September 2009 *Volume 3 Issue 2-3*

Trade Science Inc.

Research & Reviews in

BioSciences

Regular Paper

RRBS, 3(2-3), 2009 [127-132]

Hyperlipidemia - Prevalence and prediction of risk for coronary heart disease in a South Indian Population

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Received: 17th June, 2009 ; Accepted: 27th June, 2009

ABSTRACT

Hyperlipidemia is one of the major risk factor for coronary heart disease (CHD); a major leading cause of mortality and thus the study of prevalence of hyperlipidemia and the risk prediction for coronary heart disease were important and timely. A prospective study was carried out in 397 subjects who registered for Master Health Check-Up program in a tertiary care teaching hospital. There were 245 males (mean age 49.59±12.81) and 152 females (mean age 49.13 ± 10.60). The incidence of hyperlipidemia was determined as per NCEP ATP III guidelines. The prevalence of abnormal serum lipid levels was more prominent in the age group of 40-59 years in both the sexes. High levels of triglycerides were identified in 41.5%, LDL- cholesterol levels in 7.45%, where as 32.9% had high levels and total cholesterol levels in 10.57%. HDL- cholesterol levels were found to be low in 34.35%. The 10-year risk prediction for coronary artery disease was done using Coronary risk prediction algorithm using Total cholesterol and LDL-C levels. Based on LDL levels, 59% of the study population had <10% risk, 28% were in the 10-20% risk category and 13% had >20% risk. Based on total cholesterol levels, 57 % had <10% risk.31 % were under 10-20% risk category and 12% had >20% risk. The study concluded that early detection and treatment of hyperlipidemia may reduce the risk of development of CHD.

KEYWORDS

Hyperlipidemia;
Cholesterol;
Coronary heart disease;
Triglycerides;
Lipids.

INTRODUCTION

Hyperlipidemia is an elevation in atherogenic lipoprotein particles including cholesterol, cholesterol esters and triglycerides. It also includes a low level of HDL cholesterol.[1] Cholesterol is a fat like substance (lipid) that is present in cell membranes and is a precursor of bile acids and steroid hormones. Cholesterol travels in the blood in distinct particles containing both lipids and proteins (lipoproteins). Three major classes of lipoproteins are found in the serum of a fasting individual: Low density lipoproteins (LDL), High-density lipoproteins (HDL), and very low-density lipoproteins (VLDL). Another lipoprotein class, Intermediate density lipoprotein (IDL) resides between VLDL and LDL. In clinical practice, IDL is included in the LDL measurement. LDL cholesterol makes up 60-70 percent of the total serum cholesterol. LDL is the major athero-

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genic lipoprotein and has long been identified by National Cholesterol Education programme (NCEP) as the primary target of cholesterol lowering therapy. HDL cholesterol normally makes up 20-30 percent of the total serum cholesterol and the levels are inversely correlated with risk for CHD. The VLDL is triglyceride-rich lipoprotein, but contain10–15 percent of the total serum cholesterol. VLDL is produced by the liver and is the precursor of LDL; some forms of VLDL, particularly VLDL remnants, appear to promote atherosclerosis, similar to LDL. VLDL remnants consist of partially degraded VLDL and are relatively enriched in cholesterol ester. Fourth class of lipoproteins, chylomicrons, is also triglyceride-rich lipoproteins; they are formed in the intestine from dietary fat and appear in the blood after a fat-containing meal.[2]

Coronary artery disease (CHD) tends to occur earlier in life in Indians and is believed to be more severe and extensive and to follow a malignant course.[3] Projections based on the Global Burden of Disease study estimate that by the year 2020, the burden of atherothrombotic cardiovascular disease in India will surpass that in any other region in the world.[4] Over 9 million deaths in 1990 in the developing countries are due to CHD. Of this India contributed to 2.4 million deaths, which is approximately 25% of the deaths reported in India. Premature deaths seems to be more common in India as 52% of the CHD deaths occurred below the age of 70 years as compared to 22%in developed Countries. By the year 2015, India will have the largest CHD burden in the world.[5] Asian Indians have three times higher risk of developing CHD compared to Chinese and are twenty times more likely to die due to CHD compared to native blacks or white South Africans.[6]

Lipid Risk Factors and CHD

Studies across different populations reveal that those with higher cholesterol levels have more atherosclerosis and CHD than do those having lower levels. The Framingham Heart Study[7], the Multiple Risk Factor Intervention Trial (MRFIT)[8], and the Lipid Research Clinics (LRC) trial[9] found a direct relationship between the levels of LDL cholesterol (or total cholesterol) and the rate of new-onset CHD in men and women who were initially free of CHD. The same relation holds for recurrent coronary events in people with established CHD.[10]

