Introduction
Coronary artery disease is an important cause of mortality and morbidity in most industrialized nations and is gaining importance as a major disease in developing countries as well. Dyslipidaemia or hyperlipidaemia has been clearly established as a major risk factor for development of coronary artery disease and progression of atherosclerotic lesion. The level of the lipids and the lipoprotein a ILP (a) in the blood has a close relation to the severity of coronary artery disease (CAD) and predict the response to lipid lowering treatment. Prevalence of CAD, in South-east Asia is going to be the major cause of death by the year 2015 and atherosclerosis is the major cause of under lying CAD. An increase in mortality by 103% in males and 90% in females from 1985 to 2015 is expected. Coronary artery diseases (CAD) is both preventable and modifiable. Between 1965 to 1990 CAD mortality rate is fell by 60% in Japan and Finland and 50% in Australia, Canada, France and U.S.A. This decline was marginally contributed by preventive, modifiable factors & therapeutic advances. Dyslipidaemia is recognised as the major risk factor for CAD allover the world but it differs from other population among the Indian-Asian (Indian Subcontinent) abnormal lipid profile characterised by not only increase in low density lipoprotein cholesterol (LDL-c) but even their inherent atherogenicity and also markedly increase triglyceride (TG) levels and decrease high density lipoprotein cholesterol (HDL-c). For the last 30 yrs, the circulating LDL-c is regarded as the central issue in atherogenesis. By lowering the LDL-c by statin therapy only 35% of coronary events can be prevented. Other atherogenic factors like TG or Lp (a) or low HDL-c may be involved in the progression of atherosclerotic process.

Types of lipids which are clinically important
1. Total cholesterol
2. High Density Lipoprotein cholesterol (HDL-c)
3. Low Density Lipoprotein (LDL)
4. Intermediate Density Lipoprotein (IDL)
5. Triglycerides
6. LP-a.

Dyslipidaemia
Abnormality of plasma lipids and lipoprotein may be of genetic or familial (primary) or arise as a consequence of endocrine, hepatic or renal disease.

Primary:
Primary hyperlipidaemias include familial/polygenic hypercholesterolemia, familial combined hyperlipidaemia and familial hypertriglyceridaemia as well as rare dislipidaemias such as dysbetalipoprotinaemia.

Secondary:
Common causes are -
1. Untreated diabetics
2. Hypothyroidism
3. Nephrotic syndrome and 4. Alcohol abuse

Dyslipidaemia and different diseases
1. Dyslipidaemia and Cardiovascular Disease

Cholesterol: Significant relationship has been demonstrated between hypercholesterolaemia and CAD. The incidence of Myocardial Infarction (MI) is five times higher with CAD, which increases 25 times higher if the patient also have elevated levels of total cholesterol (TC). Both primary and secondary prevention trials have shown reduction of cardiovascular mortality, morbidity and need for revascularization by lipid lowering and statin group of drugs. But the total cholesterol level among the South Asian peoples 75% is usually remains within normal limit i.e. below

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200mg/dl, level of serum cholesterol even lower than 150mg/dl has been reported among Bangladeshi with CAD.

LDL cholesterol (LDL-c): Raised LDL-c has been recognised a primary risk factor by National Cholesterol Education Programme (NCEP). But level of LDL-c not always shows significant differences between with or without CAD. Oxidative modifications of LDL cholesterol (LDL-c) is the crux of atherosclerosis. Population with low LDL-c has a very low incidence of CAD.

A) Effect of LDL cholesterol
Elevated LDL levels appeared to be involved with all stages of atherogenesis. It causes -
- Endothelial dysfunction.
- Plaque formation and growth.
- Plaque instability and disruption.
- Secretion of Various inflammatory mediators and chemoattractants.
- LDL is also potent mitogen for smooth muscle cells.
- Induce apoptosis in macrophages.
- Induce development of metalloproteinases and other enzymes that participate in connective tissue matrix degradation.

B) Effect of HDL cholesterol
Numerous prospective epidemiological studies have demonstrated a continuous inverse relationship between HDL cholesterol level and incidence of CHD. The total cholesterol to HDL cholesterol ratio (4.5:1) is a better predictor of coronary heart disease than the HDL cholesterol level alone. However the national cholesterol education programme has elected to treat the individual lipoprotein levels rather than the ratio. Several studies have demonstrated that low HDL is associated with endothelial dysfunction. It is speculated that HDL-c attenuated the atherogeneity of LDL-c.

