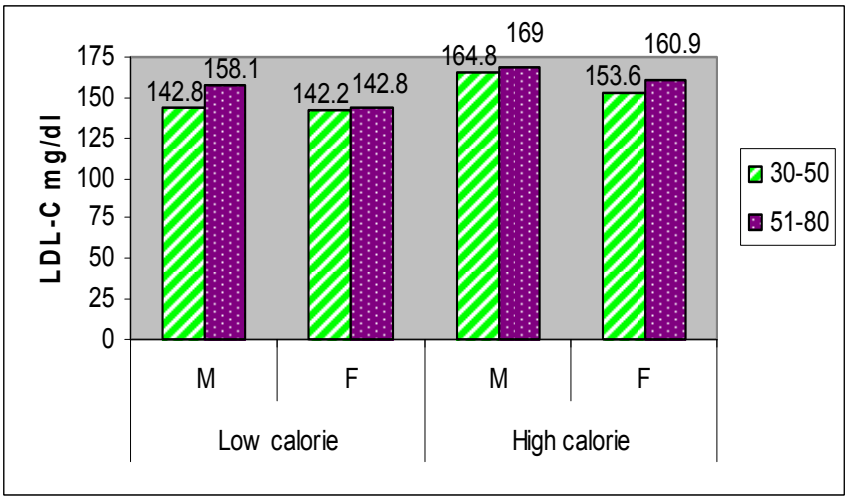
The atherogenic ratios TC/HDL-C & LDL-C/HDL-C did not show any significant rise in high calorie consuming subjects of normotensive and hypertensive group when compared to their respective low calorie consuming subjects in both the genders as well as age groups. While an extremely significant ($P<0.001$) difference was observed between high calorie hypertensive group and low calorie control group in both the genders and their age groups. In high calorie group the TC/HDL-C of hypertensive subjects in both age groups were 6.62 & 6.61 and the same in low calorie group were 4.44 & 4.50 in males while the same in females were 5.76 & 5.77 in high calorie group and 4.35 & 4.13 in low calorie group correspondingly.

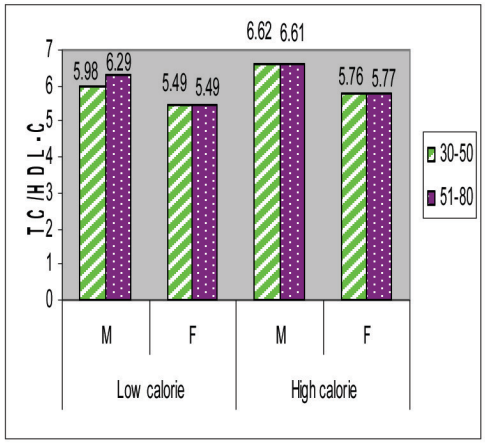
The BMI of anthropometric indices exhibited an increase in normotensive and hypertensive subjects consuming high calorie diet when compared to their respective low calorie consuming subjects and the exceptionals in this case were females in the hypertensive group. This rise and fall of BMI values in both normotensive and hypertensive subjects were found to be vastly significant ($P<0.001$) in both age groups and genders. In high calorie group, BMI value of hypertensive subjects in the two age groups were 29.25 & 27.26 kg/m^2 in males and 28.49 & 28.99 kg/m^2 in females respectively. This difference in BMI between the two diet groups in both genders and age groups were enormously significant ($P<0.001$).

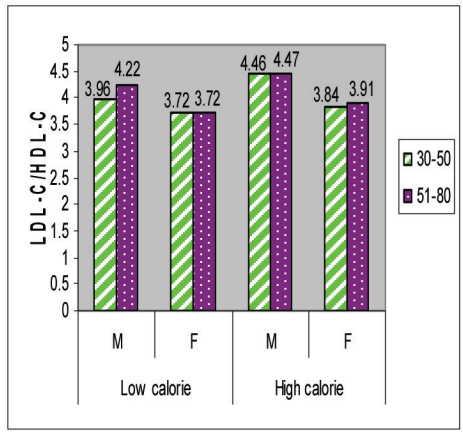
<u>Graph 4.3</u>: Effect of diet (calorie) on BP, Serum Lipids and Anthropometric Indices in Hypertensive cases:

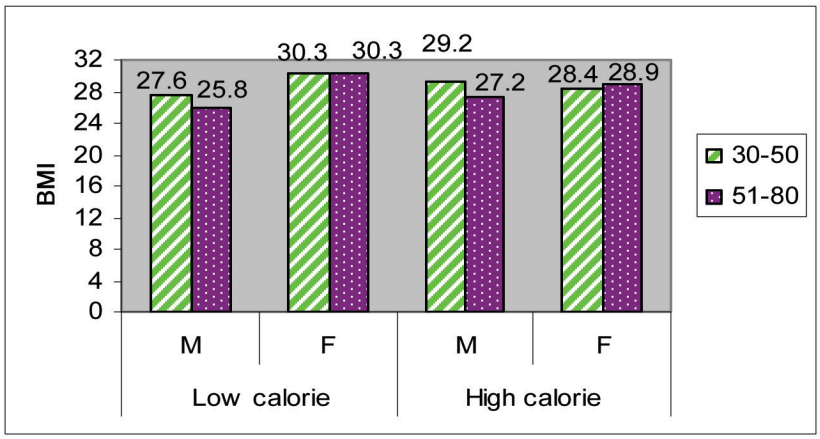

TG mg/dl
250
200
150
100
50
0
183.1
193.9
150.8
150.8
207.7
210.3
179.8
181
M
F
M
F
Low calorie
High calorie
30-50
51-80

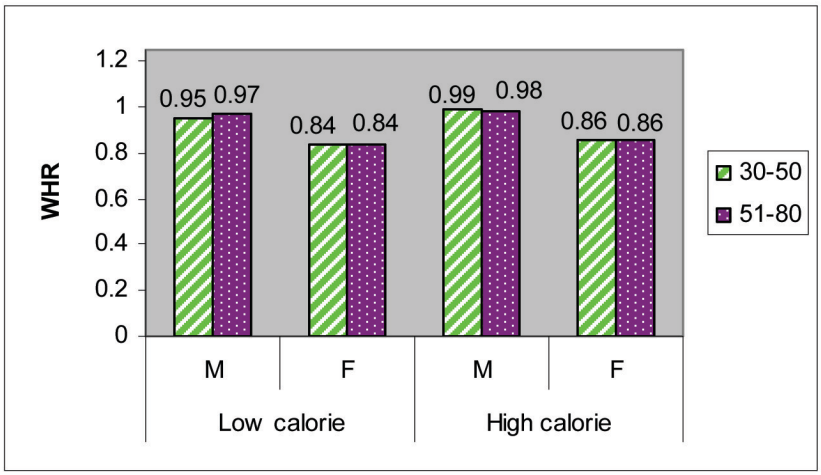

HDL-C mg/dl
48
44
40
36
32
28
24
20
16
12
8
4
0
39.6
39.45
42
42
38.6
39.5
42.9
44.4
M
F
M
F
Low calorie
High calorie
30-50
51-80


LDL-C mg/dl
175
150
125
100
75
50
25
0
142.8
158.1
142.2
142.8
164.8
169
153.6
160.9
M
F
M
F
Low calorie
High calorie
30-50
51-80

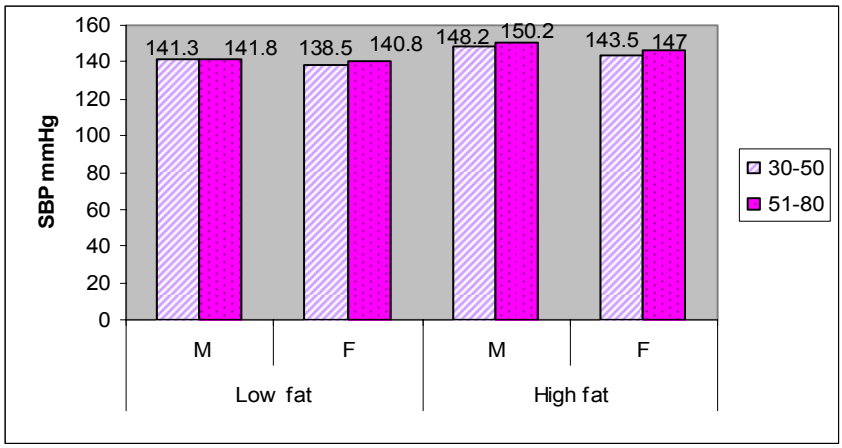

T C /H D L -C
7
6
5
4
3
2
1
0
5.98 6.29
5.49 5.49
6.62 6.61
5.76 5.77
30-50
51-80
M
F
M
F
Low calorie
High calorie

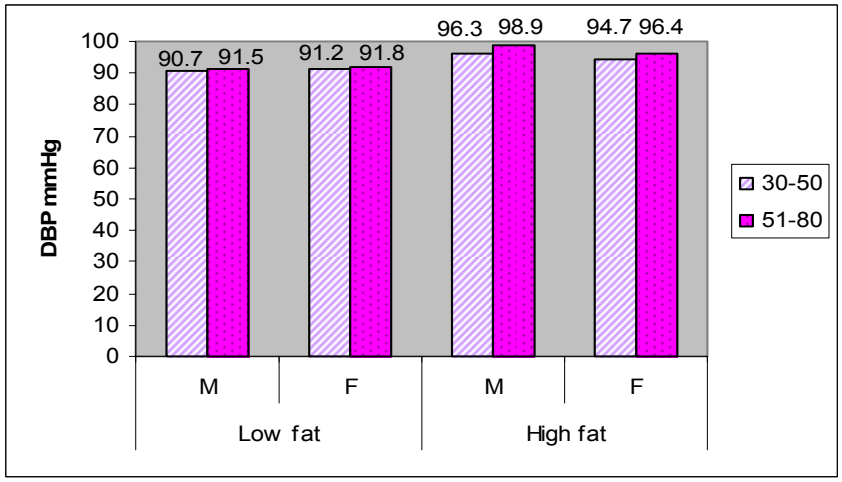

L D L -C /H D L -C
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
3.96 4.22
3.72 3.72
4.46 4.47
3.84 3.91
30-50
51-80
M
F
M
F
Low calorie
High calorie

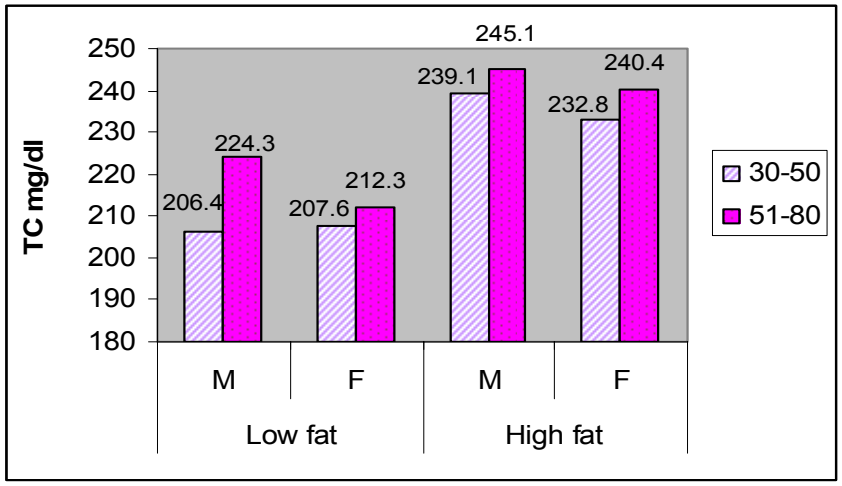

BMI
32
28
24
20
16
12
8
4
0
27.6 25.8
30.3 30.3
29.2 27.2
28.4 28.9
30-50
51-80
M
F
M
F
Low calorie
High calorie

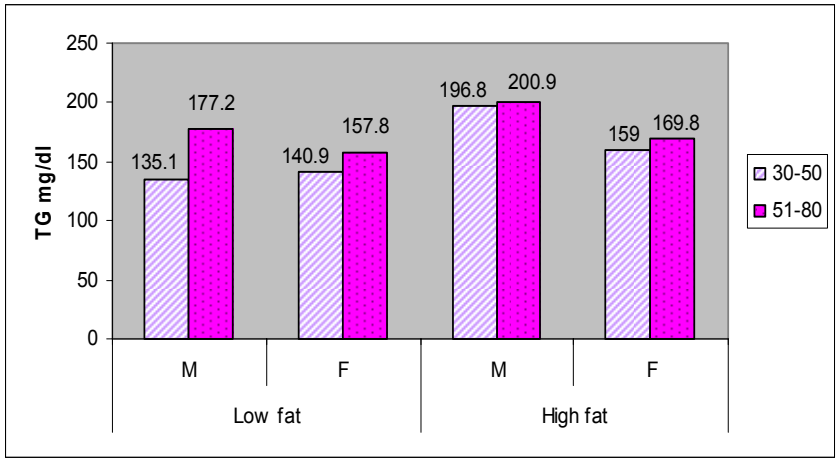

WHR
1.2
1
0.8
0.6
0.4
0.2
0
0.95 0.97
0.84 0.84
0.99 0.98
0.86 0.86
30-50
51-80
M
F
M
F
Low calorie
High calorie

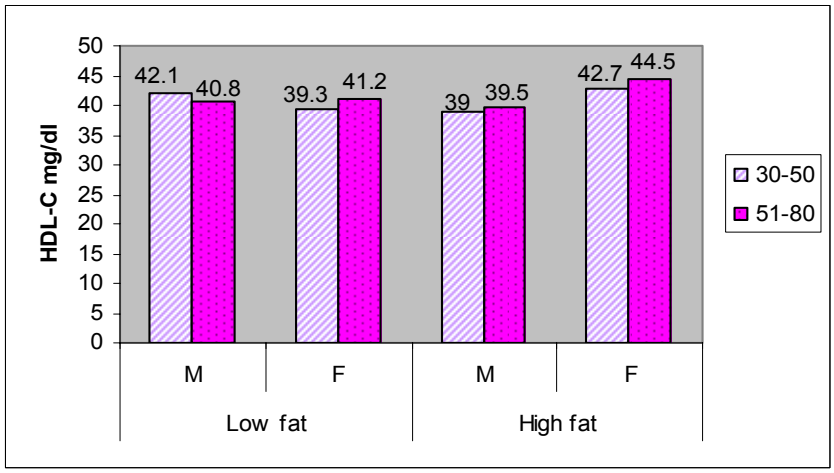
<u>Graph 4.4</u>: Effect of diet (fat) on BP, Serum Lipids and Anthropometric Indices in Hypertensive cases:

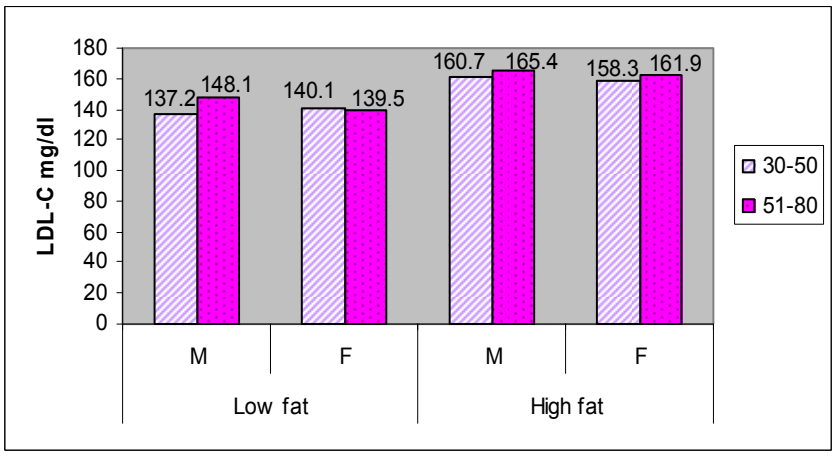


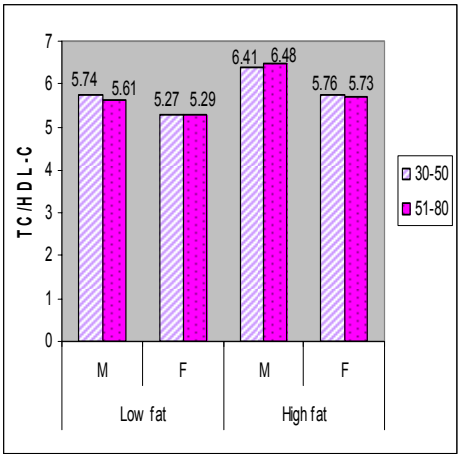


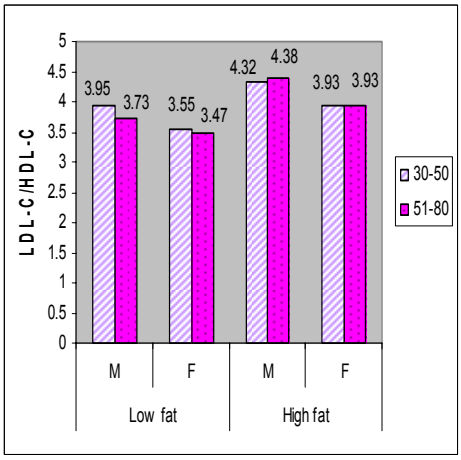


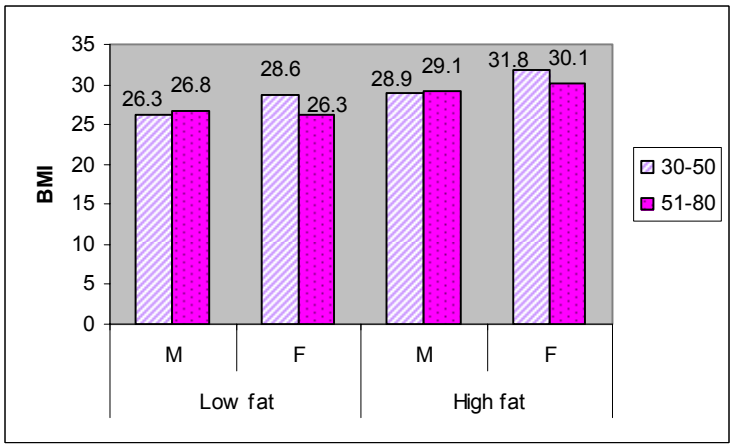

TG mg/dl
250
200
150
100
50
0
135.1
177.2
140.9
157.8
196.8
200.9
159
169.8
M
F
M
F
Low fat
High fat
30-50
51-80

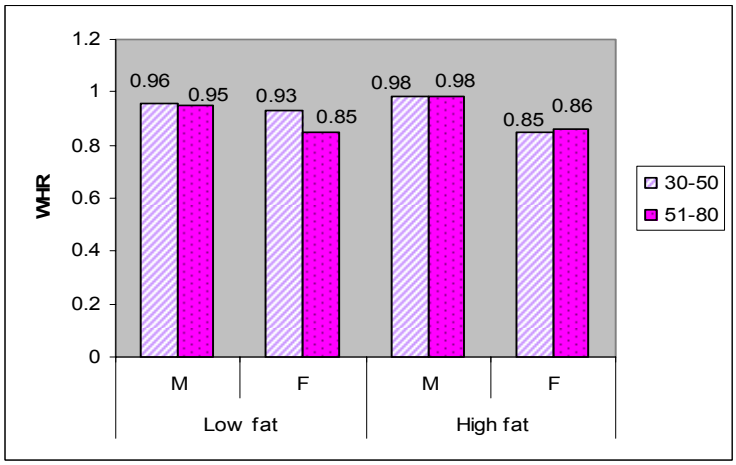

HDL-C mg/dl
50
45
40
35
30
25
20
15
10
5
0
42.1
40.8
39.3
41.2
39
39.5
42.7
44.5
M
F
M
F
Low fat
High fat
30-50
51-80


LDL-C mg/dl
180
160
140
120
100
80
60
40
20
0
137.2
148.1
140.1
139.5
160.7
165.4
158.3
161.9
M
F
M
F
Low fat
High fat
30-50
51-80









WHR also an anthropometric index did not increase but remained nearly alike in high calorie consuming normotensive and hypertensive subjects in both

the age groups and genders when compared to their individual low calorie consuming subjects. The values of WHR in hypertensive subjects consuming high calorie diet in the two age groups were 0.99 & 0.98 in males and 0.86 & 0.86 in females while in low calorie consuming control group the WHR values remained 0.94 & 0.95 in males and 0.80 & 0.84 in females. These differences in WHR between the two diet groups in both genders were outstandingly significant (P<0.001) in 30-50 years age group while it was highly significant (P<0.01) in 51-80 years age group.

Table 6.5: Effect of Diet on BP, Serum Lipids, BMI and WHR in Normotensive & Hypertensive cases

Age Group	Diet	G	N	SBP mmHg	DBP mmHg	TC mg/dl	TG mg/dl	HDL-C mg/dl	LDL-C mg/dl	TC/HDL-C	LDL-C/HDL-C	BMI	WHR
30-50	Control Low Calorie (A_1)	M	59	116.2 ±0.95	73.49 ±0.47	171.9 ±3.4	106.9 ±5.4	40.49 ±1.2	110.0 ±3.5	4.44 ±0.15	2.88 ±0.13	25.40 ±0.40	0.94 ±0.01
		F	60	115.7 ±0.57	70.67 ±0.28	168.8 ±2.6	88.8 ±4.3	42.70 ±1.7	108.4 ±3.2	4.35 ±0.19	2.90 ±0.17	24.25 ±0.58	0.80 ±0.007
	HTsive High Calorie (C_5)	M	96	152.1 ±1.5	96.1 ±1.2	245.0 ±5.7	207.7 ±8.9	38.7 ±0.96	164.8 ±5.6	6.62 ±0.19	4.46 ±0.17	29.25 ±0.58	0.99 ±0.009
		F	112	148.3 ±1.3	94.7 ±1.2	232.4 ±3.6	179.8 ±6.8	42.9 ±1.2	153.6 ±3.8	5.76 ±0.15	3.84 ±0.13	28.49 ±0.49	0.86 ±0.006
Above 50	Control Low Calorie (B_1)	M	37	119.0 ±0.69	75.3 ±0.5	174.8 ±4.5	110.3 ±8.2	41.5 ±2.0	111.2 ±4.4	4.50 ±0.21	2.94 ±0.19	24.25 ±0.58	0.80 ±0.01
		F	32	118.0 ±0.77	74.48 ±0.58	172.8 ±3.0	86.4 ±6.2	43.22 ±1.6	112.2 ±2.7	4.13 ±0.14	2.71 ±0.12	24.78 ±0.52	0.84 ±0.01
	HTsive High Calorie (D_5)	M	126	156.1 ±1.6	101.7 ±1.4	250.6 ±3.9	210.3 ±7.2	39.5 ±0.84	169.0 ±3.9	6.61 ±0.16	4.47 ±0.14	27.26 ±0.39	0.98 ±0.006
		F	160	152.2 ±1.3	98.7 ±1.1	241.5 ±3.5	181.0 ±7.1	44.4 ±0.85	160.9 ±4.2	5.77 ±0.15	3.91 ±0.15	28.99 ±0.45	0.86 ±0.005

Values are Mean ± S.E.

Table 6.5a: Statistical Analysis of Table 6.5

COMPARISON	SBP mmHg	DBP mmHg	TC mg/dl	TG mg/dl	HDL-C mg/dl	LDL-C mg/dl	TC/HDL-C	LDL-C/HDL-C	BMI kg/m^2	WHR
A_1M vs C_5M	P < 0.001	P < 0.001	P < 0.001	P < 0.001	NS	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001
A_1F vs C_5F	P < 0.001	P < 0.001	P < 0.001	P < 0.001	NS	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001
B_1M vs D_5M	P < 0.001	P < 0.001	P < 0.001	P < 0.001	NS	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.01
B_1F vs D_5F	P < 0.001	P < 0.001	P < 0.001	P < 0.001	NS	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.01

An intragroup comparison of normotensive subjects and hypertensive patients consuming high calorie diet showed a similar trend of increase with age in all the parameters except HDL-C in normotensive subjects while atherogenic ratios and anthropometric indices in hypertensive patients in both the sexes. In normotensive subjects BP and TG exhibited significance while in hypertensive subjects, along with BP, TC also showed significance. In relation to male and female, the females pointed out a lower BP, serum lipids, atherogenic ratios and anthropometric indices excluding HDL-C and BMI in both the age groups of normotensive subjects as well as hypertensive patients consuming high calorie diet than those of males. In the hypertensive patients, all the parameters while in normotensive subjects only BP, TG and the anthropometric indices exhibited significance for the difference between male and female of the two age groups.

(b) **Fat**: The normotensive and hypertensive subjects were also regrouped according to their amount of fat intake per day within the two age groups. In high fat consuming hypertensive and normotensive group the BPs exhibited an increase but huge significance ($P<0.01$) was seen in only hypertensive subjects. The BPs in the two age groups were 148.2/96.3 & 150.2/98.9 in males and 143.5/94.7 & 147/96.4 mmHg in females of high fat consuming hypertensive group while the BPs in the low fat consuming control group were 116.3/73.33 & 118.5/75.7 mmHg in males and 118.3/71.54 & 118.6 75.7 in females respectively. The difference in BPs between high fat and low fat groups were tremendously significant ($P<0.001$).

TC & TG concentrations illustrated a significant increase in both hypertensive and normotensive high fat consuming group when compared to their relevant low fat consuming groups. In the two age groups of hypertensive subjects consuming high fat, TC concentration were 239.1 & 245.1 mg% in males and 232.8 & 240.4 mg% in females while in low fat consuming control group the same were 167.8 & 174.8 mg% and 167.2 & 167.2 mg% in females respectively. TG concentration in high fat consuming hypertensive subjects were 196.8 & 200.9 mg% in males and 159.0 & 169.8 mg% in female while the same in low fat control group were 109.3 & 99.5 mg% in males and 76.8 & 70.9 mg% in females respectively. The differences in TC & TG concentrations in both groups were exceptionally significant in both the two genders and age groups ($P<0.001$).

HDL-C concentration increased in high fat consuming hypertensive and normotensive subjects except in the males of hypertensive groups in both age groups when compared to their respective low fat consuming hypertensive and normotensive subjects. This rise and fall of HDL-C concentration was insignificant. In high fat consuming hypertensive subjects the HDL-C conc in both age group were 39.01 & 39.5 mg% in males and 42.7 & 44.5 mg% in females while HDL-C conc in low fat consuming normotensive subjects were 40.25 & 39.2 mg% in males and 42.3 & 39.3 mg% in females respectively. This difference of

HDL-C conc between the two diet groups remained insignificant in both genders and age groups.

Table 6.6 : Effect of Diet on BP, Serum Lipids, BMI and WHR in Normotensive & Hypertensive cases

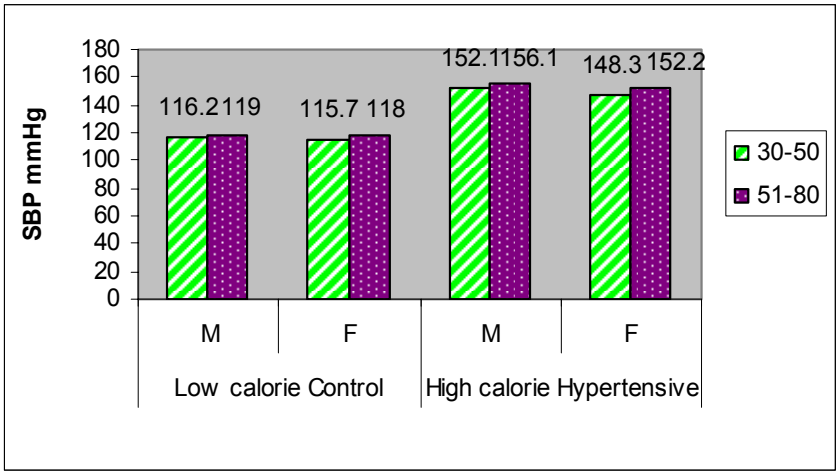
Age Group	Diet	G	N	SBP mmHg	DBP mmHg	TC mg/dl	TG mg/dl	HDL-C mg/dl	LDL-C mg/dl	TC/HDL-C	LDL-C/HDL-C	BMI	WHR
30-50	Control Low Fat (A_3)	M	12	116.3 ±1.8	73.33 ±1.4	167.8 ±5.7	109.3 ±13.0	40.25 ±2.5	105.7 ±7.1	4.38 ±0.33	2.83 ±0.33	24.25 ±0.97	0.98 ±0.01
		F	13	118.3 ±0.98	71.54 ±2.6	167.2 ±6.7	76.8 ±7.5	42.3 ±1.6	109.5 ±6.6	4.01 ±0.21	2.64 ±0.19	26.31 ±1.2	0.80 ±0.01
	HTsive High Fat (C_7)	M	134	148.2 ±1.5	96.3 ±1.0	239.1 ±4.4	196.8 ±7.5	39.01 ±0.8	160.7 ±4.3	6.41 ±0.16	4.32 ±0.14	28.91 ±0.47	0.98 ±0.007
		F	137	143.5 ±1.1	94.7 ±0.87	232.8 ±3.3	159.0 ±6.3	42.7 ±0.96	158.3 ±3.4	5.76 ±0.15	3.93 ±0.11	31.8 ±0.46	0.85 ±0.005
Above 50	Control Low Fat (B_3)	M	12	118.5 ±1.8	75.7 ±4.3	174.8 ±8.5	94.5 ±11.0	39.2 ±1.8	116.6 ±10	4.63 ±0.40	3.13 ±0.38	23.75 ±1.1	0.99 ±0.02
		F	13	118.6 ±1.7	73.8 ±3.5	167.2 ±9.3	70.9 ±10.0	39.3 ±1.6	113.7 ±7.8	4.32 ±0.28	2.95 ±0.24	21.46 ±1.0	0.86 ±0.01
	HTsive High Fat (D_7)	M	187	150.2 ±1.0	98.9 ±0.8	245.1 ±3.8	200.9 ±6.3	39.5 ±0.71	165.4 ±3.6	6.48 ±0.14	4.38 ±0.12	29.17 ±0.45	0.98 ±0.005
		F	110	147.0 ±1.0	96.4 ±0.73	240.4 ±3.1	169.8 ±6.1	44.5 ±0.74	161.9 ±3.5	5.73 ±0.13	3.93 ±0.13	30.13 ±0.37	0.86 ±0.004

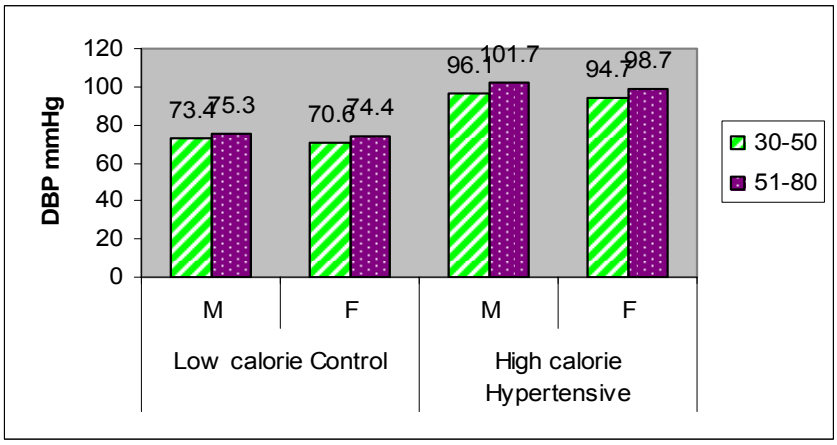
Values are Mean ± S.E.

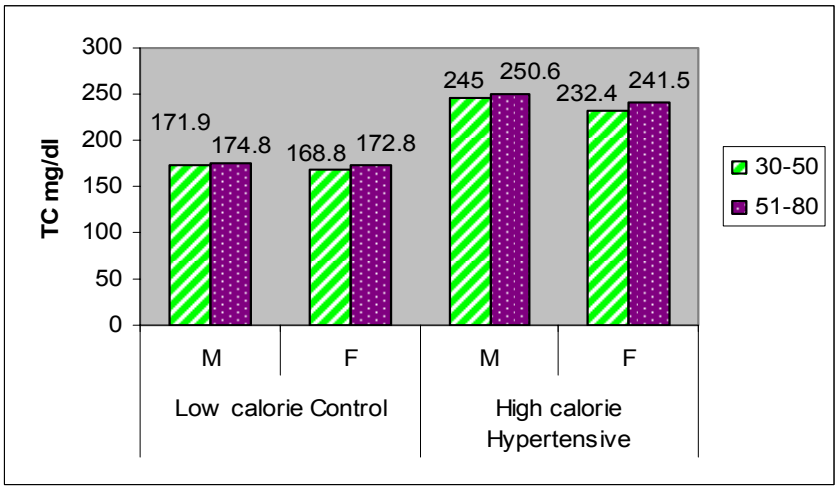
Table 6.6a: Statistical Analysis of Table 6.6

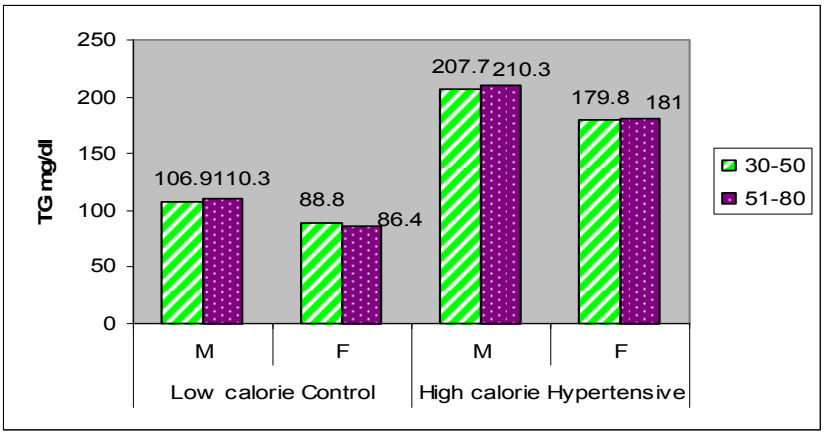
COMPARISON	SBP mmHg	DBP mmHg	TC mg/dl	TG mg/dl	HDL-C mg/dl	LDL-C mg/dl	TC/HDL-C	LDL-C/HDL-C	BMI kg/m^2	WHR
A_3M vs C_7M	P < 0.001	P < 0.001	P < 0.001	P < 0.001	NS	P < 0.001	P < 0.001	P < 0.001	P < 0.001	NS
A_3F vs C_7F	P < 0.001	P < 0.001	P < 0.001	P < 0.001	NS	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001
B_3M vs D_7M	P < 0.001	P < 0.001	P < 0.001	P < 0.001	NS	P < 0.001	P < 0.001	P < 0.001	P < 0.001	NS
B_3F vs D_7F	P < 0.001	P < 0.001	P < 0.001	P < 0.001	NS	P < 0.001	P < 0.001	P < 0.001	P < 0.001	NS

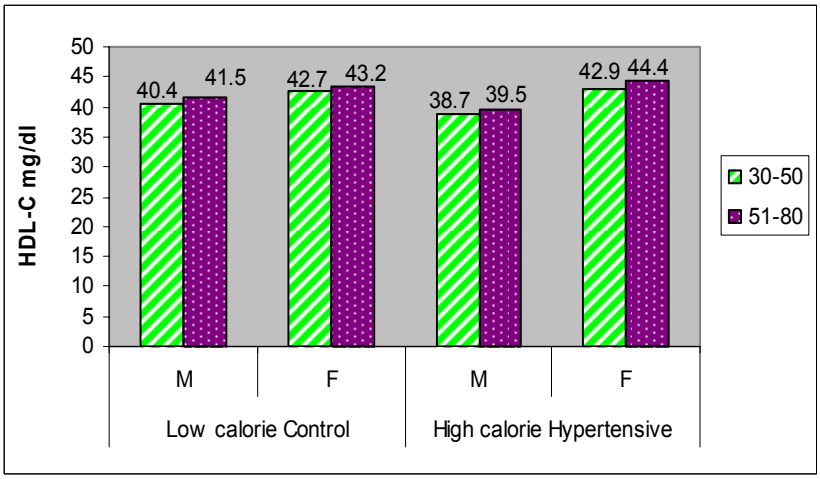
<u>Graph 4.5</u>: Effect of diet (calorie) on BP, Serum Lipids, BMI and WHR in Normotensive and Hypertensive cases:

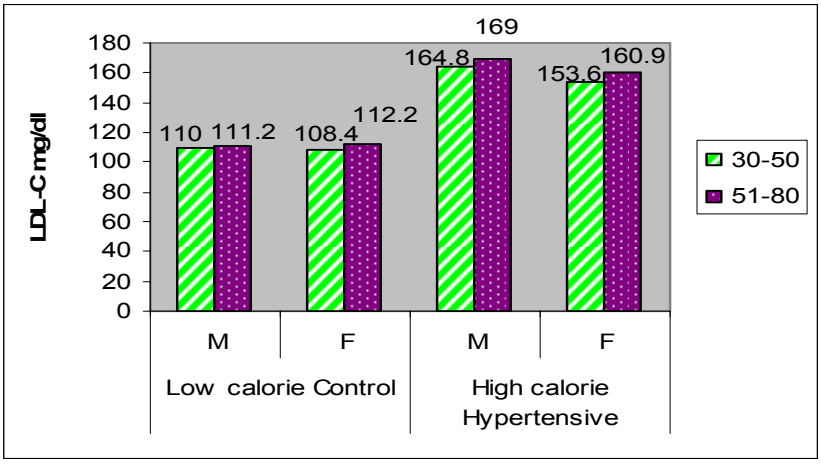


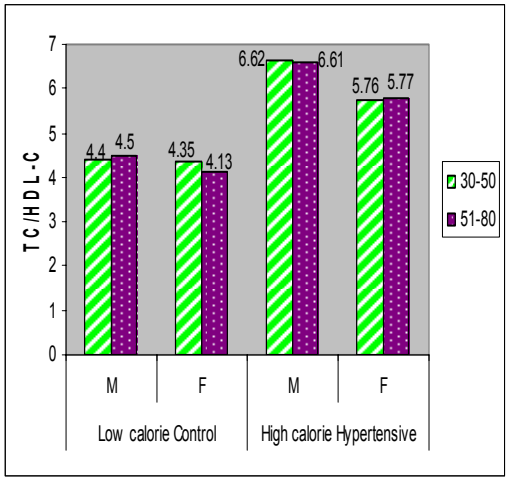


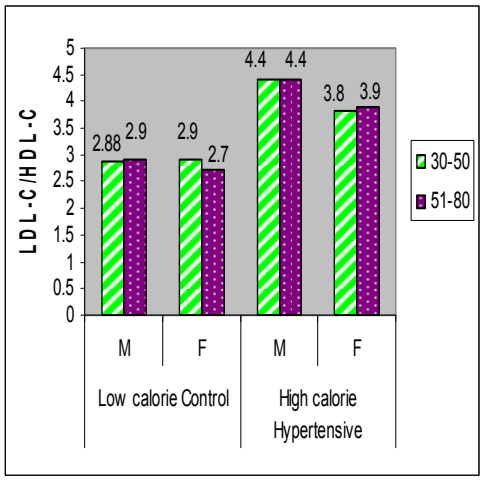


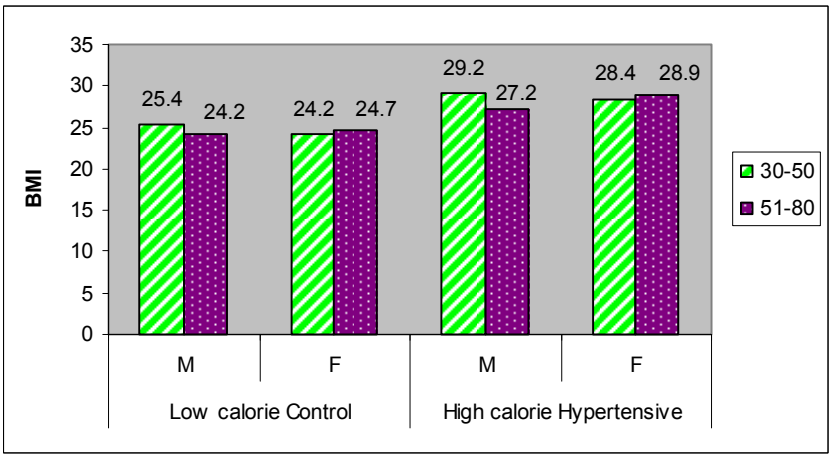

250
200
150
100
50
0
TG mg/dl
106.9
110.3
88.8
86.4
207.7
210.3
179.8
181
30-50
51-80
M
F
M
F
Low calorie Control
High calorie Hypertensive

