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Clinical Utility of Different Lipid Measures in Acute Coronary Syndrome in Young: An Observational Study in North Kerala

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Abstract

Background

Lipoprotein (a) is an emerging independent and compounding risk factor for the development of CAD (coronary artery disease. The present study was done to assess the fasting lipid profile, fasting Apo B-ApoA1 ratio and Lipoprotein (a) levels in patients with acute coronary and to evaluate whether these parameters predicts the risk of developing acute coronary syndrome in young subjects.

Patients and Methods

The present observational study was carried out in patients with first episode acute coronary syndrome, presented in Calicut Medical College during the study period.All patients were evaluated with baseline investigations like ECG, fasting blood sugar, fasting lipid profile- {total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides total cholesterol –HDLratio}, fasting apoB-apoA1 ratio, & lipoprotein (a).cardiac enzyme makers and echocardiography in indicated cases.

Results

This study clearly proves the role of hypertension, diabetes mellitus, obesity, family history of hypertension, diabetes and acute coronary syndrome. Metabolic syndrome is very prevalent in South Asians and should be screened for accordingly. Waist-hip ratio or waist circumference rather than BMI should be used to screen for central obesity. Smokers have a high risk of developing ACS, but association of alcohol consumption and ACS is not statistically significant. Emerging risk factors such as apoB-apoA1 ratio.Lp(a)_ are significant risk markers of acute coronary syndrome. But this study suggest that replacement of traditional lipid values with apoB-apoA1 ratio, Lp(a) adds little to risk assessment in acute coronary syndrome.

Conclusion

Thus the study exemplifies that, in the present study, patients belong to poor economic status, total cholesterol – HDL ratio is as efficient, as the emerging risk factors, included in this study.

Keywords: Coronary artery disease, lipoprotein (a)

Introduction

Human coronary atherosclerosis is a chronic inflammatory disease that is superimposed on background of lipid abnormalities. Studies highlights that proinflammatory oxidized LDL cholesterol may be a unifying link between lipid accumulation & inflammation in vessel wall & LDL cholesterol was the primary target in CAD preventing guidelines [1].Lipoprotein(a) is an

emerging independent and compounding risk factor for the development of CAD and, unlike other lipids, its levels are almost entirely determined by genetics and thought to multiply the effect of traditional CAD risk factors (low HDL, high LDL, DM). Screening for lipoprotein(a) is most important in younger age group since the lipoprotein(a)-associated CAD risk is highest between 45-55 years of age and declines in old age. In acute coronary syndrome Liporotein (a) concentration is predictive of an increased risk of cardiac deaths and serum level more than 30 mg/ dl is associated with 62% increase in cardiac death [2].Apolipoprotein A1 is the main structural protein of antiatherogenic HDL cholesterol and Apolipoprotein B is the structural protein of VLDL, IDL and LDL cholesterol Apo B reflects the entire spectrum of proatherogenic particles [3].Large studies like AMORIS (Apolipoprotein Related Mortality Risk) and INERHEART have unambiguously shown that ApoB-Apo A1 ratio predicts CAD events better than traditional lipid values [4, 5]. Thus the present study was undertaken to assess the fasting lipid profile, fasting Apo B-ApoA1 ratio and Lipoprotein (a) levels in patients with acute coronary syndrome of age below 55 years, within 24 hours of onset of, and to compare with that of age and sex matched controls. Further, the lipid parameters predict the risks of developing acute coronary syndrome in young were also evaluated.

Patients and Methods

The present observational study was done from September 2009 to July 2010 at the Department of General Medicine, Calicut Medical College. All patients were evaluated with baseline investigations like ECG, fasting blood sugar, fasting lipid profile- {total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides total cholesterol –HDL ratio}, fasting apoB-apoA1 ratio, & lipoprotein (a).cardiac enzyme makers and echocardiography in indicated cases.Controls also selected and evaluated in the same way- with history, clinical examination & relevant investigations.All samples were collected and processed with the use of a standardized protocol and were analysed in the central biochemistry lab.

Statistical analysis of sociodemographic and biochemical parameters between the cases and controls were done using SPSS software program version 15. the quantitative variables were analysed by using t test and qualitative variables using pearson's chi square test.

Results

Seventy five patients with acute coronary syndrome and 75 age matched controls in the age group 15-55 years were studied.The mean age of the cases was 49.28 and that of controls was 51.76 ($p<0.05$). Of the 150 subjects studied, 124 (82.7%) were males and 26 (17.3%) were females.

The occupation of 64% (48) of cases and 66.7% (50) of the control group was unskilled work.In the study group, 39 cases (52%) and 5 controls (6.67%) were hypertensive. 36(48%) cases and 10 (13.33%) controls were diabetic. Pearson Chi square value for past history of hypertension is 14.01($p<0.05$) and that for past history of Diabetes is 6.10 ($p<0.05$).

