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RESEARCH ARTICLE

Apo lipoprotein B, Total Cholesterol, HDL-C, Non HDL-C, LDL-C and Triglycerides as Risk factors of Atherosclerotic Vascular disease

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Objective: To find out the relative significance of serum levels of Apolipoprotein B versus Total Cholesterol, HDL cholesterol, Non HDL cholesterol, LDL cholesterol and Triglycerides in atherosclerotic vascular disease as risk factors

Methods:

Design: Observational case control study

Setting: Medical College Chest Hospital, ThrissurKerala

We measured fasting serum Apolipoprotein B and conventional fasting lipid profile in 59 clinically normal subjects (mean age 38 years) and 39 patients with atherosclerotic vascular disease admitted to Medical College Chest Hospital (mean age 59 years) .Patients on lipid lowering drugs were excluded in the study.The currently used ATP III guidelines [9] was used to select the cut off values of Total cholesterol (TC->200 mg %), HDL (<40 mg %), LDL-C (>100mg %) Non HDL (>130 mg %) and TG (>150 mg %) and cut off value for apo B (105 mg%) adopted from a previous study done by of Sakurabayashi, I, etal12which is close to the third quartile of our study (104mg%).Chi square test was used to test the significance of association of different study variables with the outcome (atherosclerotic vascular disease). Odds ratio was used to find out the degree of association of each parameter with the disease process.

Result: In the present study serum Apolipoprotein B levels ≥105mg% were strongly associated with atherosclerotic vascular accidents ($P < 0.001$).

Conclusion: Among various fasting lipid parameters – Total cholesterol, HDL-C, Non HDL-C, LDL-C, Triglycerides and Apolipoprotein B, ≥105mg% of Apolipoprotein B ($P < 0.001$) is found to be most significantly associated with atherosclerotic vascular disease. Hence measurement of Apolipoprotein B levels is highly recommendable in the risk assessment of atherosclerotic vascular disease for the early recognition of the problem and the institution of appropriate preventive treatment strategy.

INTRODUCTION

Atherosclerosis of the vascular system is the basis of wide spectrum of clinical outcomes like coronary artery disease, cerebro vascular disease and peripheral vascular occlusive disease.The epidemiology of coronary artery disease will give us an idea about the gravity of the problem in our country. Indians world wide has the highest rates of coronary artery disease (CAD) with those settled in the United states have a four fold higher prevalence[1,2]. The prevalence of CAD in urban India (10%) is double than that of rural India (5%) and about 4 fold

higher than in the US(2.5%)[3] The prevalence rates of CAD appear to be higher in South India [4] and it is highest in Kerala with Thiruvananthapuram having a prevalence of 7 % in rural and 13 % in urban areas[5]

The escalating epidemic of coronary artery disease in India is due to the combination of genetic predisposition and life style changes.[6,7.] Atherosclerotic vascular disease is the major cause of morbidity and mortality from middle age onwards. [8]

Dyslipidemia is considered to be the forerunner of atherosclerotic vascular disease. Adult Treatment Panel (ATP) III guidelines[9] are widely practised to identify the dyslipidemia. Current ATP III guidelines recommend lipid screening in all adults > 20 years. The screen should include a fasting lipid profile (total cholesterol, LDL cholesterol, HDL cholesterol and Triglycerides) repeated every 5 years.But this approach cannot find out all individuals at the risk of developing atherosclerotic vascular disease.

Within a population, as the levels of cholesterol rise, the risk of coronary artery disease also increases. But only a small portion of the population has very high levels of cholesterol. A major finding of Framingham study[10] is that most cases of premature vascular disease occurred in individuals with total and LDL cholesterol levels that were indistinguishable from those who did not develop premature disease. But at the same time, elevated LDL –C is the type of dyslipidemia most closely associated with coronary artery disease.[9] These two contradictory observations point towards the necessity of concentrating on the non lipid part of the lipoproteins, namely apoproteins. Since LDL – C is considered to be more linked to the atherosclerotic disease, it is better to study the apoprotein of LDL-C i.e., apolipoproteinB. Oxidatively modified apo B initiate the atherosclerotic process. Evidence suggest that the unstable atherosclerotic lesions which are susceptible to rupture or erosion have thin rupture prone fibrous caps, large lipid cores and a plenty of lipid laden macrophages.[7]

In the presence of excess of small dense sub fraction of LDL-C, total cholesterol level may not be raised, but the individual may have the disease process started. In short, atherosclerosis is initiated by apo lipoprotein B and the lesion progress by the deposition of lipids. Hence the role of lipid assay in the risk assessment of atherosclerosis cannot be neglected totally.

It is better to measure a substance that is directly involved in the pathogenic process, rather than a surrogate parameter like cholesterol. In this context, this study attempts to find out the role of apo B against the routinely tested lipid parameters - Total cholesterol, HDL-C, LDL-C, Non HDL-C and Triglycerides.