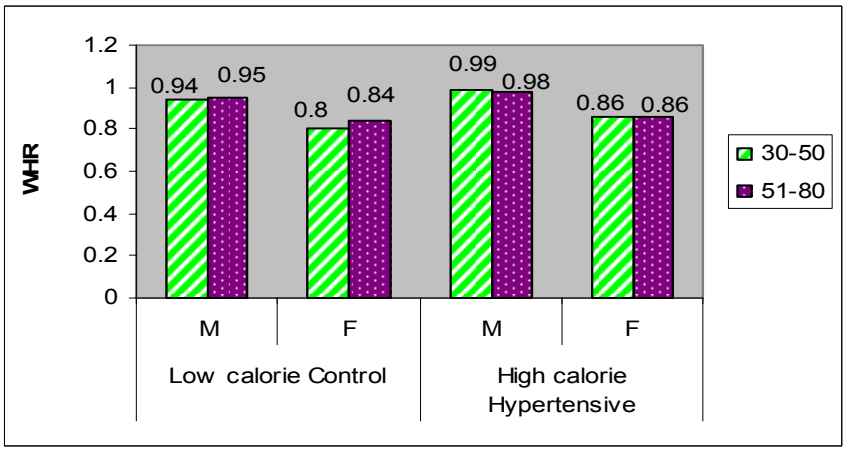

50
45
40
35
30
25
20
15
10
5
0
HDL-C mg/dl
40.4
41.5
42.7
43.2
38.7
39.5
42.9
44.4
30-50
51-80
M
F
M
F
Low calorie Control
High calorie Hypertensive


180
160
140
120
100
80
60
40
20
0
LDL-C mg/dl
110
111.2
108.4
112.2
164.8
169
153.6
160.9
30-50
51-80
M
F
M
F
Low calorie Control
High calorie
Hypertensive

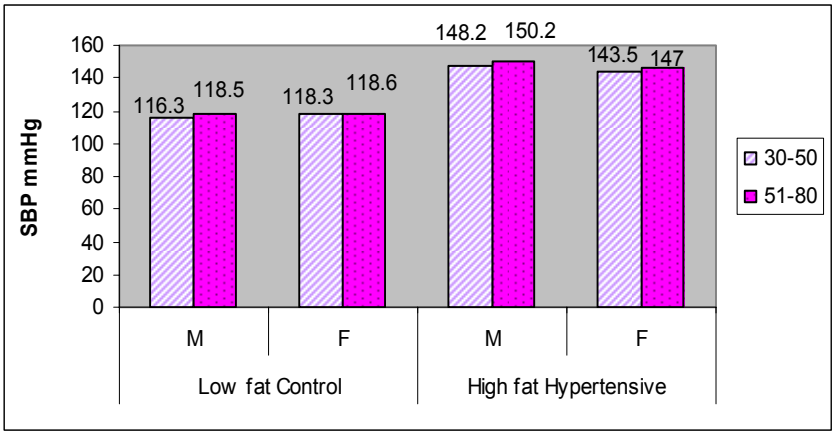

TC/HDL-C
7
6
5
4
3
2
1
0
4.4
4.5
4.35
4.13
6.62
6.61
5.76
5.77
M
F
M
F
Low calorie Control
High calorie Hypertensive
30-50
51-80

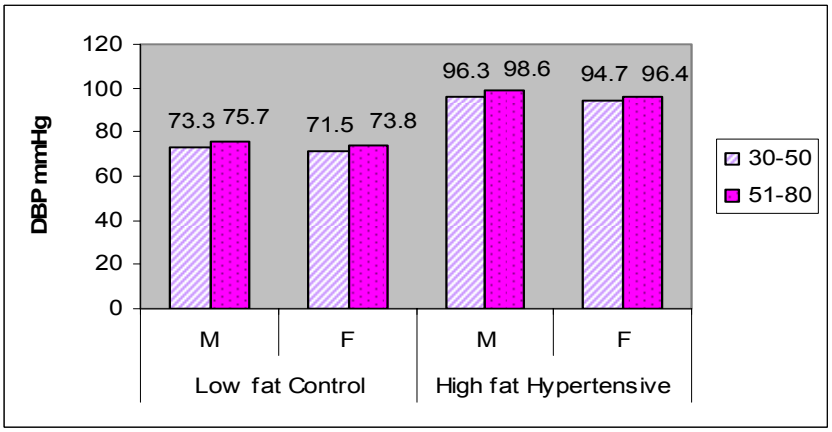

LDL-C/HDL-C
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
2.88
2.9
2.9
2.7
4.4
4.4
3.8
3.9
M
F
M
F
Low calorie Control
High calorie Hypertensive
30-50
51-80

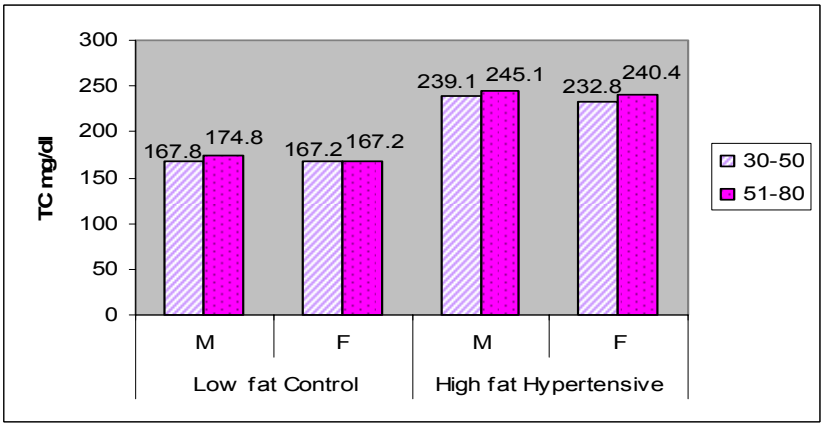

BMI
35
30
25
20
15
10
5
0
25.4
24.2
24.2
24.7
29.2
27.2
28.4
28.9
M
F
M
F
Low calorie Control
High calorie Hypertensive
30-50
51-80

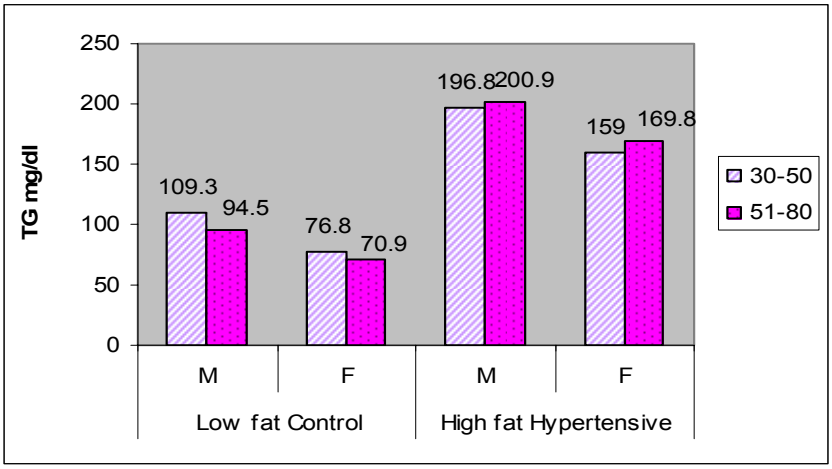

WHR
1.2
1
0.8
0.6
0.4
0.2
0
0.94
0.95
0.8
0.84
0.99
0.98
0.86
0.86
M
F
M
F
Low calorie Control
High calorie Hypertensive
30-50
51-80

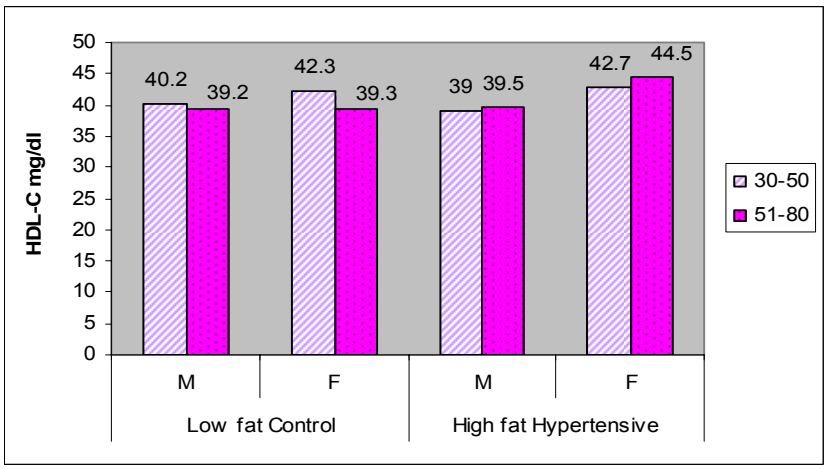
<u>Graph 4.6</u>: Effect of diet (fat) on BP, Serum Lipids, BMI and WHR in Normotensive and Hypertensive cases:

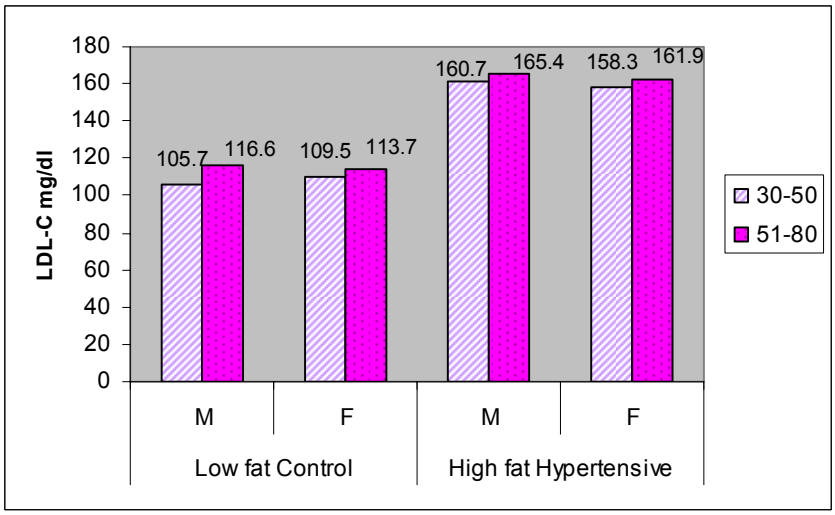


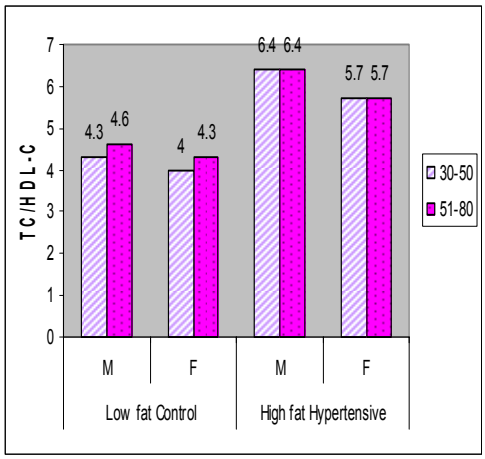


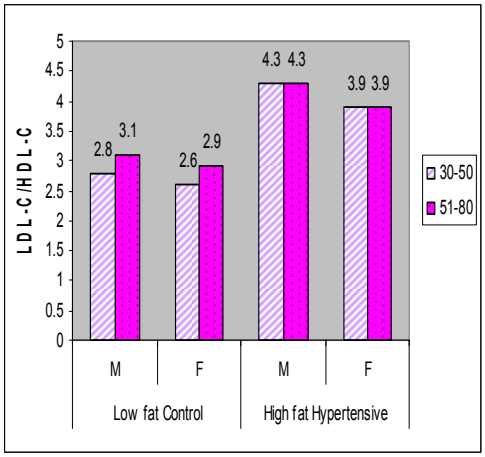


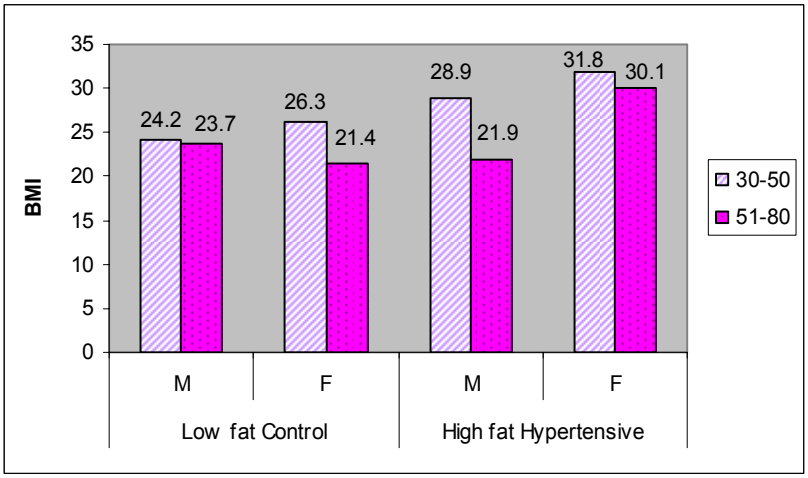

TG mg/dl
250
200
150
100
50
0
109.3
94.5
76.8
70.9
196.8
200.9
159
169.8
M
F
M
F
Low fat Control
High fat Hypertensive
30-50
51-80

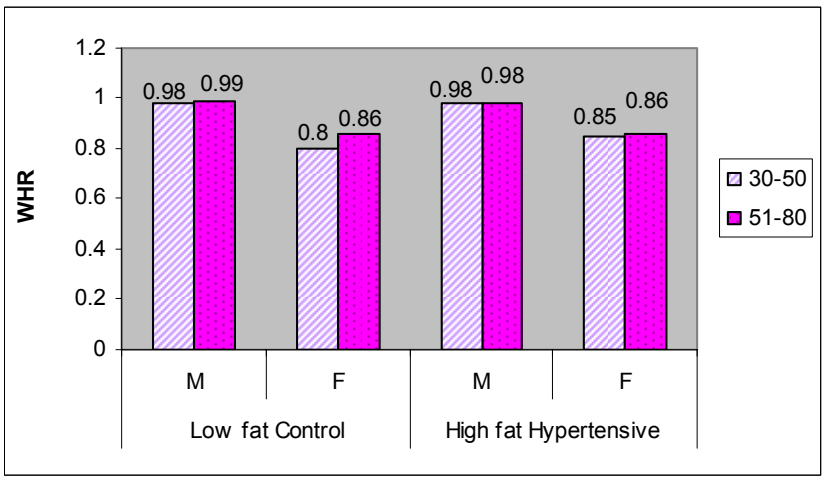

HDL-C mg/dl
50
45
40
35
30
25
20
15
10
5
0
40.2
39.2
42.3
39.3
39
39.5
42.7
44.5
M
F
M
F
Low fat Control
High fat Hypertensive
30-50
51-80


LDL-C mg/dl
180
160
140
120
100
80
60
40
20
0
105.7
116.6
109.5
113.7
160.7
165.4
158.3
161.9
M
F
M
F
Low fat Control
High fat Hypertensive
30-50
51-80


TC/HDL-C
7
6
5
4
3
2
1
0
4.3 4.6
4 4.3
6.4 6.4
5.7 5.7
M F M F
Low fat Control
High fat Hypertensive
30-50
51-80


LDL-C/HDL-C
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
2.8 3.1
2.6 2.9
4.3 4.3
3.9 3.9
M F M F
Low fat Control
High fat Hypertensive
30-50
51-80


BMI
35
30
25
20
15
10
5
0
24.2 23.7
26.3 21.4
28.9 21.9
31.8 30.1
M F M F
Low fat Control
High fat Hypertensive
30-50
51-80


WHR
1.2
1
0.8
0.6
0.4
0.2
0
0.98 0.99
0.8 0.86
0.98 0.98
0.85 0.86
M F M F
Low fat Control
High fat Hypertensive
30-50
51-80

LDL-C concentration also showed an increase in both hypertensive and normotensive high fat consuming subjects but in hypertensive only this rise was highly significant ($P<0.01$) when comparison was done with reverence to their low fat consuming subjects. Also, the LDL-C concentration in high fat consuming hypertensive subjects was much higher than those observed in low fat consuming normotensive subjects and exceedingly significant ($P<0.001$).

The atherogenic ratios exhibited a pattern similar to LDL-C concentration showing an increase in both hypertensive and normotensive high fat consuming subjects but no significance was seen in normotensive subjects. TC/HDL-C ratio in both age groups of hypertensive subjects with high fat diet were 6.41 & 6.48 in males and 5.76 & 5.73 in females while the low fat diet of normotensive subjects exhibited 4.38 & 4.63 in males and 4.01 & 4.32 in females respectively. Also the ratio of LDL-C/HDL-C in high fat diet of hypertensive subjects illustrated values likes 4.32 & 4.38 in males and 3.93 & 3.73 in females while the same in low fat diet of normotensive individuals were 2.83 & 3.13 in males and 2.64 & 2.95 in females respectively. This distinction of these atherogenic ratios in both high fat and low fat consuming hypertensive and normotensive volunteers were extremely significant ($P<0.001$) in the two age groups and genders.

In the anthropometric indices, BMI demonstrated a trend like atherogenic ratios wherein increase in high fat consuming hypertensive as well as normotensive was noticed but highly significant ($P<0.01$) rise was seen in only hypertensive subjects. The value of BMI in high fat consuming hypertensive volunteers were 28.91 & 29.17 kg/m^2 in males and 31.8 & 30.13 kg/m^2 in females while the same in low fat consuming normotensive individuals were 24.25 & 2.75 kg/m^2 in males and 26.31 & 21.46 kg/m^2 in females respectively. This diversity of BMI index in both diet groups was tremendously significant ($P<0.001$) in the age groups and genders.

In case of WHR, also an anthropometric index, an insignificant decrease in high fat consuming normotensive subjects and an insignificant increase in hypertensive volunteers were observed when comparison was done with respect to their low fat groups. Also WHR values in high fat consuming hypertensive subjects were nearly alike in low fat consuming normotensive volunteers, thus no significance was observed.

An intragroup comparison of normotensive subjects and hypertensive patients consuming high fat diet illustrated a specific manner of increase with age in BP, serum lipids, atherogenic ratios and anthropometric indices in both the sexes except BMI in normotensive subjects while atherogenic ratios and anthropometric indices in hypertensive patients. A significant difference was seen with BP in normotensive subjects while in hypertensive patients, significance was

prevalent with BP, TC, HDL-C and the atherogenic ratios in the females. Furthermore, in male to female comparison, females demonstrated lower BP, serum lipids, atherogenic ratios and anthropometric indices excluding HDL-C and BMI in both the age groups of normotensive and hypertensive subjects consuming high fat diet than those of males. In the hypertensive patients, all the parameters excluding TC while in normotensive subjects only BP, TC, TG and WHR exhibited significance for the difference between male and female in the age groups.

5. Effect of Tobacco Consumption on BP, Serum Lipids and Anthropometric indices:

Smoking and tobacco habits play an important role in precipitation of HT and also have a more firmly established pernicious influence on cardiovascular mortality and morbidity. To understand the same, normotensive and hypertensive subjects were regrouped into two subgroups i.e. tobacco consumption and tobacco nonconsumption within the age groups: 30-50 years & 51-80 years.

The tobacco consuming normotensive volunteers exhibited an increase in BP in both genders with regard to their age groups when compared to tobacco nonconsuming normotensive volunteers, while in hypertensive subjects consuming tobacco, an increase like normotensive volunteers was observed in BP in both genders in30-50 years age group while a decrease was seen in 51-80 years age group in both genders. This rise and fall in BP values were extremely significant ($P<0.001$) in hypertensive subjects whereas normotensive volunteers showed significance in only 30-50 years age group in both genders. Tobacco consuming hypertensives demonstrated 147.4/96.1 & 144/92.1 BP values in males and 143.8/95.1 & 142.7/91.3 in females in both age groups while tobacco nonconsuming normotensive showed BP values like 115.8/74.7 & 118.6/78.0 in males and 112.4/72.4 & 117.1/75.6 in females correspondingly. This dissimilarity of BP values in both tobacco subgroups was exceedingly significant ($P<0.001$) in both genders with respect to their age groups.

TC & TG concentration exhibited a similar trend in relation to tobacco. Tobacco consuming normotensive and hypertensive subjects showed a highly significant increase ($P<0.01$) of both TC & TG concentration in men and women of 30-50 years age group while an insignificant decrease was seen in case of 51-80 years age group in both men and women when compared to their individual nonconsuming tobacco groups. TC concentration of tobacco consuming

hypertensive subjects in the two age groups were 248.9 & 243.1 mg% in males and 238.3 & 236.3 mg% in females while the same in non consuming

Table 7.1: Effect of Tobacco on BP, Serum Lipids, BMI and WHR in Normotensive cases

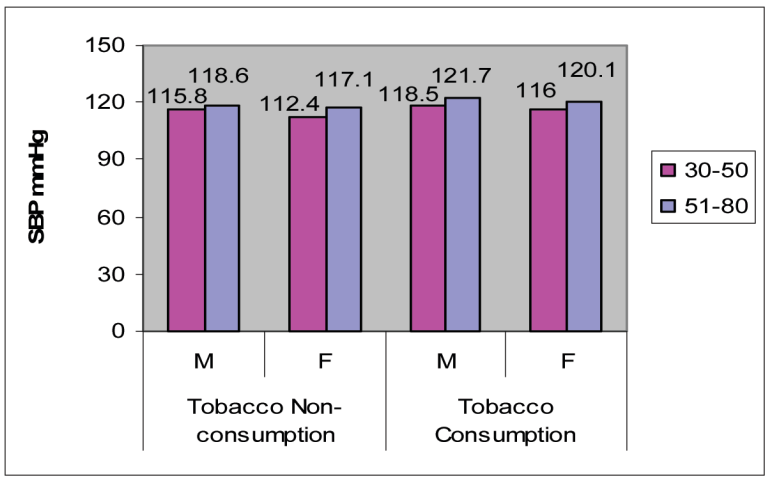
Age Group	Tobacco	G	N	SBP mmHg	DBP mmHg	TC mg/dl	TG mg/dl	HDL-C mg/dl	LDL-C mg/dl	TC/HDL-C	LDL-C/HDL-C	BMI	WHR
30-50	Tobacco Non-Consumption (A_5)	M	79	115.8 ±0.89	74.7 ±1.5	162.8 ±3.8	98.4 ±4.3	46.1 ±1.5	97.0 ±4.0	3.79 ±0.14	2.34 ±0.14	24.44 ±0.48	0.93 ±0.009
		F	52	112.4 ±0.65	72.4 ±0.3	159.4 ±2.5	93.6 ±2.9	49.2 ±0.97	91.5 ±2.7	3.42 ±0.08	2.01 ±0.07	25.30 ±0.32	0.82 ±0.006
	Tobacco Consumption (A_6)	M	31	118.5 ±1.3	77.5 ±1.2	180.3 ±4.3	118.1 ±6.7	41.4 ±1.8	115.2 ±4.5	4.66 ±0.29	3.04 ±0.26	23.23 ±0.81	0.93 ±0.01
		F	12	116.0 ±1.4	75.5 ±1.2	176.8 ±6.2	101.3 ±2.3	46.5 ±2.4	110.0 ±7.4	3.93 ±0.29	2.49 ±0.29	25.5 ±1.4	0.81 ±0.01
Above 50	Tobacco Non-Consumption (B_5)	M	151	118.6 ±0.53	78.0 ±0.32	182.3 ±6.0	115.4 ±6.9	41.0 ±1.5	118.1 ±5.8	4.85 ±0.29	3.22 ±0.25	24.17 ±0.78	0.82 ±0.006
		F	41	117.1 ±0.75	75.6 ±0.5	171.1 ±4.5	95.1 ±10.0	48.3 ±1.8	103.8 ±5.0	3.73 ±0.16	2.30 ±0.15	24.61 ±0.46	0.83 ±0.008
	Tobacco Consumption (B_6)	M	21	121.7 ±1.9	80.4 ±1.5	175.4 ±7.2	111.1 ±6.3	44.2 ±2.9	108.9 ±6.5	4.18 ±0.24	2.63 ±0.22	21.14 ±1.0	0.91 ±0.01
		F	12	120.1 ±1.3	79.1 ±1.0	173.1 ±6.6	96.8 ±4.9	50.3 ±1.8	103..4 ±7.2	3.48 ±0.19	2.10 ±0.19	23.42 ±1.2	0.83 ±0.01

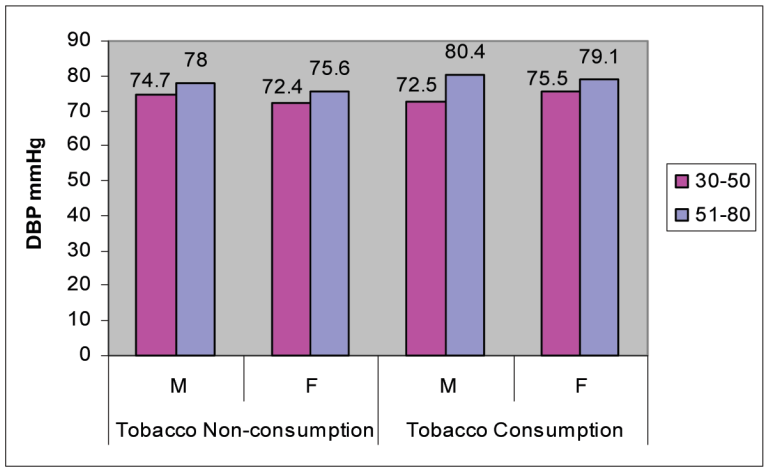
Values are Mean ± S.E.

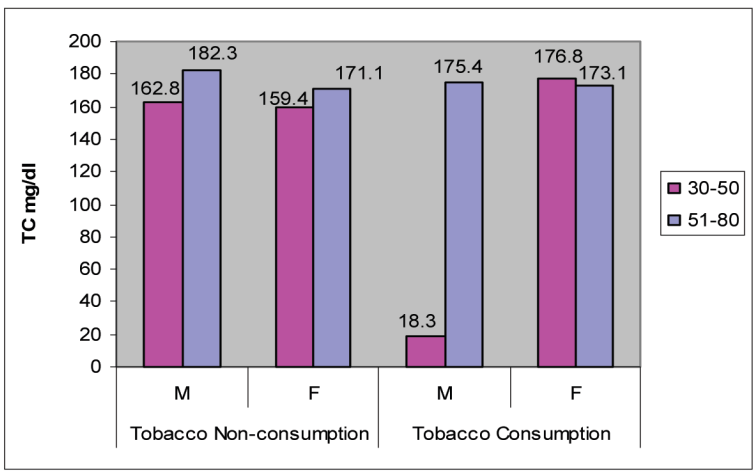
Table 7.1a: Statistical Analysis of Table 7.1

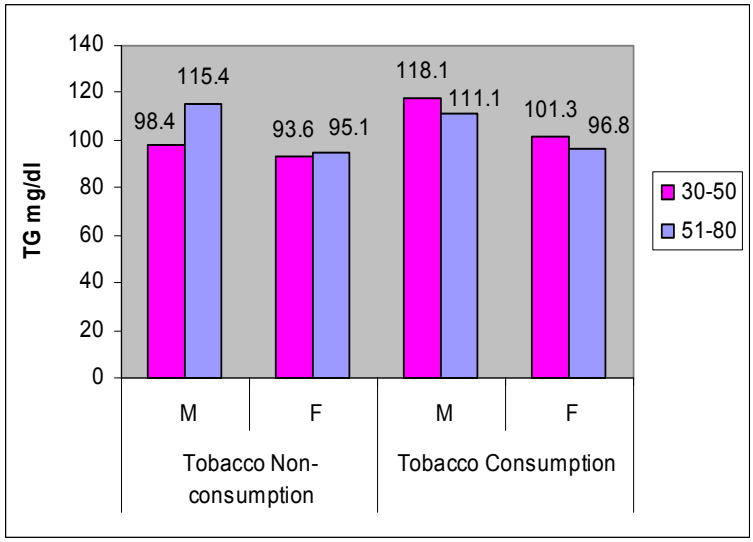
COMPARISON	SBP mmHg	DBP mmHg	TC mg/dl	TG mg/dl	HDL-C mg/dl	LDL-C mg/dl	TC/HDL-C	LDL-C/HDL-C	BMI kg/m^2	WHR
A_5M vs A_6M	P < 0.05	NS	P < 0.001	P < 0.01	P < 0.01	P < 0.001	P < 0.01	P < 0.01	NS	NS
A_5F vs A_6F	P < 0.01	P < 0.01	P < 0.01	P < 0.01	NS	P < 0.01	P < 0.05	P < 0.05	NS	NS
B_5M vs B_6M	NS	NS	NS	NS	NS	NS	NS	NS	P < 0.01	P < 0.001
B_5F vs B_6F	NS	P < 0.005	NS	NS	NS	NS	NS	NS	NS	NS
A_6M vs A_6F	NS	NS	NS	P < 0.01	P < 0.05	NS	P < 0.05	NS	NS	P < 0.001
B_6M vs B_6F	NS	NS	NS	P < 0.05	P < 0.05	NS	P < 0.01	P < 0.05	NS	P < 0.001
A_6M vs B_6M	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
A_6F vs B_6F	P < 0.01	P < 0.01	NS	NS	NS	NS	NS	NS	NS	NS

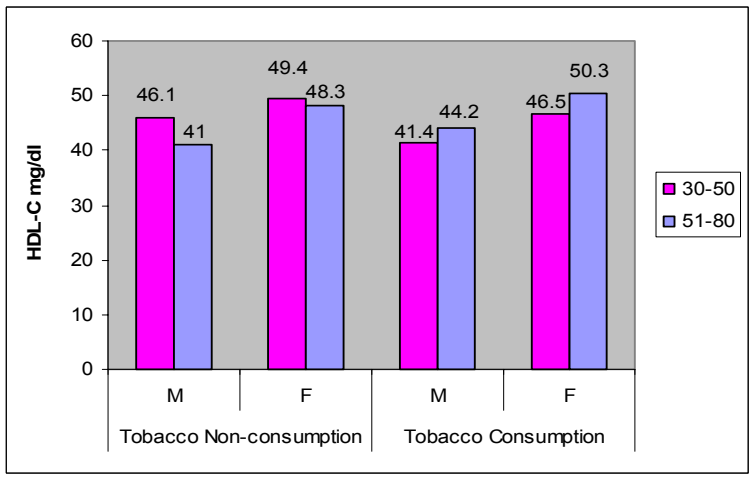
<u>Graph 5.1</u>: Effect of tobacco consumption on BP, Serum Lipids and Anthropometric Indices in Normotensive cases:

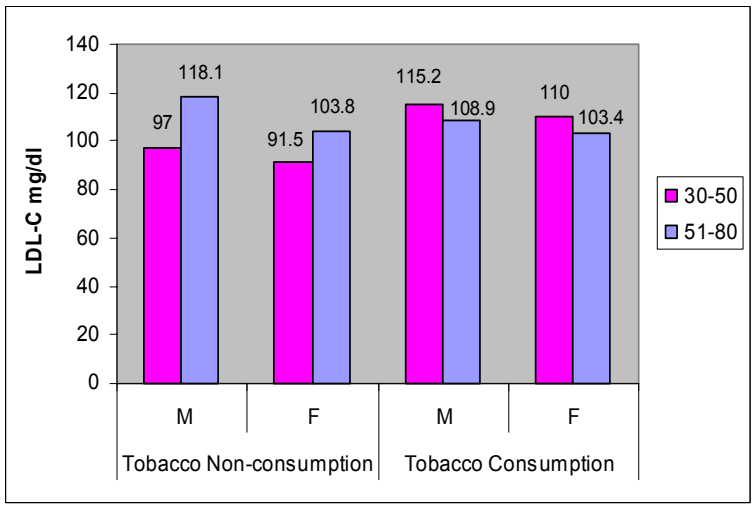


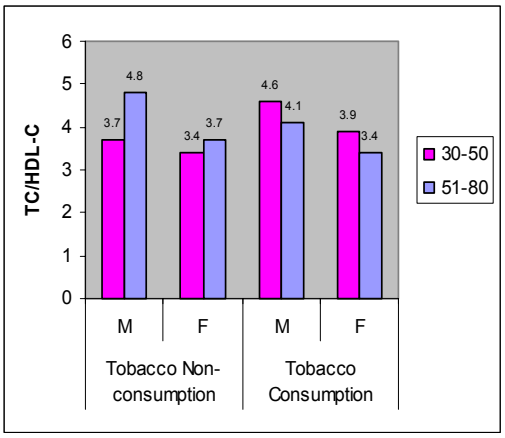


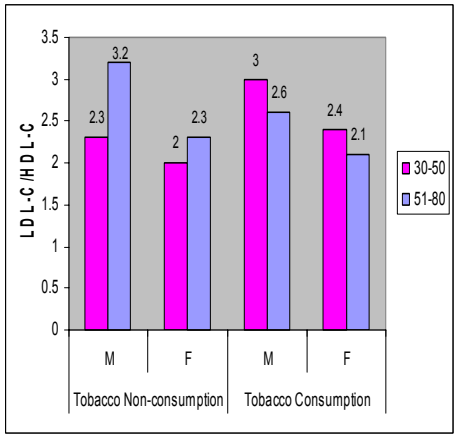


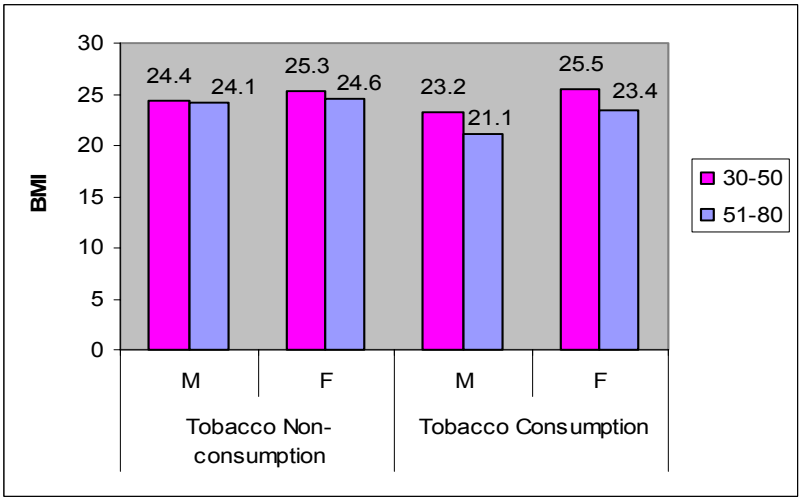

TG mg/dl
140
120
100
80
60
40
20
0
98.4
115.4
93.6
95.1
118.1
111.1
101.3
96.8
M
F
M
F
Tobacco Non-consumption
Tobacco Consumption
30-50
51-80


HDL-C mg/dl
60
50
40
30
20
10
0
46.1
41
49.4
48.3
41.4
44.2
46.5
50.3
M
F
M
F
Tobacco Non-consumption
Tobacco Consumption
30-50
51-80


LDL-C mg/dl
140
120
100
80
60
40
20
0
97
118.1
91.5
103.8
115.2
108.9
110
103.4
M
F
M
F
Tobacco Non-consumption
Tobacco Consumption
30-50
51-80


TC/HDL-C
6
5
4
3
2
1
0
3.7
4.8
3.4
3.7
4.6
4.1
3.9
3.4
M
F
M
F
Tobacco Non-consumption
Tobacco Consumption
30-50
51-80


LDL-C /HDL-C
3.5
3
2.5
2
1.5
1
0.5
0
2.3
3.2
2
2.3
3
2.6
2.4
2.1
M
F
M
F
Tobacco Non-consumption
Tobacco Consumption
30-50
51-80


BMI
30
25
20
15
10
5
0
24.4
24.1
25.3
24.6
23.2
21.1
25.5
23.4
M
F
M
F
Tobacco Non-consumption
Tobacco Consumption
30-50
51-80

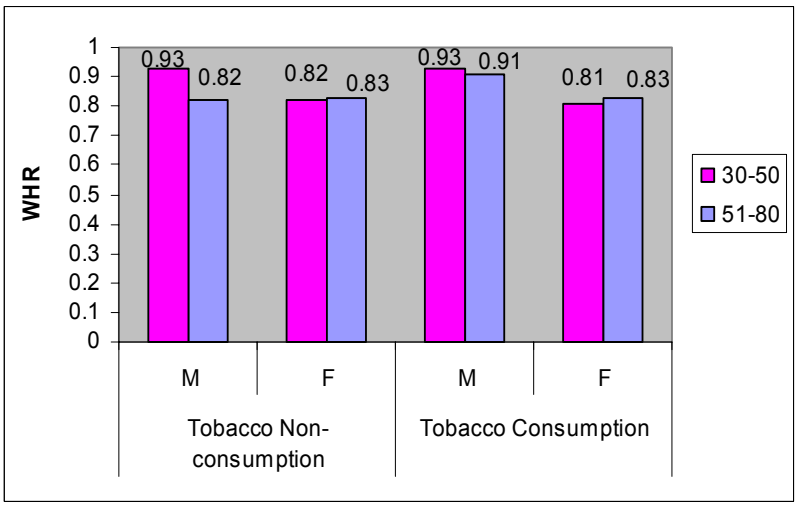

WHR
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0.93
0.82
0.82
0.83
0.93
0.91
0.81
0.83
M
F
M
F
Tobacco Non-consumption
Tobacco Consumption
30-50
51-80

Table 7.2: Effect of Tobacco on BP, Serum Lipids, BMI and WHR in Htsive cases

Age Group	Tobacco	G	N	SBP mmHg	DBP mmHg	TC mg/dl	TG mg/dl	HDL-C mg/dl	LDL-C mg/dl	TC/HDL-C	LDL-C/HDL-C	BMI	WHR
30-50	Tobacco Non-Consumption (C_8)	M	79	136.5 ±2.5	87.3 ±1.4	234.3 ±5.5	185.3 ±8.9	38.7 ±1.3	128.2 ±5.6	6.40 ±0.25	4.35 ±0.22	29.05 ±0.72	1.00 ±0.01
		F	52	134.7 ±1.3	86.8 ±0.9	218.5 ±3.2	155.6 ±7.4	44.4 ±1.2	142.9 ±3.5	5.25 ±0.15	3.47 ±0.13	29.28 ±0.72	0.85 ±0.006
	Tobacco Consumption (C_9)	M	31	147.4 ±1.6	96.1 ±1.4	248.9 ±4.5	206.7 ±6.5	32.36 ±0.79	175.2 ±4.7	8.07 ±0.24	5.75 ±0.23	27.25 ±0.52	0.97 ±0.009
		F	12	143.8 ±1.9	95.1 ±1.6	238.3 ±5.3	186.2 ±7.0	36.11 ±1.9	164.9 ±5.2	6.87 ±0.34	4.79 ±0.30	28.11 ±1.1	0.86 ±0.01
Above 50	Tobacco Non-Consumption (D_8)	M	151	148.4 ±1.5	99.1 ±1.6	244.5 ±3.5	204.1 ±8.0	41.32 ±0.91	162.4 ±3.7	6.22 ±0.17	4.17 ±0.15	27.05 ±0.46	0.98 ±0.008
		F	41	146.0 ±1.4	95.1 ±1.2	239.3 ±4.1	179.2 ±6.9	45.7 ±0.91	157.8 ±4.5	5.53 ±0.16	3.70 ±0.15	28.54 ±0.43	0.87 ±0.006
	Tobacco Consumption (D_9)	M	21	144.0 ±1.5	92.1 ±0.76	243.1 ±5.4	199.2 ±8.5	35.47 ±0.76	167.8 ±5.4	7.1 ±0.19	4.93 ±0.18	26.20 ±0.47	0.97 ±0.006
		F	12	142.7 ±1.9	91.3 ±1.2	236.3 ±7.5	156.2 ±7.9	39.9 ±1.7	165.1 ±8.1	6.43 ±0.35	4.60 ±0.33	27.24 ±0.71	0.86 ±0.01

Values are Mean ± S.E.