The relation of elevated LDL cholesterol to the development of CHD must be viewed as a multi-step process beginning relatively early in life**.** The first stage of atherogenesis is the fatty streak, which consists largely of cholesterol filled macrophages; and most of the cholesterol in fatty streaks is derived from LDL cholesterol. The second stage consists of fibrous plaques in which a layer of scar tissue overlies a lipid rich core. Other risk factors contribute to plaque growth at this phase. The third stage is represented by the development of unstable plaques that are prone to rupture and formation of luminal thrombosis. Plaque rupture (or erosion) is responsible for most acute coronary syndromes (myocardial infarction, unstable angina, and coronary death).[11]

Non-Lipid Risk Factors and CHD

A number of non lipid risk factors are associated with increased CHD risk and must be considered in preventive efforts. They are hypertension, cigarette smoking, thrombogenic/ haemostatic state, diabetes, obesity, physical inactivity, age, male sex and family history of premature CHD. Some of these factors are modifiable and are appropriate targets for intervention efforts in themselves.[12] Though several fixed risk factors cannot be modified, abnormality in lipid levels is modifiable risk factor; early monitoring and treating lipid abnormalities reduces the risk of CHD.[13]

METHODOLOGY

A prospective study was carried out in a1650 bedded multispecialty tertiary care teaching hospital, for a period of eight months in a population of 397 individuals (245 males and 152 females) who registered for Master Health Check up after obtaining institutional ethical committee approval and informed consent form the subjects. Details such as age, gender, blood pressure values (classified as per JNC VII guidelines)[14], fasting, random and post prandial blood sugar levels (as per American Diabetes Association guidelines)[15], fasting lipid profile values (classified as per the NCEP ATP III guidelines)[2], family history of CAD, smoking history (persons who smoked regularly during the previous 12 months were classified as smokers) of the study population were obtained from the patient case sheets and documented in the patient data

collection proforma designed for the study. The prevalence of hyperlipidemia (high LDL cholesterol, triglycerides and total cholesterol levels and low HDL cholesterol levels) was determined based on cut off values of serum lipid profile stated in the National Cholesterol Education Program: Adult treatment Panel III guidelines[2].

Risk Prediction

The risk for the development of CHD over a period of 10 years was calculated, according to the Framingham Heart Study Coronary risk prediction Scale[14] for men and women. The score sheet included total cholesterol and LDL cholesterol levels of the study population as lipid risk factors and age, hypertension (systolic and diastolic blood pressure values) diabetes and smoking as the non-lipid risk factors. A step wise calculation of the number of points for each risk factor was done and the total risk score was calculated by summing the points for each risk factor. The 10-year risk for myocardial infarction and coronary death was estimated from total points and the patients were categorized as those who have a 10-year risk of >20 percentage and those patients who have a 10-year risk of 10-20 percent. The primary endpoint for 10-year risk assessment was "hard CHD" (myocardial infarction+ CHD death).

RESULTS

The study included 245 males (mean age 49.45 ±12.81) and 152 females (mean age 49.13 ± 10.60). There were 77 males (31.4%) and 29 females (19.1%) in the age range of < 40 years, 126 males (51.4%) and 103 females (67.8%) in the age range of 40-59 years and 42 males (17.1%) and 20 females (13.2%) in the age range of = 60 years.

The systolic and diastolic blood pressure of the study group was categorized as per JNC VII guidelines. 57(23.26%) males and 55(36.18%) females had a normal systolic BP, 54(22.04%) males and 25(10.44%) females had prehypertensive systolic BP, 88(35.91%) males and 39 (25.65%) females were diagnosed to have a systolic BP of 140-159mmHg and were under Stage I hypertension. 46(18.78%) males and 33(21.71%) females were observed to be under Stage II hypertension as they had a systolic BP of =160 mm Hg. The diastolic BP was found to be normal (<80 mmHg) in 61(25%) males and 63(54.6%) females. 36(14.7%) males and 20(1.9%) females had prehypetension (diastolic BP of 80-89 mmHg), 71(29%) males and 36(23.7%) females had Stage I hypertension (diastolic BP of 90-99 mmHg) and 77(31.42%) males and 30(19.73%) females had Stage II hypertension (diastolic BP of =100 mmHg).

The fasting and post prandial blood sugar levels of the patients are given in TABLE 1. As per ADA guidelines, patients with fasting blood sugar =126mg/dl and post prandial blood sugar =200mg/dl were considered to be diabetic. Accordingly 137 males and 84 females were diabetic among the study population, of which many of them were in the age range of 40-59 years. There were 88(35.9%) smokers in the study group and all were males (28 in the age group of <40 years, 42 in the age range of 40-59 years and 12 in the age range of = 60 years).