MATERIAL AND METHODS

We performed an observational case control study at Medical College Chest Hospital, Thrissur.59 clinically normal and 39 cases with atherosclerotic vascular disease were included in the study. It was undertaken over 3 months period (March – May 2008)

Inclusion criteria:

Cases: Patients of any age with atherosclerotic vascular disease admitted to Medical College Chest Hospital (coronary artery disease, cerebro vascular disease or peripheral vascular disease)

Controls: Clinically normal persons with normal ECG & ECHO findings

Exclusion criteria:

Cases: Patients on lipid lowering drugs

Controls: Those with diabetes and hypertension and those on lipid lowering drugs or any other drugs.

Approval was obtained from institutional ethics committee.

Measurements:

Specimen: Fasting blood sample

Assay techniques used: Given in table –I

Data analysis:

Results were expressed as mean ± 2SD. Frequency of each serum lipid variable among controls and cases were presented. Chi square test was the test of significance used to study the association of different study variables with the outcome (atherosclerotic vascular disease). The currently used ATP III guidelines [9] was used to select the cut off values of Total cholesterol (TC->200 mg %), HDL-C (<40 mg %), LDL-C (>100mg %) Non HDL-C (>130 mg %) and TG (>150 mg %) and cut off value for apo B (105mg%) adopted from a previous study done by of Sakurabayashi,I,et al[12] which is close to the third quartile of our study (104mg%). Odds ratio was used to find out the degree of association of each parameter with the disease process.

RESULTS

Figures 1 and table 4 shows frequency of controls and cases falling within the optimum and above optimum levels of serum Total Cholesterol (TC) ,High density lipoprotein cholesterol (HDL-C) ,Non HDL –C , Low density lipoprotein (LDL-C), Triglyceride and apolipoprotein B(apo B) . Different quartile values of apo B was shown in table – 2. Odds ratio for the association of different variables with atherosclerotic vascular accident are presented in table 3.

Table -1 Assay technique

Instrument	Assay technique	Method	Parameter
Semiautoanalyzer (Microlab 300 – MERCK)	Photoelectric colourimetry	Immunoturbidimetry	Apolipoprotein B
		Enzymatic (Cholesterol esterase, Cholesterol oxidase and Peroxidase)	Total cholesterol (TC)
		Phosphotungstic precipitation method	HDL
		Enzymatic (GPO- Lipase ,glycerol kinase &Peroxidase	Triglyceride(TG)
		Indirect - Calculated value using Friedwald equation [11]	LDL
		= TC – HDL –C	Non HDL

Table -2 Quartile values of Serum Apolipoprotein B

Quartile values of Serum Apolipoprotein B (mg%)			
4	3	2	1
127	104	97	86

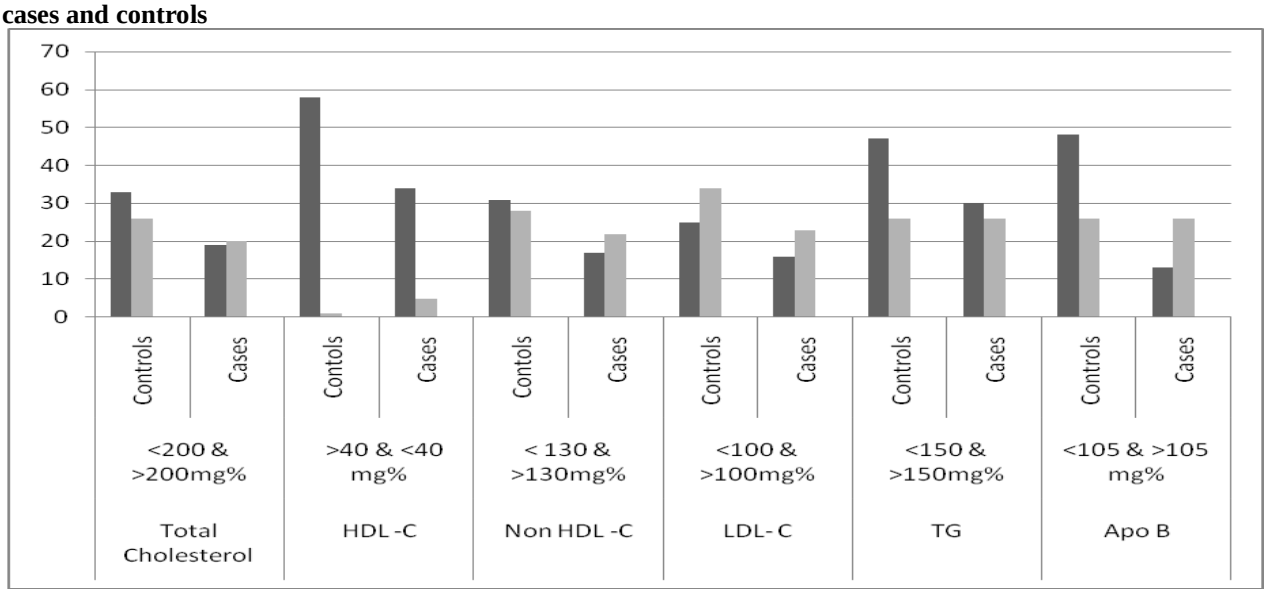
Table -3 Comparison of Serum Lipid variables