Table 7.2: Statistical Analysis of Table 7.2

COMPARISON	SBP mmHg	DBP mmHg	TC mg/dl	TG mg/dl	HDL-C mg/dl	LDL-C mg/dl	TC/HDL-C	LDL-C/HDL-C	BMI kg/m^2	WHR
C_8M vs C_9M	P < 0.001	P < 0.001	P < 0.01	P < 0.05	P < 0.005	P < 0.01	P < 0.001	P < 0.001	P < 0.01	NS
C_8F vs C_9F	P < 0.001	P < 0.001	P < 0.01	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001	NS	NS
D_8M vs D_9M	P < 0.01	P < 0.005	NS	NS	P < 0.001	NS	P < 0.001	P < 0.001	NS	NS
D_8F vs D_9F	P < 0.05	P < 0.01	NS	P < 0.01	P < 0.001	NS	P < 0.01	P < 0.01	P < 0.05	NS
C9M vs C9F	P < 0.05	NS	P < 0.05	P < 0.01	P < 0.05	NS	P < 0.001	P < 0.01	NS	P < 0.001
D9M vs D9F	NS	NS	NS	P < 0.001	P < 0.01	NS	P < 0.05	NS	NS	P < 0.001
C9M vs D9M	P < 0.05	P < 0.01	NS	NS	P < 0.001	NS	P < 0.001	P < 0.001	NS	NS
C9F vs D9F	NS	P < 0.05	NS	P < 0.001	P < 0.05	NS	NS	NS	NS	NS

normotensive counterparts were 162.8 & 182.3 mg% in males and 159.4 & 171.1 mg% in females respectively. The concentration exhibited by TG in tobacco consuming hypertensive were 206.7 & 156.2 mg% in men and 199.2 & 186.8 mg% in women whereas the nonconsuming normotensive volunteers showed

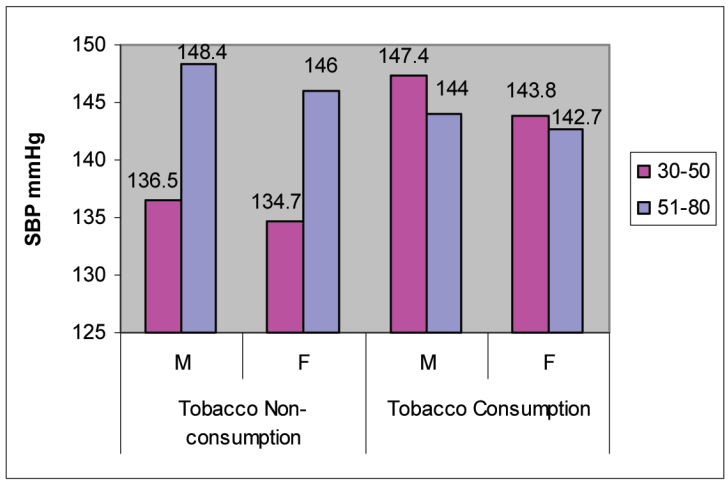
values like 98.4 & 115.4 mg% in men and 93.6 & 95.1 mg% in women. These differences of TC & TG conc in the two subgroups of tobacco were found to be enormously significant (P<0.001) in both the genders and their age groups.

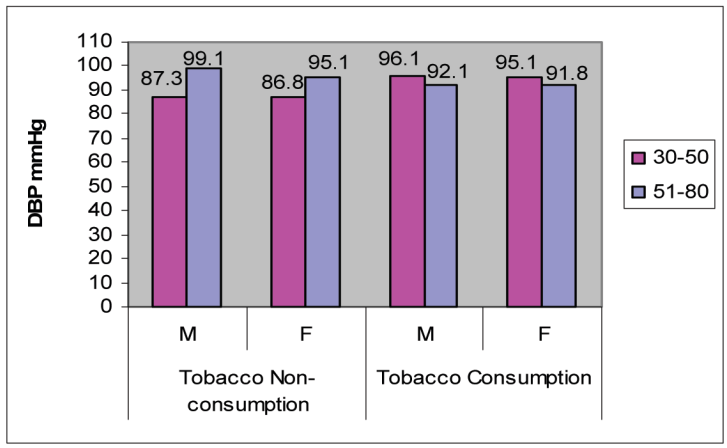
HDL-C concentration illustrated an extremely significant (P<0.001) decrease in tobacco consuming hypertensives in male and female of both age groups while an insignificant increase in 30-50 years age group and a decrease in 51-80 years age group was observed in tobacco consuming normotensives when compared to their respective non consuming counterparts. HDL-C concentration in tobacco consuming hypertensives were 32.36 & 35.47 mg% in males and 36.11 & 39.9 mg% in females while the same in nonconsuming normotensives were 46.1 & 41.0 mg% in males and 49.2 & 48.3 mg% in females in the two age groups respectively. This divergence of HDL-C concentration in the two tobacco subgroups were outstandingly significant (P<0.001).

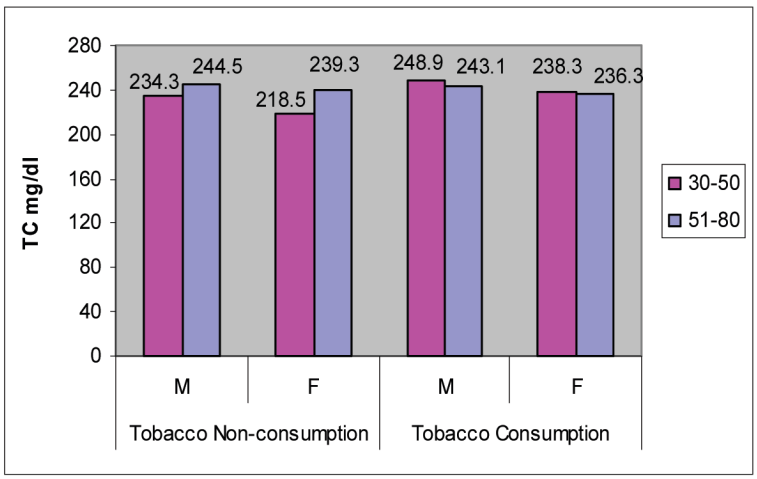
LDL-C concentration of serum lipids demonstrated an increase in both normotensive and hypertensive tobacco consuming volunteers in either of the genders with relation to their age groups except in 51-80 years age group of normotensive subjects. But in these, only 30-50 year subjects in both normotensives and hypertensives displayed significance (P<0.01). LDL-C concentration of tobacco consuming hypertensives in the two age groups were 175.2 & 167.8 mg% in men and 164.9 & 165.1 mg% in women while their tobacco non consuming normotensive counterparts exhibited 97.0 & 118.1 mg% in men and 91.5 & 103.8 mg% in women respectively. This variation in LDL-C concentration among the two subgroups of tobacco was remarkably significant (P<0.001).

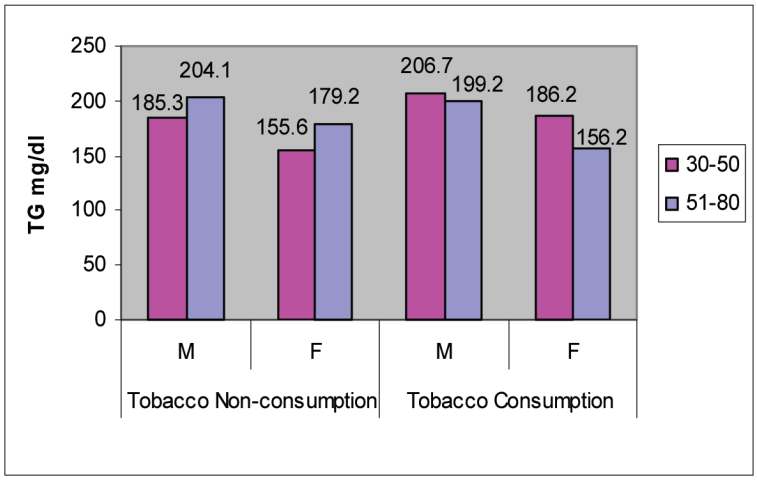
The atherogenic ratios showed a pattern, alike LDL-C concentration wherein a highly significant increase was illustrated with tobacco consuming normotensives and hypertensives in both genders and their relevant age groups but an insignificant decrease was also observed in 51-80 years normotensives when compared to their respective tobacco nonconsuming counterparts. TC/HDL-C exhibited ratios like 8.07 & 7.1 in males and 6.87 & 6.43 in female tobacco consuming hypertensives whereas the same in non consuming normotensives were 3.79 & 4.85 in males and 3.42 & 3.73 in females respectively. Also LDL-C/HDL-C showed 5.75 & 4.93 in men and 4.79 & 4.60 in women hypertensives while non consuming normotensives illustrated 2.34 & 3.22 in men and 2.01 & 2.30 in women correspondingly. The atherogenic ratios in hypertensives was considerably higher than the normotensives in the tobacco subgroups and was found to be exceptionally significant (P<0.001).

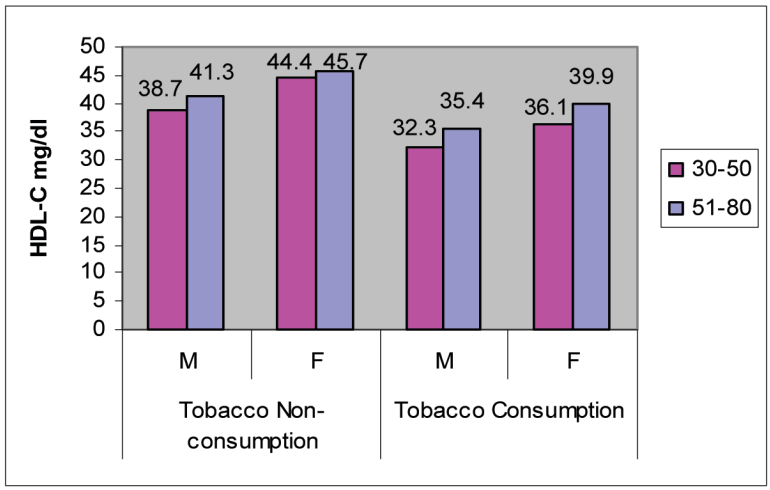
<u>Graph 5.2</u>: Effect of tobacco consumption on BP, Serum Lipids and Anthropometric Indices in Hypertensive cases:

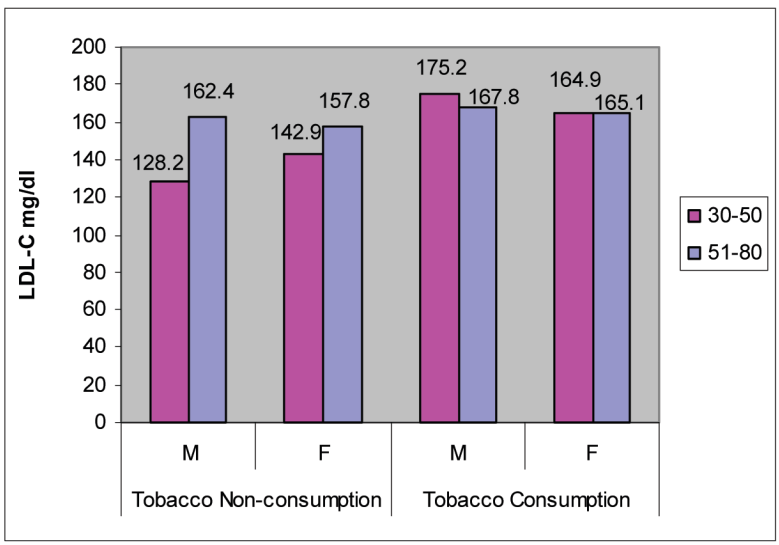


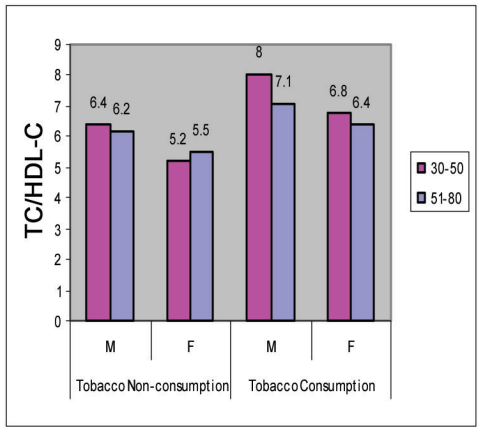





TG mg/dl
250
200
150
100
50
0
185.3
204.1
155.6
179.2
206.7
199.2
186.2
156.2
M
F
M
F
Tobacco Non-consumption
Tobacco Consumption
30-50
51-80


HDL-C mg/dl
50
45
40
35
30
25
20
15
10
5
0
38.7
41.3
44.4
45.7
32.3
35.4
36.1
39.9
M
F
M
F
Tobacco Non-consumption
Tobacco Consumption
30-50
51-80


LDL-C mg/dl
200
180
160
140
120
100
80
60
40
20
0
128.2
162.4
142.9
157.8
175.2
167.8
164.9
165.1
M
F
M
F
Tobacco Non-consumption
Tobacco Consumption
30-50
51-80


TC/HDL-C
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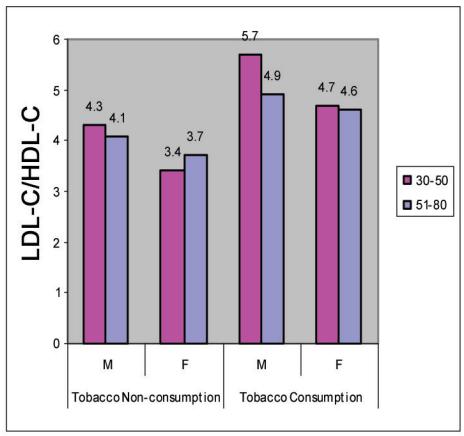
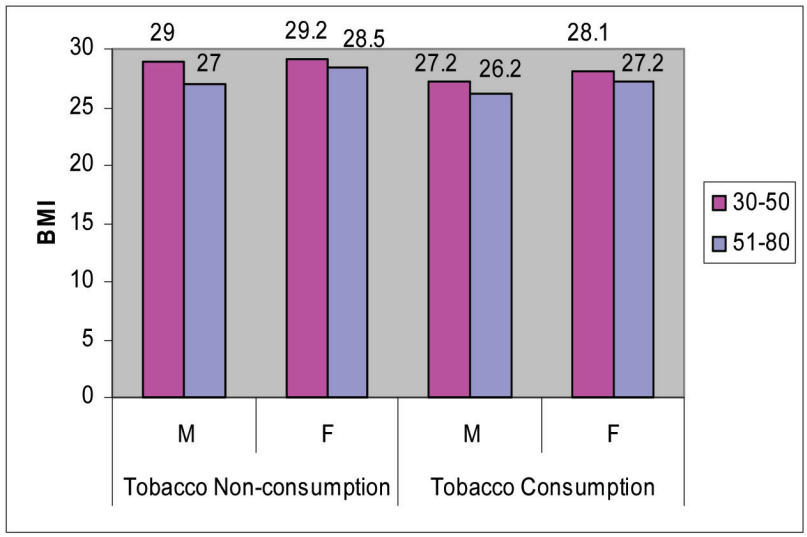
8
7
6
5
4
3
2
1
0
6.4 6.2
5.2 5.5
8 7.1
6.8 6.4
M F M F
Tobacco Non-consumption
Tobacco Consumption
30-50
51-80


LDL-C/HDL-C
6
5
4
3
2
1
0
4.3 4.1
3.4 3.7
5.7 4.9
4.7 4.6
M F M F
Tobacco Non-consumption
Tobacco Consumption
30-50
51-80


BMI
30
25
20
15
10
5
0
29 27
29.2 28.5
27.2 26.2
28.1 27.2
M F M F
Tobacco Non-consumption
Tobacco Consumption
30-50
51-80

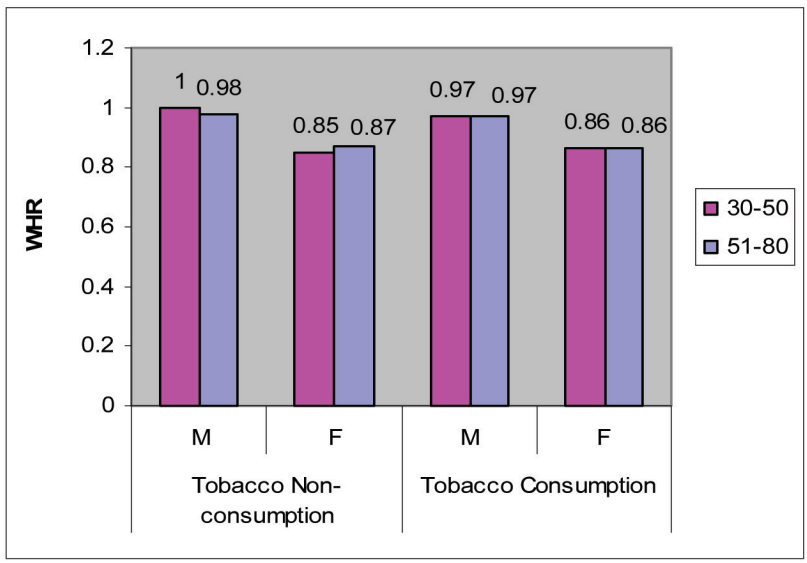

WHR
1.2
1
0.8
0.6
0.4
0.2
0
1 0.98
0.85 0.87
0.97 0.97
0.86 0.86
M F M F
Tobacco Non-consumption
Tobacco Consumption
30-50
51-80

Table 7.3: Effect of Tobacco on BP, Serum Lipids, BMI and WHR in Normotensive & Htsive cases

Age Group	Tobacco	G	N	SBP mmHg	DBP mmHg	TC mg/dl	TG mg/dl	HDL-C mg/dl	LDL-C mg/dl	TC/HDL-C	LDL-C/HDL-C	BMI	WHR
30-50	Tobacco NC Control (A_6)	M	79	115.8 ±0.89	74.7 ±1.5	162.8 ±3.8	98.4 ±4.3	46.1 ±1.5	97.0 ±4.0	3.79 ±0.14	2.34 ±0.14	24.44 ±0.48	0.93 ±0.009
		F	52	112.4 ±0.65	72.4 ±0.3	159.4 ±2.5	93.6 ±2.9	49.2 ±0.97	91.5 ±2.7	3.42 ±0.08	2.01 ±0.07	25.30 ±0.32	0.82 ±0.006
	Tobacco Consump-tion HT (C_6)	M	31	147.4 ±1.6	96.1 ±1.4	248.9 ±4.5	206.7 ±6.5	32.36 ±0.79	175.2 ±4.7	8.07 ±0.24	5.75 ±0.23	27.25 ±0.52	0.97 ±0.009
		F	12	143.8 ±1.9	95.1 ±1.6	238.3 ±5.3	186.2 ±7.0	36.11 ±1.9	164.9 ±5.2	6.87 ±0.34	4.79 ±0.30	28.11 ±1.1	0.88 ±0.01
Above 50	Tobacco NC Control (B_5)	M	151	118.6 ±0.53	78.0 ±0.32	182.3 ±6.0	115.4 ±6.9	41.0 ±1.5	118.1 ±5.8	4.85 ±0.29	3.22 ±0.25	24.17 ±0.78	0.82 ±0.006
		F	41	117.1 ±0.75	75.6 ±0.5	171.1 ±4.5	95.1 ±10.0	48.3 ±1.8	103.8 ±5.0	3.73 ±0.16	2.30 ±0.15	24.61 ±0.46	0.83 ±0.008
	Tobacco Consump-tion HT (D_6)	M	21	144.0 ±1.5	92.1 ±0.76	243.1 ±5.4	199.2 ±8.5	35.47 ±0.76	167.8 ±5.4	7.1 ±0.19	4.93 ±0.18	26.20 ±0.47	0.97 ±0.006
		F	12	142.7 ±1.9	91.3 ±1.2	236.3 ±7.5	156.2 ±7.9	39.9 ±1.7	165.1 ±8.1	6.43 ±0.35	4.60 ±0.33	27.24 ±0.71	0.86 ±0.01

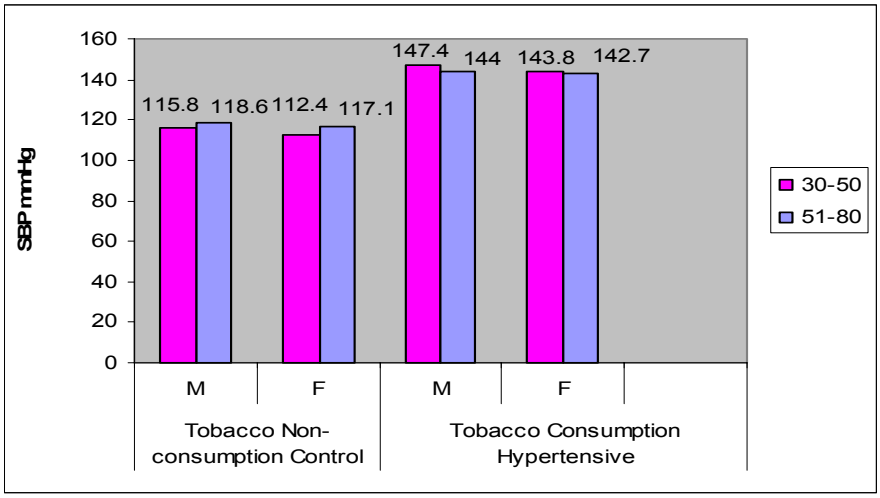
Values are Mean ± S.E.

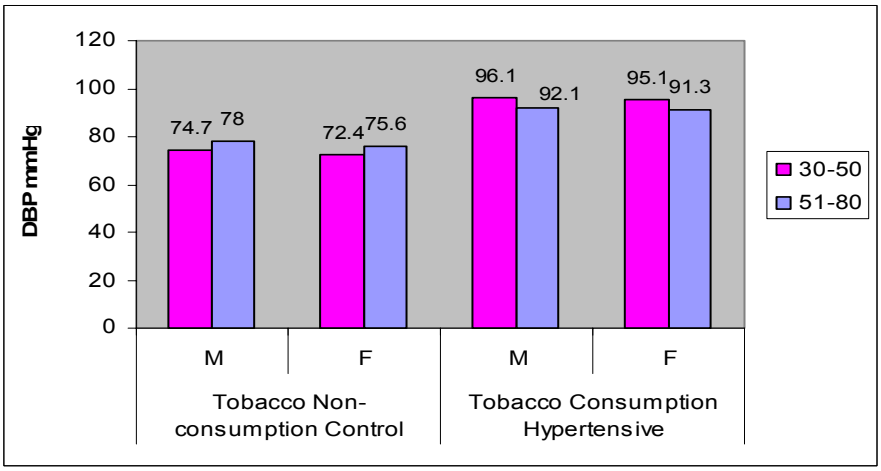
Table 7.3a: Statistical Analysis of Table 7.3

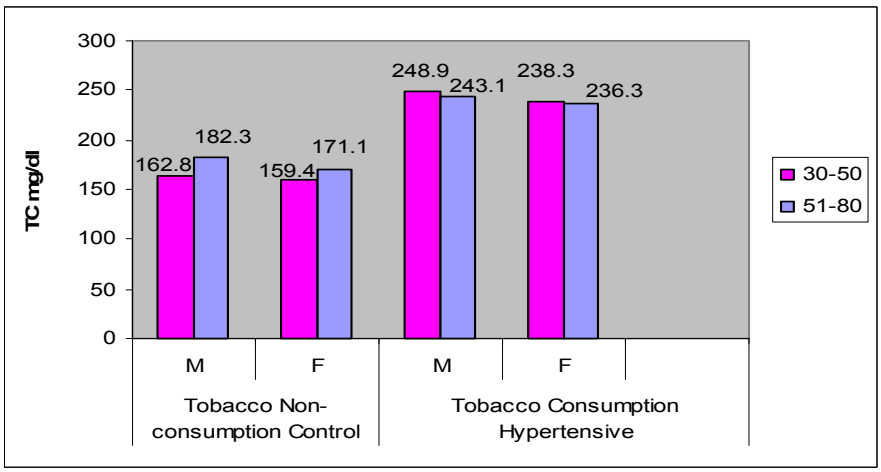
Comparison	SBP mmHg	DBP mmHg	TC mg/dl	TG mg/dl	HDL-C mg/dl	LDL-C mg/dl	TC/HDL-C	LDL-C/HDL-C	BMI kg/m^2	WHR
A_6M vs C_6M	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001
A_6F vs C_6F	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.01	P < 0.01
B_5M vs D_6M	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.01	P < 0.001
B_5F vs D_6F	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.05

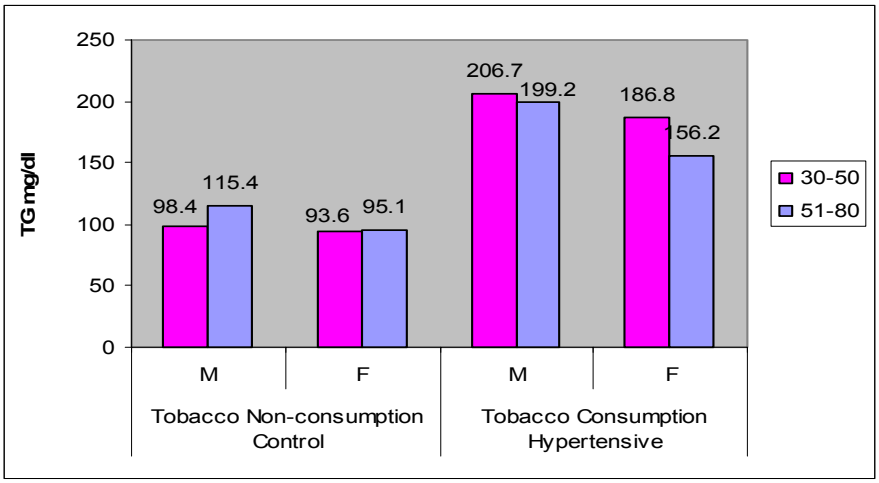
In the anthropometric indices, BMI in both normotensive and hypertensive tobacco consuming subjects showed an insignificant decrease in both genders and their age groups while WHR remained nearly alike in both tobacco consuming and nonconsuming groups of normotensive and hypertensive subjects. Both BMI & WHR values of hypertensive patients consuming tobacco were much higher than those observed in tobacco nonconsuming normotensives and were extremely significant (P<0.001).

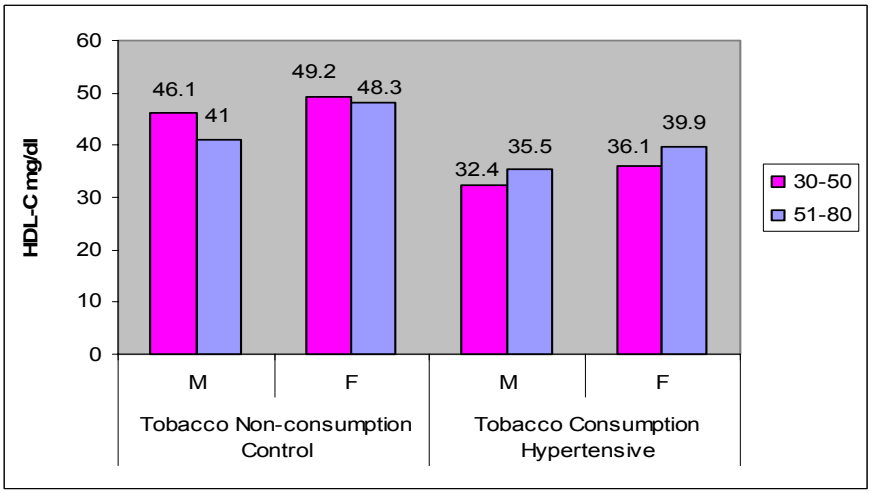
<u>Graph 5.3</u>: Effect of tobacco consumption on BP, Serum Lipids and Anthropometric Indices in Normotensive and Hypertensive cases:

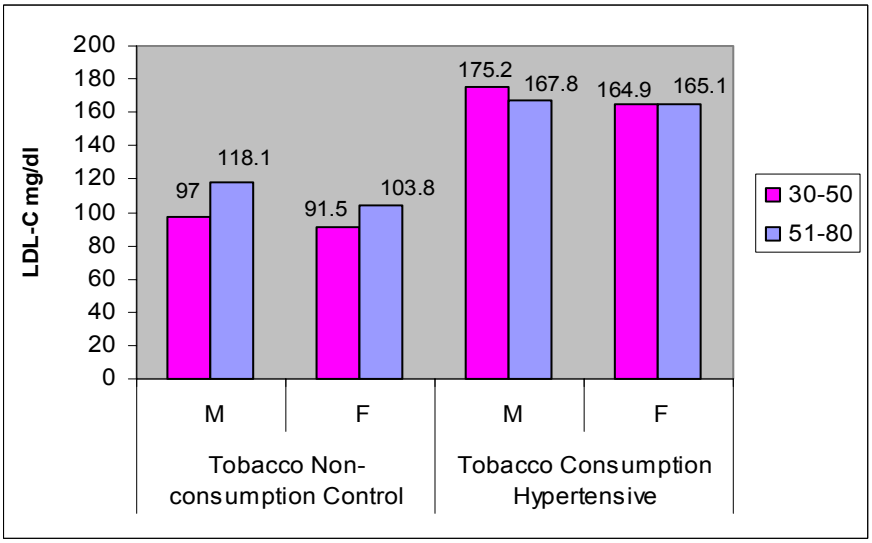


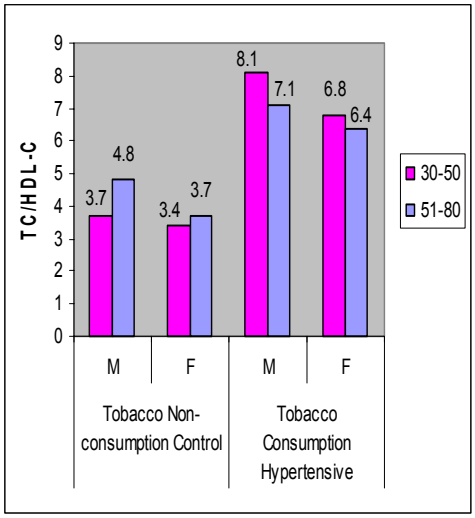


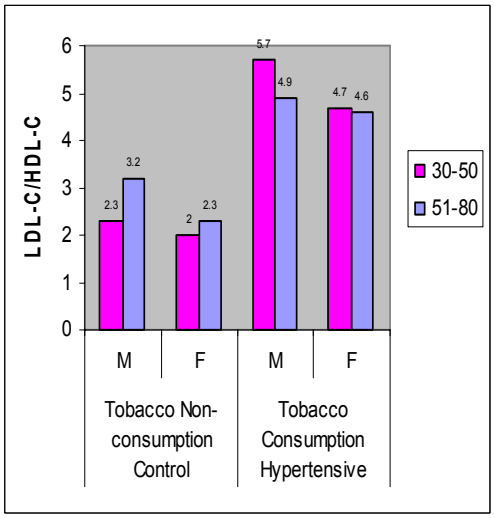


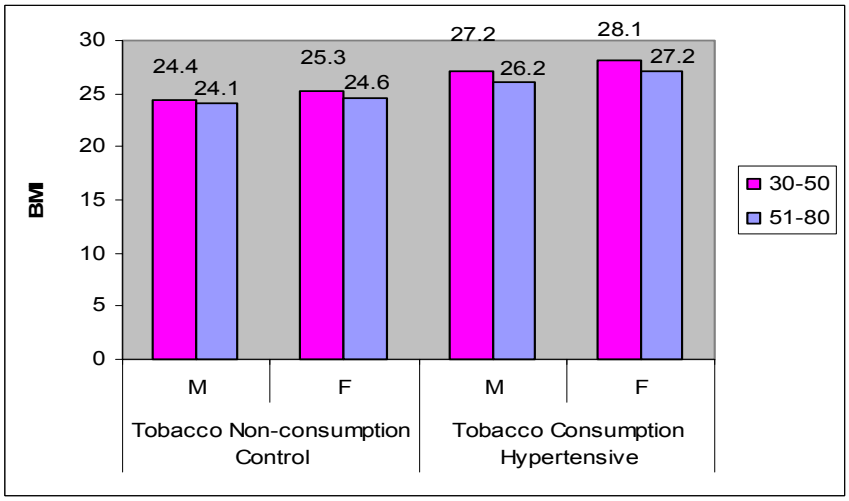

TG mg/dl
250
200
150
100
50
0
98.4
115.4
93.6
95.1
206.7
199.2
186.8
156.2
M
F
M
F
Tobacco Non-consumption Control
Tobacco Consumption Hypertensive
30-50
51-80

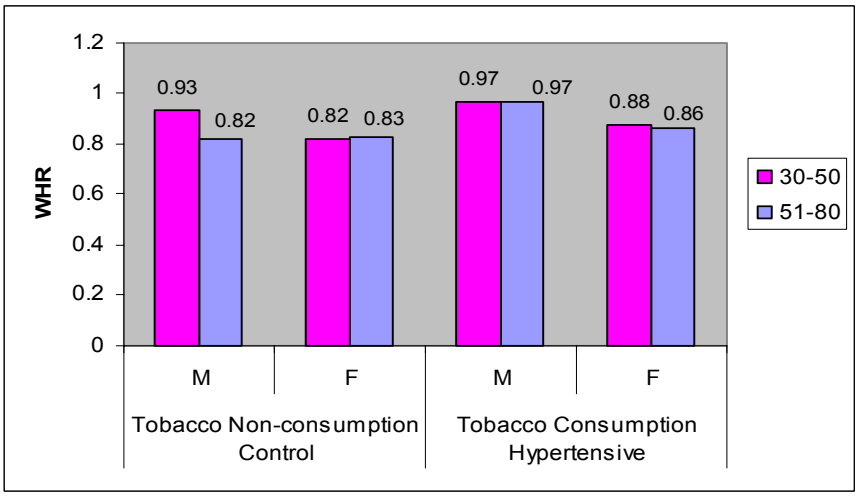

HDL-C mg/dl
60
50
40
30
20
10
0
46.1
41
49.2
48.3
32.4
35.5
36.1
39.9
M
F
M
F
Tobacco Non-consumption Control
Tobacco Consumption Hypertensive
30-50
51-80


LDL-C mg/dl
200
180
160
140
120
100
80
60
40
20
0
97
118.1
91.5
103.8
175.2
167.8
164.9
165.1
M
F
M
F
Tobacco Non-consumption Control
Tobacco Consumption Hypertensive
30-50
51-80


TC/HDL-C
9
8
7
6
5
4
3
2
1
0
3.7
4.8
3.4
3.7
8.1
7.1
6.8
6.4
M
F
M
F
Tobacco Non-consumption Control
Tobacco Consumption Hypertensive
30-50
51-80


LDL-C/HDL-C
6
5
4
3
2
1
0
2.3
3.2
2
2.3
5.7
4.9
4.7
4.6
M
F
M
F
Tobacco Non-consumption Control
Tobacco Consumption Hypertensive
30-50
51-80


BMI
30
25
20
15
10
5
0
24.4
24.1
25.3
24.6
27.2
26.2
28.1
27.2
M
F
M
F
Tobacco Non-consumption Control
Tobacco Consumption Hypertensive
30-50
51-80


WHR
1.2
1
0.8
0.6
0.4
0.2
0
0.93
0.82
0.82
0.83
0.97
0.97
0.88
0.86
M
F
M
F
Tobacco Non-consumption Control
Tobacco Consumption Hypertensive
30-50
51-80

An intragroup comparison of normotensive and hypertensive patients consuming tobacco displayed an analogous mode of decrease in all parameters except BP and HDL-C in normotensive subjects and only HDL-C in hypertensive patients. Significance was seen with only BP, TG, HDL-C and atherogenic ratios. Besides, in male and female assessment also, both the control and hypertensive gp illustrated similarity among them with decrease in females than those of males in all the parameters except HDL-C and BMI and significance being prevalent with TG, HDL-C, atherogenic ratios and WHR.

6. Effect of Heredity on BP, Serum Lipids and Anthropometric indices:

Heredity has a positive correlation in the development of HT or cardiac events. To appreciate the same, normotensive and hypertensive individuals were regrouped into two subgroups explicitly, with and without family history.

Table 8.1: Effect of Heredity on BP, Serum Lipids, BMI and WHR in Normotensive cases

Age Group	Heredity	G	N	SBP mmHg	DBP mmHg	TC mg/dl	TG mg/dl	HDL-C mg/dl	LDL-C mg/dl	TC/HDL-C	LDL-C/HDL-C	BMI	WHR
30-50	Negative Family History (A_7)	M	35	127.5 ±2.1	83.1 ±1.2	180.9 ±3.1	108.3 ±6.1	42.74 ±1.6	116.5 ±2.7	4.40 ±0.15	2.85 ±0.12	24.64 ±0.61	0.94 ±0.01
		F	76	122.8 ±1.2	80.6 ±0.77	171.0 ±2.7	91.4 ±5.4	48.17 ±1.1	104.6 ±2.7	3.69 ±0.10	2.28 ±0.08	25.30 ±0.46	0.82 ±0.006
	Positive Family History (A_8)	M	66	123.0 ±1.1	80.7 ±0.68	176.3 ±3.7	118.9 ±5.0	42.02 ±1.2	110.5 ±3.7	4.39 ±0.15	2.80 ±0.13	26.39 ±0.54	1.02 ±0.01
		F	82	125.7 ±1.4	82.4 ±0.87	184.2 ±1.9	106.5 ±3.9	46.44 ±1.0	116.5 ±2.2	4.09 ±0.08	2.62 ±0.08	26.83 ±0.55	0.87 ±0.04
51-80	Negative Family History (B_7)	M	34	130.5 ±2.5	85.9 ±1.7	187.9 ±5.5	107.6 ±6.5	41.40 ±2.0	125.0 ±5.9	4.83 ±0.24	3.26 ±0.22	24.37 ±0.61	0.94 ±0.01
		F	39	129.3 ±2.3	82.2 ±1.0	179.5 ±3.7	114.9 ±3.5	48.8 ±1.9	107.7 ±3.6	3.87 ±0.16	2.37 ±0.14	25.56 ±0.80	0.83 ±0.009
	Positive Family History (B_8)	M	33	126.4 ±1.4	83.7 ±1.6	180.5 ±4.7	122.2 ±5.7	41.0 ±1.7	115.0 ±4.2	4.63 ±0.21	3.01 ±0.19	26.30 ±0.62	0.96 ±0.01
		F	14	133.7 ±4.9	86.4 ±2.3	186.9 ±6.6	99.8 ±10.0	50.64 ±2.0	116.3 ±7.3	3.74 ±0.17	2.36 ±0.19	27.93 ±1.10	0.84 ±0.01

Values are Mean ± S.E.

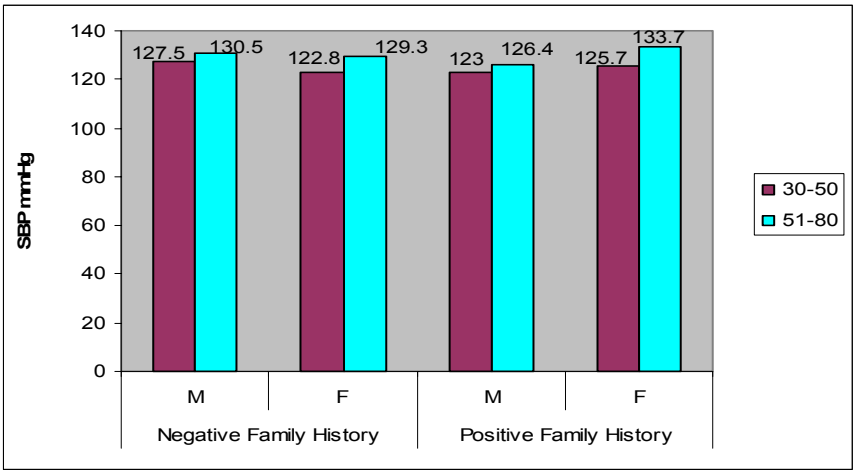
Table 8.1a: Statistical Analysis of Table 8.1										
COMPARISON	SBP mmHg	DBP mmHg	TC mg/dl	TG mg/dl	HDL-C mg/dl	LDL-C mg/dl	TC/HDL-C	LDL-C/HDL-C	BMI kg/m^2	WHR
A_7M vs A_8M	P < 0.05	P < 0.05	NS	NS	NS	NS	NS	NS	P < 0.01	P < 0.001
A_7F vs A_8F	P < 0.05	P < 0.05	P < 0.001	P < 0.01	NS	P < 0.001	P < 0.001	P < 0.005	P < 0.01	NS
B_7M vs B_8M	NS	NS	NS	P < 0.05	NS	NS	NS	NS	P < 0.01	NS
B_7F vs B_8F	NS	P < 0.05	NS	NS	NS	NS	NS	NS	P < 0.05	NS
A_8M vs A_8F	NS	P < 0.05	P < 0.05	P < 0.05	P < 0.005	NS	P < 0.05	NS	NS	P < 0.001
B_8M vs B_8F	NS	NS	P < 0.05	P < 0.05	P < 0.001	NS	P < 0.001	P < 0.01	NS	P < 0.005
A_8M vs B_8M	P < 0.05	P < 0.05	NS	NS	NS	NS	NS	NS	P < 0.05	P < 0.001
A_8F vs B8F	P < 0.05	P < 0.05	NS	NS	P < 0.05	NS	P < 0.05	NS	NS	NS

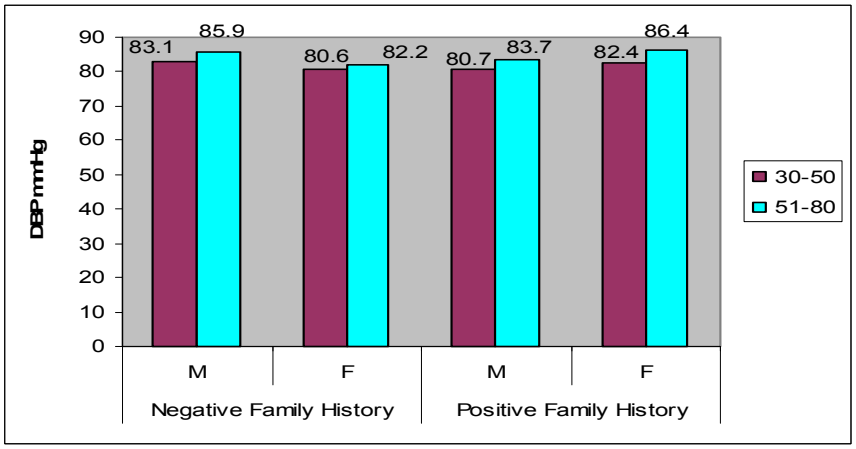
The normotensives and hypertensives with positive family history showed significant rise (P<0.05) in BPs in both the age groups and their respective genders except the males in normotensives when compared to their concerned negative family history counterparts. The BPs exhibited by hypertensives with positive family history in the two age groups were 142.7/90.0 and 148.3/96.8 in males and 146.2/94.4 & 151.8/98.6 in females while the same in normotensives with negative family history were 127.5/83.1 & 130.5/85.9 in males and 122.8/80.6 & 129.3/82.2 in females respectively. The divergence of BPs between these two groups of heredity were excessively significant (P<0.001).