TABLE 1 : Age, gender vs fasting and post prandial blood sugar levels

Age in Years	Fasting BloodSugar(mg/dl)				Post PrandialBlood Sugar(mg/dl)			
	Males n=245		Females n=152		Males n=245		Females n=152	
	No n (%)	Yes* n (%)	No n (%)	Yes* n (%)	No n (%)	Yes* n (%)	No n (%)	Yes* n (%)
< 40	69(28.2)	8(3.2)	27(17.7)	2(1.31)	61(24.9)	17(6.9)	18(11.8)	10(6.6)
40-59	96(39.2)	30(12.2)	87(57.2)	16(10.5)	71(28.9)	54(22.0)	58(38.6)	44(28.9)
≥ 60	35(14.3)	7(2.8)	18(11.8)	2(1.3)	21(8.7)	21(8.6)	10(6.6)	10(6.6)

***Patients with Fasting Blood Sugar ≥ 126 mg/dl and Post prandial blood sugar ≥ 200mg/dl were considered to be diabetic as per ADA guidelines.**

The prevalence of abnormal serum lipid levels was more prominent in the age group of 40-59 years in both the sexes. A high triglyceride level (200-499mg/dl) was identified in 50 (20.4%) males and 32(21.1%) females and a very high level (> 500mg/dl) of triglycerides in 3 (1.2%) males (TABLE 2). HDL- Cholesterol levels

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were found to be low (<40mg/dl) in 52(21.2%) males and 20(13.15) females (TABLE 3). LDL- Cholesterol levels were found to be very high (>190mg/dl) in 7 (2.85%) males and 7(4.60%) females, where as 47(19.1%) males and 21(13.8%) females had a high LDL- Cholesterol (160-189 mg/dl) and 89 (36.8%) males and 57(37.5%) females had a borderline high cholesterol levels (130-159 mg/dl) (TABLE 4). Total Cholesterol levels were high(= 240 mg/dl) in 30(12.2%) males and 20(13.15%) females and borderline high (200-239mg/dl) in 92(37.5%) males and 50(32.9%) females (TABLE 5).

TABLE 2 : Age & gender vs triglycerides

Triglycerides (mg/dl)	Males (n =245)				Females (n=152)			
	Age in Years			Total n (%)	Age in Years			Total n (%)
	<40 (n=77)	40-59 (n=126)	≥ 60 (n=42)		<40 (n=29)	40-59 (n=103)	≥ 60 (n=20)	
Normal (<150)	34	36	15	85 (34.7)	13	68	14	95(62.5)
Borderline high (150-199)	31	61	15	107(43.7)	6	16	3	25(16.4)
High (200-499)	12	26	12	50 (20.4)	10	19	3	32(21.1)
Very high (≥500)	0	3	0	3 (1.2)	0	0	0	0

TABLE 3 : Age & gender vs HDL-cholesterol

HDL-C (mg/dl)	Males (n =245)				Females (n=152)			
	Age in Years			Total n (%)	Age in Years			Total n (%)
	<40 (n=77)	40-60 (n=126)	> 60 (n=42)		<40 (n=29)	40-60 (n=103)	> 60 (n=20)	
Low (<40)	14	32	6	52(21.2)	6	11	3	20(13.2)
Normal (40-59)	56	92	31	179(73.1)	9	84	14	107(70.4)
High (≥60)	7	2	5	14(5.71)	14	8	3	25(16.4)

TABLE 4 : Age & gender vs LDL-cholesterol

LDL-C (mg/dl)	Males (n =245)				Females (n=152)			
	Age in Years			Total n (%)	Age in Years			Total n (%)
	<40 (n=77)	40-59 (n=126)	≥ 60 (n=42)		<40 (n=29)	40-59 (n=103)	≥ 60 (n=20)	
Optimal (<100)	9	4	3	16(6.53)	0	2	2	4(2.63)
Near optimal (100-129)	21	35	30	86(35.1)	17	44	2	63(41.4)
Borderline high (130-159)	33	51	5	89(36.3)	5	45	7	57(37.5)
High (160-189)	11	33	3	47(19.1)	4	10	7	21(13.81)
Very High (≥190)	3	3	1	7(2.85)	3	2	2	7(4.60)

TABLE 5 : Age & gender vs total cholesterol (TC)