C) Effect of Hypertiglyceridaemia
There is growing evidence that hypertriglyceridaemia is a marker of increased risk for CAD; in fact it can serve as a marker for several atherogenic factors. A simple way to interpret the clinical significance of elevated serum TGL concentration is to consider it as a marker for the atherogenic factors. The association between a high serum TGL and other atherogenic factors theoretically would exist at three levels. First a high TG level would be a marker for raised concentration of atherogenic TG rich LDL. Second an elevated serum TG could be a marker for other lipoprotein abnormalities with which they frequently coexist namely abnormally small particles of LDL’s and low serum concentration of HDL.

2. Diabetes & Dyslipidaemia
The risk of coronary heart disease (CHD) death & serious nonfatal CHD events are markedly increased in diabetic patients relative to non-diabetic subjects. Furthermore, clinically manifested CHD has a worst prognosis in a diabetic patient than a non-diabetic subject. The excessive CHD risk in diabetic patients is in part explained by adverse effects of diabetes on serum lipids and other general cardiovascular risk factors but a large part of the excessive risk is evidently caused by enhancing effects of diabetic state itself on atherogenesis and / or thrombogenesis.

Adverse effects of diabetes on S. lipids are more pronounced in NIDDM than IDDM. Dyslipidaemia also causes insulin resistance. Three major conditions are important in the dyslipidaemia that characterizes insulin resistance:
- Increase TG level. • Decreased HDL cholesterol level.
- Compositional changes in LDL cholesterol.

Insulin resistance and hyperinsulinaemia enhance alteration in the vasculature leading to atherosclerosis. In addition hyperlipidaemia,
hyperglycaemia, hypertension, smoking and homocystine, damage the endothelium, leading to an imbalance in endothelial production of vasoconstrictors versus vasodilators.

Clinical trial in-patients with the dyslipidaemia characteristic of insulin resistance illustrate the potential benefit of successful treatment of dyslipidamia. Both weight loss and exercise can improve the insulin resistance and associated dyslipidaemia. In patients with type II DM certain anti-diabetic therapies can improve the lipid profile by improving insulin resistance.

3. Dyslipidaemia and Hypertension
High plasma cholesterol levels are frequently seen in patients with systemic hypertension. Recent experimental and clinical studies have demonstrated strong correlation between high plasma cholesterol levels and impaired endothelium dependent vascular relaxation. The hypercholesterolaemia contribute to increase the vascular reactivity and systemic hypertension. Hypertension may interact with risk factors in the development of atherosclerosis in coronary and cerebral blood vessels.

4. Dyslipidaemia and Peripheral Vascular Diseases
Deposition of lipid materials in the blood vessels like carotid artery and other peripheral vasculature causes formation of atherosclerotic plaque, which interferes the blood circulation in the respective portion of the body. As a result there may be ischaemic cerebral stroke, TIA and other peripheral vesicular diseases.

5. Dyslipidaemia and cerebrovascular diseases
Dyslipidaemia has become and important risk factor for stroke. Recent CARE trial showed a significantly lower incidence of stroke in paravastatin treated group. So statin therapy is now considered as a mode of primary prevention for stroke.

Treatment of dyslipidaemia
Reduction of cholesterol is just one part of a program to reduce cardiovascular disease. Other measures including smoking cessation, hypertension control should be addressed properly. If the decision to treat a patient with an lipid lowering drug is made, the clinician must select an appropriate agent based on the Safety, Efficacy, Cost, Effects on lipid level, Set a goal for treatment

As with all therapies for chronic conditions the therapeutic goal is best approached slowly and steadily, watching carefully for side effects and encouraging continued compliance with non pharmacologic measures but at first, we have to stratify the patients into different risk group.

1. Primary prevention
Primary prevention is for those groups of persons who don't have clinically manifest coronary heart disease but might have catastrophic cardiac event in future. They could be classified into three groups -

a) High Risk group: Persons without clinical coronary heart disease whose risk for major coronary events equal that of patients with established coronary heart disease can be said to have coronary heart disease risk equivalent. This group of people is called high-risk group. For these patients, aggressive risk reduction therapy should be introduced. This group includes (1) Non-coronary forms of atherosclerotic disease, (2) Type 2 diabetes & (3) Multiple risk factor patients.

b) Intermediate risk group: Those with two or more risk factor are considered to be at interim-diate risk of coronary artery disease.

c) Low risk group: Patient having less than 2 risk factors compromises the low risk group

Table -1: Primary Prevention
2. Secondary prevention
Secondary prevention is for those who already have clinically manifest coronary heart disease. The group has the same treatment guideline as for the high-risk group of primary prevention including treatment for then underlying cause.