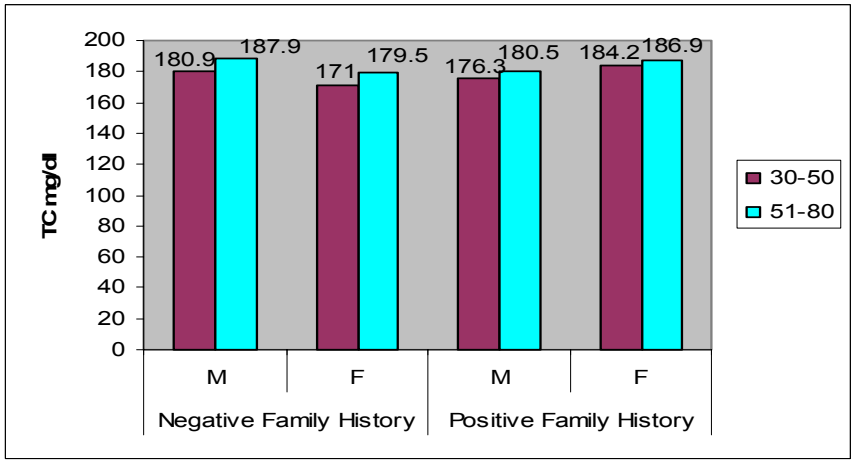
TC & LDL-C concentrations illustrated similar trends like an insignificant decrease in both normotensives and hypertensives with positive family history in both age groups and their genders except the females in normotensive cases. TC concentration in positive family history hypertensives in the two age groups were 224.6 & 239.3 mg% in men and 229.3 & 231.9 mg% in women while the same in negative family history normotensive were 180.9 & 187.9 mg% in men and 171.0 & 179.5 mg% in women respectively. Similarly, the concentration of LDL-C in hypertensives with positive family history were 148.4 & 159.6 mg% in males and 152.5 & 152.6 mg% in females where in normotensives with negative family history, the concentration were 116.5 & 125 mg% in males and 104.6 & 107.7 mg% in females respectively. Thus the dissimilarity in TC & LDL-C concs between the heredity subgroups were exceedingly significant (P<0.001).

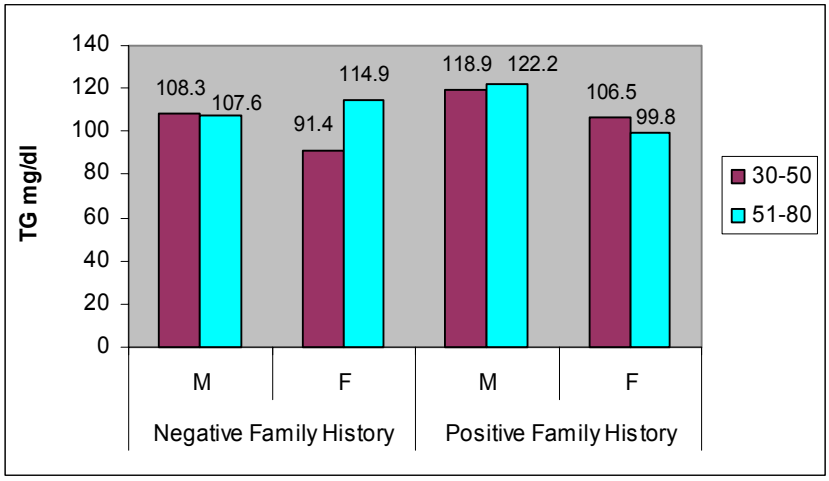
TG concentration increased significantly (P<0.05) in normotensive with positive family history while the hypertensives exhibited nearly alike concentration when compared to their relevant negative family history counterparts. In hypertensive with positive family history the TG concentration in the two age groups were 192.7 & 201.2 mg% in men and 163.7 & 169.4 mg% in women whereas the normotensives with negative family history illustrated 108.3 & 107.6 mg% in men and 91.4 & 114.9 mg% in women respectively. Thus the disparity of TG concentration in both the heredity groups were enormously significant (P<0.001).

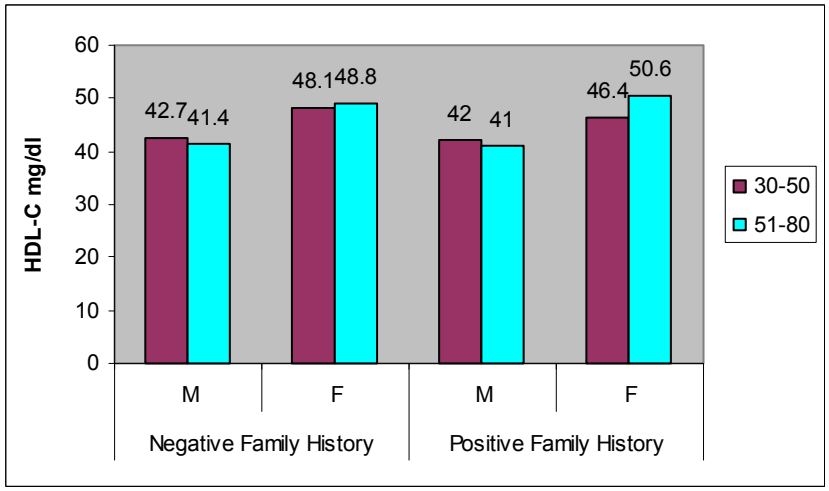
<u>Graph 6.1</u>: Effect of Heredity on BP, Serum Lipids and Anthropometric Indices in Normotensive cases:

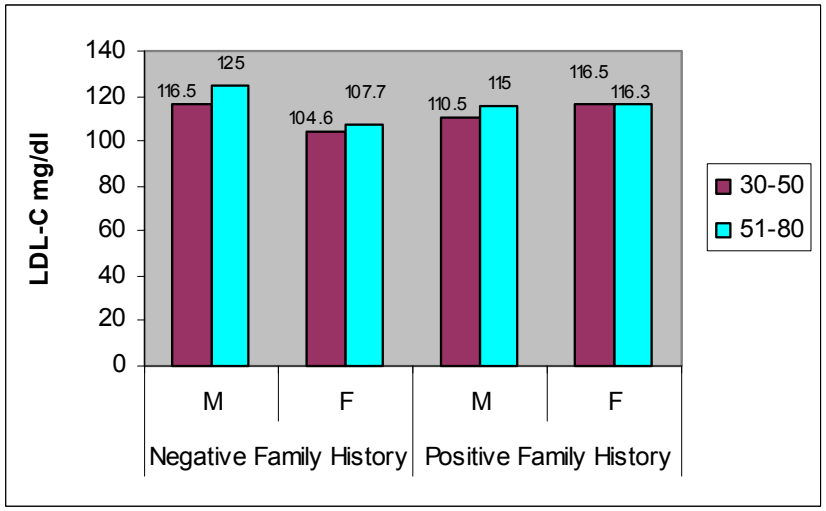


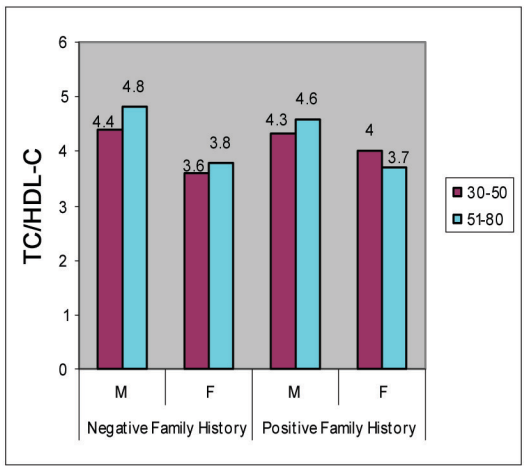


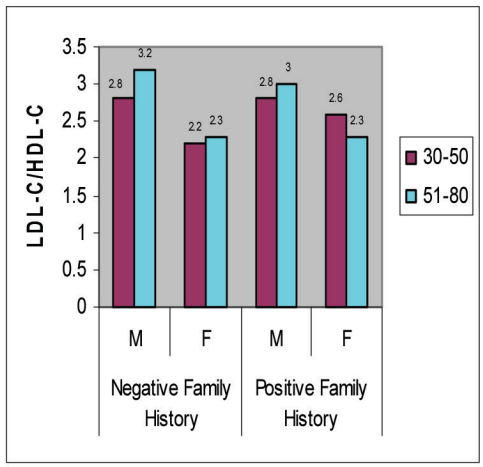


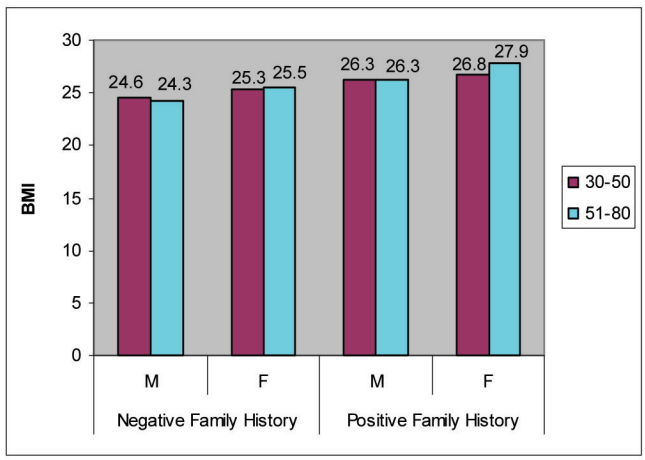

TG mg/dl
140
120
100
80
60
40
20
0
108.3
107.6
91.4
114.9
118.9
122.2
106.5
99.8
M
F
M
F
Negative Family History
Positive Family History
30-50
51-80


HDL-C mg/dl
60
50
40
30
20
10
0
42.7
41.4
48.1
48.8
42
41
46.4
50.6
M
F
M
F
Negative Family History
Positive Family History
30-50
51-80


LDL-C mg/dl
140
120
100
80
60
40
20
0
116.5
125
104.6
107.7
110.5
115
116.5
116.3
M
F
M
F
Negative Family History
Positive Family History
30-50
51-80


TC/HDL-C
6
5
4
3
2
1
0
4.4
4.8
3.6
3.8
4.3
4.6
4
3.7
M
F
M
F
Negative Family History
Positive Family History
30-50
51-80


LDL-C/HDL-C
3.5
3
2.5
2
1.5
1
0.5
0
2.8
3.2
2.2
2.3
2.8
3
2.6
2.3
M
F
M
F
Negative Family History
Positive Family History
30-50
51-80


BMI
30
25
20
15
10
5
0
24.6
24.3
25.3
25.5
26.3
26.3
26.8
27.9
M
F
M
F
Negative Family History
Positive Family History
30-50
51-80

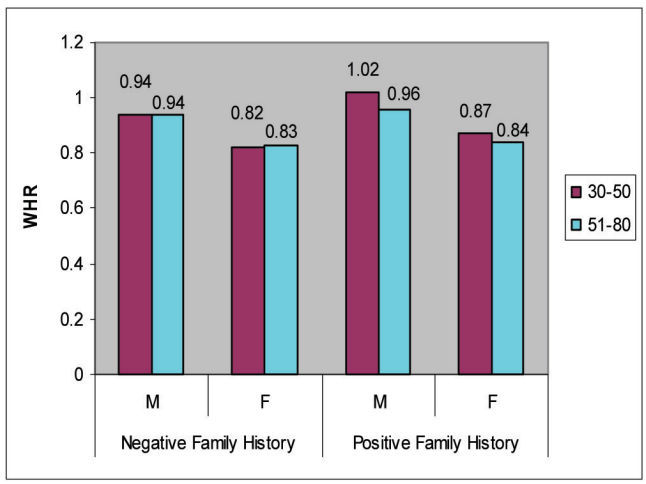

WHR
1.2
1
0.8
0.6
0.4
0.2
0
0.94
0.94
0.82
0.83
1.02
0.96
0.87
0.84
M
F
M
F
Negative Family History
Positive Family History
30-50
51-80

Table 8.2: Effect of Heredity on BP, Serum Lipids, BMI and WHR in Hypertensive cases

Age Group	Heredity	G	N	SBP mmHg	DBP mmHg	TC mg/dl	TG mg/dl	HDL-C mg/dl	LDL-C mg/dl	TC/HDL-C	LDL-C/HDL-C	BMI	WHR
30-50	Negative Family History (C_{10})	M	62	145.8 ± 2.0	92.6 ± 1.2	251.6 ± 7.6	187.7 ± 11.0	41.1 ± 1.4	173.0 ± 7.2	6.50 ± 0.26	4.49 ± 0.22	27.44 ± 0.61	0.96 ± 0.01
		F	56	143.3 ± 2.0	91.04 ± 1.0	236.2 ± 5.5	161.9 ± 11.0	39.9 ± 1.1	163.9 ± 5.9	6.09 ± 0.18	4.21 ± 0.17	28.25 ± 0.63	0.84 ± 0.009
	Positive Family History (C_{11})	M	90	142.7 ± 1.8	90.0 ± 1.1	224.6 ± 4.2	192.7 ± 9.9	37.6 ± 0.9	148.4 ± 4.1	6.25 ± 0.18	4.15 ± 0.15	29.74 ± 0.63	1.01 ± 0.01
		F	95	146.2 ± 1.4	94.4 ± 1.0	229.3 ± 4.0	163.7 ± 8.1	44.2 ± 1.3	152.5 ± 4.1	5.53 ± 0.16	3.70 ± 0.14	31.56 ± 0.64	0.86 ± 0.006
51-80	Negative Family History (D_{10})	M	94	145.0 ± 1.5	94.4 ± 0.84	240.9 ± 5.5	201.0 ± 8.6	38.19 ± 0.89	162.5 ± 5.5	6.59 ± 0.22	4.48 ± 0.20	26.67 ± 0.48	0.98 ± 0.008
		F	95	148.4 ± 1.5	92.79 ± 0.83	242.9 ± 5.2	170.4 ± 10.0	42.6 ± 1.0	166.2 ± 6.0	6.08 ± 0.23	4.24 ± 0.23	26.58 ± 0.49	0.87 ± 0.008
	Positive Family History (D_{11})	M	118	148.3 ± 1.4	96.8 ± 1.2	239.3 ± 4.6	201.2 ± 8.7	40.5 ± 0.87	158.6 ± 4.2	6.16 ± 0.15	4.08 ± 0.13	27.75 ± 0.38	0.97 ± 0.006
		F	128	151.8 ± 1.4	98.6 ± 1.2	231.9 ± 4.0	169.4 ± 7.0	45.4 ± 0.94	152.6 ± 4.2	5.38 ± 0.14	3.58 ± 0.13	30.09 ± 0.45	0.85 ± 0.005

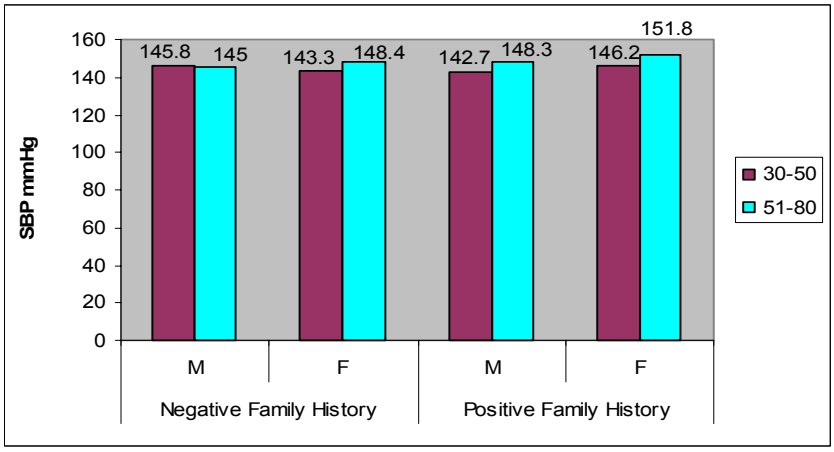
Values are Mean ± S.E.

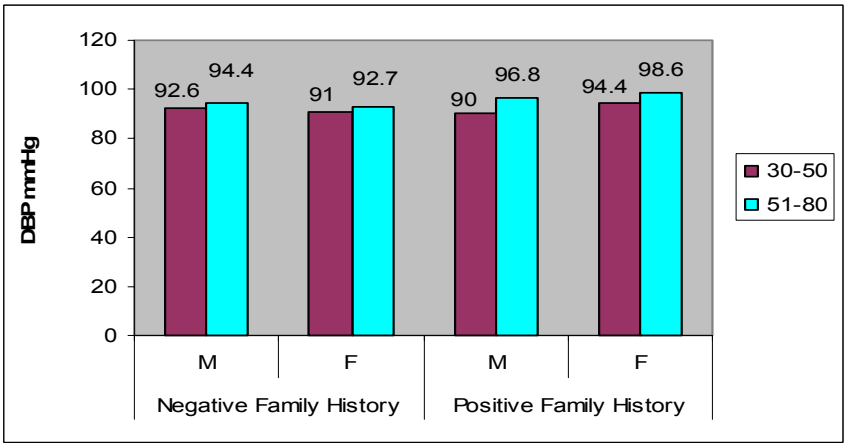
Table 8.2a: Statistical Analysis of Table 8.2

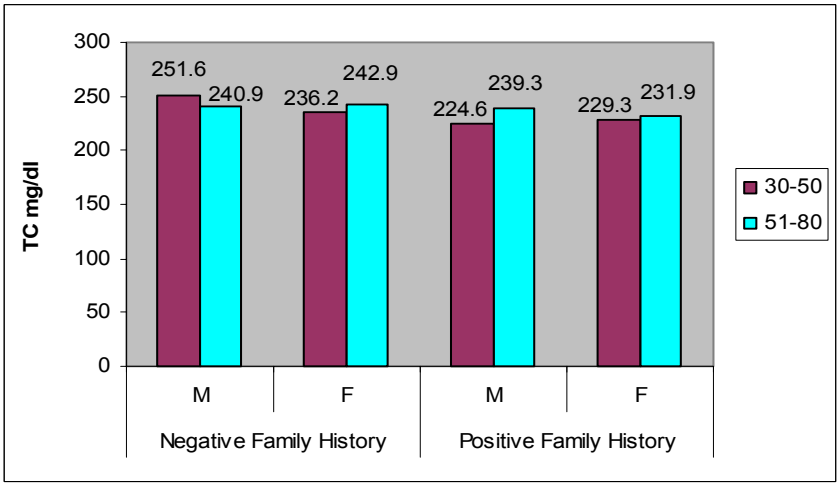
COMPARISON	SBP mmHg	DBP mmHg	TC mg/dl	TG mg/dl	HDL-C mg/dl	LDL-C mg/dl	TC/HDL-C	LDL-C/HDL-C	BMI kg/m^2	WHR
$C_{10}M$ vs $C_{11}M$	NS	P < 0.05	P < 0.001	NS	P < 0.01	P < 0.001	NS	NS	P < 0.01	P < 0.001
$C_{10}F$ vs $C_{11}F$	NS	P < 0.01	NS	NS	P < 0.01	P < 0.05	P < 0.01	P < 0.01	P < 0.05	NS
$D_{10}M$ vs $D_{11}M$	P < 0.05	P < 0.05	NS	NS	P < 0.05	NS	P < 0.05	P < 0.05	P < 0.001	NS
$D_{10}F$ vs $D_{11}F$	P < 0.05	P < 0.001	P < 0.05	NS	P < 0.01	P < 0.05	P < 0.005	P < 0.01	P < 0.001	P < 0.05
$C_{11}M$ vs $C_{11}F$	P < 0.05	P < 0.001	NS	P < 0.01	P < 0.001	NS	P < 0.001	P < 0.01	P < 0.01	P < 0.001
$D_{11}M$ vs $D_{11}F$	P < 0.05	NS	NS	P < 0.005	P < 0.001	NS	P < 0.001	P < 0.005	P < 0.001	P < 0.001
$C_{11}M$ vs $D_{11}M$	P < 0.01	P < 0.001	P < 0.01	NS	P < 0.01	P < 0.05	NS	NS	P < 0.005	P < 0.001
$C_{11}F$ vs $D_{11}F$	P < 0.005	P < 0.01	NS	NS	NS	NS	NS	NS	P < 0.05	NS

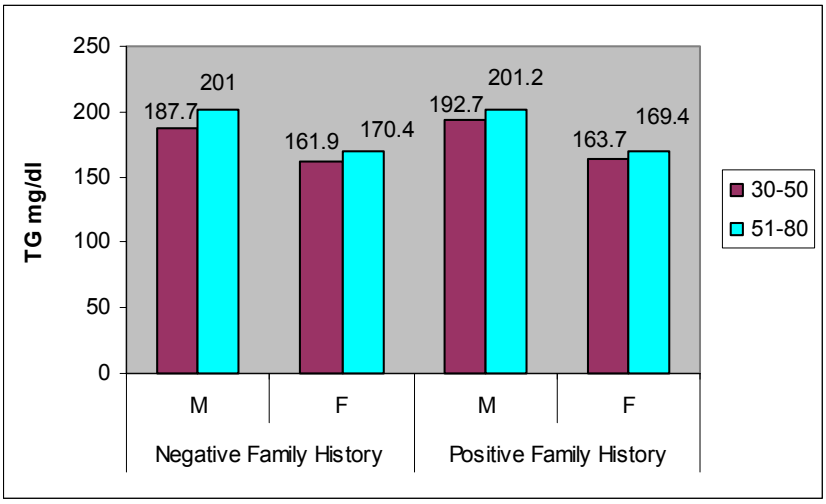
Among the serum lipids, HDL-C concentration in normotensives with positive family history was nearly alike in males in both age groups while the females showed an insignificant decrease in 30-50 years and an increase in 51-80 years. On the other hand, the hypertensives with positive family history illustrated a highly significant increase in both age groups and their genders except 30-50 years males wherein a significant decrease was observed. The concentration of HDL-C displayed in hypertensives with positive family history were 37.6 & 40.5 mg% in males and 44.2 & 45.4 mg% in females while the same in normotensives with negative family history were 42.74 & 41.4 mg% in males and 48.17 & 48.8 mg% in females respectively. These differences were found to be greatly significant (P<0.01) among the heredity subgroups.

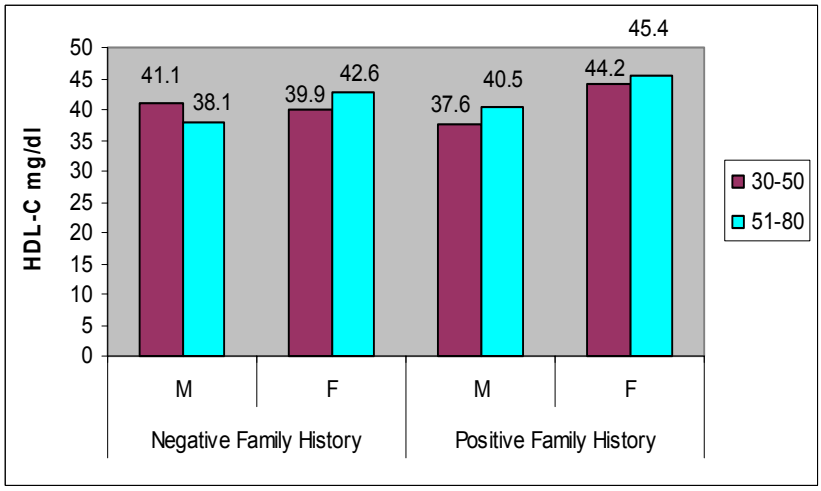
<u>Graph 6.2</u>: Effect of Heredity on BP, Serum Lipids and Anthropometric Indices in Hypertensive cases:

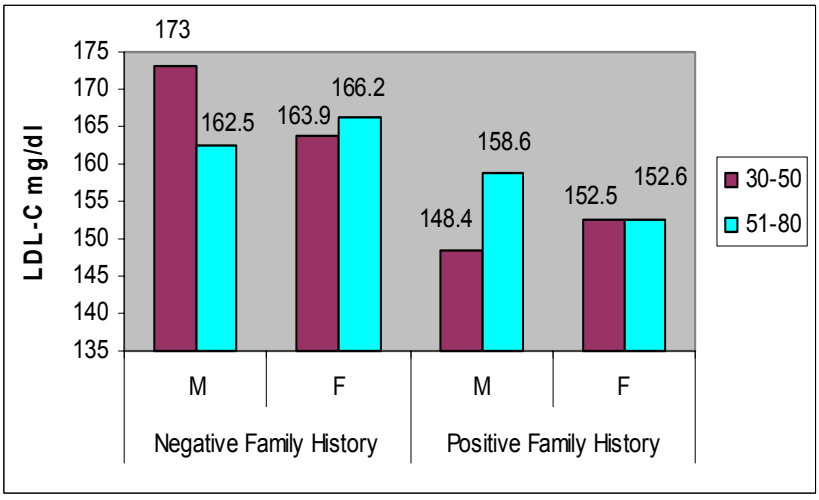


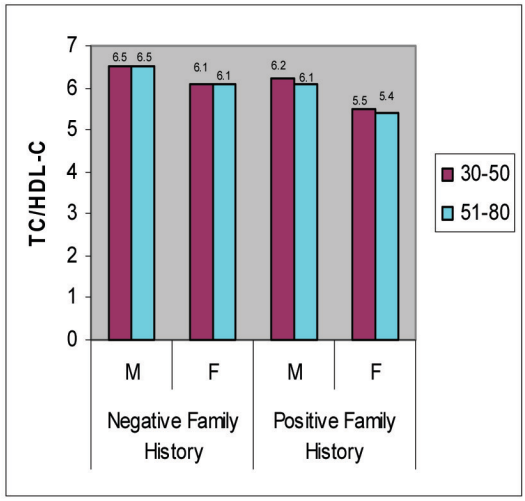


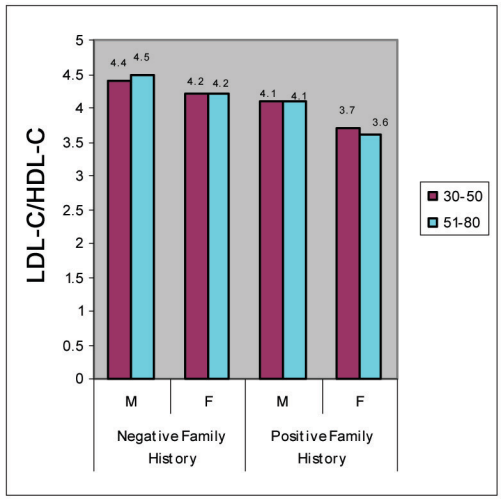


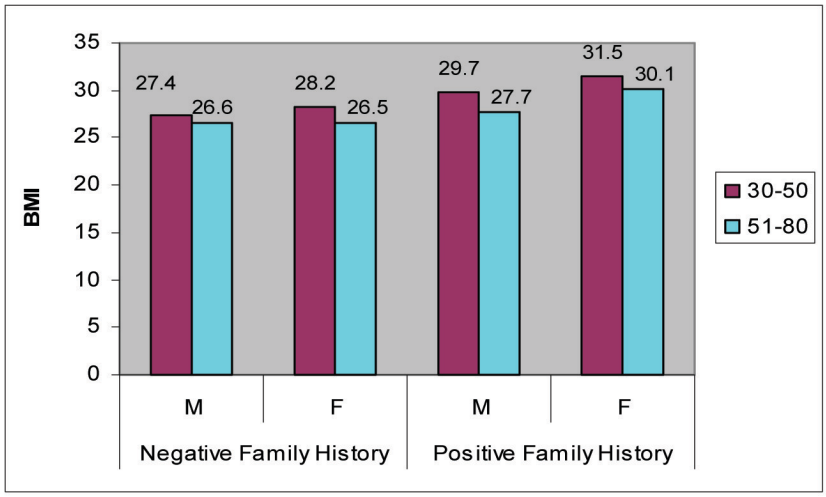

TG mg/dl
250
200
150
100
50
0
187.7
201
161.9
170.4
192.7
201.2
163.7
169.4
M
F
M
F
Negative Family History
Positive Family History
30-50
51-80


HDL-C mg/dl
50
45
40
35
30
25
20
15
10
5
0
41.1
38.1
39.9
42.6
37.6
40.5
44.2
45.4
M
F
M
F
Negative Family History
Positive Family History
30-50
51-80


LDL-C mg/dl
175
170
165
160
155
150
145
140
135
173
162.5
163.9
166.2
148.4
158.6
152.5
152.6
M
F
M
F
Negative Family History
Positive Family History
30-50
51-80


TC/HDL-C
7
6
5
4
3
2
1
0
6.5 6.5
6.1 6.1
6.2 6.1
5.5 5.4
M
F
M
F
Negative Family History
Positive Family History
30-50
51-80


LDL-C/HDL-C
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
4.4 4.5
4.2 4.2
4.1 4.1
3.7 3.6
M
F
M
F
Negative Family History
Positive Family History
30-50
51-80


BMI
35
30
25
20
15
10
5
0
27.4 26.6
28.2 26.5
29.7 27.7
31.5 30.1
M
F
M
F
Negative Family History
Positive Family History
30-50
51-80

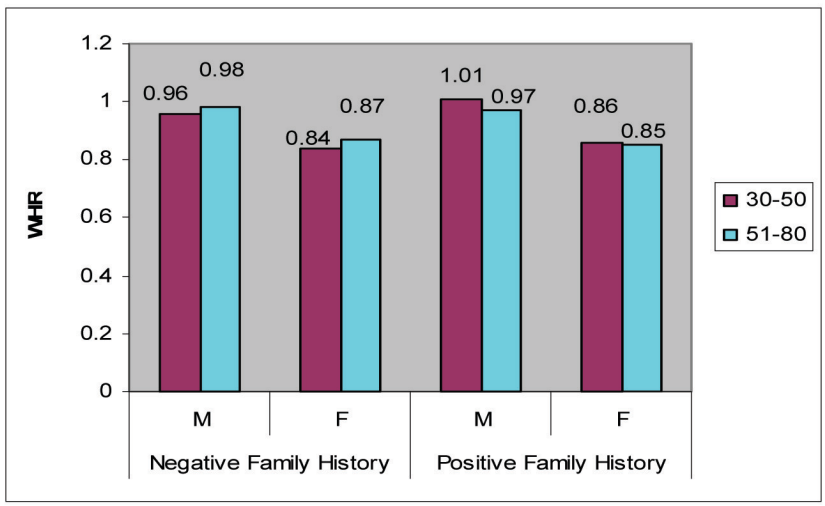

WHR
1.2
1
0.8
0.6
0.4
0.2
0
0.96 0.98
0.84 0.87
1.01 0.97
0.86 0.85
M
F
M
F
Negative Family History
Positive Family History
30-50
51-80

Table 8.3: Effect of Heredity on BP, Serum Lipids, BMI and WHR in Normotensive & Hypertensive cases

Age Group	Heredity	G	N	SBP mmHg	DBP mmHg	TC mg/dl	TG mg/dl	HDL-C mg/dl	LDL-C mg/dl	TC/HDL-C	LDL-C/HDL-C	BMI	WHR
30-50	Non Heredity Control (A_7)	M	35	127.5 ±2.1	83.1 ±1.2	180.9 ±3.1	108.3 ±6.1	42.74 ±1.6	116.5 ±2.7	4.40 ±0.15	2.85 ±0.12	24.64 ±0.61	0.94 ±0.01
		F	76	122.8 ±1.2	80.6 ±0.77	171.0 ±2.7	91.4 ±5.4	48.17 ±1.1	104.6 ±2.7	3.69 ±0.10	2.28 ±0.08	25.30 ±0.46	0.82 ±0.006
	Heredity HTsive (C_{11})	M	90	142.7 ±1.8	90.0 ±1.1	224.6 ±4.2	192.7 ±9.9	37.6 ±0.9	148.4 ±4.1	6.25 ±0.18	4.15 ±0.15	29.74 ±0.63	1.01 ±0.01
		F	95	146.2 ±1.4	94.4 ±1.0	229.3 ±4.0	163.7 ±8.1	44.2 ±1.3	152.5 ±4.1	5.53 ±0.16	3.70 ±0.14	31.56 ±0.64	0.86 ±0.006
Above 50	Non Heredity Control (B_7)	M	34	130.5 ±2.5	85.9 ±1.7	187.9 ±5.5	107.6 ±6.5	41.40 ±2.0	125.0 ±5.9	4.83 ±0.24	3.26 ±0.22	24.37 ±0.61	0.94 ±0.01
		F	39	129.3 ±2.3	82.2 ±1.0	179.5 ±3.7	114.9 ±3.5	48.8 ±1.9	107.7 ±3.6	3.87 ±0.16	2.37 ±0.14	25.56 ±0.80	0.83 ±0.009
	Heredity HTsive (D_{11})	M	118	148.3 ±1.4	96.8 ±1.2	239.3 ±4.6	201.2 ±8.7	40.5 ±0.87	158.6 ±4.2	6.16 ±0.15	4.08 ±0.13	27.75 ±0.38	0.97 ±0.006
		F	128	151.8 ±1.4	98.6 ±1.2	231.9 ±4.0	169.4 ±7.0	45.4 ±0.94	152.6 ±4.2	5.38 ±0.14	3.58 ±0.13	30.09 ±0.45	0.85 ±0.005

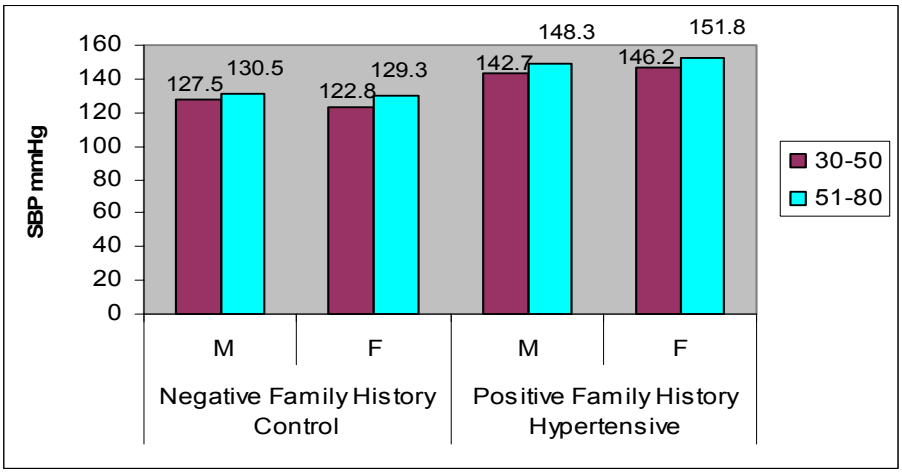
Values are Mean ± S.E.