P value	X^2 Value	Odds Ratio & CI	Controls(n=59)Mean (Mean age – 38 years) Mean □ 2SD	Cases(n=39) (Mean age-59 years) Mean □ 2SD	Variable
0484	0.491	1.34 0.59-3.0	195 □ 72	203 □ 116	Total Cholesterol (mg%)
0.025	5.057	8.53 0.96-76.01	63 □ 26	56 □ 32	HDL-C (mg%)
0.386	0.753	1.4 0.64-3.23	130 □ 80	146 □ 102	Non HDL-C (mg%)
0.895	0.018	1.057 0.47-2.4	108 □ 78	121 □ 96	LDL –C (mg%)
0.746	0.105	1.2 0.44-3.23	107 □ 100	129 □ 106	TG (mg%)
0.001	23.041	8.7 3.429-22.2	95 □ 28	116 □ 46	Apo lipoprotein B (mg%)

Table 4. Total Cholesterol, HDL-C,Non HDL –C,LDL-C, Triglycerides and Apolipoprotein B levels in cases and controls

Apo B (mg%)			Triglyceride (mg%)			LDL- C (mg%)			Non HDL –C (mg%)			HDL –C (mg%)			Total Cholesterol(mg%)		
Cases	Controls		Cases	Controls		Cases	Controls		Cases	Controls		Cases	Controls		Cases	Controls	
13	48	<105	30	47	<150	16	25	<100	17	31	< 130	34	58	>40	19	33	<200
26	11	>105	9	12	>150	23	34	>100	22	28	>130	5	1	<40	20	26	>200

Figure -1 Total Cholesterol , HDL-C, Non HDL –C, LDL-C, Triglycerides and Apolipoprotein B levels in cases and controls



DISCUSSION

In the present study the significant variable associated with atherosclerotic vascular disease was found to be high values of apolipoprotein B (≥105 mg %) (p-0.001).The close association of apo B with atherosclerotic vascular disease is supported by Quebec Cardiovascular study which showed that apolipoprotein B was associated with Coronary artery disease, independent of low density lipoprotein (LDL) [13] .

Another study by SamanMiremadi et al[14] suggests that use of single index namely serum apo B is as efficient for categorization and follow up of patients with dyslipidemia as the currently used lipid profile. The Caerphilly study[15] corroborated the lack of a lipid independent association between apolipoprotein B levels and coronory artery disease. That means a mere elevation of apo B cannot produce atherosclerosis even though the modified apo B could initiate the plaque formation. It is because the pathophysiolgy of atherosclerosis involves initiation by oxidatively modified residues of apo B and progression of the lesion requires subintimal deposition of lipids. Constitutively synthesized apo B is degraded by the proteasome as and when synthesized, if there are no enough lipids available to form lipoprotein complexes.[16] It is suggested that Apo B should not be the only parameter measured for the risk evaluation of atherosclerotic vascular disease in an individual. It should be combined with TC, HDL and triglycerides, in the initial screening and for the follow up Apo B is a better than other lipid variables.[14] Apolipoprotein B being a protein unlike lipid variables, the assay of apo B can be performed on non fasting blood

samples and this is definitely an added advantage over the routine lipid profile which requires a fasting blood sample[17].

In this study serum Total Cholesterol, HDL –C, Non HDL, LDL and TG are found to be insignificantly associated with atherosclerotic vascular accidents. Several studies have now shown that apo B and apo A1, remain predictive of the outcome in patients on lipid lowering therapy, where as lipids in the lipoproteins (TC &TG) do not.[18.19.] The risk attributed to TC and LDL-C is not linear and increases sharply over the higher ranges.Reduction of serum cholesterol is important in reducing the risk of ischemic heart disease but cholesterol and other lipids are poor screening tests for risk evaluation of atherosclerotic vascular disease.[20] The reason for this discrepancy is that the screening potential of a factor depends not only on the power of its relationship with disease but also on it's variation in magnitude across individuals in a community. Moreover multi factorial nature of the disease creates complication in the selection of a single screening tool.

The protective effect offered by HDL-C is attributable to unique Apo lipoprotein of HDL-C, Apolipoprotein A1 .Future research required to find out the role of Apo A1 along with Apo B in the risk assessment of atherosclerotic vascular disease.

CONCLUSION

Plasma/serum Apolipoprotein B is a better marker of atherosclerotic vascular disease than total cholesterol, HDL-C, NonHDL-C, LDL-C and Triglycerides. Other advantage of ApolipoproteinB assay is that it can be performed on nonfasting blood sample also.

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