Treatment plan
Most treatment algorithms recommend diet therapy as the initial step for all patients with high cholesterol. The three recommended regimens are as follows -

<table>
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<tr>
<th>Step I Diet</th>
<th>Step II Diet</th>
<th>Mediterranean Diet</th>
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<tbody>
<tr>
<td>10% of Calories</td>
<td>7% of Calories</td>
<td>6% of Calories</td>
</tr>
<tr>
<td>20% of Calories</td>
<td>10% of Calories</td>
<td>9% of Calories</td>
</tr>
<tr>
<td>40% of Calories</td>
<td>20% of Calories</td>
<td>15% of Calories</td>
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2. Drug Therapy
A. Statin group: These agents work by inhibiting the rate limiting enzyme HMG-CoA reductase inhibitor in the formation of cholesterol. Recent CARE & LIPID trial have shown significant reduction in stroke, MI and mortality. These agents are an exitng advance with relatively few side-effects and are now the drugs of first choice. The benefciial effects of statin on clinical events may involve non lipid mechanism that modify endothelial function, inflammatory response, plaque stability and thrombus formation. It also inhibits platelet aggregation and maintains a favourable balance between prothrombotic and fibrinolytic mechanism.

B. Fibrate group
They act by activating plasma lipoprotein lipase & thus removing cholesterol from blood. These agent are preferable, when there are high blood triglycerides. Fibrate changes the LDLc structural size (increases the LDLc particles size)

C. Nicotinic Acid: It reduces synthesis and secretion of VLDL particles from liver, with secondary reduction of LDL and increases in HDL level. Nicotinic acid also increases the LDLc particles size, and prevents easy filtration of ox LDL in to arterial wall.

D. Bile acid binding resin (cholestyramine): These resins work by binding bile acid in the intestine, resulting reduction in enterohepatic circulation. This causes live to increase production of bile acid using hepatic cholesterol. So plasma cholesterol level decreases.

E. Probucol: This probably causes increased excretion of cholesterol in the bile and also reduces amount of oxidized LDL thus preventing progression of atheroma.

Table-2: Selection of Lipid modifying drug

<table>
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<th>PRIMARY PREVENTION</th>
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<tr>
<td>- Postmenopausal women: Statin, Nicin, resin.</td>
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<tr>
<td>- Men (55-75 yrs): Statin, Nicin, resin.</td>
</tr>
<tr>
<td>- Men: Statin, Nicin, Combination.</td>
</tr>
<tr>
<td>- Women: Statin, Nicin, Combination.</td>
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Benefit of lipid lowering therapy
Several secondary prevention trial have shown that LDL lowering therapy can reduce mortality after myocardial infarction. This was first shown in the scandinavian simvastatin survival study (4S) in high-risk group. The cholesterol and recurrent event. (CARE) and the long-term intervention with par- avastation in Ischaemic heart disease (LIPID) study, further supported the benefit in patients with average cholesterol group. Primary prevention trial have also shown significant benefit both in a high risk group in west of Scotland coronary prevention study group (WOSCOPS) and in a low risk population in AFCAPS trial. More than 80% individual in AFCAPS study, who did benefit would not have qualified for these therapy under existing guideline. The impressive result of the AFCAPS study raises the important question of whether the NCEP treatment guideline should be broadened.
New paradigm is based on the following observations
1. 85% of myocardial infarctions develop at sites of relatively less severely occluded, lipid-rich plaque, which rupture, followed by thrombosis and spasm.
2. Coronary atherosclerosis is diffuse and subject to plaque rupture throughout the length of the epicardial coronary artery.
4. The diagnostic accuracy of coronary arteriography for diffuse coronary atherosclerosis is poor (as low as 10%) compared with intracoronary ultrasound.
5. Vigorous cholesterol lowering markedly decreases the rate of cardiac events and mortality more than invasive procedures that do not alter long-term survival or cardiovascular events.
6. New techniques for interpreting PET perfusion images and absolute flow measurements reflect the presence of diffuse coronary atherosclerosis, endothelial dysfunction, and their changes with vigorous cholesterol lowering therapy.

Conclusion
The available cholesterol lowering therapies prescribing practice have not resulted in widespread use of these important preventive therapies. So education~l message about could be more beneficial if they were better utilized. Our current guidelines and guideline and benefits of cholesterol lowering therapy should be incorporated in our national health program to expand patient-physician activities in coronary artery disease prevention.

Reference
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