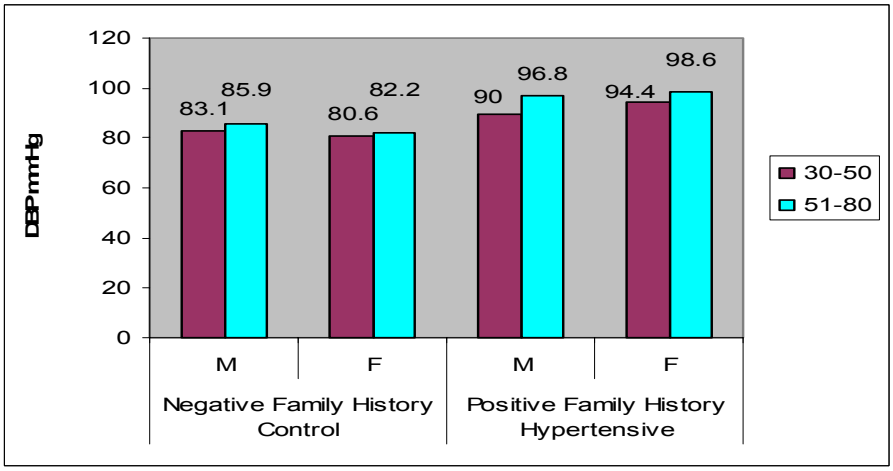
Table 8.3a: Statistical Analysis of Table 8.3

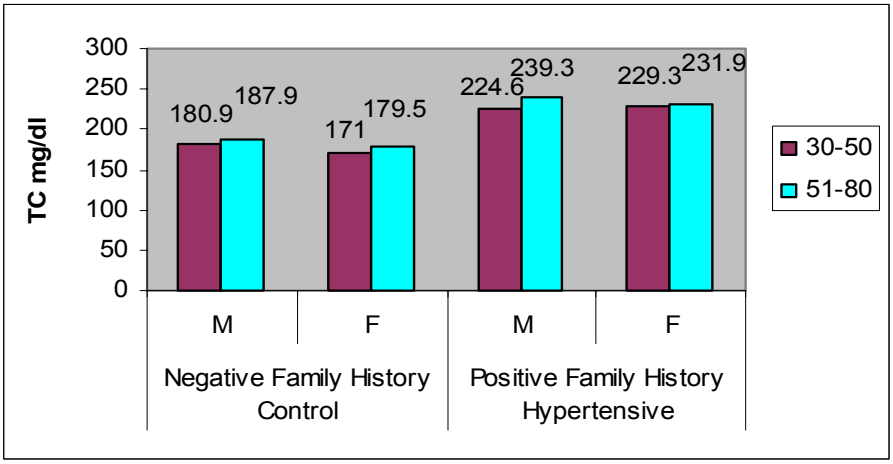
Comparison	SBP mmHg	DBP mmHg	TC mg/dl	TG mg/dl	HDL-C mg/dl	LDL-C mg/dl	TC/HDL-C	LDL-C/HDL-C	BMI kg/m^2	WHR
A_7M vs $C_{11}M$	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001
A_7F vs $C_{11}F$	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.01	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001
B_7M vs $D_{11}M$	P < 0.001	P < 0.001	P < 0.001	P < 0.001	NS	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.01
B_7F vs $D_{11}F$	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.05	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.05

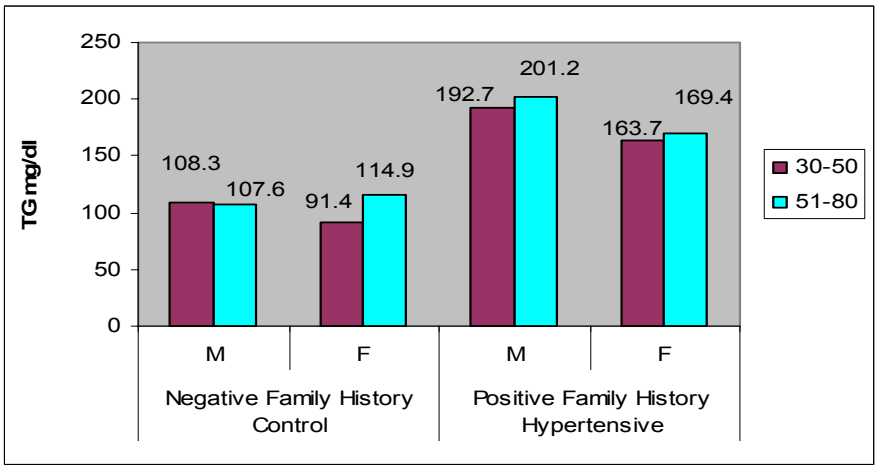
The atherogenic ratios remained nearly similar in normotensives with and without family history whereas the hypertensives with family history demonstrated a vastly significant (P<0.01) decrease when compared to their negative family history counterparts. TC/HDL-C displayed values like 6.25 & 6.16 in men and 5.53 & 5.38 in women of hypertensives with positive family history in both age groups whereas the same in normotensives with negative family history were 4.40 & 4.83 in men and 3.69 & 3.87 in women respectively. The same in LDL-C/HDL-C were 4.15 & 4.08 in males and 3.70 & 3.58 in females of hypertensives whereas the normotensives showed 2.85 & 3.26 in males and 2.28

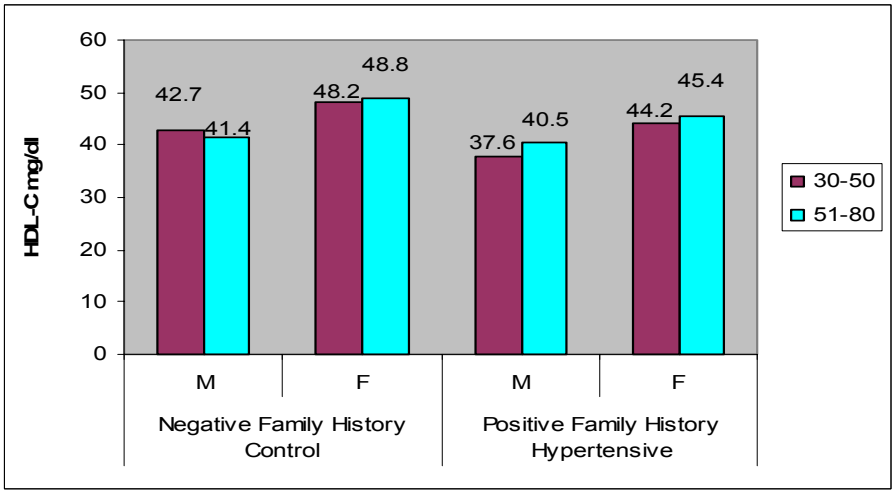
<u>Graph 6.3</u>: Effect of Heredity on BP, Serum Lipids and Anthropometric Indices in Normotensive and Hypertensive cases:

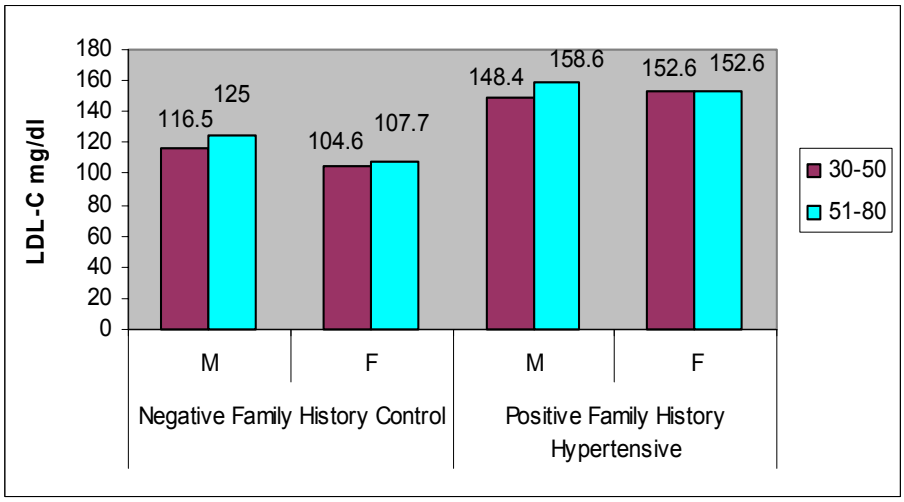


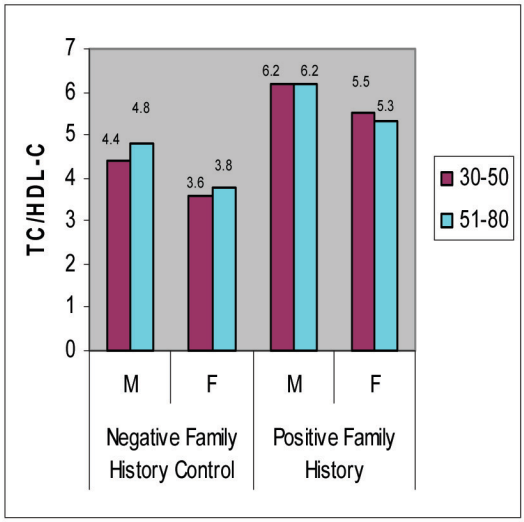


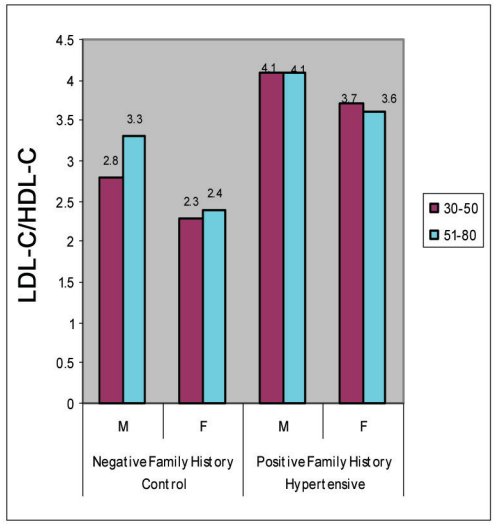


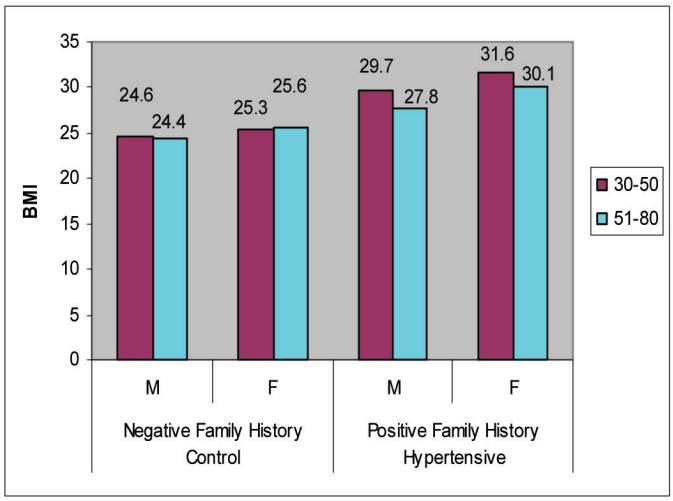

TG mg/dl
250
200
150
100
50
0
108.3
107.6
91.4
114.9
192.7
201.2
163.7
169.4
M
F
M
F
Negative Family History Control
Positive Family History Hypertensive
30-50
51-80

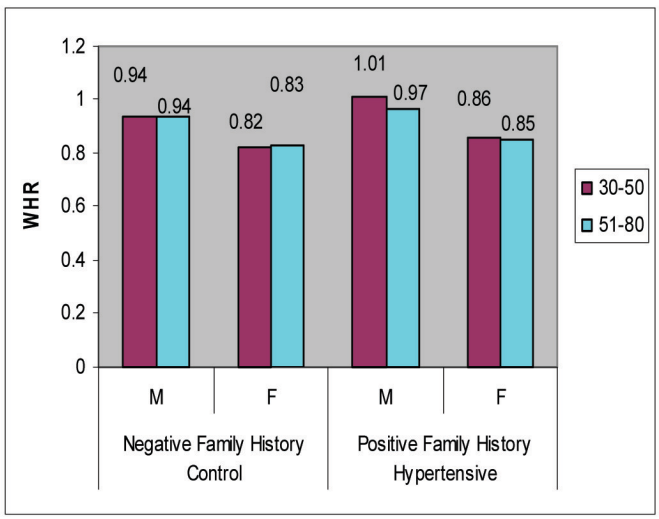

HDL-C mg/dl
60
50
40
30
20
10
0
42.7
41.4
48.2
48.8
37.6
40.5
44.2
45.4
M
F
M
F
Negative Family History Control
Positive Family History Hypertensive
30-50
51-80


LDL-C mg/dl
180
160
140
120
100
80
60
40
20
0
116.5
125
104.6
107.7
148.4
158.6
152.6
152.6
M
F
M
F
Negative Family History Control
Positive Family History Hypertensive
30-50
51-80


TC/HDL-C
7
6
5
4
3
2
1
0
4.4
4.8
3.6
3.8
6.2
6.2
5.5
5.3
M
F
M
F
Negative Family History Control
Positive Family History
30-50
51-80


LDL-C/HDL-C
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
2.8
3.3
2.3
2.4
4.1
4.1
3.7
3.6
M
F
M
F
Negative Family History Control
Positive Family History Hypertensive
30-50
51-80


BMI
35
30
25
20
15
10
5
0
24.6
24.4
25.3
25.6
29.7
27.8
31.6
30.1
M
F
M
F
Negative Family History Control
Positive Family History Hypertensive
30-50
51-80


WHR
1.2
1
0.8
0.6
0.4
0.2
0
0.94
0.94
0.82
0.83
1.01
0.97
0.86
0.85
M
F
M
F
Negative Family History Control
Positive Family History Hypertensive
30-50
51-80

& 2.37 in females correspondingly. The values of atherogenic ratios in the hypertensives with family history of both genders among the two age groups were much higher than those seen in normotensive with negative family history and these divergences were exceptionally significant ($P<0.001$).

In the anthropometric indices both, BMI & WHR exhibited an increase in normotensives and hypertensives with positive family history when compared to their corresponding negative family history counterparts but highly significant rise ($P<0.01$) was observed in only BMI. Also, their values in both genders and their age groups of hypertensives with positive family history were considerably higher than those seen in normotensives with negative family history and were found to be outstandingly significant ($P<0.001$).

An intragroup comparison of control and hypertensive cases with positive family history put forward a parallel manner of increase with age in all parameters except in control group of males in HDL-C. Significance was seen in only BP and anthropometric indices in hypertensive cases while in control group only BP showed significance. Moreover in male and female evaluation, normotensive subjects of both age groups and hypertensive patients of 30-50 age group, displayed increase in BP, serum lipids and BMI and a decrease in TG, atherogenic ratios and WHR among the females than the males of the corresponding age groups. In hypertensive patients, the females in 51-80 age group had lower values in serum lipids, atherogenic ratios and WHR whereas higher BP, HDL-C and BMI were observed than those of males.

DISCUSSION

1. Effect of age on BP, Serum Lipids and Anthropometric indices in Normotensive subjects:

Aging is the biological process common to all living organisms. It is a non-modifiable, but major risk factor in the anticipation of HT risk. Studies in humans have found that arterial wall thickening and dilatation are prominent structural changes that occur within large elastic arteries during aging. BP is determined by the interplay of peripheral vascular resistance and arterial stiffness. Peripheral vascular resistance raises both systolic and diastolic pressures to a similar degree whereas, arterial stiffness raises systolic but lowers diastolic pressure.

In the present study, SBP and DBP have been found to increase with age in both sexes as shown in table 3 and graph 1. These findings were in agreement to those of Mathur, [455] Indrayan, [456] Boe [455] and others wherein an increasing tendency of both SBP and DBP; with advancement of age in both sexes were observed. Also the third NHANES and Framingham data have shown a rise in SBP with increase in age which also agrees to the results observed in this study. [21,22]

Age related increase of BP is a common but not a universal phenomenon. This is predominantly influenced by environmental factors as certain non-migrant or tribal populations, who follow a primitive life style do not develop age related rise in BP. [457] But in most cases, BP rises with advancement of age. [458] MiaII [459] opined that age, sex and race were the variables to which the BP was largely related. Boe [455] in Norway found that both SBP and DBP increased progressively with age in both sexes.

In this study it was also found that SBP and DBP were higher in males than in females of the corresponding age group. There seems to be a positive correlation between BP and gender differences. It may be due to the protective effect of female sex hormones against stress. In agreement to this study, Shyamal Das *et al* also showed an influence of gender on BP among men. [13] The progressive urbanization, lifestyle modification and sedentary habits are probably some of the important factors considered to be responsible for increase in BP with advancement of age in Jamnagar. Also structural, functional and

biochemical changes occurring in the vascular system of human body due to aging process are some other factors which are again influenced by sex, race socioeconomic, etc. [13]

Serum lipids (cholesterol, triglyceride) and lipoprotein levels (VLDL, LDL, HDL) do have immense importance in coronary artery disease patients because variation from normal levels can predict the cause of CAD to a great extent. [371] Thus increased level of serum lipids is considered to be one of the important factor for the development of atherosclerotic diseases.

In the present study an increase in the serum lipids (TC &TG) and lipoproteins (VLDL, LDL) are observed with the advancement of age in both sexes. A similar observation was revealed by Ritu Sharma *et al.* [371] But Onitri and coworkers [460] showed that serum concentration of TG did not rise with age in adults but concentration of cholesterol did. Lipids Research Clinics (LCR) prevalence study carried out cross sectional age specific plasma lipid distribution in North American population. [461] This data also confirmed a rise in TC levels among male and female from teenage years to middle age. A substantial rise in TG levels between the late teens and middle age in males and a steady rise in women were also observed. B.M. Gandhi [462] also stated an increase in TC and TG with age in both the sexes. Reddy [463] for South Indian people of coastal Andhra Pradesh and Tirupati and Puri [464] highlander community of Himalayan range showed an increase in TC concentration with advancement of age. However the rate of increase in total serum cholesterol was very high and highly significant in urban population. [463] TG showed a slight increase with increase in age, but females were possessing higher TG values than males. While in this present study females always showed a value significantly lower to the males of the corresponding age groups of serum lipids (TC & TG) and lipoproteins (VLDL-C & LDL-C) which was in agreement with Chadha's study [465] for Gujaratis, LRC data for North American population [466] and Reddy's [463] findings for urbanization of Andhra Pradesh.

HDL-C levels in the present study did not vary with increase in age in males while it increased in females. In females the elevated HDL-C maybe due to estrogens and thus they might have lower incidence of CAD before the age of 50. [160] Also a study by B.M. Gandhi [462] showed a marginal increase of HDL-C with age but the difference between the two sexes was insignificant. Abdul Rehman [466] showed an average serum HDL-C level of 58.4% with significant variation between age

groups 20 to 49 years in Kuwaiti males. Contrary to all these above findings, serum HDL-C was found to decrease with advancing age in normotensive people in Ritu Sharma *et al* study. [371]

Factors associated with weight change during puberty due to differential effect by gonadal hormones, smoking and sucrose intake play a major role in the difference in HDL-C and TC concentration according to sex. [467] The sex difference in HDL-C is due to lower levels of HDL2-C subfractions in men. [468] Schaefer *et al* [469] concluded that higher apo A-I level normally found in women was associated with a greater synthetic rate of HDL-C. Thus the sex difference in lipoproteins may be resulted from difference in the effects of factors that influence lipoprotein levels between the two sexes. [469] In communities like Japanese, Greenland Eskimos [470] with little or no CHD had minimal sex difference in lipoprotein levels as compared with societies where CHD is a significant health problem as found in North West London. [471]

Age and Sex related changes in LDL-C levels documented in this study closely resemble those for total plasma cholesterol. This is because 70% of TC is transported in this lipoprotein in the ultracentrifugal low density range. LDL-C in males and females increase with age which was in agreement with Heiss *et al*. [472] Also study by B.M.Gandhi [462] illustrated an increase of LDL-C with age in both sexes up to the age of 50 years. This increase in LDL-C with age has not been reported in older age groups. The change may be related to calorie intake in relation to requirements for growth and physical activity. VLDL-C concentration demonstrated little but gradual change with age in males and females and resembles almost with respect to TG as VLDL-C was estimated with the use of Friedwald formula.

Increased concentration of LDL-C in the plasma is the primary factor for increase in TC while a small part is due to an increase in VLDL-C with age which is also a form in which a little amount of cholesterol is transported. HDL-C hardly changes in men at this time and no increase in TC is related to HDL-C. In women LDL-C and VLDL-C increase more slowly, thus accounting for the major differences according to sexes [472] in plasma TC concentration. The presence of estrogen has a protective effect on the females from incidences of CAD but a shift in hormonal balance created with the deficiency of estrogen after 50 years, gradually increase the concentration of LDL-C in women and after 60 years LDL-C reaches its peak concentration. Miller [473] showed an inverse relationship between fractional catabolic rate (FCR)

of LDL-C and apo-B on one hand and age on the other. Brown and Goldstein [474] reported that increase in LDL-C with age is a consequence of a reduction in LDL-C receptors mediated catabolism due to decrease in numbers of LDL-C receptors with age. Angelin [475] also proposed that hepatic bile acid synthesis decreased with age, while biliary cholesterol increased which caused changes in intrahepatic cholesterol pool, down regulation of LDL-C receptors and a reduction in the LDL-C FCR.

According to Simons [476] in an individual population TC and HDL-C estimations were enough to predict the risk for CHD. In a study by K.P. Misra *et al* [477] it emphasizes the significance of HDL-C and more so of the ratios of TC/HDL-C and LDL-C/HDL-C as major lipid risk factors for CHD. This is understandable in view of the proposed hypothesis that HDL facilitates the uptake of cholesterol from peripheral tissues and helps in its transport to the liver for degradation and excretion. [139] Therefore for efficient transport of tissue cholesterol to the liver the proportion of HDL-C to TC and LDL-C is more important than the individual values of any of these. Also TC/HDL-C and LDL-C/HDL-C were used to compare and explain the international differences observed in the rate of development of CHD in various population studies. In this study the data confirmed the rise in these atherogenic ratios in the males with increase in age.

Obesity predispose to many disease conditions like HT, diabetes, coronary and vascular disease. The percent of fat in a young individuals body weight is somewhere between 15 to 25% and this tends to increase to increase with age which may not be desirable. When the body fat content is greater than 25 to 30%, an individual is termed to be obese. Measuring the BMI and WHR in an individual is necessary to identify them as obese. In this study BMI decreased with age but showed no significance while WHR increased with age. Obesity has more recently been shown to decrease life expectancy by 7 years at the age of 40 years. [478] The increase in risk of death with each unit increase in BMI declines progressively with age but remains substantial until the age-group of 75 years and older. [479] Central adiposity is a predictor of CVD independently of major risk factors, including BMI. [402] Also dyslipidaemic individuals are more frequently “centrally obese”. [eg. with a high WHR] [404]

Thus the non-modifiable structural, metabolic and hormonal change in the body due to aging can be one of the factor which accounts for an increase in BP, dyslipidaemia and obesity.

2. Effect of age on BP, Serum Lipids and Anthropometric indices in Hypertensive subjects:

HT is becoming an important public health problem worldwide. It is the third leading killer in the world and responsible for one in every eight deaths. A recent report on the global burden of HT indicates that nearly 1 billion adults (more than a quarter of the world's population) had HT in 2000, and this is predicted to increase to 1.56 billion by 2025. [480] HT is a precursor to major diseases like myocardial infarction, stroke, renal failure, etc. Also it has been identified as one of the leading risk factors for mortality and is ranked third as a cause of DALYs. [481]

In this study hypertensive volunteers showed a similar pattern as observed for normotensive subjects in relation to age and gender. Hypertensive volunteers exhibited an increase in BP with age in both the genders and female values remained significantly lower to the males of the corresponding age groups. This result is in agreement with a study by Mohan *et al* wherein the prevalence of HT steadily increased with age in both sexes and was 3.5% in men and 3.1% in women at the age group of 20-29 years which increased rapidly and reached a prevalence of 50.8% in men and 51% in women at the age of 60years and above. Also in the same study it showed that compared to those below 35years, subjects between 35-49 years were at 3 times higher risk of HT; subjects between 50-64 years at >8 times higher risk while those above 65years were >13 times higher risk of HT. Thus an increase in prevalence of HT with aging has been observed in earlier studies also. [482]

Several epidemiological studies have been carried out in the past in India and abroad to find out prevalence of HT and its relation with age. Age was related with HT in the urban population of Istanbul. [483] Age was also the key predictor of HT in Brazil [484] and Mexico. [485] Age is a

known risk factor for high BP. In general BP rises as people get older. Proof is in the numbers. Upto 80% of people over 65years old have measurable high BP. [486]

Various studies in developing countries estimated a prevalence rate of HT among urban population ranging from 1.24% in 1949 to 36.4% in 2003. [487] The difference in prevalence rates could be due to different cut points used in defining the level of HT and also differing age groups constituting the study population. The prevalence of HT in Jaipur representing an urban north Indian population aged 20years and above was 30% in men and 33% in women using JNC V criteria. [8] The prevalence of HT in the urban population of West Bengal representing eastern India as reported to be 24.9%, based on JNC VII criteria. [13]

Another study showing the influence of age and sex on distribution of both systolic and diastolic HT among the sample population exhibited a higher prevalence of both systolic and diastolic HT in men below 40years. After 40years systolic HT showed progressive age-dependent increase upto eighth decade in both sexes and only in women, the prevalence of diastolic HT remained higher upto eighth decade. [13] A study by Hazarika *et al* on HT in the native rural population of Assam established age as not only a factor among others associated with an increase in the risk of HT but also as a significant determinant of HT. [488]

As seen in this study, influence of gender in HT prevalence has been observed among men by Shymal Kumar Das *et al* also. [13] A higher prevalence of both systolic and diastolic HT in young age among men, but higher prevalence of diastolic HT in women after 40years may be related to increasing family stress and obesity which is common in middle aged women. [489]

The reasons why HT increases with age are still poorly understood but are a topic of intense research. Some known contributors include: [490]

- Age related changes in hormone profiles.

- A tendency for older people to over salt their food because of decreased taste bud sensitivity.
- Changes that happen in the walls of arteries and other blood vessels.
- Decreased efficiency of the heart.

HT is an important association of systemic atherosclerosis and is a strong risk factor for major cardiovascular and cerebrovascular events. These events are further increased in the presence of dyslipidaemia. [63] Both HT and dyslipidaemia coexist more often than by a chance alone. [66] A few studies in Western populations have established the relationship between hyperlipidemia and HT. [66,67] Also most studies on HT and dyslipidaemia in India so far have been confined to metropolitan cities. [491,492] Asian Indians have a high prevalence of CAD and the risk factors are still not clear. [493]

In this study a strong correlation between age and serum lipids in hypertensive volunteers of both sexes was found. TC and TG values rose with the advancement of age in both sexes. In both gender LDL-C and VLDL-C concentrations remained parallel to that of TC and TG concentrations. Also HDL-C concentration increased in both sexes with increase in age but this rise was found to be insignificant. However in each age group of both genders the hypertensive patients showed an increase in TC, TG, LDL-C and VLD-C concentrations except HDL-C concentration as compared to normotensives. TC/HDL-C and LDL-C/HDL-C values were also much above the normal upper limit (4.5 & 3.0) in hypertensive volunteers as compared to normotensives.

Various studies on lipids in Asian Indians have shown a mixed picture of dyslipidaemia. Studies among immigrant Indians have shown high TGs and low HDL-C as the common lipid abnormalities. [493] Studies from North West India have shown high TC, high TG and low HDL-C as the predominant abnormalities in normal as well as among hypertensive population. [494,495] Studies from Southern India have shown lipid abnormalities predominantly of TC, LDL-C and TG rather than low HDL-C. [17,496] Also Zavaroni *et al* [497] have reported significantly raised systolic and diastolic pressures in subjects who have raised TGs and reduced HDL-C. In a retrospective study by Joglekar *et al* on the prevalence of lipid profile abnormalities in HT, it was found that 57% of

these subject had total cholesterol >200mg/dl. Also an elevated total to HDL-C >4.5 was found in 47% and 34% of subjects had serum TGs above 200mg/dl. [491] Thakur and Achari in their study on lipid level in uncomplicated HT found that with an increase in BP, the LDL-C was also elevated. [17] When these hypertensives were classified according to age the mean TC, HDL-C and TG levels were significantly different in hypertensives below 40 years of age as compared to controls. Within the hypertensive group, the mean HDL-C tended to rise and TG levels to fall with increasing age, when TC/HDL-C ratio were compared, a significantly higher proportion of hypertensives had an abnormal TC/HDL-C ratio (50.3% vs 44.4%) ($p \leq 0.001$); this applied to all the age groups and both the sexes. [17] Thomas and Mann [498] found 30% of patients seen in their lipid clinics to be hypertensive and many patients attending HT clinics had hyperlipidemia. In Bogalusa Heart Study, Newman [499] also found a strong and significant association between aortic fatty streaks and TC and LDL-C while an inverse association with HDL-C. SBP and DBP were also found to be related to coronary artery fatty streaks. Thus a positive correlation was established between atherosclerosis, BP and atherogenic index. Chadha *et al* [500] reported for Gujaratis settled in Delhi that 3.9% in control group with negative CAD were hypertensive and their lipid profile was quite high in both the genders.

A slight tendency for HT in normal men with negative CHD was noticed by Albrink [501] along with higher serum lipid levels. He also observed an increase in lipid concentration with age and observed marked increase in concentration in older age group volunteers. Albrink found the increase in TG with age only in some persons rather than an obligatory change. Conway and Smith [502] in their study of aging and HT found lack of arterial elasticity in a group of older hypertensive people. He also found a negative correlation of atherosclerosis with chronological aging by the way of obtaining increased arterial rigidity index with increase in age and concluded that hardening of arteries may be the one cause of diastolic HT.

The risk of HT is upto 5 times higher among obese people than among those of normal weight. [414] Upto two third of cases of HT are linked to excess weight [415] and cross sectional population surveys [416] suggest that more than 85% of HT arises in individuals with BMI values above 25kg/m^2. The anthropometric indices in this study showed a negative correlation with the advancement of age but the BMI values were greater than 25kg/m^2 in both genders of the two age groups in hypertensive patients. Females exhibited BMI values greater than males

of the corresponding age groups while an inverse was seen in case of WHR values. At all ages and throughout the world, women are generally found to have a higher mean BMI and higher rates of obesity than men for biological reasons. [395] Contrary to this study, the relation of HT with advancing of age and BMI has been documented in the past among Indian subjects. [4] In agreement to this finding an Indian study reported the occurrence of IHD even in patients with lower BMI. [503] According to the analysis by Brown et al; [504] the prevalence of HT as low at younger ages and high at older ages. At older ages, the prevalence is high even in normal weight individuals (BMI<25). Among men aged 60 to 79 years with BMI values <25, the prevalence of HT is 50%. Because the preponderance of cases of HT occur in the old age groups, even a considerable reduction in the prevalence of overweight and obesity as defined by BMI, might not necessarily lead to a large change in the population prevalence of HT. As stated earlier age, BMI and smoking were related with HT in the urban population of Istanbul [483] and also age and obesity were the key predictors of HT in Brazil [484] and Mexico. [485] Thus the possible explanations for the changes in BP, serum lipids and anthropometric indices with age in relation to hypertensive subjects might be same as those of normotensives as explained earlier. [18,160,474,475]

3. Levels of Serum Lipids and Anthropometric indices with regard to Levels of HT:

HT is becoming an important public health problem worldwide. It is also an important direct cause of cardiovascular morbidity and mortality in general and CHD in particular. Elevated BP and hypercholesterolemia in a healthy person without CHD predicts an increase in future risks of CAD, where as in population with abnormal ECG or with symptoms of angina pectoris the presence of HT or high cholesterol, increase CHD development.

According to the recommendations of JNC VII [2] an attempt had been made to find out a correlation between levels of HT (on basis of

DBP), serum lipids and anthropometric indices in comparison to normotensive subjects. Normal BP was defined as SBP <120mmHg and DBP <80mmHg. This classification includes preHT values from 80-89mmHg; stage-I HT from 90-99 mmHg and stage-II HT ≥100mmHg.

In this study the levels of HT from preHT to stage-II HT with respect to DBP was positively correlated with SBP in all three subgroups in both sexes as well as age groups. SBP in all three HT groups were significantly higher when compared to normotensives. DBP is the hallmark of essential HT and the CV sequelae of HT were derived entirely from diastolic component of BP. Kannel [505] specifically showed that SBP rises with age, while DBP tends to fall. This is true for people with high BP and those with no history of high BP. Goteborg multivariate analysis illustrated higher predictive capacity of SBP while DBP did not change the risk when SBP had been computed. [506] Also Anderson [507] pointed out that SBP, rather than DBP, was the most important indicator for overall CV mortality.

In the Chennai Urban Rural Epidemiology Study (CURES), the overall prevalence of preHT, stage-I and stage-II HT were 36.01%, 15.1% and 4.9% respectively. In addition, the prevalence of these levels of HT increased with increasing age. National health and nutritional survey of US obtained from 1976 to 1980, showed that, in adults (18-74 years of age) about 7% had preHT, 15% had stage-I, about 2% had stage-II HT, about 8% had borderline systolic and 2% had ISH. [508] These data indicated that about 60% million Americans had abnormal levels of BP. Framingham Study [509] demonstrated that the risk of all major CV complications increased progressively with levels of DBP over 82mmHg and of SBP over 130mmHg. The CURES study showed large proportion of sample population in the prehypertensive group. Even at the youngest age group studied (20-29years), the proportion of subjects with preHT was 33%, which was very high. In recognizing 'preHT' as clinical condition, JNC VII pointed out that BP related mortality is linear and that higher BP levels within what was earlier called 'high normal' or 'normal' range is associated with increasing morbidity and mortality. The Trial of Preventing Hypertension (TROPHY) study [510] on individuals with high normal BP suggests clearly the risk of CVD begins to rise before the diagnosis of HT is evident.

In the Framingham Heart study Castelli [511] found powerful interaction between HT and hypercholesterolemia. A few studies in

Western populations have established the relationship between hyperlipidaemia and HT. [66,67] Most studies in HT and hyperlipidaemia in India so far have been confined to metropolitan cities. [491,492] A study from Assam showed the prevalence of lipid abnormalities among the hypertensive to be 54%. [512]

In this study TC concentration showed significant rise with increase in DBP in both sexes as well as age groups. Moreover, in all three hypertensive groups as DBP increased from preHT to stage-II HT, cholesterol also elevated significantly. Males and females in this study also had increased LDL-C, TG and atherogenic ratios in comparison to normotensives. In addition, HDL-C decreased with each levels of HT and was lower to the normotensive values thus suggesting increased rise of CHD in hypertensive patients. LDL-C increased with levels of HT just like TC as 70% of TC are transported in the plasma as LDL-C.

Willum *et al* [513] had also shown that more than 25% of persons, 60years or younger, in whom HT developed and who also had a sibling with early onset of HT, will have a major lipid abnormality as well. Study by Kotokey *et al* [512] reported TC, TG and LDL-C cholesterol values to be significantly higher, whereas HDL-C value was lower among the hypertensive than the normotensives. The findings of this study were similar to those of Shankar Shiv *et al* on essential HT. [514] These findings suggest the coexistence of HT and hyperlipidaemia in a hypertensive population. The atherogenic ratios in hypertensive volunteers was not only significantly higher than that in normotensives of sexes but also significantly increased with the increase in DBP from preHT to stage-II HT. These ratios can be the best predictors to the risk of CHD in hypertensive subjects as higher the values greater is the risk and thus it is advisable to keep the ratio below 4.5 and 3.0.

Obesity being one of the risk factors for HT was correlated with levels of HT. The anthropometric indices, BMI and WHR exhibited similar pattern in relation to levels of HT. Both demonstrated an increase with increase in DBP among individuals with less than 50years in both gender while above 50years no change in these indices were illustrated. Compared to the normotensive the values of these indices were significantly high in each levels of HT. A study by Hazarika *et al* [488] is in agreement with this finding where in HT was associated with increased values of BMI and WHR.

Thus from this study the coexistence of HT, hyperlipidaemia and obesity can be well established. Moreover, the occurrence of coronary events is exaggerated with the presence of BMI and central obesity along with HT and dyslipidemia.

4. Effect of Diet on BP, Serum Lipids and Anthropometric indices:

Many risk factors for CVD, including high blood cholesterol, HT, obesity and diabetes are substantially influenced by dietary factors. Several population studies [167,168] correlated severity of atherosclerosis, serum cholesterol level and dietary fats. The Seven Countries study by Keys *et al* in the 1960s showed a relation between saturated fat intake, fasting blood cholesterol concentration and CHD mortality in various populations, [175] which suggests the protective effect of traditional Mediterranean-type diets. The diet in the high-risk group usually is high in animal foodstuffs, total calories, saturated fat cholesterol and refined carbohydrate. This does not imply that diet is the sole cause of HT and CHD. Nevertheless, diet must be considered as a major factor in the widespread occurrence of these clinical diseases since the disease occurs only rarely in the absence of diets habitually high in total calories, total and saturated fats, cholesterol and refined sugar.

Calorie: In this part of the study, the effects of high calorie consumption on the parameters were positively correlated. The BPs, SBP and DBP exhibited an increase in relation to age groups and genders in the hypertensive subjects consuming high calorie when compared to the hypertensive low calorie consuming subjects. A similar significant increase was prevalent among the serum lipids TC, TG and LDL-C concentration. HDL-C illustrated an increase in females of both age groups while males did not show much change in relation to low calorie diet consuming hypertensive patients. The atherogenic ratios also demonstrated an increase with high calorie consuming hypertensive subjects but this rise was not significant. The anthropometric indices, BMI increased in males but not females; in hypertensive, high calorie

consuming subjects while WHR remained nearly alike when comparison was done with low calorie consuming hypertensive subjects. However, in relation to normotensive individuals consuming low calorie diet all parameters demonstrated a tremendously significant increase except HDL-C concentration when compared to hypertensive patients consuming high calorie diet.

Several short-term laboratory studies have demonstrated that very low carbohydrate diets can have substantial effects on metabolism including weight loss and ketonemia. [515] Seven Countries study [296] and International atherosclerotic project [164] demonstrated a positive relationship between the saturation of dietary fat, serum cholesterol levels and CHD. In relation to BP, SBP did not change significantly in either low-carbohydrate diet (Atkins Diet) or high carbohydrate diet (conventional diet) during a study [213] but DBP decreased in both groups. Regarding lipids, HDL-C increased and TG concentration decreased in the group on low-carbohydrate diet. [213] The mechanism responsible for the decreased energy intake induced by a low carbohydrate diet with unrestricted protein and fat intake is not known, but may be related to the monotony of simplicity of the diet, alterations in plasma or central satiety factors, or other factors that affect appetite and dietary adherence. [213] Excessive caloric intake from sources like fats, carbohydrates, proteins or alcohol promotes hyperlipidaemia. A carbohydrate rich diet increases serum lipids in persons having higher baseline serum lipid levels than in those with low or normal serum lipids. [213]

Several epidemiological studies have reported reduced BP linked to Mediterranean dietary pattern (α linolenic acid rich diet). [209,210] The DASH trial has shown that a dietary pattern rich in fruit vegetables and low fat dairy products and with reduced total and saturated fat can be effective in the prevention of HT. [52,219] Also fruit and vegetable intake may reduce CVD risk through the beneficial combination of micronutrients, AOs, phytochemicals and fiber in these food. Several prospective studies have directly related fruit and vegetable intake with CVD. [516] Findings from ecologic studies show that populations with lower intake of animal products and higher intakes of fruit and vegetables have lower prevalence of CVD than do populations with higher intakes of animal products. [517] Also in a recent study the co-administration of garlic pearls with fish oil was found to be more effective than placebo in the management of dyslipidemia. [240] Walker *et al* [518] demonstrated in two men that an excess of calories over a short period of time caused striking increases in serum cholesterol and lipoprotein

levels even though the diet was low in fat. Anderson *et al* [519] found that a daily excess of 600 calorie cause a significant elevation in the total serum cholesterol of 20mg/100ml.

Obesity is common in patients who have essential HT although there is no direct relationship. For this reason, the total calorie intake should be restricted in such patients. Thus the low-carbohyrate, high protein, high-fat Atkins diet produces greater weight loss (an absolute difference of approximately 4%) than a conventional high-carbohyrate, low fat diet. Christakis *et al* [520] reported the effect of a cholesterol lowering diet on hypercholesterolemia in obese and normal weight subjects in experimental and control groups. In the experimental group 42% of the normal weight subjects were hypercholesterolemic. In the control group, 44% of the normal weight men were hypercholesterolemic. After 4years of observation, the proportion of hypercholesterolemic men in the experimental group was significantly lower than that in the control group, thus suggesting that the dietary protocol of the study was effective in lowering serum cholesterol levels without regard to initial or final weight status or change in weight status.

Fat: The intake of total fat exerts a strong influence on the BP and serum lipid levels. In this study it was evident that in hypertensive volunteers fat played a significant and positive role. Subjects taking high fat diet showed increased BP, serum lipid levels, atherogenic ratios and anthropometric indices. In normotensive subjects, all these parameters demonstrated a decreased value with low fat diet when compared to their high fat consuming hypertensive subjects.

Populations with diets high in total fat usually have high SBP, DBP and serum cholesterol levels. Dodson and Paul [521] separately were able to get the findings that a combination of dietary interventions with a low sodium, low fat and high fibre diet caused a greater fall in both SBP and DBP (11.6 and 7.6mmHg) than any of those interventions alone in treated hypertensive patients. In hypertensive North Karelian volunteers, Pekka and James [522] were able to reduce BP from 138.9/88.9 to 129.5/81.3 mmHg on low fat (23% energy) diet.

Food consumption patterns in a particular study [523] showed that important difference in relation to CAD were higher intake of total visible fat, milk and milk products, meat, eggs, sugar and jaggery in urban compared to rural subjects. Prevalence of CAD in relation to visible fat intake showed a higher prevalence rate with higher visible fat intake in both sexes and the trend was significant for total prevalence rates both for rural and urban men and women. Another study [524] reported that urban subjects had three times better socioeconomic status than rural subjects and were thus eating higher total and saturated fat, cholesterol and refined carbohydrates and lower total and complex carbohydrates compared to rural men and women. Also energy expenditure during routine and spare time physical activity was significantly higher in rural compared to urban subjects. Those patients who had risk factors, showed lesser physical activity and had greater adverse factors in the diet compared to subjects without risk factors. Thus, this finding suggested that decreased consumption of total and SF and increased physical activity may be useful for prevention of HT and CAD among urban as well as immigrants. [524]

The dietary intake of cholesterol in human adults varies between 200 and 800 mg/day and is highest in those with a high intake of SF. The body synthesizes approximately 2000mg daily from various sources. Wilson [525] noted that 60 to 80% of serum cholesterol was derived from endogenous source when a diet high in cholesterol is fed. Taylor *et al* [526] reported that subjects of cholesterol free and cholesterol rich diets showed essentially the same rates of daily endogenous cholesterol synthesis. Thus restriction of exogenous cholesterol has; been recommended as helpful in reducing serum cholesterol. In relation to TGs, elevations of serum TGs have been reported with diets low in total fat and high in carbohydrates. This hypertriglyceridemia is transient, however as shown by Antonis and Bersohm, in a carefully controlled study on South African white Bantu prisoners. [527] They showed that a diet low in total fat (15%) and high in carbohydrate (70% of total calories), when followed for a period of 39 weeks caused a lowering of all serum lipids, including cholesterol and TGs in both groups (European and Bantu) to the usual low levels found in Bantu natives. [527]

Also it has become apparent that changes in serum lipids and cholesterol are dependent on the degree of saturation or unsaturation of the fats, rather than on their source. [528] The highly SFs such as butter, coconut oil and cocoa butter produce high levels of serum cholesterol, while iso-caloric amounts of highly unsaturated oils such a safflower oil, corn and cotton seed oil, produce lower levels of cholesterol. Contrary to

the above statement, in 1957, Ahrens et al [192] reported that cocoa butter does not raise the plasma cholesterol level in humans as much as butter fat since cocoa butter is rich in stearic acid. Thus results suggested that this fatty acid is not "hypercholesterolemic" in humans. Also a study by Bronte-Steward *et al* [529] exhibited that the essential unsaturated fatty acids, linoleic acid, linolenic acid and arachidonic acid, which are present in most oils but not butter, exert a lowering effect in the serum cholesterol. Further they went on to show that when these polyunsaturated fatty acids were hydrogenated their favorable effect on serum cholesterol was lost and they acted to elevate it just as did certain highly SFs such as butter and coconut oil. [529] Some metabolic studies suggest that fatty acids containing at least one double bond in the transconfiguration, which are found in hydrogenated fat, have a detrimental effect on serum lipoprotein cholesterol levels as compared with unsaturated fatty acids containing double bonds only in the cis configuration. Also considerable attention has been focused on the effects of trans FAs on HDL-C levels after initial reports suggested not only a LDL-C raising effect but also an HDL-C lowering effect. [262] Similarly FAs have been reported to increase serum Lp(a) levels in some, but not all, studies. [530,531]

In relation to anthropometric indices, an analysis of potential anthropometric predictors of the risk factor response to diet showed significant correlations between the indices of adiposity and changes in LDL-C concentration, but not with change in HDL-C or TG concentration. [264] In this above study the men with a BMI ≥25.3 had 30% smaller reductions in LDL-C concentration than did the men with a BMI <25.3. This effect of BMI on the LDL-C response is consistent with data from dietary intervention and epidemiologic studies. Katan and Beynen [532] first reported that TC response to increases in dietary cholesterol was negatively correlated with BMI in women but not in men. In studies conducted in premenopausal women, Cole et al [533] found that women with a BMI between 24.8 and 30 had smaller reductions in LDL-C concentration than did women with BMI <24 when switched from a typical American diet to one lower in total fat, SF and cholesterol. Additionally TGs increased the most in women with a BMI >30. Additional studies conducted in both men and women and with diets of varying FA composition have shown a positive correlation between BMI and LDL-C in response to reduction in dietary SF. [210,221-224] Thus these data suggest that weight reduction may be required to fully derive the benefit of dietary changes on CVD risk.