Total Cholesterol mg/dl	Males (n =245)				Females (n=152)			
	Age in Years			Total n (%)	Age in Years			Total n (%)
	<40 (n=77)	40-59 (n=126)	≥ 60 (n=42)		<40 (n=29)	40-59 (n=103)	≥ 60 (n=20)	
Desirable (<200)	42	69	12	123(50.2)	11	66	5	82(54)
Borderline High (200-239)	18	53	21	92(37.5)	12	28	10	50(32.9)
High (≥240)	17	4	9	30(12.2)	6	9	5	20(13.15)

The 10-year risk prediction for coronary artery disease was done using Coronary risk prediction algorithm based on total cholesterol and LDL-C levels. The scoring based on LDL- cholesterol levels have shown

that majority of the study population 232 (128 males and 104 females) had <10% risk, 110 (75 males and 35 females) were in the 10-20% risk category and 55 patients (42 males and 13 females) had >20% risk. The scoring based on total cholesterol levels have shown that 225 (123 males and 102 females) had <10% risk.125 (87 males and 38 females) were under 10-20% risk category and 47(37 males and 10 females) had >20% risk (TABLE 6).

TABLE 6 : Risk percentage using total cholesterol and LDL-cholesterol levels

Risk percentage as per coronary risk prediction scale	LDL-cholesterol levels				Total cholesterol levels			
	Males		Females		Males		Females	
	n= 245	%	n= 152	%	n=245	%	n=152	%
<10%	128	52.24	104	68.4	123	50.20	102	67.11
10-20%	75	30.61	35	23.02	87	35.51	38	15.51
>20%	42	17.14	13	8.55	37	15.10	10	4.08

Since the South Asians have 3 times the higher risk of developing CHD when compared to western population, the percentage risk can be tripled in the study population. Based on this, subjects who have <10% risk were considered to have <30% risk, those with 10-20% risk has 30-50% risk and subjects with > 20 % risk has >50% risk.

DISCUSSION

CHD is now becoming the major leading cause of mortality in India, and thus the study of hypercholesterolemia and other risk factors for CHD is important and timely.[17] This study reveals the prevalence of hyperlipidemia, a well-known factor for cardiovascular disease. Male preponderance was found to be higher in the study and also an increased prevalence of serum lipids was more prominent in the age group of 40-59 years in both the sexes.

In comparison with western population, a relatively lower level of cholesterol appears to predispose Indians to CHD. A Chennai based hospital study has shown that around 75% of patients with MI had TC levels < 200mg/dL indicating that the threshold for the TC levels above which it possess a risk for CHD is low in Indians.[18] In this study we have observed 123(50.20%) of male patients and 82(54%) of female patients were in the desired range, yet they might be at risk for CHD.

A positive relationship exists between serum LDL-cholesterol levels and the development of first or subsequent attacks of CHD, the higher the levels greater the risk. Data from Framingham study suggest that the serum triglyceride level is also an independent risk factor CHD. Similarly low HDL-C levels are strong predictor of occurrence and reoccurrence of MI and stroke and are also associated with premature and severe CHD.[19]

Diets with high fat and caloric intake and lack of physical activity would be the major culprits of dyslipidemia in our population. References have shown that our diets are rich in saturated fats. Besides it also involves over cooking of food which results in destruction of nutrients like folate, deep frying and refrying in the same oil leading to trans fatty acid formation which probably contributes to increased levels of lipids in our population.[20]

Hypertension, diabetes and smoking are the other risk factors of CHD and the coexistence of these with hyperlipidemia adds on to the percentage of risk. Subjects with hypertension possess two fold higher risk of developing CHD.[21] Diabetics have two to three times higher risk of developing CHD. More than 80% of all deaths in diabetic patients are due to CHD. Currently India has approximately 20 million diabetics, which is expected to increase to 57.2 million by the year 2025.[22]

Apart from the established lipid risk factors, intensive research is being carried out to identify new atherogenic risk factors that will enhance predictive power in individuals. These newer factors can be called as emerging lipid risk factors. These can be divided in to: Triglycerides, Lipoprotein remnants, Lipoprotein (a), Small LDL particles, HDL subspecies, Apolipoproteins and Total cholesterol/HDL- cholesterol ratio.[23]

Abnormality in lipid levels is one of the major risk factor for CHD. Since it is a modifiable risk factor, monitoring and treating lipid abnormalities in normal adults will have a bearing on reducing the rates of CHD.

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CONCLUSION

The study reveals that the incidence of hyperlipidemia was higher in the age group of 40-59 years in both the sexes. Though majority had <30% risk for CHD based on both LDL and total cholesterol values, presence of other factors like hypertension, diabetes and smoking may increase the risk by three fold. Therefore primary prevention with health measures focusing on life-style modification, diet and management of all the risk factors have to be implemented in order to prevent the epidemic of CHD which can be effectively performed by a pharmacist.

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