Introduction
Introduction

Atherosclerosis is the leading cause of death and serious morbidity in the present human civilization. It is a progressive disease which begins in childhood and has manifestations in the middle to late adulthood.

Although any artery may be involved the aorta, the coronary and the cerebral systems are the prime targets. Hence myocardial infarction, cerebral infarction and aortic aneurysms are the major consequences of the disease. Moreover, extensive atheromas are friable often yielding of their grumous contents into the distal circulation (atheroemboli) more commonly noted in the kidneys.

Other consequences of acutely or chronically diminished arterial perfusion are gangrene of the legs, mesentric occlusion, chronic ischemic heart disease, ischemic encephelopathy and sudden cardiac death.

Despite a continuing decline in the incidence of atherosclerosis-related death in the past 35 years, deaths from CHD, cerebrovascular disease and peripheral vascular disease accounted for 30% of the 2.3 million deaths in the United states during 1997. Two-thirds of atherosclerosis deaths were due to CHD, about 85% of CHD deaths occurred in individual over 65 yrs.of age. Among the 15% dying prematurely (below age 65), 80% died during their first CHD event. Among those dying of sudden cardiac death in 1997, 50% of the men and 63% of the women had been previously asymptomatic.

These studies illustrate the importance of identifying and management of risk factors for CHD. The major known risk factors are
elevated LDL-C, reduced HDL-C cigarette smoking, hypertension, type II Diabetes mellitus, advancing age and a family history of premature [men 55yr women <65yr] CHD events in a first degree relative, control of the modifiable risk factors is especially important in preventing premature CHD. Observational studies suggest that modifiable risk factors account for 85% of excess risk (risk over and above that of individual with optimal risk factor profiled for premature CHD).

Furthermore these studies indicates that, when total cholesterol levels are below 160 mg/dl, CHD risk is markedly attenuated, even in the presence of additional risk factor.

This pivotal role of hypercholesterolemia in atherogenesis gave rise to the almost- universally accepted cholesterol-diet-CHD hypothesis.

Relation between an elevated total serum cholesterol (STC) and atherosclerosis (AS) was first noted in 1930’s in independant studies by Muller and by Thannhauser and Magendantz. A strong direct co-relation was reported between STC levels and development of IHD in more than 5000 subjects followed for 14 years in Framingham Heart Study (Kannel and co-workers, 1971). Although AS is polygenic in nature and multifactorial in development, the evidence for improvement in coronary disease outcome consequent to lowering low density lipoprotein (LDL) is incontrovertible.

A direct relation exists between LDL levels and development of IHD (Hulley and Rhodes, 1982; Kannel et al, 1984; Ross et al, 1986). In contrast an inverse relationship exists between high density lipoprotein (HDL) levels and development of IHD. (Miller and Miller, 1975; Gordon et al, 1981; Goldbourt et al, 1985).

An understanding of lipoprotein metabolism and how it influences diabetes is of particular importance because of the association of
lipoproteins with CAD, presently the leading cause of death among diabetics. In DM (one of the risk factors for CAD) disturbances of serum lipoprotein concentrations may account for the increased frequency of atherosclerosis in affected patients. (Biermann, 1978; Ganda, 1980).

Increased levels of very low density lipoprotein (VLDL) cholesterol and low density lipoprotein (LDL) cholesterol and a decreased concentration of high density lipoprotein (HDL) cholesterol have been frequently described (Lopes - Virella, 1978; Taylor, 1981; Briones, 1984) in both individuals with non insulin dependant diabetes (NIDDM) and insulin dependant diabetes (IDDM).

Hypertension is quantitatively the largest risk factor for CAD because of early intrinsic vascular abnormalities (probably genetically determined) that are exaggerated by concomitant risk factors and by high blood pressure itself.

New emphasis is now being laid on management of lipid disorders as an area of critical importance in reducing the morbidity and mortality due to coronary events, as evidenced by National Cholesterol Education Programme's (NCEP) aim to target the coronary patients for aggressive lipid lowering therapy. This can be achieved by dietary therapy (as 50% of body cholesterol comes from exogenous sources) or by lipid lowering drugs. The dietary cholesterol can be reduced by reducing oral intake of saturated fats (eg. dairy milk products) and increasing polyunsaturated fat intake.

**Statins (Atorvastatin):**

Statins are the HMG-CoA reductive inhibitor which catalyze a early, rate limiting step in cholesterol biosynthesis. [Conversion of HMGCoA To Mevalenate]. By this statins inhibit cholesterogenesis in liver. it also increases the synthesis of LDL receptors, which help in increased removal
of LDL from blood. Statins exert their main effect by reduction of LDL levels although it also reduces the triglyceride level. Some studies show that it helps in increasing HDL levels.

Along with its lipid lowering property statins also stabilizes the plaque and reduces the thromboembolic phenomenon.

**Nicotinic Acid (Niacin):**

One of the oldest drug used to treat dyslipidemia and is most versatile in that it favorably affects virtually all lipid parameters. Niacin is the best available agent for increasing HDL-C [30%-40%] it also lowers triglycerides by 35%–45% and reduces LDL-C levels by 20% -30%, only lipid lowering drug that reduces LP(a) level significantly (40%).

**Fibric Acid Derivatives (Fenofibrate):**

Mechanism by which fibrates lower lipoproteins levels or raise HDL levels remain unclear, recent studies suggest by interacting with peroxisome proliferator activated receptors (PPAR) they increase LPL synthesis and enhance the clearance of triglycerides-rich lipoproteins, Fibrate mediated increase in HDL-C are due to PPARα stimulation of apoA-I and apo A-II expression, which increase HDL levels.

Most of the fibric acid agents have potential antiatherothrombotic effects including inhibition of coagulation and enhancement of fibrinolysis. These salutary effects also could alter cardiovascular outcomes by mechanisms unrelated to any hypolipidomic activity.

Fibrates usually are the drug of choice for treating severe hypertriglyceridemias (decrease up to 50%), also increase HDL-C, LDL-C levels may be unchanged or increase.