5. Effect of tobacco consumption on BP, Serum Lipids and Anthropometric indices:

Smoking is a major risk factor for CVD. Cigarette smoking contributes to heart disease through induction of a hypercoagulable state, reduced oxygen delivery, coronary vasoconstriction and nicotine-induced hemodynamic effects. The epidemiological studies have mounted ample evidences of a strong positive association between cigarette smoking and the risk of CVD morbidity and mortality in men and women under 65years. [296,534,535] MRFIT, MRC and prospective cardiovascular studies found 35%, 34% and 20% hypertensive volunteers having smoking habits in USA, UK and North Europe respectively. [536] More than 1.1 million individuals are affected by MI each year in North America and >20% of these individuals are habitual smokers. [288] Cigarette smoking is associated with an increased risk of sudden death, angina, MI, peripheral vascular disease and stroke. [289,290]

The effect of tobacco consumption on BP and serum lipids was seen in hypertensive subjects. The risk of smoking is dependent on the presence of HT and concomitant hyperlipidaemia. The landmark Framingham study have not only established smoking as cardiovascular risk factor, but also revealed a synergetic effect with the risk factors, such as HT, hypercholesterolemia, glucose intolerance and DM. [537]

Hypertensive tobacco consumers in this study showed a age dependent variation in BP. An increase in BP in both genders in 30-50 years age group but yet both these values in the two age groups were considerably higher to normotensive cases. This finding was in agreement with the epidemiological finding of Israel population [538] in which nonsmokers had lower BP. Also other epidemiological studies had shown a sudden rise in BP of 10/8mmHg or 11/9mmHg in hypertensive volunteers after smoking two cigarettes and this happened as a result of increase in nicotine content which caused rise in epinephrine and norepinephrine concentrations in blood. [539] Also the nicotine mediated hemodynamic effects of smoking include an increase in heart rate and BP, which increases myocardial risk. [301] Also in another study by Sharma *et al* pan masala intake causing acute increase in PP and BP was reported. [540]

In seven countries study Keys [296] could not find an association between smoking and CHD in population with low plasma cholesterol levels and low risk of CHD. On the contrary, a study by Pais *et al* reports smoking 10 cigarettes or beedies/day carries an independent four-fold increased risk of AMI. [541] Khurana *et al* showed that though different mode of addictions, smoking and tobacco chewing have an equal and comparable effects on lipid profile and therefore raising cardiovascular risk in same proportion. [542] Cigarette smoking is associated with reduced HDL-C, [128] lecithin cholesterylacyl transferase (LCAT)activity [306] and cholesteryl ester transfer protein (CETP) activity. [307] In chain smokers there was increased risk of CHD with high levels of TC, TG, LDL-C and low levels of HDL-C and also decreased capacity of liver and kidney functions. In this study TC and TG concentration of tobacco consumers in hypertensive volunteers showed a increase in 30-50 years age group while a decrease in 51-80 years age group when compared to hypertensive tobacco nonconsuming counterparts. This study showed a consistent positive association between tobacco consumption and LDL-C values, while an inverse relation between tobacco consumption and HDL-C. The atherogenic ratios were also positively associated with tobacco consumption. Thus variations at hypertensive level of tobacco consumers might occur but when compared to their normotensive counterparts a significantly positive correlation was exhibited between serum lipids, atherogenic ratios and tobacco consumption.

The Framingham Offspring Study showed that smoking was significantly associated with lower HDL-C levels of 4mg/dl in men and 6mg/dl in women. [293] Also there is a linear dose dependent effect between the number of cigarettes smoked per year and HDL-C level. Nesje [543] showed that in Northern Norway HDL-C levels were more pronounced between heavy smokers (≥20 cigarettes) and nonsmokers particularly for HDL2-C levels. Cigarette smoking habit interfering with LCAT activity causes decrease in esterification of free cholesterol and results in the rise of free cholesterol in the plasma and this in turn is related to decreased levels of HDL-C concentration [544] Thus tobacco consumption increase atherogenic lipids in blood and decrease the protective effect of HDL-C by decreasing HDL2-C fraction. Nicotine in the cigarette smoke increases oxygen demand and causes arterial constriction, which impairs blood flow to the heart. [301] Also smoking further accelerates endothelial atherosclerosis through damage to the endothelium and increased fibrinogen levels. [303,330] In these ways tobacco consumption impairs the lipid metabolism and promotes the development of CHD and atherosclerosis. Thus there is a synergistic interaction of tobacco smoking with HT and high blood cholesterol which greatly increase CHD risk as well as sudden death and stroke. [545]

Among the anthropometric indices, BMI showed a decrease in hypertensive tobacco consumer while WHR did not vary much when compared to hypertensive tobacco nonconsumers. But yet these indices were significantly higher compared to their normotensive counterparts. In agreement to this finding a study shows that the factor for pathogenesis of obesity is addiction to smoking among others. [546] Also an inverse relationship between cigarette smoking and weight is well documented [547] which again is in agreement to part of this study.

Thus in hypertensive tobacco consumers, HT itself being a risk factor for CHD, the possibility is enhanced by additive effect of hyperlipidaemia, smoking and obesity.

6. Effect of heredity on BP, Serum Lipids and Anthropometric indices:

There are several challenges in the prevention and management of atherosclerotic heart disease. The principal challenge is to identify susceptible individuals before they develop the disease. Knowledge of genetic risk factors will help define the mechanisms of the disease and could ultimately assist in the rational design of selective prophylaxis or therapy. Many single genes have been identified as the basis for different CVDs. Family history as an isolated event for genetic implications of recurrence of disease is more suggestive when the illness occurs early.

In 2004, the *Journal of American Medical Association* published a study entitled, “Parental CVD as a Risk Factor for CVD in Middle-aged Adults.” The study found that a parental history of CVD is an independent predictor of cardiovascular events in middle aged men and women. After adjustment for other risk factors, premature CVD in atleast 1 parent was associated with a significant doubling (100% increase) in cardiovascular risk for men and a 70% increase in risk for women over 8years. Some workers have observed positive family history as an independent predictive factor for CHD in men aged less than 50years. [335] In a study by Trivedi *et al* CHD was significantly associated with

increased BP, family history and smoking.[548] Also in an epidemiological study to find the influence of risk factors on the prevalence of CHD in a total rural community of Punjab, it was found that of the various risk factors tested, HT, hypercholesterolemia and a positive family history showed an association with CHD. [549]

In this part of the study an effort was made to study the effect of heredity and its relation to BP, serum lipids and anthropometric indices in hypertensive volunteers. There was a significant increase in BP in the hypertensives with positive family history in both genders along with their corresponding age groups. HT is a serious disease that can result in heart attack, strokes or kidney failure and scientists have known for some time that HT is a heritable condition that runs in families. Elizabeth *et al* [550] showed significantly higher BP and TC in men less than 60years of age with positive history of heart attack and thus was found to be independent of all other risk factors studied. She also showed a five fold excess risk of cardiovascular death in younger men with positive family history of heart attack. Heller [551] also found on an average the first degree relatives of hypertensive patients to have higher BP than those relatives of normotensive controls. Some studies have suggested that high blood pressure may be associated with the presence of E_4 allele, when studies aimed to find out the association of apo E genotypes with HT were carried out. [351,552] The genetic variations at apo E have also been shown to affect lipid and lipoprotein levels in the general population. [553]

With regard to lipids in this study, TC and LDL-C concentrations showed an insignificant decrease in hypertensive with positive family history while TG concentration did not vary in both age groups and their genders when compared to hypertensives with negative family history. But yet, when compared to the normotensive negative family history all serum lipids demonstrated tremendous significant increase among the hypertensives with positive family history except HDL-C concentration. One of the best understood inborn error of metabolism determining elevated levels of plasma cholesterol and LDL-C is the autosomal dominant disorder of familial hypercholesterolemia (FH). Studies indicate that 5-10% of individuals with premature MI may have FH. [114] A study on FH indicated that there exist mutational heterogeneity if the LDL receptor gene among the Indians, wherein, none of the mutation were reported to be common among Indian immigrants. [554] In recent times new markers like the apo E gene polymorphism stated earlier have been found associated with CHD and are being extensively studied. [347] A small study from the Southern parts of rural India on tribal communities

suggested that the low frequency of the apo E_4 allele was a contributing factor for the low prevalence of CHD in this community. [363] A significant relation was found between cholesterol levels and the family history of CAD. Persons with high family history scores were found to have cholesterol values of 213mg% while those with intermediate or low scores had average cholesterol values of 192 and 189mg% respectively. [555] Mowar *et al* [556] also studied coronary risk factors in family members, close or distant relatives of patients having MI. He observed highly significant TC and TG concentrations in brothers and sisters of the patients having MI in comparison to those without having MI or positive history of CHD.

A genetic predisposition to CAD is suggested by high levels of lipoprotein in Asian Indians. [557] Pometta *et al* [558] found lower HDL-C and did not find any significant differences in TC or LDL-C in young males with family history of AMI in comparison with control group. Kukita [558] also found significantly lower apo A and higher apo B in first degree relative of CHD patients. Backer [558] observed (LDL-C+VLDL-C)/apo B and HDL-C/apoA-1 values to be very high in offspring group in comparison to the control group. These ratios of serum lipids and apo proteins reflected internal composition of LDL-C and HDL-C. HDL-C concentration also was less and TC/HDL-C ratio was high in those with positive family history which suggested that the protective role of HDL-C against atherosclerosis was very much reduced. Widhalm *et al* [559] showed that the progeny of families with manifestation of CHD could be distinguished from children with negative family history with the help of HDL-C, TC/HDL-C and LDL-C/HDL-C, where as apoA-1/apo B was the strongest discriminator.

Lp(a) level is an important determinant if CHD among patients with FH and non FH. [560] Higher Lp(a) levels were reported in individuals as a strong family history of CHD than in those without such history. [561] A study by Rajashekhar *et al* found higher Lp(a) levels in patients with hypercholesterolemia than normocholesterolemia but not significant. [563] The pathogenecity of Lp(a) is increased with high LDL-C and vice-versa. [562] In 1958, research conducted in Singapore first established that Indians have thicker blood and more of Lp(a) than the Chinese. The significance was not well understood, till 1990 when a subsequent 10year study conducted by Enas confirmed that one of four Indian-American had high levels of Lp(a) as compared to the Japanese, Chinese, Caucasians and Hispanics. Recently, a study in Singapore which took blood from the natal chord of 5000 babies of Indian origin, found extraordinarily high contents of Lp(a) present, indicating that

genetics, not lifestyle or diet, was the major cause of such abnormal levels of Lp(a). Thus Lp(a) levels correlate with both early and advanced atherosclerosis, severity, extent and progression of atherosclerosis and all complication of CHD. [564]

The causes of obesity are many, but there is little doubt that genetic factors play an important role in its etiology. Humans carry probably dozens of genes that are directly related to body size. In this study the anthropometric indices, BMI and WHR showed a positive correlation with hypertensive positive family history patients. Statistical analyses suggest that 50% or more of the variation between individuals in BMI has a genetic basis [565] but these effects are dominated by polygenic environmental interactions that reflect many genetic influences affecting spontaneous physical activity, twitchiness, BMR, propensity to synthesize diurnally lean rather than fat tissues and appetitive behavior. The increasing epidemic of obesity in the world has stimulated interest in identifying or predicting individuals who are at greatest health risk at an early age. [378] This is particularly important to allow early implementation of preventive strategies.

The role of apoE polymorphism in causing atherosclerotic events have been reported. [345,346] ApoE is an exchangeable protein which acts as an ligand for LDL receptors. It plays an essential role in lipid metabolism specially in the removal of atherogenic remnants of TG-rich lipoproteins [347] and by reversing cholesterol transport in plasma and intercellular lipid transport within tissues. These common isoforms of apo E including E2, E3, E4 [348] have been identified. It is well known that the E4 isoform is associated with increased levels of TC and β-lipoprotein [349] and increased susceptibility to CVD. [350] Some studies have suggested that high BP may be associated with the presence of the E4 allele [351,352] while others have found its association with E2 allele [353]. Mechanisms of apoE such as increased rigidity and decreased elasticity of the aorta and other large vessels [354] may contribute to the development of HBP and thus explain the lack of association in the elderly subject. Thus significant association of E4 allele is observed with HT in addition to other well known risk factors and positive family history. These observations emphasize the need to monitor HT and lipid metabolism especially in middle aged males and those with a positive family history to reduce the susceptibility to CAD.

However genes alone don't explain the spurt in HT and heart diseases among the young. The answer, in a word, is lifestyle. While over 10% of urban Indians succumb to HT and heart diseases, the figure is only 3-5% in rural areas. Thus lifestyle changes due to rapid urbanization are the precipitating cause of these diseases in India. The solution to these, sky-rocketing figures are – Simply tweaking our lifestyles a little.

SUMMARY AND CONCLUSION

Summary and Conclusion:

HT occupies the no.1 position as a major public health problem in most industrialized countries of the world. Existing data suggests that the prevalence of HT has remained stable or has decreased in economically developed countries during the past decade, while it has increased in developing countries. [4] (ht32) However, the increase in the prevalence rates of HT needs to be quantified to plan for effective prevention strategies, which are urgently needed in developing countries. Given the rising prevalence of HT in developing countries undergoing epidemiological transition like India, increased awareness treatment and control of high BP are critical to the reduction of CVD risk and prevention of the associated burden of illness. This study was undertaken with the objective to gather the effect of diet, tobacco and heredity on lipid metabolism and HT.

In normotensive and hypertensive subjects a positive correlation with BP and serum lipids were observed while HDL-C showed a negative correlation with the advancement of age in both sexes. Thus, age was an important atherogenic factor, which indicated that with increase in age, the older individuals are more susceptible to the development of HT and CVDs.

In relation to gender, males had values higher to females in all the parameters but still both are prone to develop HT and atherosclerotic disease as the values were above normal in both the genders. Thus gender specific increase of development of HT in both men and women indicate significant role of environmental factors. This suggests public health remedial measures to address growing HT in the community. Thus health education about lifestyle changes, dietary modification and avoidance of urban stress are required to be taught.

In hypertensives with respect to age in both genders, the levels of HT from preHT to stage-II illustrated an increase in serum lipids and anthropometric indices. As lipid levels increased and HDL-C decreased with increase in DBP, the risk of development of CAD increased from preHT to stage-II HT (severe HT). Thus, the levels of HT show an increase in levels of serum lipids and anthropometric indices, which may be major contributors to increased risk of CAD in patients of HT. Patients

with preHT, are at increased risk for progression to HT as they usually remain unnoticed with their asymptomatic behavior and thus become easy targets to develop severe HT. Therefore subjects with preHT should be monitored regularly and life style altered to curb them from progressing to stage-I or stage-II level of HT.

Diet plays a positive and significant role in hypertensive patients. The increased consumption of both calorie and fat exhibited an increased BP, serum lipids and anthropometric indices when comparison to their low consuming calorie and fat in normotensive counterparts were conducted. Thus, the patient who has essential HT should eat as much as is necessary to maintain strength and nutrition but should avoid excesses. This restriction of the quantity and quality of the diet should be extended to total calories, total volume of fluids protein and salt. Special modification of the diet for the patient with hypertensive vascular disease may be indicated because of coincidental or associated disturbances in lipid and carbohydrate metabolism. *Moderation* as a watchword should apply to the diet as well as to all other aspects of treatment.

This study showed a consistent positive association between tobacco consumption, BP, serum lipids and anthropometric indices, while an inverse relation was established between HDL-C and tobacco consumption among hypertensive individuals. Several smoking related mechanism are responsible for the development of atherosclerosis and the induction of cardiac events. Benefits from quitting are seen in former smokers even after many years of heavy smoking. Investigations also have demonstrated benefits from cessation for smokers who have already developed smoking related diseases or symptoms. Persons with diagnosed CHD experience as much as 50% reduction in risk of reinfarction, sudden cardiac death and total mortality if they quit smoking after the initial infarction. Thus, there is overwhelming evidence demonstrating both the cardiovascular hazards of smoking and the prompt benefit that occurs with smoking cessation. Therefore, tobacco consumption is the single most alterable risk factor contributing to premature morbidity and mortality that can be reversed by quitting consumption of tobacco.

Heredity also among the above parameters demonstrated a positive relation with BP, serum lipids and anthropometric indices except HDL-C in the hypertensive subjects. Nothing can be done about ones'

family history, but if a strong family history of CHD or HT is present one must:

- Change lifestyle
- Lose weight
- Stop smoking
- Lower cholesterol levels
- Eat more fiber, more vegetables and fruits

Furthermore, the principal challenge is to identify susceptible individuals before they develop the disease. Advance in the field of genomics and proteomics will help in preventing and treating this multifactorial disease.

However, several potential limitations should be considered while interpreting the results of this study. First, the dietary data were obtained from a structured questionnaire and therefore underestimation or overestimation of calorie and fat intake cannot be ruled out. In addition, the correlation of socio-economic status with HT was not analyzed, as participants did not want to reveal their actual income status. Lastly, the lipid parameters analyzed are not enough to come to a particular conclusion due to limitations in the infrastructure. Thus, further studies on apolipoproteins and other risk factors are required to be conducted to find out the effect of these observations stated in this study.

The results of the present study show, there is a long way to go to accomplish the goal of optimal control among the Saurashtrian population. Undoubtedly, a similar situation exists in other parts of the country as well. It took 30 to 40years of sustained effort to substantially improve HT, detection and control in western countries and the rates are still far from optimal. HT itself being a risk factor for CAD, further deteriorates the patients with presence of all atherogenic parameters. Thus, screening of the population for detecting HT at the earliest and timely intervention could curb the sequel events to a certain extent. Therefore hypertensive patient can more appropriated be targeted for, therapy for risk factor clusters rather than HT alone. Thus, it is obvious that considerable effort is needed to prevent or reduce the increasingly large burden of disease related to increasing rates of HT in countries in epidemiological transition, such as India.

BIBLIOGRAPHY

Bibliography:

1. Wasir HS Hypertension- The need for Primary prevention. Regional Health Forum (WHO SC-Asia). 1996; 1: 1.

2. Chobanian AV, Bakris GL, Black HR. The seventh report of the joint national committee on prevention, detection, evaluation and treatment of high blood pressure- the JNC 7 report. *JAMA* 2003; 289: 2560-2572.

3. Yasan RS, Beiser A, Seshadri S. Residual lifetime risk for developing HT in the middle aged women & men: the Framingham Heart Study. *JAMA* 2002; 287: 1003-10.

4. Gupta R. Meta analysis of prevalence of HT in India. *Indian Heart Journal*. 1997; 49: 43-48.

5. Dutta BB. Studies on BP, height, weight, chest & abdominal measurement of 2500 members of the Calcutta police with short notes on their medical impediments. *Indian Med. Gazette*. 1949; 84: 238-243.

6. Washir HS, Ramachandran P, Nath LM. Prevalance of HT in a closed urban community. *Ind Heart J*. 1984; 36: 250-253.

7. Hussain SA, Nayak KC, Gupta A. A study of prevalence of HT with reference to economic, education, environmental and hereditary factors in general population of north- west rajastan *Ind Heart J*. 1988; 40: 148-151.

8. Gupta R, Gupta S, Gupt VP, Prakash H. The prevalence of determinants of HT in the urban population of Jaipur in Western India. *J Hypertension*. 1995; 13: 1193-1200.

9. Anand MR. Epidemiology of HT. *In*: (ed) Anand MP. HT: an international monograph 2001. New Delhi: IJCP. 2001: 20-25

10. Indian Council of Medical Research – Annual Reprt 2002- 2003.

11. Grassi GM, Somers VK Renk WS, Abboud FM, Mark AL. Effects of alcohol intake of BP & sympathetic nerve activity in normotensive humans: A preliminary report. *J Hypertension*. 1989; 7(suppl 6): S20-S21.

12. Smit M, von der Kooij-Meijis E, Frants RR, Haviks I, Klasen EC. Apo gene duster on chromosome 19, Definite localization of the apo C2 gene & the polymorphic Hpa I site associated with type III hyperlipoproteinemia. *Hum genet*. 1988; 78: 90-93.

13. Das SK, Sanyal K, Basu A. Study of urban community survey in India: growing trend of high prevalence of HT in a developing country. *Int J Med Sci*. 2005; 2: 70-78.

14. Vasan RS, Larson MG, Leip EP, *et al*. Assessment of freq of progression to HT in non hypertensive patient in the Framingham Heart Study: A cohort study. *Lancet* 2001; 358 : 1682-6.

15. Levington S, Clarke R, Qizilbash N, *et al*. Age specific relevance of usual BP to vascular mortality. A meta–analysis of individual data for 1 million adults in 61 prospective studies. *Lancet* 2002; 360: 1903-13.

16. Xavier J, Florent S, Yuri VK, *et al*. Molecular Basis of Human HT: Role of Angiotensiongen. *Cell* 1992; 71: 169-180.

17. Thakur Ak, Achari V. A study of lipid levels in uncomplicated HT. *Ind Heart J* 2000; 52: 173-177.

18. Shaper AG, Cook DG, Walker M. Prevalence of IHD in middle aged British men. *Brit Heart J* 1984; 51: 595-605.

19. Logan RL, Thompson M, Olior ME, Carlson LA, *et al.* Risk factors for IHD in normal men aged 40 years. *Lancet* 1978; 2: 949-954

20. Curb JD, Borhani NO, Entwisle G. Isolated systatolic HT in 14 communitis. *Am J Epidemiol.* 1985; 21-362-70.

21. Burt NL, Whelton P, Rocella EJ. Prevalence of HT in the US adult population. Results from the third National Health & Nutrition Examination survey, 1988-1991. *Hypertension* 1995; 25: 305-13.

22. Franklin SS, Gustin WT, Wong ND. Hemodynamic patterns of age related changes in BP. The Framingham Heart Study. *Circulation* 1997; 96:308-15.

23. Gubner RS. Systolic HT : A pathogenetic entity. *Am J Cardiol*. 1962; 9: 773-6.

24. Garland C, Barrett-Conner E ,Suarez L. ISH and mortality after age 60 years. A prospective population based study. *Am J Epidemiol* 1983; 118: 365-76.

25. Tumilehto J, Salonen JT, Nissinen A. ISH & its relationship to the risk of MI, CVD & death in middle aged population. *Eur Heart J.* 1984; 5: 739-44.

26. Kannel WB, Gordon T, Schwartz MI. Systolic versus diastolic BP & risk of CHD. The Framingham Study. *Am J Cardiol*. 1971; 27: 335-46.

27. Kannel WB, Wolf PA, Mcgee DL; Systolic BP, arterial rigidity & risk of stoke. The Framingham Study. *JAMA* 1981; 245: 1225-9.

28. Rutan GH, Kaller LH, Neaton JD. Mortality associated with diastolic HT & ISH among men screened for the MRFIT. *Circulation* 1988; 77: 504-14.

29. Stamler J, Stramler R, Neaton JD. BP, systolic & diastolic & CV risks. US population data. *Arch Int Med* 1993; 153: 598-615.

30. Chae W, Pfeffer MA, Glynn RJ. Increase PP & risk for heart failure in the elderly. *JAMA* 1999; 281: 634-9.

31. Franklin SS, Khan SA , Wong ND. Is Pulse pressure useful in predicting risk for CHD? The Framingham Heart Study. *Circulation* 1999; 100: 354-60.

32. Domanski MJ, Davis BR, Pfeffir MA. ISH: prognostic information provided by PP. *Hypertension* 1999; 34: 375-80.

33. Blacher J, Staessen JA, Girerd X. PP not mean pressure determines CV risk in older hypertensive patients. *Arch Intern Med* 2000; 160: 1085-9.

34. Glynn RJ, Chae CU, Guralnik JM. PP & mortality in older people. *Arch Intern Med* 2000; 160: 2765-72.

35. Domanski M, Norman J, Wolz M, *et al*. CV risk assessment using PP in the NHANES-I. *Hypertension* 2001; 38: 793-7.

36. Mitchell GF, Moye ha, Braunwald E, *et al*. Sphygmomanometrically determined PP is a powerful independent predictor of recurrent events following MI in patients with impaired left ventricular function. *Circulation* 1997; 96: 4254-60.

37. SHEP Cooperative Research Group. Prevention of stroke by antihypertensive drug treatment in older patients with ISH. *JAMA*. 1991; 265: 3255-64.

38. Stassen JA, Fagard R, Thigs L. Randomized doubt blind comparison of placebo & active treatment for older patients with ISH. The systolic HT in Europe (Syst-Eur) Trial Investigations. *Lancet* 1997; 350: 757-64.

39. Liu L, Wang JG, Gong L. Comparison of active treatment & placebo in older Chinese patients with ISH. Systolic HT in China (Syst-China) Collaborative Group. J *Hypertension* 1998; 16:1823-9.

40. Domanski M, Mitchell G, Pfeffer M. PP & CV disease related mortality: follow up study of the MRFIT. *JAMA* 2002; 287: 2677-83.

41. Franklin SS , Larson MG, Khan SA. Does the relation of BP to CHD risk change with aging? The Framingham Heart Study. *Circulation* 2001; 103: 1245-9.

42. Venkataram CS. Systemic Hypertension. In: *Cardiology.* 1995, p 403-414.

43. Vajpayee S. Role of PGs & bioactive substances in HT. Satellite meeting on HT & heart research in souvenir. 1994 Abst. pg no 11.

44. Willis J, Hurst & Robert S, Schlant. The Heart 7th edition – 1990, Mcgraw Hills book comp. Page no : 961 -1028, 877-925.

45. Robert GL. Essential HT. A review & update of the evidence. *Hypertension* 1993; 21: 380-390.

46. Vincent Dequattro, Yukio Miura. Neurogenic factors in human HT mechanism or myth. *Am Jr of Med.* 1973; 55: 362-375.

47. Stevo Julius. Sympathetic hyperactivity & coronary risk in HT. *Hypertension* 1993; 21: 386-393.

48. Neal B, MacMohan S, Chapman N. Effects of ACE inhibitors, calcium antagonists & other blood pressure lowering drugs: Result of prospectively designed overviews of randomized trials. Blood Pressure Lowering Treatment TrialistS Collaboration. *Lancet* 2000; 356: 1955-64.

49. Mulrow C, Lau J, Cornell J, *et al*. Pharmaco-therapy for HT in the elderly. *Cochrane Database Syst Rev* 2000; 2: CD 000028.

50. Ogden LG, He J, Lydick E, Whelton PK. Long term absolute benefit of lowering BP in hypertensive patients according to the JNC VI risk stratification. *Hypertension* 2000; 35: 539-43.

51. The Trials of HT Prevention Collaborative Research Group. Effects of weight loss & sodium reduction intervention on BP & HT incidence in overweight people with high normal BP. The Trials of HT Prevention, phase II. *Arch Intern Med* 1997; 157: 657-67.

52. Sacks FM, Svetkey LP, Vollmer WM, *et al.* Effects on BP of reduced dietery sodium & the DASH diet. DASH-sodium Collaborative Research Group. *N Engl J Med*. 2001; 344: 3-10.

53. Vollmer WM, Sacks FM, Ard J, *et al.* Effects of diet & sodium intake on BP: Subgroup analysis of the DASH-sodium trial. *Ann Intern Med*. 2001; 135: 1019-28.

54. Kelley GA, Kelley KS. Progressive resistance exercise & resting BP: A meta-analysis of randomized controlled trails. *Hypertension* 2000; 35: 838-43.

55. Xin X, He J, Frontine MG, *et al*. Effects of alcohol reduction on BP: A meta analysis of randomized controlled trials. *Hypertension* 2001; 38:1112-7. [30] (HT -19).

56. Hajjai J, Kotchem TA. Trends in prevalence, awareness, treatment & control of HT in the US, 1988-2000. *JAMA* 2003; 290:199-206.

57. National center for helath statistics healthy people 2000 final review. Hyattsville (Md): Public Health Services; 2001.

58. Burt VL, Whelton D, Roccella EJ, *et al*. Pervalence of HT in the US adult population. Results from the NHANES III, 1988-1991. *Hypertension*: 1995; 25; 305-13.

59. The JNC on Detection, Evaluation & Treatment of High BP. The 1988 Reoport of the JNC on Detection, Evaluation and Treatment of high BP. *Arch Intern Med*
1988; 148:1023-38.

60. National Institute of Health, National Heart, Lung & Blood Institute. Diagnosis & management of HT -1987. A nation wide survey of physicians' knowledge, attitudes & reported behaviour. Washington (DC): US Dept of Health & Human Services, Public health Service; 1989[publication no 89-2968].

61. Weiler PG, Camel GH, Chiappini M, *et al*. Systolic HT of the Elderly Program (SHEP). Part 9: Behavioral characteristics. *Hypertension* 1991; 17(3 Suppl): 152-61.

62. Gueyffier F, Frament A, Gouton M. New meta-analysis of treatment trials of HT: improving the estimate of therapeutic benefit. *J Hum Hypertens*. 1996; 10: 1-8.

63. Malhotra P, Kumar R, Kumar S, Singh MM. Dysglycemia and risk of cardiovascular disease. *Lancet* 1996; 347: 1835.

64. Ostrander LD, Lamphiear DE. Coronary risk factors in the community: findings in Tecumsch, Michigan. *Circulation* 1976; 53: 152-56.

65. Criqui MH, Barrett-Conor E, Holdbrook MJ, Austin M, Turner JD. Clustering of cardiovascular disease risk factors. *Prev Med* 1980; 9: 523-33.

66. Goode GK, Miller JP, Heagerty AM. Hyperlipidemia, HT and coronary heart disease. *Lancet* 1995; 345: 362-4.

67. Bonaa KH, Thelle DS. Association between BP and serum lipids in a population. *Circulation* 1991; 83: 1305-1314.

68. Chadha SL, Radhakrishnan S, Ramachandran K, Kaul U, Gopinath N. Prevalence, awareness and treatment status of hypertension in urban population of Delhi. *Indian J Med Res* 1990; 92: 233-240.

69. Chadha SL, Radhakrishnan S, Ramachandran K, Kaul U, Gopinath N. Epidemiological study of coronary heart disease in urban population of Delhi. *Indian J Med Res* 1990; (B) 92: 424-430.

70. Wander GS, Khurana SB, Gulati R, Sachar RK, Gupta RK, Khurana S, *et al*. Epidemiology of coronary heart disease in a rural Punjab population-prevalence and correlation with various risk factors. *Ind Hear J* 1994; 46: 319-323.

71. Joglekar SJ, Nanivadekar AS. Prevalence of lipid and Glycemic Abnormalities in hypertensive patients: A Retrospective Survey. *Indian Heart Journal* 1996; 48: 371-374.

72. Joglekar SJ, Kulkarni SS, Nanivadekar AS. Prevalence of dyslipidaemia in hypertensive patients: A retrospective survey. *Ind Practitioner* 1996; 19: 405-410.

73. Gray T, Callos AR, McMurry MT, Richards ML and Strong JP: Serum Cholesterol and triglyceride level in two human populations. *Ciruclation* 1968; Suppl VI: 15.

74. Kannel WB, Castelle WP, Gordon T and McNamara PM : Serum cholesterol, lipoprotein and the risk of CHD- The Framingham Study. *Ann Intern Med* 1971; 74: 1

75. Carlson LA and Bottiger LE. Ischemic heart disease in relation to fasting values of plasma trighycerides and cholesterol. *Lancet* 1972;1: 865.

76. Miller NE, Forde OH, Thelle DS and Mjos OD. The Tromso Heart Study- HDL and CHD: A prospective case-control study. *Lancet* 1977; 1: 65.

77. Malcom Silver. Cardiovascular diseases in tropics. Cardiovascular pathology: edition 2; 1992; 2: 231-1277.

78. Lynborg K. The major CVD entities of the 20th century editorial. *The Indo European Med J* 1987; 2: 4-6.

79. Coronary drug project research group natural history of MI in the CDP lay from prognostic importance of serum lipid levels*. Am J of Cardio*. 1978; 42: 489-498.

80. Robert WW. Update on the atherosclerosis. *Am J of Med*. 1991; supp-1B: 38-98.

81. Simons LA. Interrelations of Lipids and Lipoproteins with coronary artery diseases in 19 countries. *Am J of Cardiology*. 1986; 57(SuppG): 5G-10G.

82. Eugene Braunwald. The heart diseases. The textbook of cardiovascular medicine. WB Saunders Comp 4th edition 1992: 1106-1200.

83. Gotto AM. Diet and cholesterol guidelines and coronary heart disease. *Am J Cardiology* 1989; 13: 503-7.

84. Kannel WB. Contributions of the Framingham Study to the conquest of CHD. *Am J Cardiology*. 1988; 62: 1109-12.

85. Expert Panel. Report of the National Cholesterol Education Programme Expert Panel on detection, evaluation and treatment of high blood cholesterol adults. *Arch Intern Med.* 1988; 148: 36-69.

86. Canner P, Berge K, Wenger N. Fifteen year mortality in Coronary Drug Project patients. Long-term benefit with niacin. *Am J Cardiology* 1986; 8: 1245-55.

87. Blankernhor D, Nessim S, Johnson R, Sammarco M, Azen S, HemphillL. Beneficial effects of combined colestipol-niacin therapy on coronary atherosclerosis and coronary venous bypass grafts. *JAMA* 1987; 257: 3233-40.

88. Marshall WJ. Lipids and lipoproteins. *In*: Marshall WJ (3rd eds), *Clinical Chemistry*. 1995, p 213-228.

89. Eisenberg S. HDL metabolism *J Lipid Res*. 1984; 25:1 017-1058.

90. Hussain MM and Zannis VI. Intracellular modification of human apolipoprotein AII (apo AII) and sites of apo AII Mrna synthesis comparison of apo AII with apo CII and apo CIII isoproteins. *Biochemistry* 1990; 29: 209-217.

91. Rifkind BM. Cholestrol lowering and reduction of CHD risk. *JAMA* 1986; 256: 2872-2883.

92. Marenah CB. Lipid metabolism, hyper and hypolipidaemias and atherosclerosis. *In*: Marshall B (eds), *Clinical Biochemistry* (Metabolic and Clinical Aspects). 1996, p 621-640.

93. Rifai N, Bachorik PS, Albers JJ. Lipids, lipoproteins and apolipoproteins. *In*: Burtis CA, Ashwood ER (3rd eds), *Teitz Textbook OF Clinical Chemistry*. 1999, p 809-861.

94. A joint statement for physicians by the committee on atherosclerosis and hypertension in childhood of the council on cardiovascular disease in the young and the Nutrition Committee. American Heart Association: Diagnosis and treatment of primary hyperlipidemia in childhood. *Circulation* 1986; 74: 1181-1188A.

95. Ginsberg HN. Lipoprotein physiology and its relationship to atherosclerosis. Lipid disorders, Endocrinology and metabolism Clin. of North America. 1990; 19: 211-465.

96. National Cholesterol Education Program. *Arch Intern Med* 1988; 148: 36-69.

97. Austin MA. Plasma triglycerides and CAD. *Arterioscler Thromb* 1991; 11: 2-14.

98. Hokanson JE, Austin MA. Plasma triglycerids level as a risk factor for cardiovascular disease independent of HDL level: a meta-analysis of population-based prospective studies. *J Cardivasc Risk* 1996; 3:213-219.

99. Brown DF, Kinch SH, Doyle JJ. Serum triglycerides in health and in ischemic heart disease. *N Engl J Med* 1965; 273: 947-952.

100. Criqui MH, Heiss G, Cohn R, *et al*. Plasma triglycerids level and mortality from coronary heart disease. *N Engl J Med* 1993; 328: 1220-1225.

101. Hulley SB, Rosenman RH, Bawol RD, Brand RJ. Epidemiology as a guide to clinical decisions: the association between triglyceride and CHD. *N Engl J Med* 1980; 302: 1383-1389.

102. Rosenman RH, Brand RJ, Jenkin CD, *et al*. CHD in the Western Collaborative Group Study: final follow up experience of 81/2 years. *JAMA* 1975; 233: 872-877.

103. Scott MG. Hypertroglyceridemia, Atherogenic Dyslipidemia and the Metabolic Syndrome. *American J Cardiol* 1998; 81[4A]:18B-25B.

104. Mahley RW,Rall SC Jr. Type III hypolipoproteinemia (dysbetalipoproteinemia): the role of apolipoprotein E in normal and abnormal

lipoprotein metabolism. *In*: Scriver CR, Beaudet AL, eds. *The Metabolic and Molecular Bases of Inherited Disease*. New York: McGraw Hill 1995; 1953-1980.

105. Minnich A. Zilversmit DB. Impaired triacylglycerol catabolism in hypertriglyceridemia of the diabetic, cholesterol-fed rabbit: a possible mechanism for protection from atherosclerosis. *Biochem Biophys Acta* 1989; 1002: 324-332.

106. Austin MA, King MC, Vranizan KM, Krauss RM. Atherogenic lipoprotein phenotype : a proposed genetic marker for coronary artery risk. *Circulation* 1990; 82: 495-506.

107. Richards EG, Grundy SM, Cooper K. Influence of plasma TGs on lipoproterin patterns in nnormal subjects and in patients with coronary artery disease. *Am J Cardiol* 1989; 63: 1214-1220.

108. Grundy SM, Vega GL. Fibric acids : Effects on lipids and lipoprotein metabolism. *Am J Med* 1987; 83: 9-20.

109. de Graf J, Hak-Lemmers HLM, Hectors PNM. Enhanced susceptibility to invitro oxidation of the dense low density lipoprotein subfractions in healthy subjects. *Arterioscler Thromb* 1991; 11: 298-306.

110. Grundy SM, Vega GL. Two different views of the relationship of hypertriglyceridemia to CAD : implications for treatment. *Arch Intern Med* 1992; 152: 28-34.

111. Grundy SM. Small LDL, atherogenic dyslipidaemia and the metabolic syndrome. *Circulation* 1997; 95:1-4.

112. GottoAM Jr., Brinton EA. Assesing low levels of HDL-C as a risk factor in CHD: a working group report and update. *J Am Coll Cardiology* 2004; 43: 717-24.

113. Strong JP. Atherosclerosis in primates: Introduction and overview: *Primates Med* 1976; 9: 1-15.

114. Goldstein JL, Brown MS. Familial hypocholesterolemia. *In* : Scriver R, Beaudet AL, Sly WS, Valle D, eds. *The Metabolic and Molecular Bases of Inherited Disease*. New York: McGraw Hill, 1995; 1981-2030.

115. Steinberg D, Parathasarathy S, Carew TE, Khoo JC, Witztum JL. Beyond cholesterol: modifications of low density lipoprotein that increase its atherogenicity. *N Eng J Med*. 1989; 320: 915-24.

116. Ross R. The pathogenesis of atherosclerosis: a perspective for the 1990s *Nature* 1993; 362: 801-09.

117. Gambhir DS, Gambhir JK. Oxidized low density lipoprotein, antioxidants and coronary atherosclerosis. *Indian Heart J* 1997; 49:19-22.

118. Leake DS, Rankin SM. The oxidative modification of low density lipoprotein by macrophages. *Biochem J* 1990; 270: 741-748.

119. Witzum JL, Steinberg D. Role of oxidized low density lipoprotein in atherogenesis. *Br Heart J* 1993; 69: S12-18.

120. Diplock AT. Antioxidants and disease prevention. *Mol Aspects Med* 1994; 15: 295-376.

121. Esterbauer H, Gebicki J, Paul H, Jurgens G. The role of lipid peroxidation and antioxidants in oxidative modification of LDL. *Free Radical Biol Med* 1992; 13: 341-90.

122. Sasahara M, Raines EW. Carew TE, *et al*. Inhibition of hypercholesterolemia- induced atherosclerosis in Macaca nemestrina by protocol I: intimal lesion area correlates inversely with resistance of lipoprotein to oxidation. *J Clin Invest* 1994; 94: 155-209.

123. Expert Panel on Detection, Evaluation AND Treatment of High Blood Cholesterol in Adults. Executive Summary of The Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adults Treatment Panel III). *JAMA* 2001; 285: 2486-2497.

124. Rader DJ. HDL as an emerging therapeutic target for atherosclerosis. *JAMA* 2003; 290: 2322-2324.

125. Miller NE, Thelle DS, Forde OH, Mjos OD. The Tromso Heart-Study : HDL and CHD: a prospective case control study. *Lancet* 1977; 1: 965-8.

126. Shah PK, Amin J. Low HDL level is associated with increased restenosis rate after coronary angioplasty. *Circulation* 1992; 85: 1279-85.

127. Wilson PW, Abbott RD, Castelli WP. HDL-C and mortality: The Framingham Heart Study. *Atherosclerosis* 1988; 8: 737-41.

128. Goldbourt U, Yaari S, Medalie JH. Isolated low HDL-C as a risk factor for CHD mortality: a 21 year followup of 8000 men. *Arterioscler Thromb Vac Biol* 1997; 17: 107-13.

129. Dominique Ashen M, Roger Blumenthal S. Low HDL-C levels. *N Eng J Med* 2005; 353: 1252-60.

130. Brewer HB Jr. HDL: a new potential therapeutic target for the prevention of cardiovascular disease. *Arterioscler Thromb Vac Biol* 2004; 24: 387-91.

131. Gotto AM, Brinton EA. Assesing low levels of HDL-C as a risk factor in CHD. *J Am Coll Cardiol* 2004; 43: 717-724.

132. Castelli WP, Anderon K, Wilson PW, Levy. Lipids and risk of CHD: The Framingham Study. *Ann Epidemiol* 1992; 2: 23-28.

133. Lipids Research Clinics Program. The Lipid Research Clinics Coronary Primary Prevention Trial Results.I: Reduction in incidence of CHD. *JAMA* 1984; 251: 351-364.

134. Frick MH. Elo O, Haapa K, *et al*. Helsinki Heart Study: primary prevention trial with gemfibrozil in middle aged men with dyslipidemia. *N Engl J Med* 1987; 317: 1237-1245.

135. Kannel WB. HDL: epidemiologic profile and risks of coronary artery disease. *Am J Cardiol* 1983; 52: 9B-12B.

136. Belacazar LM, Ballantyne CM. Defining specific goals of therapy in treating dyslipidemia in the patient with low HDL-C. *Progress on CVDs* 1988; 41: 151-174.

137. Gordon T, Castelli WP, Hjortland MC, *et al*. HDL as a protective factor against CHD. The Framingham Heart Study. *Am J Med* 1977; 62: 707.

138. Gordon DJ, Knoke J, Probstfield JL, *et al*. HDL-C and CHD in hypocholesterolemic men: The Lipid Research Clinics Coronary Primary Prevention Trial. *Circulation* 1986; 74: 1217-25.

139. Miller GJ, Miller NE. Plasma HDL concentration and development of IHD. *Lancet* 1976; 1: 16.

140. Fielding CJ, Fielding PE. Molecular physiology of reverse cholesterol transport. *J Lipid Res* 1995; 36: 211-228.

141. Remaley AT, Rust S, Rosier M, Knapper C, *et a*l. Human ATP-binding cassette transporter-1 (ABC1): genomic organization and identification of the genetic defect in the original Tangier disease kindred. *Proc Nat Acad Sci USA* 1999; 96: 12685-12690.

142. Acton S, Rigotto A, Landschiltz KT, *et al*. Identification of scavenger receptor SR-BI as a high density lipoprotein receptor. *Science* 1996; 271: 518-520.

143. Tall A. Plasma lipid transfer proteins. *Ann Rev Biochem* 1995; 64: 235-257.

144. Steinberg. A docking receptor for HDL-C esters. *Science* 1996; 271: 460-461.

145. Shah PK, Kaul S, Nilsson J, Cereck B. Exploiting the vascular protective effects of high density lipoprotein and its apolipoproteins: an idea whose time for testing is coming. *Circulation* 2001; 104: 2376-83.

146. Rosenson RS. Statins in atherosclerosis: lipid lowering agents with antioxidant capabilities. *Atherosclerosis* 2004; 173: 1-12.

147. Stafforini DM, Zimmerman GA, McIntyre TM, Prescott SM. The platelet activating factor acetylhydrolase from human plasma prevents oxidative modification of LDL. *Trans Am Assoc Physiol* 1993; 106: 44-63.

148. Navab M, Imes SS, Hama SY, et al. Monocyte transmigration induced by modification of LDL in cocultures of human aortic wall cells is due to induction of monocyte chemotactic protein-I synthesis and is abolished by HDL. *J Clin Invest* 1991;88: 2039-2046.

149. Uttenbogard A, Shaul PW, Yuhanna IS, et al. HDL prevents oxidized LDL induced inhibitiob of endothelial nitric oxide synthase localization and activation in caveolac. *J Biochem* 2000; 275: 11278-11283.

150. Vinab M, Martinez-Gonzalez J, Badimon JJ, et al. HDL-induced prostacyclin release in smooth muscle cells is depemdent on cyclooxygenase-2 (Ox-2). *Arterioscler Thromb Vasc Bio* 1997; 17: 3481-3488.

151. Xia P, Vadas MA, Rye K, et al. HDL interrupt the sphingosine kinase signaling pathway. *J Biol Chem* 1999; 274: 33143-33147.

152. Saku K, Ahmad T, Glas-Greenwalt P, Kashyap ML. Activation of fibrinolysis by apolipoproteins of HDL in man. *Thromb Res* 1985; 39: 1-8.

153. Peter OK, Jr. The Antiatherogenic Role of HDL-C. *Am J Cardiol*. 1998; 82: 13Q-21Q.

154. Criqui MH, Wallace RB, Heiss G, et al. Cigarette smoking and plasma HDL-C. The Lipid Research Clinics Program Prevalence Study. *Circulation.*1980; 62: IV70-IV76.

155. Dietschy JM. Theoretical considerations of what regulates LDL and HDL-C. *Am J Clin Nutri* 1997; 65: 1581S-1589S.

156. Glueck CJ, Taylor HL, Jacobs D, et al. Plasma HDL-C: Association with measurements of body mass. The Lipid Research Clinics Program Prevalence Study. *Circulation* 1980; 62: IV62-IV69.

157. Gordon DJ, Witztum JL, Hunning D, et al. Habitual physical activity and HDL-C in men with primary hypocholesterolemia. The Lipid Research Clinics Coronary Primary Prevention Trial. *Circulation* 1983;67: 512-520.

158. Dattilo AM, Kris-Etherton PM. Effects of weight reduction on blood lipids and lipoproteins: a meta analysis. *Am J Clin Nutr* 1992; 56: 320-328.

159. Enas. Coronary artery disease epidemic in Indians: A cause for alarm and call for action. *J Ind Med Assoc* 2000; 98: 694-702.

160. Third Report of the NCEP Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Available at: http://www.nhibi.nih.gov.

161. Bhavani AB, Sastry KB, Krishna RN, Padma T. Lipid Profile and Apolipoprotein E Polymorphism in Essential Hypertension. *Indian Heart J*. 2005; 57: 151-157.

162. Lopez AD. Assessing the burden of mortality from CVDs. *World Health Stat Q*. 1993; 46: 91-6.

163. Manson JE, Ridker PM, Gaziano JM, Hennekens CH. Prevention of myocardial infarction. New York: Oxford University Press; 1996.

164. Levy RIM, Rifking BM, Dennis BH, Nancy Ernst. (International atherosclerosis Project, 1968). Nutrition, Lipids in CHD, *A Global view*. 1979; 25: 364.

165. Renaud S. Dietary lipids and their relation to IHD: from epidemiology to prevention. *J Intern Med*, 1987; 225: 39-46.

166. WHO. Prevention of CHD. Report of a WHO Expert Committee. Technical Report Series 678. Geneva: WHO, 1982.

167. Keys Ancel. CHD in seven countries. Circulation, 1970; 41: supp 1st: S1-S212.

168. Ishi T, Newnan WP. Coronary atherosclerosis in young men from Tokyo snf New Orleans. *Lab Inves*. 1986; 54: 561-565.

169. (NI-HON-SAN Study) Marmot MG, Syme SL. Epidemiology studies of CHD and stroke in Japanese men living in Japan, Hawaii and California. Prevalence of coronary hypertensive heart diseases and association of risk factors. *Am J Epidemiol*, 1975; 102: 514-525.

170. Leren P. The Oslo diet-heart study. Eleven year report. *Circulation*, 1970; 42: 935-42.

171. Buer ML, Fehily AM, Gilbert JF, *et al*. Effects of changes in fat, fish and fiber intakes in death and myocardial reinfarction: diet and reinfarction trial (DART). *Lancet* 1989; 334: 757-61.

172. Morris JN, Bali KP, Antonis A, *et al*. Controlled trial of soya-bean oil in myocardial infarction. *Lancet* 1968; 11: 694-700.

173. Hjerman I, Holme I, Leren P. Oslo study diet and antismoking trial. Results after 102 months. *Am J Med* 1992; 327: 669-77.

174. Phillips RL, Lemon FR. Seventh study Adventists study. CHD mortality among seventh day Adventists with differing dietary habits. Preliminary report.*Am J Clinical Nutr* 1978; 31(suppl): S191-S198.

175. Keys A, Menotti A, Karvonen MJ, *et al*. The diet and 15-year death rate in the seven countries study. *Am J of Cardiology*. 1962; 9: 343-354.

176. Martinez-Gonzalez MA, Fernandez-Jarne E, Sersano-Martinez M, *et al*. Mediterranean diet and reduction in the risk of a first acute myocardial infarction : an operational healthy dietary score. *Eur J Nutr* 2002; 41: 153-60.

177. Trichopoulou A, Costacou T, Bamia C, Trichopoulou D. Adherence to a Mediterranean diet and survival in a Greek population. *N Engl J Med* 2003; 348: 2599-608.

178. Hu FB, Willett WC. Diet and CHD findings from the Nurses Health Study AND Health Professionals: Followup study. *J Nutr Health Aging* 2001; 5: 132-8.

179. Willet WC, Sacks F, Trichopoulou A, *et al*. Mediterranean diet pyramid: a cultural model for healthy eating. *Am J Clin Nutr*. 1995; 61(suppl): 1402S-6S.

180. Singh RB, Dubnov G, Niaz MA, *et al*. Effect of and Indo-Mediterranean diet on progression of CAD in high risk patients (Indo-Mediterranean Diet Heart Study): a randomized single-blind trial. *Lancet* 2003; 360: 1455-61.

181. Baudey SV, Defroort C, Gerber M, *et al*. The Medi-RIVAGE study: reduction of CVD risk factprs after a 3-mo intervention with a Mediterranean type diet of a low-fat diet. *Am J Clin Nutr* 2005; 82: 964-71.

182. Ghafoorunissa. Fish for a healthy heart. *Nutrition News* 1992; 13: 2.

183. Krauss RM, Deckerbaum RJ, Ernst N, *et al*. Dietary guidelines for healthy American adults. *Circulation* 1996; 94: 1795-1800.

184. Summary of the second report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation and treatment of high blood cholesterol in adults. (Adult Treatment Panel II). *JAMA* 1993; 269: 3015-3023.

185. Denke MA. Individual responsiveness to a cholesterol lowering diet in postmenopausal women with moderate hypercholesterolemia. *Arch Intern Med* 1994; 154: 1977-1982.

186. Weisburger JH. Dietary fat and risk of chronic disease: mechanistic insights from experiment studies. *J Am Diet Assoc* 1997; 97: S16-S23.

187. Ginsberg HN, Kris-Etherton P, Dennis B, Elmer PJ, Ershaw A, *et al*. Effects of reducing dietary saturated fatty acids on plasma lipids and lipoproteins in healthy subjects: the DELTA Study, protocol 1. *Arteriscler Thromb Vasc Biol* 1998; 18: 441-449.

188. de Lorgeril M, Renaud S, Mamella N, Salen P, *et al*. Mediterranean alpha-linolenic acid rich diet in secondary prevention of coronary heart disease. *Lancet* 1994; 343: 1454-1459.

189. Grundy SM, Bilheimer D, Blackburn H, *et al*. Rationale of the diet-heart statement of the American Heart Association: report of Nutrition Committee. *Circulation.* 1982; 65: 839A-854A.

190. Ginsberg SM. Lipoprotein physiology and its relationship to atherosclerosis. Lipid disorders, endocrinology and metabolism. *Clin of North America*. 1990; 19: 211-465.

191. Hashim SA, Arteaga A, van Ilallie TB. Effect of a saturated medium chain TG on serum lipids in man. *Lancet* 1960; 1: 1105-8.

192. Ahrens EH Jr., Hersch J, Insull W Jr., *et al*. The influence of dietary fats on serum lipid levels in man. *Lancet*. 1957; 1: 943-53.

193. Hegsted DM, McGandy RB, Myers ML, *et al*. Quantitative effects of dietary fat on serum cholesterol in man. *Am J Clin Nutr*. 1965; 17: 281-95.

194. Keys A, Anderson JT, Grande F. Serum cholesterol response to changes in the diet. IV. Particular saturated fatty acids in the diet. *Metabolism* 1965; 14: 776-87.

195. Wilson RB, Martin JM, Hartrolt WS. Dietary control of serum cholesterol levels in rats fed high-fat cholate containing diets. *Can J Physiol Pharma* 1966; 44: 267-73.

196. Renaud S, Gauthern P. Influence of dietary fats on atherosclerosis, coagulation and platelet phospholipids in rabbits. *Atherosclerosis* 1975; 21: 119- 24.

197. Renaud S. Linoleic acid, platelet aggregation and myocardial infarction. *Atherosclerosis*. 1990; 80: 255-256.

198. Elwood P, Renaud S, Sharp DS, *et al*. ISH and platelet aggregation, the Caerphilly collaborative heart disease study. *Circulation* 1991; 83: 38-44.

199. Thaulow R, Eriksen J, Sandvik L, *et al.* Blood platelet count and function are related to total and cardiovascular death in apparently healthy men. *Circulation* 1991; 84: 613-17.

200. Reaven P, Parthasarathy S, Grasse BJ, Miller F, *et al*. Effects of oleate-rich and linoleate-rich diets in the susceptibility of low density lipoprotein to oxidative modification in mildly hypercholesterolemic subjects. *J Clin Invest* 1993; 91: 668-76.

201. Renaud S, Nordoy A. Small is beautiful: α-linolenic acid and eicosapentaenoic acid in man. *Lancet* 1983; i: 1169.

202. Sinnopoulos AP, Norman HA, Gillapsy JE, *et a*l. Common purslanc: a source of omega-3 fatty acids and antioxidants. *J Amer Coll Nutr* 1992; 11: 374-82.

203. Rinum EB, Stampfer MJ, Ascherio A, Giovannucci E, *et al*. Vitamin E consumption and the risk of CHD in men. *N Engl J Med* 1993; 328: 1450-56.

204. Kardinal AFM, lol FJ, Ringsted J, *et a*l. Antioxidants in adipose tissue and risk of myocardial infarction the Euramic study. *Lancet* 1993; 342: 1379-84.

205. Singh RB, Rastogi SS, Verma R, *et al*. An Indian experiment with nutritional modulation in acute myocardial infarction. *Am J Cardiol* 1992; 69: 879-85.

206. Foster GD, Wyatt HR, Hill JO, McGuckin BG, *et al*. A ramdomized trial of a low-carbohydrate diet for obesity. *N Engl J Med* 2003; 348: 2082-90.

207. Olefskey J, Reaven GM. Effects of weight reduction on obesity. *J Clin Invest* 1974; 53: 64-76.

208. Whelton PK, He J, Appel LJ, *et al*. Primary prevention of HT: clinical and public health advisory from the National High Blood Pressure Education Program. *JAMA* 2002; 288: 1882-8.

209. Panagiotakos DB, Pitsavos CH, Chrysohoou C, *et al*. Status and management of HT in Greece: role of the adoption of a Mediterranean diet: the Attica study. *J Hypertens* 2003; 21: 1483-9.

210. Psaltopoulou T, Naska A, Orfanos P, Trichopoulos D, *et al*. Olive oil, the Mediterranean diet and arterial blood pressure: the Greek European Prospective Investigation into Cancer and Nutrition (EPIC) Study. *AM J Clin Nutr*. 2004; 80: 1012-8.

211. Bray GA. Obesity: An endocrine perspective In: DeGroot LJ ed. *Endocrinology*, vol 3, 2nd edn. WB Saunders Co. (Pub) 1989; 2303-2337.

212. Felding P, Tryding N, Hyltoft P, *et al*. Effects of posture on comcentrations of blood constituents in healthy adults: Practical application of nlood specimen collection procedures recommended by the Scandinavian Committee in Reference Values. *Scand J Clin Lab Invest* 1980; 40: 615-621.

213. Solberg H. International federation of clinical Chemistry, Expert Panel on Theory of Reference Values: Approved Recommendation on the theory of reference values. Part 4. Control of analytical variation in the production transfer and application of reference values. *Eur J Clin Chem Clin Biochem*. 1991; 29: 531-535.

214. Stamm D. A new concept for quality control of clinical laboratory investigations in the light of clinical requirements and based on reference method values. *J Clin Chem Clin Biochem* 1982; 20: 817-824.

215. Whitehead TP, Robinson D, Hale AC and Bailey AR. Clinical chemistry and Haematology: Adult reference values. London: BUPA Medical Research and Development Ltd. 1994.

216. Friedwald WT, Levy RI and Fredrickson DS. Estimation of the concentration of LDL-C in plasma, without the use of the preparative ultracentrifuge. *Clin Chem* 1972; 18: 499.

217. Bhise A, Krishnan PV, Aggarwal R, Gaiha M, Battacharger J. Effect of low dose omega-3 fatty acids substitution on blood pressure, hyperinsulinemia and dyslipidemia in Indians with essential HT: A pilot study. *Indian J of Clin Biochem* 2005; 2: 4-9.

218. Enas EA. Cooking oil, cholesterol and coronary artery disease. *Indian Heart J* 1996; 48: 423-428.

219. Appel LJ, Moore TJ, Obarzanek E, *et al*. A clinical trial of the effects of dietary patterns on blood pressure. *N Engl J Med* 1997; 336: 1117-24.

220. Miura K, Greenland P, Stampler J, Liu K, *et al*. Relation of vegetable, fruit and meat intake to 7-year blood pressure change in middle-aged men: the Chicago Western Electric Study. *Am J Epidemiol* 2004; 159: 572-80.

221. Pereira MA, Jacobs DR Jr., Van Horn L, et al. Dairy consumption, obesity and the insulin resistance syndrome in young adults: the CARDIA Study. *JAMA* 2002; 287: 2081-9.

222. Moore LL, Singer MR, Bradke ML, *et al*. Intake of fruits, vegetables and dairy products in early childhood and subsequent blood pressure change. *Epidemiology* 2005; 16: 4-11.

223. Kelemen LE, Kushi LH, Jacobs DR Jr., Cuhan JR. Association of dietary protein with disease and mortality in a prospective study of postmenopausal women. *Am J Epidemiol* 2005; 161: 239-49.

224. Hjerman I, Valve Byre K, Holme I, Leren P. Effect of diet and smoking intervention on the incidence of CHD. *Lancet* 1981; 2: 1303-10.

225. Jorde R, Bonaa KH. Calcium from dairy products, vitamin intake and BP: the Tromso study. *Am J Clin Nutr* 2000; 71: 1530-5.

226. Fitzgerald RJ, Murray BA, Walsh DJ. Hypertensive peptides from milk proterin. *J Nutr* 2004; 134: 9805-8.

227. Vaskonen T. Dietary minerals and modification of cardiovascular risk factors. *J Nutr Biochem* 203; 14: 492-506.

228. Sethi KL. CAD in Indians. *Cardiology Today* 1997; 2: 21-26.

229. American Heart Association. Dietary guidelines for healthy American adults: a statement for physicians and health professionals by the Nutrition Committee. *Circulation* 1988; 77: 721A-724A.

230. Brinton EA, Eisenberg S, Breslow JL. A low-fat diet decreases high density lipoprotein cholesterol levels by decreasing HDL apolipoprotein transport rates. *J Clin Invest* 1990; 85: 144-151.

231. Mensink RP and Katan MB. Effects of dietary fatty acids on serum lipids and lipoproteins. A meta analysis of 27 trials. *Arterioscler Thromb Vasc Biol* 1992; 12: 911-919.

232. Berglund L, Oliver EH, Fontanez N, *et al*. HDL subpopulation patterns in response to reductions in dietary total and saturated fat intakes in healthy subjects. *Am J Clin Nutr* 1999; 70: 332-1000.

233. Schaefer EJ, Levy RI, Ernst ND, Van Sant ED. The effects of low cholesterol, high polyunsaturated fat and low fat diets on plasma lipid and lipoprotein cholesterol levels in normal and hypercholesterolemic subjects. *Am J Clin Nutr* 1981; 34: 1758-1763

.

234. Thursen I, Henriksen LB, Engley B. One-year experience with a low fat, low cholesterol diet in patients with CHD. *Am J Clin Nutr* 1986; 44: 212-219.

235. Barr SL, Ramakrishnan R, Johnson C, et al. Reducing total dietary fat without reducing saturated fatty acids does not significantly lower total plasma cholesterol concentrations in normal males. *Am J Clin Nutr* 1992; 55: 675-68.

236. Aeller AJ, Holub BJ. Effect of garlic and fish oil supplementation on serum lipid and lipoprotein concentrations in hypercholesterolemic men. *Am J Clin Nutr* 1997; 65: 445-450.

237. Conner SL, Conner WE. Are fish oils beneficial in the prevention and treatment of CAD ? *Am J Clin Nutr* 1997: 66(suppl 4): 1020-1031.

238. Griffin BA. The effect of n-3 fatty acids on low density lipoprotein subfractions. *Lipids* 2001; 36 (suppl 5): 897.

239. Enas A, Mehta J. Malignant coronary artery disease in young Asian Indians: thoughts on pathogenesis, prevention and therapy. *Cardiothorac* J. 3: 26-30.

240. Krishnamoorthy S. Onions and garlic, 2nd ed, DK Publishers, New Delhi, 1995.

241. Lau HS. Anticoagulant and lipid regulatory effects of garlic. *Lancet* 1988; 4: 150-156.

242. Clevidence BA, Judd JT, Schatzkin A, *et al*. Plasma lipid and lipoprotein concentration of men consuming a low fat, high-fiber diet. *Am J Clin Nutr* 1992; 55: 689-694.

243. Lichtenstein AH, Ausman LM, Carrasco W, *et al*. Short-term consumption of a low fat diet beneficially affects plasma lipid concentration only when accompanied by weight loss. *Arteriscler Thromb* 1994; 14: 1751-1760.

244. Schaefer EJ, Lichtenstein AH, Lanon-Fara S, *et al*. Body weight and LDL-C changes after consumption of a low fat addibitum diet. *JAMA* 1995; 274: 1450-1455.

245. Liz, MeNamara JR, Fruchart JC, Bard JM. Effects of gender and menopausal status on plasma lipoprotein sunspecies and particle size. *J Lipid Res* 1996; 37: 1886-1896.

246. Castelli WP, Garrison RJ, Wilson PWF, *et al*. Incidence of CHD and lipoprotein cholesterol levels: the Framingham Study. *J Am Med Assoc* 1986; 256: 2835-2838.

247. Heiss G, Johnson NJ, Retland S, *et al*. The epidemiology of plasma HDL-C levels. *Circulation* 1980; 62 (suppl IV): 116-136.

248. Assman G, Schulte H, von Eckaidstein A and Huang Y. HDL-C as a predictor of CHD risk. The PROCAM experience and pathophysiological implications for reverse cholesterol transport. *Atherosclerosis* (124 Suppl): S11-S20.

249. Breslow JL. Familial disorters of HDL metabolism. *In the metabolic basis of inherited disease*, 6th ed. Scriver CR, Beaudet AL, Sly WS and Valle D, editors. McGraw Hill, New York, NY. 1989: 2031-2052.

250. Hayek T, Ito Y, AZROLAN n, Verdery RB, *et al*. Dietary fat increases HDL levels both by increasing the transport rates and decreasing the fractional catabolic rates of HDL-C ester and apolipoprotein (apo) A-I. *J Clin Invest* 1993; 91: 1665-1699.

251. Asztalos B, Sloop CH, Wong L and Tohelm PS. Two-dimensional electrophoresis of plasma lipoproteins recognition of new apo A-I containing subpopulations. *Biochem Biophys Acta* 1993; 1169: 291-300.

252. Asztalos BF, Lefevre M, Foster TA, Tulley R, *et al*. Normolipidemic subjects with low HDL-C levels have altered HDL subpopulations. *Arterioscler Thromb Vasc Biol.* 1997; 17: 1885-1893.

253. Asztalos B Lefevre M, Wong L, Foster TA, *et al*. Differential response to low fat diet between low and normal HDL-C subjects. *J Lipid Res* 2000; 41: 321-328.

254. Tato F,Vega GL, Grundy SM. Bimodal distribution of cholesteryl ester transfer protein activities in normotriglyceridemic men with low HDL-C concentrations. *Arterioscler Thromb Vasc Biol*. 1995; 15(4): 446-451.

255. Knuiman JT, Hermus RJJ, Hautvast JG. Serum total and HDL-C concentrations in rural and urban boys from 16 countries. *Atherosclerosis* 1980; 36: 529-37.

.

256. Gerasinova E, Perova N, Ozerova I, *et al*. The effect of dietary n-3 polyunsaturated fatty acids on HDL-C IN Chukot residents Vs Muscovits. *Lipids* 1991; 26: 261-5.

257. Pelkman CL, Fishell VK, Maddox DH, *et al*. Effects of moderate-fat (from monounsaturated fat) and low-fat weight loss diets on the serum lipid profile in overweight and obese men and women. *Am J Clin Nutr* 2004; 79: 204-12.

258. Slyper A, Jurva J, Pleuss J, Hoffmann R, Gutterman D. Influence of glycemic load On HDL-C in youth. *Am J Clin Nutr* 2005; 81: 376-9.

259. McNamara JR. Schaefer EJ. Automated enzymatic standardized lipid analyses for plasma and lipoprotein fractions. *Clin Chem Acta* 1987; 166: 1-8.

260. Hu FB, Stampfer MJ, Manson JE, *et al*. Dietary fat intake and the risk of CHD in women. *N Engl J Med* 1997; 337: 1491-9.

261. Kromhout D, Menotti A, Bloemberg B, *et al*. Dietary saturated and trans fatty acids and cholesterol and 25-year mortality from CHD: the Seven Countries Study. *Prev Med* 1995; 24: 308-15.

262. Mensink RP, Katan MB. Effect of dietary trans fatty acids on high density and low density lipoprotein cholesterol levels in healthy subjects. *N Engl J Med* 1990; 323: 439-45.

263. Zock PL, Mensink RP. Dietary transfatty acids and serum lipoproteins in humans. *Curr Opin Lipidol* 1996; 7: 34-7.

264. Bonanome A, Grundy SM. Effect of dietary stearic acid on plasma cholesterol and lipoprotein levels. *N Engl J Med* 1988; 318: 1244-8.

265. Bemelmans WJ, Broer J, Feskens EJ, *et al.* Effect of an increased intake of α-linolenic acid and group nutritional education on cardiovascular risk factor: the Mediterranean Alpha-linolenic Enriched Groningen Dietary Intervention (MARGARIN) Study. *Am J Clin Nutr* 2002; 75: 221-7.

266. Rinm EB, Ascherio A, Giovannucci E, *et al*. Vegetable, fruit and cereal fiber intake and risk of coronary; heart disease among men. *JAMA* 1996; 275: 447-51.

267. Holub DJ, Holub BJ. Omega-3 fatty acids from fish oils and CVD. *Mil Cell Biochem* 2004; 263: 217-25.

268. Hu FB, Willett WC. Optimal diets for prevention of CHD. *JAMA* 2002; 288: 2569-78.

269. Law MR, Wald NJ, Thompson SG. By how muc and how quickly does reduction in serum cholesterol concentration lower risk of IHD *? BMJ* 1994; 308: 367-72.

270. Stunkard AJ. Current views on obesity*. Am J Med* 1996; 100: 230-236.

271. Blackburn G. Effect of degree of weight loss on health benefits. *Obes Res* 1995; 3(suppl 2): 211S-216S.

272. Grilo CM. Physical activity and obesity. *Biomed Pharmacother* 1994; 48: 127-136.

273. Hegsted DM, Ausman LM, Johnson JA, Dallal GE. Dietary fat and serum lipids: an evaluation of the experimental data. *Am J Clin Nutr* 1993; 57: 875-883. Correction in Am J Clin Nutr 1993; 58: 245.

274. Keys A, Anderson JT, Grande F. Prediction of serum cholesterol responses of man to change in fats in the diet*. Lancet* 1957; 2: 959-966.

275. Brown MS, Goldsterin JL. A receptor-mediated pathway for cholesterol homeostasis*. Science* 1986; 232: 34-47.

276. Frayn KN, Kingman SM. Dietary sugars and lipid metabolism in humans. *Am J Clin Nutr* 1995; 62(suppl): 250S-263S.

277. Carroll KK. Review of clinical studies on cholesterol lowering response to soyprotein. *J Am Diet Assoc* 1991; 91: 820-827.

278. Connor WE, Defrancesco CA, Conner SL. N-3 fatty acids from fish oil: effects on plasma lipoproteins and hypertriglyceridemic patients. *Ann N Y Acad Sci* 1993; 638: 16-34.

279. National Cholesterol Education Program. 2nd report of the Expert Panel on Detection, Evaluation and Treatment of HIGH Blood Cholesterol in Adults (Adult Treatment Panel II). *Circulation* 1994; 89: 1333-1445.

280. Stamler J, Shekelle R. Dietary cholesterol and human CHD: the epidemiologic evidence. *Arch Pathol Lab Med* 1988; 112: 1032-1040.

281. Shekelle RB, Shryock AM, Lepper M, *et al*. Diet, serum cholesterol and death from CHD: the Western Electric Study. *N Engl J Med* 1981; 304: 65-70.

282. Kromhout D, Coulander CD. Diet, prevalence and 10-year mortality form CHD in the HonoluluHeart Program: relationship to nutrient intake. *Am J Epidemiol*. 1984; 119: 667-676.

283. Whyte JL, McArthur R, Topping D, Nestel P. Oat bran lowers plasma cholesterol levels in mildly hypercholesterolemic men. *J Am Diet Assoc* 1992; 92: 446-449.

284. He J, Tell GS, Tang YC, Mo PS, *et al.* Relation of electrolytes to blood pressure in men: the Yi people study. *Hypertension* 1991; 17: 378-385.

285. Stamler J, Rose G, Elliot P, Dyer P, *et al*. Findings of the International Cooperative INTERSALT Study. *Hypertension* 1991; 17(suppl-I): I-9-I-15.

286. Cutler JA, Follmann D, Elliott P, *et al.* An overview of randomized trials of sodium reduction and BP. *Hypertension*. 1991; 17(suppl-I): I-27-I-33.

287. Midgley JP, Mathew AG, Guenwood CM, Logam AG. Effect of reduced dietary sodium on blood pressure: a meta-analysis of randomized controlled trials. *JAMA* 1996; 275: 1590-1597.

288. 2002 Heart and stroke statistical update. Dallas, Tex: *American Heart Association*; 2001.

289. Benowitz NL, Gourlay SG. Cardiovascular toxicity of nicotine: implications for nicotine replacement therapy. *J Am Coll Cardiol* 1997; 29: 1422-31.

290. Ferry LH. Non-nicotine pharmacotherapy for smoking cessation. *Prim Care* 1999; 26: 653-9.

291. Jeferey BL. Smoking and CVDs. *Am J of Med* 1992-93; supp 1A: 85-125.

292. Kannel WB, McGee DL. Latest prospective on cigarette smoking and CVDs. The Framingham heart study. *Tr Cardiac Rehabil* 1984; 4: 267-277.

293. Garrison RJ, Kannel WB, Feinleib M, *et al*. Cigarette smoking and HDL-C: the Framingham offspring study. *Atheroscerlosis* 1978; 30: 17-25.

294. Moffatt RJ. Effects of cessation of smoking on serum lipids and HDL-C. *Atherosclerosis* 1988; 74: 85-89.

295. Cullen P, Schulte H and Assmann G. Smoking, lipoproteins and CHD risk. Data from the Munster Heart Study (PROCAM). *Eur Heart J* 1998; 19: 1632-1641.

296. Pooling project research group relationship of BP, cholesterol, smoking relative weight and ECG abnormalities to incidences of major coronary events. *J of Chronic Diseases* 1978; 31: 201-306.

297. Keys A, Taylor HL. CHDs among Minnesota business and professional men followed for 15 years. *Circulation* 1963; 28: 381-395.

298. Benowitz NL, Fitzgerald GA, Wilson M, *et al*. Nicotine effects on eicosanoid formation and hemostatic function-comparison of transdermal nicotine and cigarette smoking. *J Am Coll Cardiol* 1993; 22: 1159-67.

299. McBride Patrick. The health consequences of smoking. *Med Clin of North Am* 1992; 76: 333-352.

300. Piandadosi CA. Perspective- carbon monoxide poisoning *N Engl J Med* 2002; 347: 1054-5.

301. Quillen JE, Rossen JD, Oskarsson HJ, et al. Acute effects of cigarette smoking on the coronary circulation; constriction of epicardial resistance vessels. *J Am Coll Cardiol* 1993; 22: 642-7.

302. Winniford MD, Jansen DE, Reynolds GA, *et al*. Cigarette smoking-induced coronary vasoconstriction in atherosclerotic CAD and prevention by calcium antagonists and nitroglycerin. *Am J Cardiol* 1987; 59: 203-7.

303. Kannel WB, Dagastino RB, Belanger AJ. Fibrinogen, cigarette smoking and risk of CVDs-insights from the Framingham Study. *Am Heart J* 1987; 113: 1006-10.

304. Goldstein MG, Niaura R. Methods to enhance smoking cessation after myocardial infarction. *Med Clin North Am* 2000; 84: 63-80.

305. Astrup P, Kjelsen K. Carbon monoxide, smoking and CVDs. Symposium on atherosclerosis. *Med Clin North Am* 1974; 58: 323-350.

306. Imamura H, Teshima K, Miyamoto N. Cigarette smoking, HDL-C subfractions and lecithin cholesterol acyltransferase in young women. *Metabolism* 2002; 51: 1313-6.

307. Mero N, Van Tol A, Scheck LM, *et al*. Decreased postprandial HDL-C and apolipoproteins A-I and E in normolipidemic smoking men: relations with lipid transfer proteins and LCAT activities. *J Lipid Res* 1998; 39: 1493-502.

308. Jenssen J. Cigarette smoking and serum estrogen and bone loss during hormone theory. *NEJM* 1985; 313: 973-975.

309. Francis T. IL1, IL6 and PDGF messenger RNA expression in alveolar cells following stimulation with tobacco-derived antigen. *Cell Immunol* 1992; 145: 156-74.

310. Rose RM, Kozbik L, Filderman AE, *et al*. Characterization of colony stimulating factor activity in the human respiratory tract. Comparison of healthy smokers and non smokers. *Am Rev Respir Dis* 1992; 145: 394-9.

311. Harrats D, *et al*. Cigarette smoking renders LDL susceptible to peroxidative modification and enhance metabolism by macrophages. *Atherosclerosis* 1989; 79: 245-52.

312. Rajavashisth TB, Andaibi A, Territo MC, *et al*. Induction of endothelial cell expression of granulocyte and macrophage colony stimulating factors by modification of low density lipoproteins. *Nature* (Lond) 1990; 344: 254-7.

313. Roth P, Stanley ER. The biology of CSF-1 and its receptor. *Current topics in microbiology and immunology*, Berlin: SonnegVerlag 1992; 181: 141-58.

314. Patrons C, Davi G, Giabattani G. Thromboxane biosynthesis and metabolism in relation to cardiovascular risk factors. *Trends Cardiovasc Med* 1992; 2: 15-20.

315. Narahara N, Enden T, Wiger M, *et al*. Polar expression of tissue factor in human umbilical vein endothelial cell. *Atherioscler Thromb* 1994; 14: 1815-20.

316. Bauer J, Gantu U, Griger T, *et al*. Regulation of IL-6 expression in cultred human blood monocytes and monocyte derived macrophages. *Blood* 1988; 72: 1134-40.

317. Bataille R, Klein B. C-reactive protein levels as a direct indicator of IL-6 levels in humans *in vivo*. *Arthritis Reum* 1992; 35: 982-4.

318. Rohde LE, Ridker PM. Survey of C-reactive protein and cardiovascular risk factors in apparently healthy men. *Am J Cardiol* 1999; 84: 1018-22.

319. Matetzky S, Tani S, Kangavair S, *et al*. Smoking increases tissue factor expression in atherosclerotic plaques: implications for plaque thrombo genicity. *Circulation* 2000; 102: 602-4.

320. Hulthe J, Wilksrand J, Fagerberg B. Relation between C-reactive protein and intima thickness in the carotid and femoral arteries and to antibodies against oxidized LDL in healthy men: the Atherosclerosis and Insulin Resistance (AIR) Study. *Clin Sci* (Lond) 2001; 100: 371-8.

321. Ishibashi S, Inaba T, Shimano H, *et al*. Monocyte colony stimulating fator enhances cholesterol uptake and degradation of acetylated LDLs and

cholesterol esterification in human monocyte derived macrophages. *J Biol Chem* 1990; 265: 14109-17.

322. Sheshiah PN, Keriales DJ, Vasudevan SS, *et al*. Activated monocytes induce smooth muscle cell death. The role of macrophage colony stimulating factor and cell contact. *Circulation* 2002; 105: 174-8.

323. Huh HY, Pearce SF, *et al*. Regulated expression of CD36 during monocyte to macrophage differentiation potential role of CD36 in foam cell formation. *Blood* 1996; 87: 2020-8.

324. Ikonemidis I, Lekakis J, Vamvakou G, *et al*. Cigarette smoking is associated with increased circulating proinflammatory and procoagulant markers in patients with chronic CAD: Effects of aspirin treatment. *Am Heart J* 2005; 149: 832-9.

325. Balfour DJ. Neural mechanisms underlying nicotine dependence. *Addiction* 1994; 89: 1419-23.

326. Wilson K, Gibson N, Willan A, *et al*. Effect of smoking cessation on mortality after myocardial infarction- meta analysis of cohort studies. *Arch Intern Med* 2000, 160: 939-44.

327. Gordon T, Kannel WB. Death and coronary attacks in men after giving up smoking. *Lancet* 1974; 2: 1345-1348.

328. Rosenberg L, Palmer Jr. Decline in risk of myocardial infarction among women who stopped smoking. *N Engl J Med* 1990; 322: 213-217.

329. Maeda K, Naguchi Y, Fukui T. The effects of cessation from cigarette smoking on the lipid and lipoprotein profiles: a meta analysis. *Prev Med* 2003; 37: 283-90.

330. Zahler R, Piselli C. Smoking, alcohol and drugs. In: Zaret BL, Moser M, Cohen LS, editors. New York: Hearst Books; Yale University School of Medicine heart book 1992; 71-83.

331. Perkins J, Dick TB. Smoking and myocardial infarction: secondary prevention. *Postgrad Med J* 1985; 61: 295-300.

332. Glantz SA, Parmley WW. Epidemiology, physiology and biochemistry. *Circulation* 1991; 83: 1-12.

333. Neufeld EJ, Mietus-Snycler M, *et al*. Passive cigarette smoking and reduced HDL-C levels in children with high-risk lipid profiles. *Circulation* 1997; 96: 1403-1407.

334. Rigotti NA. Treatment of tobacco use and dependence*. N Engl J Med* 2002; 346: 506-12.

335. Rohan MC, Risteard M. Is a family history of CHD an independent coronary risk factor. *BRI Heart J*. 1985; 53: 378-381.

336. Dhanraj TJ, Acker MS, Danaraj W, *et al*. Ethnic differences in CHD in Singapore: an analysis of necroscopy*. Am Heart J.* 1959; 58: 516-526.

337. Enas EA, Yusuf S and Mehta JL. Prevalence of CHD in Asian Indians. *Am J Cardiol*. 1992; 70: 445-449.

338. Jha P, Enas EA, Yusuf S. CAD in Asian Indians: Prevalence of risk factors. *Asian Am Pac Islander J Health* 1993; 1: 161-175.

339. Rigat B, Hubert C, Alhenec GF, Vambien F, *et al*. An insertion/deletion polymorphism in the angiotensin-converting enzyme: gene accounting for half the variance of serum enzyme levels. *J Clin Invest*. 1990; 86: 1343-1346.

340. Cambien F, Poirier O, Lecerf L, *et al*. Deletion polymorphism in the gene for angiotensin- converting enzyme is a potent risk factor for myocardial infarction. *Nature* 1992; 359: 641-644.

341. Joseph A, Nair KG, Ashavaid TF. Angiotensin converting enzyme gene polymorphism in CAD: The Indian scenario. *Clin Chem Lab Med* 1998; 36: 621-624.

342. Ashavaid TF, Shaila KK, Nair KG, *et al*. ACE and AT1R gene polymorphism and hypertension in Indian population. *J Clin Lab Anal* 2000; 14: 230-237.

343. Bonnardeaux A, Davies A, Jeunemaitre X, *et al*. Angiotensin II type I receptor gene polymorphisms in human essential hypertension. *Hypertension* 1994; 24: 63-69.

344. Jeunemaitre X, Florent S, Kotelevster YV, *et al*. Molecular basis of human hypertension: role of angiotensinogen. *Cell* 1992; 71: 169-180.

345. Uterman G. Apolipoprotein E polymorphism in health and disease. *Am Heart J* 1987; 113: 433-440.

346. Kolovu G, Daskalova D, Mikhalldis DP. Apolipoprotein E polymorphism and atherosclerosis. *Angiology* 2003; 54: 59-71.

347. Siest G, Pillot T, Regis-Bailly A, Leininger-Miller B, *et al*. Apo E: an important gene and protein to follow in laboratory medicine. *Clin Chem* 1995; 41: 1068-1086.

348. Zannis VI, Breslow JI. Human very low density lipoprotein E isoprotein polymorphism is explained by genetic variation and post translational modification. *Biochemistry* 1981; 20: 1033-1041.

349. Boerwinkle E, Visvikis S, Welsh D, *et al*. The use of measured genotype information in the analysis of quantitative phenotypes in man. II The role of apolipoprotein E polymorphism in determining levels, variability and co-variability of cholesterol, beta lipoprotein and TG in a sample of unrelated individuals. *Am J Med Genet* 1987; 27: 567-582.

350. Davignon J. Apo E polymorphism and atherosclerosis. In Born GVR Schwartz CJ (eds). New Horizons in CHD. *Curr Sci* 1993; 5: 5.1-5.21.

351. Yilmag H, Isbir T, Agachan B, *et al*. Is epsilon 4 allele of apo E associated with more severe end-organ damage in essential HT ? *Cell Biochem* 2001; 19: 191-195.

352. Li X, Du Y, Huang X. Association of apo E gene polymorphism with essential HT and its complications. *Clin Exp Med* 2003; 2: 175-179.

353. Katsuya T, Baba S, Ishikawa K, *et al*. Epsilon 4 allele of apo E gene associates the lower blood pressure in yung Japanese subjects. *J Hypertension* 2002; 20: 2017-2021.

354. Rastas S, Mattila K, Verkkoniemi A, Niinisto L, *et al*. Association of apo E genotypes, BP, blood lipids and ECG abnormalities in a general population aged 85+. *BMC Geriatr* 2004; 4:1.

355. Zerba KE, Ferrell RE, Sing CF. Genotype-environmental interaction: apo E gene effects and age as an index of time and spatial context in humans. *Genetics* 1996; 143: 463-478.

356. Reilly S, Ferrell R, Sing CF. The gender-specific apo E genotype influence on the distribution of plasma lipids and apo in the population of Rochester, MN. III. Correlations and covariances. *Am J Hum Genet* 1994; 55: 1001-1018.

357. Elehner JE, Dunn ST, Perveen G, *et al*. Apo E polymorphism and CVD: a HUGE review. *Am J Epidemiol* 2002; 155: 487-495.

358. Hobbs HH, Brown MS and Goldstein JL. Molecular genetics of the LDL receptor gene in familial hypercholesterolemia. *Hum Mutat*. 1992; 1: 445-466.

359. Ashavaid TF, Altaf AK and Nair KG. Molecular basis of familial hypercholesterolemia: an Indian experience. *Indian J Clin Biochem* 2000; 15: 11-19.

360. Kotze MJ, Loubser O, Thiart R, *et al*. CpG hotspot mutations at the LDL receptor lows is a frequent cause of familial hypercholesterolemia among South African Indians. *Clin Genet* 1997; 51: 394-398.

361. Ashavaid TF, Altaf AK and Nair KG. Identification of LDL receptor gene defect in FH family from India using combined HDX-SSCP analysis. Mol Pathol, Division Newsletter, 2001; 13: 3-4.

362. Davignon J, Gregg RE, Sing CF. Apo E polymorphism and atherosclerosis. *Arterioscleroses* 1988; 8: 1-21.

363. Venkataramana P, Reddy PC. Effects of apo E polymorphism on the lipid and lipoprotein levels related to risk for CVD. Abst *ICMR Bulletin* 1998; 28: 66-67.

364. Ito Y, Azrolan NO, Connell A, *et al.* Hypertriglyceridemia as a result of human apo C III gene expression in transgenic mice. *Science* 1990; 249: 790-793.

365. Chen M, Breslow JL, Liw and Leff T. Transcriptional regulation of the apo C III gene by insulin in diabetic mice. Correlation with change in plasma triglyceride levels. *J Lipid Res* 1994; 35: 1918-1924.

366. Brunzell JD. Familial LPL deficiency and other causes of the chylomicronemia syndrome. *In*: Scriver CR, Beaudet AL, Sly WS, Varkee D, eds. *The Metabolic and Molecular Basis of Inherited Disease*. New York: McGraw Hill 1995; 1913-1932.

367. Brunzell JD, Schrott HG, Motulsky AG, *et al*. Myocardial infarction in familial forms of hypertriglyceridemia. *Metabolism* 1976; 25: 313-320.

368. Mahley RW, Rall SC Jr. Type III hypolipoproteinemias (dyslipoproteinmia): the role of apo E in normal and abnormal lipoprotein metabolism. *In*: Scriver CR, Beaudet AL, Sly WS, Varkee D, eds. *The Metabolic and Molecular Basis of Inherited Disease*. New York: McGraw Hill 1995; 1953-1980.

369. Valentine F, Chesebro JH. Platelet survival and development of CHDs in young adult: Effect of smoking and strong family history and medical therapy. *Circulation* 1981; 63: 546-555.

370. Ashavaid TF, Todur SP and Nair KG. Apo E4 polymorphism as risk factor for CHD among Indian subjects. *Indian J Clin Biochem* 2002; 17: 83-93.

371. Ritu S, Mridula M and Ravi K. Comparative account of serum lipids, lipoproteins and apolipoprotein B in patients of CAD. *Indian J Clin Biochem* 2004; 19: 10-13.

372. Reddy KS. Epidemiology of CHD in India. In CVD prevention. Vijayaraghavan G, Sunitha Kumari K (eds) Trivandrum: Dept of Cardiology, Medical College and Hospital, Trivandrum 1996; 6-30.

373. Taskinen MR. Effect of NIDDM on VLDL,TG and VLDL, Apo B metabolism. Studies before and after sulphonylurea therapy. *Diabetes* 1986; 35: 1268-1277.

374. Khare A, Ghosh k, Kulkarni B, *et al*. Thrombophilia hereditary and acquired in CVD: a review. *Haematologia*, 2002; 32: 293-311.

375. Winkelmann BR, Hager J, Krauss WE, *et al*. Genetics of CHD: current knowledge and research principles. *Am Heart J*. 2000; 140(suppl): S11-S26.

376. Pi-Sunyer FX. Health implications of obesity. *Am J Clin Nutr* 1991; 53: 1595S-1603S.

377. WHO. Obesity: preventing and managing the global epidemic. *WHO technical Report* Series number 894. Geneva: WHO, 2000.

378. Ezzati M, Lopez AD, Rodgers A, *et al.* Comparative Rik Assessment Collaborating Group. Selected major risk factors and global and regional burden of disease. *Lancet* 2002; 360: 1347-60

379. Gray DS. Diagnosis and prevalence of obesity. *Med Clin North Amer* 1989; 73: 1.

380. Hubert HB, Feinleib M, McNamara PM. Obesity as an independent risk factor for CVD: A26year follow up of participants in the Framingham Heart Study. *Circulation* 1983; 67: 968.

381. Catersen ID. Obesity, part of the metabolic syndrome. *The clinical biochemist reviews* 1997; 18: 11-21.

382. Must A, Spadano J, Coakley EH, Field AE, *et al*. The disease burden associated with overweight and obesity. *JAMA* 1999; 282: 1523-1529.

383. Manson JE, Willett WC, Stampfer MJ, *et al*. Body weight and mortality among women. *N Engl J Med* 1995; 333: 677-685.

384. Manson JE, Colditz GA, Stampfer MJ *et al*. A prospective study of obesity and risk of CHD in women. *N Engl J Med* 1990; 322: 882-889.

385. Stamler J. Epidemiologic findings on body mass and BP in adults. *Ann Epidemiol* 1991; 1: 347-362.

386. Willett WC, Manson JE, Stampfer MJ, *et al*. Weight , eright change and CHD in women: risk within the "normal" weight range. *JAMA* 1995; 273: 461-465.

387. Bethesda MD. Clinical guidelines on the Identification, Evaluation and Treatment of Overweight and Obesity in Adults: Evidence Report. *National Institutes of Health*. 1998; Publication no. 98-4083.

388. Grundy SM, Denke MA. Dietary influences on serum lipids and lipoproteins. *J Lipid Res* 1990; 31: 1149-1172.

389. Krotkiewski M, Bjorntorp P, Sjostrom L, Smith U. Impact of obesity on metabolism in men and women (Important for regional adipose tissue) *J Clin Invest* 1983; 72: 1150-1162.

390. Larsson B, Svarsudd K, Welin L, *et al.* Abdominal adipose tissue distribution, obesity and risk of CVD and death: By follow up of the participants in the study of the men born in 1913. *Br Med J* 1988; 288: 1401-1404.

391. Huges LO, Wojeiechowski AP, Rafterey EB. Relationship between plasma cholesterol and CAD in Asians. *Atherosclerosis* 1990; 83(1): 15-20.

392. Edington JD, Geekie H, Carter C, *et al*. Serum lipid response to dietary cholesterol in subjects fed a low fat, high fiber diet. *Am J Clin Nutr* 1989; 50: 58-62.

393. Kuczmarski RJ, Flegal KM, Campbell SM , *et al*. Increasing prevalence of overweight amonbg US adults. The National Health and Nutrition Examination Surveys 1960 to 1991. *JAMA* 1994; 272: 205-211.

394. Allison DB, Fontane KR, Manson JE, *et al*. Annual deaths attributable to obesity in the US. *JAMA* 1999; 282: 1530-1538.

395. James WPT, Jackson–Laach R, *et al.* Overweight and obesity (high BMI): *In* : Ezzati M, Lopez AD, et al. eds. Comparative quantification of health risks: global and regional burden of disease attributable to selected major risk factors, vol 1. Geneva: WHO 2004: 497-596.

396. Shah M, Hannan PJ, Jeffrey RW. *Int J Obes* 1991; 15: 499-503. 1999; 23: 771-4.

397. Hoffmans AF, Kromhout D, Coulander de LC. BMI at the age of 18 and its effects on 32year mortality from CHD and cancer. *J Clin Epidemiol* 1989; 42: 513-520.

398. Donahue RP, Abbott RD, Bloom E, *et al*. Central obesity and CHD in men. *Lancet* 1987; 1: 821.

399. Andres R. *Ann Intern Med* 1985; 103: 1030-3.

400. Rabkin SW, Mathewson FAL, *et al*. *Am J Cardiol* 1977; 39: 452-8.

401. Bjorntorp P. Visceral obesity: a "civilization syndrome". *Obes Res* 1993; 1: 206-222.

402. Han TS, Van Leer EM, Scidell JC, *et al*. Waist circumference action levels in the identification of cardiovascular risk factors: prevalence study's in a random sample. *BMJ* 1995; 311: 1401-1405.

403. Shetterley SM, Marshall JA, *et al*. WHR measurement location influences association with measures of glucose and lipid metabolism. The San Luis Valley . Diabetes Study . *Ann Epidemiol* 1993; 103: 295-299.

404. Bjorntorp P. Regional patterns of fat distribution. *Ann Int Med* 1985; 103: 994-995.

405. Reeder BA, Liu L, Horlick L. Selective screening for dyslipidaemia in a Canadian population. *J Clin Epidemiol* 1996; 49: 217-222.

406. Pacccaud F, Schluter-Fasmeyer V, *et al*. Dyslipidemis and abdominal obesity: An assessment in there general populations. *J Clin Epidemiol* 2000; 53: 393-400.

407. Freedman DS, Jacobsen SJ, Barboriak JJ. Body fat distribution and male/female differences in lipids and lipoproteins. *Circulation* 1990; 81: 1498-1500.

408. Larsson B, Bengtsson C, Bjorntop P. Is abdominal body fat distribution a major explanation for the sex difference in the incidence of myocardial infarction ? The study of men born in 1913 and the study of women. *Am J Epidemiol* 1992; 135: 266-273.

409. INTERSALT Co-operative Research Group. INTERSALT Study. An international co-operative study on the relation of BP to electrolyte excretion in populations. I. Design and methods. *J Hyperstens* 1986; 4: 781-7.

410. Elliot P, Stamler R. Manual of operations for “INTERSALT” an international co-operative study on the relation of sodium and potassium to BP. *Controlled Clin Trials* 1988; 9(suppl): 1-118.

411. WHO/IASO/IOTF. The Asia-Pacific perspective: redefining obesity and its treatment. Melbourne: Health Communication Australia PTY Ltd 2000.

412. Sanchez-Castillo CP. Velasquez-Monroy O, *et al*. Diabetes and hypertension increases in a society with abdominal obesity: results of the Mexican National Health Survey 2000*. Public Health Nutr* 2005;8: 53-60.

413. Alberti KG, Zimmet PZ. Definition , diagnosis and classification of diabetes mellitus and its complication, part1: diagnosis and classification of diabetes mellitus, provisional report of a WHO consultation. *Diabetic Med* 1998; 15: 539-53.

414. Wolf HK, Tuomilehto J, Kuulasmaa K, *et al*. BP levels in 41 populations of the WHO MONIC project. *J Hum Hypertens* 1997; 11: 733-42.

415. Cassono PA, Segal MR, Vokonas PS, *et al*. Body fat distribution, BP and HT: a prospective cohort study of men in the normative aging study. *Ann Epidemiol* 1990; 1: 33-48.

416. Kastarinen MJ, Nissinen AM, Varitiainen EA, *et al*. BP levels and obesity trends in hypertensive and normotensive Finnish population from 1982 to 1997. *J Hypertens* 2000; 18: 255-62.

417. Dyer A, Elliott P. Body mass index and BP in the INTERSALT atudy of urinary electrolytes, other factors and BP. *J Hum Hypertens* 1989; 3: 299-308.

418. Keys A, Fidanza F, Karvomen MJ, *et al.* Indices of relative weight and obesity. *J Chronic Dis* 1972; 25: 329-49.

419. Dyer AR, Elliott P and Shipley M. The INTERSALT Cooperative Research Group. BMI versus height and weight in relation to BP: findings of the 10,079 persons in the INTERSALT study. *Am J Epidemiol* 1990; 131: 589-96.

420. Berglund G, Wilhelmsen L. Factors related to BP in a general population sample of Swedish men. *Acta Med Scand* 1976; 198: 291-8.

421. Doyle AE, Lovell RRH. BP and body build in men in tropical and temperate *Australia. Clin Sc*i 1961; 20: 243-7.

422. Miall WE, Bell RA, Lowell HG. Relation between change in BP and weight. *Br J Prev Soc Med* 1968; 22: 73-80.

423. Anupama K, Nandini M, Kedilaya HR, *et al*. Relation of anthropometry to CVD risk factors in young obese women. *Biomedical Research* 2005; 16(2): 137-141.

424. Rabkin SW, Chen Y, Leiter L*, et al*. Risk factor correlates of BMI: Canadian Heart Health Surveys Research Group. *Can Med Association* J 1997; 157(suppl 1):S26-31.

425. Krauss RM, Winston M. Obesity- Impact in CVD. *Circulation* 1998; 98: 1472-1476.

426. Skurk T, Hauner H. Obesity and impaired fibrinolysis: role of adipose production of plasminogen activator inhibitor-1. *Int J Obes Relat Metab Disord* 2004; 28: 1357-64.

427. Drewnowski A. Energy density palatability and satiety: implications for weight control. *Nutr Rev* 1998; 56: 347-53.

428. Raben A, Vasilaras TH, *et al*. Sucrose compared with artificial sweetners: different effects on ad libitum food intake and body weight after 10 week of supplementation in overweight subjects*. Am J Clin Nutr* 2002; 76: 721-29.

429. Denke MA, Sempos CT, Grundy SM. Excess body weight an underrecognized contributor to high blood cholesterol levels in white American men. *Arch Intern Med* 1991; 153: 1093-103.

430. Wakabayashi I. Relationship of BMI with BP and serum cholesterol concentration at different ages. *Aging Clin Exp Res* 2004; 16: 461-6.

431. Lamon-Fava S, Wilson PW and Schaefer EJ. Impact of BMI on CHD risk factors in men and women. The Framingham Offspring study . *Arterioscler Thromb Vasc Biol* 1996; 16: 1509-1515.

432. Weisweiler P. Plasma Lps and lipase and LCAT activities in obese subjects before and after weight reduction. *J Clin Endocrinol Metab* 1987; 65: 969-73.

433. Kenchaiah S, Gaziano JM, Vasan RS. Impact of obesity on the risk of heart failure and survival after the onset of heart failure. *Med Clin North Am* 2004; 88: 1273-94.

434. McKrigue PM, Shah B, Marmot MG. Relation of central obesity and insulin resistance with high diabetes prevalence and cardiovascular risk in South Asians. *Lancet* 1991; 337: 382-86.

435. Brage S, Brage N, Frank PW, *et al.* Reliability and validity of the combined heart rate and movement sensor Actiheart. *Eur J Clin Nutr* 2005; 59: 561-70.

436. Morris JN, Chave SPW, Adam C, *et al.* Vigorous exercise in leisure-time and the incidence of CHD. *Lancet* 1973; 1: 333-39.

437. Blair SN, Kohl HE, Barlow CE, *et al*. Changes in physical fitness and all cause mortality. *JAMA* 1995; 273: 1093-98.

438. US Dept of Health and Human Services. Physical activity and helth: A report of the Sugeon General. Atlanta GA: US Dept of health and human services, Centers for Disease Control and Prevention*, National Center for Chronic Disease Prevention and HEALTH Promotion* 1996.

439. King AC, Haskell WL, Young DR, *et al*. Long-term effects of varying intensities and formats of physical activity on participation rates; fitness and Lps in men and women aged 50to 65years. *Circulation.* 1995; 91: 2596-604.

440. Gupta AK, Ross EA, Myers JN*, et al*. Increased reverse cholesterol transport in athletes. *Metabolism 1*993; 42: 684-90.

441. Kokkinos PF, Holland JC, Narayan P, et al. Miles run per week and HDL-C levels in healthy, middle-aged men. A dose-response relationship. *Arch Intern Med* 155: 415-450.

442. Couillard C, Despres JP, *et al.* Effects of endurance training on plasma HDL-C levels depend on levels of TGs: evidence from men of the Health, Risk Factors, Exercise Training and Genetics (HERITAGE) Family Study. *Arteriscler Thromb Vasc Biol* 2001; 21: 1226-32.

443. Dengel DR, Hagberg JM, Coon PJ, *et al*. Comparable effects of diet and exercise on body composition and lipoproteins in older men. *Med Sci Sports Exerc* 1994; 26: 1307-1315.

444. Erlichman J, Kerbey AL, James WPT . Physical activity and its impact on health outcomes. Paper 2, prevention of unhealthy weight gain by physical activity: an analysis of the evidence. *Obes Rev* 2002; 3: 273-87.

445. Trichopoulous A, Gnardellis C, Benetou V, *et al*. Lipid, protein and carbohydrate intake in relation to BMI. *Eur J Clin Nutr* 2002; 56: 37-43.

446. Petersen L, Schnohr P, Sorensen T. Longitudianal study of the long-term relation between physical activity and obesity in adults*. Int J Obes Relat Metab Disord* 2004; 28: 105-12.

447. Pereira MA, Kartashow AI, Ebbding CB, *et al*. Fast food habits, weight gain and insulin resistance (the CARDIA study): 15year prospective analysis. *Lancet* 2005; 365: 36-42.

448. WHO. Diet, nutrition and the prevention of chronic diseases: report of a joint WHO/FAO Expert Consultation. *WHO Technical Report* Series number 916. Geneva: WHO, 2003.

449. Astrup A, Meinert Larsen T, Harper A. Atkins and other low carbohydrate diets; hoax or an effective tool for weight loss ? *Lancet* 2004; 364: 897-99.

450. Dansinger ML, Gleason JA, Griffith JL, *et al*. Comparison of the Atkins, Ornish, Weight Watchers and Zone diets for weight loss and heart disease risk reduction: a randomized trial. *JAMA* 2005; 293: 43-53.

451. Bray GA. Predicting obesity in adults from childhood and adolescent weight. *Am J Clin Nutr* 2002; 76: 497-498.

452. Enas EA, Mehta J. Malignant CAD in young Asian Indians: thoughts on pathogenesis, prevention and therapy. Coronary Artery Disease in Asian Indians (CADI) Study. *Clin Cardiol* 1995; 18: 131-135.

453. Allain CC, Poon LS, Chan CSG. Enzymatic determination of total serum cholesterol. *Clin Chem* 1974; 20: 470-75.

454. Burnstein SM. Lipoprotein MR, Lipoprotein-Metal interactions. *Adv Lipid Res* 1973; 11: 67-108.

455. Celine VJ, Mathur BBL. BP variations in aging. *JAMA* 1970; 55: 129-130.

456. Shrivastava RN, Verma BL. Kumar A, *et al*. BP in a rural adult population percentile distribution by age and sex. *Int of Med Res* 1977; 65: 142-149.

457. Whelton PK. Epidemiology of HT. *Lancet* 1994; 344: 101-106.

458. Editorial. Why does BP rise with age ? *Lancet* 1981; ii: 289-290.

459. Miall WE, Lovell HG. Relation between change of BP and age. *Br Med J* 1967; 2: 660-664.

460. Onitri AC, Sander, Monica and Boye AR. Serum lipids and lipoproteins in healthy Africans. *Clin Chem Acta* 1977; 57: 81.

461. Lipids Research Clinics Program Prevention Study. LRCPPC trial. Plasma lipid distributions in North American White population. *Circulation* 1979; 60: 427-439.

462. Gandhi BM. Lipoprotein composition of normal healthy subjects in northern India. *In J Med Res* 1982; 75: 393-401.

463. Reddy KK, Bulliyya. Effect of aging and atherogenesis factors of rural and urban population. *Ind J Clinical Biochem* 1990; 5: 18-29.

464. Puri DS, Kashyap S, Singhal SK. Serum lipids in healthy tribal living at high altitudes in the Himalayas. *J Assoc Physic Ind* 1990; 38: 777-779.

465. Joshi HD. Aetiology and incidence of heart disease in Gujarat. *ICMR* 1965; 44: 655-663.

466. Abdul RS. Assessment of selected coronary risk factors in adult Kuwaitti males. *Med Principle Practice*. 1990; 2: 199-202.

467. Robert L, Donald CT, Israel Tamir. Plasma HDL-C in children and young adults. *Circulation* 1980; 62(suppl IV): 83-92.

468. Barclay M, Barday RK. HDL-C lipoprotein concentration in men and women. *Nature* 1963; 200: 262-267.

469. Godsland JF, Wyan V, Crook D, *et al*. Sex, gender, plasma lipoprotein and atherosclerosis. Prevailing assumptions and outstanding questions special report. *Am Heart J* 1957; 114: 1467-1503.

470. Eskimos diets and diseases editorial. *Lancet* 1983; 1: 1139-1141.

471. Slack J, Nancy Noble, Miede TW, *et al*. Lipids and Lp concentration in 1604 men and women in working population in North West London. *Br Med J* 1977; 2: 353-357.

472. Heiss G, Tamir I, Davis CE. Lp cholesterol distribution in selected North American population. *The LRCPPS Circulation* 1980; 61: 302-315

473. Miller NE. Why does LDL-C in adults increased with age ? *Lancet* 1984; 1: 263-266.

474. Brown MS, Goldstein JL. LDL-C receptor influence and plasma cholesterol traffic. *J Clin Invest* 1983; 72: 743-747.

475. Angelin B, Einarsson K, Leijd B. Influence of age in secretion of cholesterol and synthesis of bile acids by livers. *N Engl J Med* 1985; 313: 277-282.

476. Simons LA. Interrelations of lipids and lipoproteins with CAD in 19 countries. *Am J Cardiology* 1986; 57(suppl G): 5G-10G.

477. Misra KP, Suresh S, Balachandran G, *et al*. Plasma lipoprotein cholesterol and CHD. *J Assoc Phys Ind* 1980; 28: 399-404.

478. Peters A, Barendregt DT, Wang C, *et al.* NECOM the Netherlands Epidemiology and Demography Compression of Morbidity Research Group. Obesity in adulthood and its consequences for life expectancy: a life-table analysis. *Ann Intern Med* 2003; 289: 187-93.

479. Stevens J, CaiJ, Panuk ER. The effect of age on the association between BMI and mortality. *N Engl J Med* 1998; 338: 1-7.

480. Kearney PM, Whelton M, Reynolds K, *et al*. Global burden of HT: analysis of worldwide data. *Lancet* 2005; 365: 217-23.

481. Ezzati M, Lopez AD, Rodger A, *et al*. Selected major risk factors and global and regional burden of disease. *Lancet* 2002; 360: 1347-60.

482. HT Study Group. Prevalence, awareness, treatment and control of HT among the elderly in Bangladesh and India: A multicenter study. *Bull World Health Organ* 2001; 79: 490-500.

483. Onal AE, Eebil S, Ozel S, *et al.* The prevalence of and risk factors for HT in adults living in Istanbul. *Blood Press* 2004; 13(1): 31-36.

484. Carneiro G, Faria AN, Rineiro FF, *et al*. Influence of body fat distribution on the prevalence of arterial HT and other cardiovascular risk factors in obese patients. *Rev Assoc Med Bras* 2003; 49(3): 306-11. Epub 2003 Nov 5.

485. Rosas PM. Arterial HT in Mexico and its association with other risk factors. *Arch Cardiol Mex* 2003; 73(suppl 1): S137-40.

486. Burt VL, et al. Prevalence of HT in the US adult population. Results from the Third National Health and Nutrition Examination Survey. 1988-1991. *Hypertension* 1995; 25(3): 305-13.

487. Nissinen A, Bothig S, Granroth H, *et al.* HT in developing countries. *World Health Stat Q* 1988; 41: 141-54.

488. Hazarika NC, Nalain K, Biswas D, *et al*. T in the native rural population of Assam. *Natl Med J India* 2004; 17: 300-4.

489. Isles CS. Prevalence, epidemiology and pathology of HT. In: (ed) Warrell DA *Oxford textbook of Medicine*, 4th ed. Oxford: Oxford University Press 2000; 1153-1160.

490. Whelton PK, *et al.* Sodium restriction and weight loss in the treatment of HT in older persons. A randomized controlled trial of non-pharmacologic interventions in the elderly (TONE). TONE Collaborative Research Group. *JAMA 1*998; 279(11): 839-43.

491. Joglekar SJ, WarrenSL, Prabhu AT, *et al.* Co-existence of HT and abnormal lipid profile. A hospital-based retrospective survey *Indian Heart J* 1997; 49: 275-298.

492. Hakim AS, Kamath SA, Mehta PJ, *et al*. A retrospective study of the lipid profile in 500 hypertensive patients. *J Assoc Phys India* 1997; 45: 943-944.

493. Malhotra P, Singh MM, Kumar R, *et al*. CHD and its risk factors in first-generation immigrant Asian Indians to the USA. *Ind Heart J* 1996; 48: 737.

494. Gopinath N, Chadha SL, Sehgal A, *et al.* What is desirable lipid profile*. Ind Heart J* 1994; 46: 325-327*.*

495. Chadha SL, Gopinath N, Shekhawat S. Urban-rural differences in the prevalence of CHD and its risk factors in Delhi*. Bull WHO* 1997; 75: 31-8.

496. Joseph A, Kutty VR, Soman CR. High risk for CHD in Thiruvananthapuram city: A study of serum lipids and their risk factors. *Ind Heart J* 2000; 52: 29-39.

497. Zavoroni I, Bonora E, Pagliara M, *et al*. Risk factors for CAD in healthy persons with hyperinsulinemia and normal glucose tolerance*. N Engl J Med* 1989; 320: 702-06.

498. Thomas GW, Mann JI, Beilin LN, *et al*. HT and raised serum lipids. *BMJ* 1977; Sept: 805.

499. Newman WP, David SF. Relation of serum Lp levels and SBP to early atherosclerosis. Bogalusa Heart Study*. N Engl J Med* 1986; 314: 138-143.

500. Chadha SL, Gopinath N and Ramachandran K. Epidemiological study of CHD in Gujaratis in Delhi. *Indian J Med Res* 1992; 96: 115-121.

501. Albrink MJ, Man EB, Meigs JW. Serum lipids and CHD. *Am J Med* 1961; 31: 4-23.

502. Balanntyne D, Davine BL. Interrelation of age, obesity, smoking and BP in hypertensive patients. *Br Med J* 1978; i: 880-881.

503. Thomas CS, Krishnaswami S. Distribution of BMI in Indian patients with CAD. *Ind Heart J* 1995; 47: 134-137.

504. Brown CD, Higgins M, Donato KA, *et al*. BMI and the prevalence of HT and dyslipidemia. *Obes Res* 2000; 8: 605-619.

505. Kannel WB. BP as cardiovascular risk factor. Prevention and Treatment. *JAMA* 1996; 275(20): 1571-6.

506. Wilhelmsen D, Wedel B, Tibblin K. Risk of CHD. *Circulation* 1973; 48: 949-957.

507. Andersen TW. Reexamination of some of the Framingham BP data. *Lancet* 1978; ii: 1139-1141.

508. Ibrahim AM. HT prevalence and status of awareness and control in USA. *Hypertension* 1985; 7: 457-468.

509. Kannel WB, Dawber TR. HT as an ingredient of a cardiovascular risk profile. *J Appl Med 1*975; 499-510.

510. Nesbitt SD, Julius S, Leonard D, *et al*. Is low risk HT fact or fiction ? Cardiovascular risk profile in the TROPHY study. *American J of Hypertension* 2005; 18: 980-5.

511. Castelli WP, Anderson K. Population of risk prevalence of high blood cholesterol levels in hypertensive patients in the Framingham study. *Am J Med 1*986; Suppl 2A: 23-32.

512. Kotokey RK, Hazarika S, *et al.* Lipid abnormalities in hypertensive urban population of Dibrugarh District of Upper Assam. Available at: http://indianheartjournal.com/NOVDEC_HTML

513. Willum RR, Hunt SC. Familial dyslipidemia in HT. Evidence form 58 Utah families for a syndrome present in approximately 12% of patients with essential HT. *JAMA* 1988; 289: 3579-3586.

514. Shankar S, Shankae A*, et al*. Study of insulinemia and lipid profile in patients of essential HT. *J Assoc Phys India* 1993; 41: 12-851.

515. Hays JH, DiSabatino A, Gorman RT, *et al.* Effect of a high saturated fat and no-starch diet on serum lipid subfractions in patients with documental atherosclerotic CVD. *Mayo Clin Oroc* 2003; 78: 1331-1336.

516. Ness AR, Powles JW. Fruit and vegetables and CVD: a revuew. *Int J Epidemiol* 1997; 26: 1-3.

517. Joshipura KJ, Ascherio A, Mnson JE, *et al*. Fruit and vegetable intake in relation to risk of ischaemic stroke. *JAMA* 1999; 282: 1233-9.

518. Walker L, Mann L, *et al*. *Am J Med* 1953; 4: 654.

519. Anderson TW, *et al*. *J Clin Invest* 1957; 36: 81.

520. Christakis RA, *et al*. *JAMA* 1966; 195(6): 129.

521. Paul L, Willum G, Anne H, *et al*. A controlled trial of low sodium, low fat high fibre diet in treated hypertensive patients. *Postgraduatee Med J* 1990; 66: 616-621.

522. Pekka P, James MI, *et al*. Controlled randomized trial of the effect of dietary on BP. *Lancet* 1983; i: 1-5.

523. Singh RB, Niaz MA, Ghosh S, *et al*. Association of trans FAs (vegetable ghee) and clarified butter (Indian ghee) intake with higher risk of CAD in rural and urban populations with low fat consumption. *Int J Cardiol* 1996; 56(3): 289-98.

524. Singh RB, Niaz MA, Ghosh S, *et al*. Epidemiologic study of diet and coronary risk factors in relation to central obesity and insulin levels in rural and urban populations of North India. *Int J Cardiol* 1995; 47(3): 245-55.

525. Wilson L. *J of Clin Invest* 1965; 44: 1805.

526. Taylor M, Anderson TW, *et al*. *Minnesota Medical* 1966; 46: 728.

527. Anronis B. Am J Clin Nutr 1962; 10: 484.

528. Keys and Blackburn. *Prog Cardiovascular Disease* 1963; 6: 14.

529. Bronte-Stewart, Antonis E, *et al*. *Lancet* 1956; 1: 521.

530. Lichtenstein AH, Ausman LM,*et al*. Hydrogenation impairs the hypolipidemic effect of corn oil in humans: hydrogenation, trans FAs and plasma lipids. *Arterioscler Thromb* 1993; 13: 1493-501.

531. Nestel P, Noakes M, Belling B, *et al*. Plasma Lp lipid and Lp(a) changes with substitution of elaidic acid for oleic acid in the diet. *J Lipid Res* 1992; 33: 1029-36.

532. John JH, Ziebland S, Yudkin P, *et al*. Effects of fruit and vegetable consumption on plasma AO concentration and BP: a randomized controlled trial. *Lancet* 2002; 359: 1969-74.

533. Alonso A, dela Fuente C, Martin AM, *et al*. Fruit and vegetable consumption is inversely associated with BP in a Mediterranean population with a high vegetable fat intake: the Seguimiento Universidad de Navarra (SUN) Study. *Br J Nutr* 2004; 92: 311-9.

534. Stamler J. Research related to risk factors. *Circulation* 1979; 60: 1775-1787.

535. Medical Research Council (MRC) Working party trial. *Br Med J* 1985; 297: 97-104.

536. Manica G, Fitzgerald GA. Symposium- smoking and CVD. *Am Heart J* 1988; 115: 240-296.

537. Kannel WB. Some lesions in cardiovascular epidemiology from Framingham Heart Study. *Am J Cardiol* 1976; 37: 269-289.

538. Green MS, Jucha E. BP in smokers and non-smokers epidemiological findings. *Am Heart J* 1986; 11: 932-940.

539. Leslie B, Ildiko R. Cigarette smoking in hypertensive patients. BP and endocrine response. *Am J Med* 1985; 78: 564-565.

540. Sharma K, Gupta R, Gupta HP, *et al*. Haemodynamic effects of pan masala in healthy volunteers. *J Assoc Phys India* 2000; 48(4): 400-1.

541. Pais P, Fay MP, Yusuf S. Increased risk of AMI associated with beedi and cigarette smoking in Indians: final report on tobacco risks from a case-controlled study. *Ind Heart J* 2001; 53(6): 731-5.

542. Khurana M, Sharma P, Khandelwal PD. Lipid profile in smokers and tobacco chewers- a comparative study. *J Assoc Phys India* 2000; 48(9): 895-7.

543. OK D Mjos. Lipid effects on smoking: *Am Heart J* 1988; 155: 272-275.

544. Kulkarni KA, Dangarwale P, *et al*. Study of quantitation of compositional changes in levels of TC and HDL-C fraction in smokers and its relation with that of non smokers. *Ind J Clinic Chem* 1991; 6: 133-137.

545. Pandey MR. Tobacco smoking and HT. *Ind Med Assoc* 1999; 97(9): 367-9.

546. Haslam DU, Jamer WPT. Obesity. *Lancet* 2005; 366:1197-209.

547. Albaner D, Jones Y, Micozzi MS, *et al*. Assocociations between smoking and body weight in the US population: analysis of NHANES II. *Am J Public Health* 1987; 77: 437-444.

548. Trivedi DH, Sharma V, et al. Longitudinal epidemiological study of CHD in a rural population of Kheda district. Gujarat. *Soz Preventiv Med* 1996; 41(6): 373-9.

549. Wander GS, Khurans SB, *et al*. Epidemiologyof CHD in a rural Punjab population- prevalence and correlation with various risk factors. *Ind Heart J* 1994; 46(6) 319-23

550. Elizabeth BC, Kay-tee Khaw. Family history of heart attack as an independent prediction of death due to CVD. *Circulation* 1984; 69: 1065-1069.

551. Heller RF, Robinson N, Peart WS. Value of BP measurements in the relatives of hypertensive patients. *Lancet* 1980; ii: 1206-1208.

552. Dembinska Kice A, Kaweela-Jaszez K, Kwasnaik GI, *et al.* Apo E isoforms, insulin output and plasma lipid levels in essential HT. *Eur J Clin Invest* 1998; 28: 95-99.

553. Breslow JL. Apolipoprotein genetic variation and human disease. *Physiol Rev* 1988; 68: 85-98.

554. Ashavaid TF, Kondkar AA and Nair KG. Identification of two LDL receptor mutation causing FH in Indian subjects. *J Clin Lab Anal* 2000; 14: 293-298.

555. Lynn BJ, Roger RW. Relation between family history of CAD coronary risk variables. *Am J Cardiol* 1988; 62: 708-713.

556. Mowar SM, Pal SK, Ghosh KK. Coronary risk factors in families. *Ind Heart J* 1977; 29: 112-117.

557. Jha P, Enas E, *et al*. CAD in Asian Indians: Prevalence and Risk factors. *Asian AM Pac Isl J Health* 1993; 1(2): 163-175.

558. De Backer G, Hulstarrt F, *et al*. Serum lipids and apoproteins in students whose parents suffern prematurely MI. *Am Heart J*. 1996; 112: 478-484.

559. Widhalm K, Koch S, Pakesta R, *et al*. Serum lipids, lipoproteins and apolipoproteins in children with and with out family history of premature CHD. *J Am College of Nutr* 1992; 11(suppl): 323-355.

560. Schaefer EJ, LamonFava S, Jenner JL, *et al.* Lp(a) levels and risk of CJD in men. The Lipid Research Clinics Coronary Primary Prevention Trial. *JAMA* 1994; 271: 999-1003.

561. Durrington PN, Ishola M, Hunt L, *et al*. Apolipoprotein (a), AI and B and parental history in men with early onset IHD. *Lancet* 1988; 1: 1070-1073.

562. Armstrong VW, Crimer P, Eberle E, *et al*. The association between serum Lp(a) concentration and angiographically assessed coronary atherosclerosis: Dependence on serum LDL levels. *Atherosclerosis* 1986; 62: 249-257.

563. Rajashekhar D, Saibaba KSS, *et al.* Lp(A): Better assessor of CHD risk in south Indian population. *Ind J Clin Biochem* 2004; 19(2): 53-59.

564. Enas EA, Senthilkumar A. Role od Lp(a): Reality and Prevalence. In; Gambhir D (ed) *Cardiology Update*. CSI, New Delhi p 8-25.

565. Allison D, Matz PE, Pietrobelli A, et al. Genetic and environmental influences on obesity. In: Bendich A, Deckelbaum RJ, eds. *Primary and secondary preventive nutrition*. Totowar NJ: Humana Press, 2001: 147-64.