Out of the 75 cases studied, 54 (72%) had positive family history of hypertension. Out of the 75 controls studied, 18 (24%) had positive family history of hypertension and the value was found to be statistically significant ($p<0.05$). The Odds ratio calculated for family history of hypertension is 8.143.

Regarding family history of diabetes, 48(64%) cases had positive family history of diabetes and 24 (32%) controls had positive family history of diabetes mellitus ($p<0.05$). The Odds ratio is 3.778.

Out of the 75 cases studied, 33 (44%) had positive family history of CAD. Out of which 62.7% had occurrence of

CAD <55 years. Among the control group 36(48%) had positive family history of CAD, but 92% had family history of CAD >55 years (p<0.05). Odds ratio for family history <55 years is 6.85.63 cases and 38 controls were smokers. Odd ratio for smoking was 5.112 (p<0.05).

Current alcohol user constitutes 47 cases and 19 controls. Odd ratio is 0.690 with p value 0.497.Only 2 cases and 2 controls were strict vegetarians (p<0.05). Out of 75 cases, 48 were very active, 17 moderately active and 10 not active. Among the control group, 48 very active, 18 moderately active and 9 were sedentary (p<0.05).

Mean systolic BP for cases was 148.77 and for controls were 115.15. Mean diastolic BP for cases were 95.57 and for controls were 77.01. Odds ratio for systolic BP was 15.7 with p value <0.05. Odds ratio for diastolic BP was 11.3 with p value < 0.05.The mean BMI for cases was 24.41 and for control was 20.53.Odd ratio is 9.894 and p value is <0.05.Mean waist circumference of cases is 92.73 and controls 86.69. Odd ratio is 8.73 with p value <0.05.

The mean, standard deviation, Odd ratio and p value of the biochemical parameters studied explained in the Table1 given below.

Table1: Lipid and biochemical parameters level in the study

	Study Group	Mean	Standard Deviation	Odds Ratio	P Value
APO-B	CASE CONTROL	188.165 89.48	39.496 35.469	11.677	<.05
APO-A1	CASE CONTROL	104.41 185.37	32.13 48.58	5.083	<.05
APO-B/APO-A1	CASE CONTROL	2.00998 0.54469	0.78805 0.37899	11.725	<.05
LP(A)	CASE CONTROL	31.03 20.63	9.15 8.41	11.714	<.05
Total Cholesterol	CASE CONTROL	222.29 173.15	52.56 25.95	5.954	<.05
Triglycerides	CASE CONTROL	183.37 148.17	61.20 41.86	1.659	<.05
HDL-C	CASE CONTROL	35.47 40.81	8.42 6.91	4.955	<.05
LDL-C	CASE CONTROL	140.23 106.49	46.28 14.04	7.825	<.05
TC/HDL-C	CASE CONTROL	6.4257 4.5327	1.8688 2.4835	11.951	<.05
FBS	CASE CONTROL	123.93 96.41	39.86 9.46	9.418	<.05

Further, the level of apo A1 was less in cases as that of the control, whilst the levels of apo B were found to be vice versa. Meanwhile, apo B apo A1 ratio was more in cases as that of the control (Table 1).

There was significant (p<0.05) elevation the Lp (a) level in the cases as that of the control (Table 1).

Discussion

The mean of apo-B – apoA1 ratio was high in cases. 2.00998 (SD = 0.78805) than control 0.54469 (SD = 0.37899). The Odds ratio was 11.725 (p value <0.05) which clearly indicates apo B – apoA1 ratio is a significant risk marker of acute coronary syndrome. The mean of apoB in cases 188.165 (SD = 39.496) is higher than in control group. 89.480 (SD = 35.469). The Odd's ratio for apoB is 11.677 (p value <0.05). The mean apo A1 is lower in cases 104.41 (SD = 32.13), when compared to controls 185.37 (SD = 48.58). The Odds ratio for apo A1 in the study group is 5.083 (p value <0.05). The results obtained for apoA1 and apoB separately, definitely indicates that a low apoA1 and high apoB levels are risk predictors in acute coronary syndrome. The apoB and apoB – apoA1 ratio has almost same risk estimate for acute coronary syndrome.The odds ratio of apo B is much higher than LDL.This may be because apo B includes other atherogenic lipoproteins like VLDL and chylomicrons.

The mean Lp(a) in the cases was 31.03 (SD = 9.15) higher than the mean Lp(a) in control group20.63(8.41).The Odds ratio for Lp(a) is 11.714 (p value <0.05). The Lp(a) risk estimate reveals that it is also a significant risk factor for acute coronary syndrome.

Considering the fasting lipid profile, the mean of total cholesterol, triglycerides, LDL was higher in cases than in control. The mean HDL cholesterol in cases is lower than in control. The Odds ratio was different for each biochemical parameter in the fasting lipid profile. The Odd's ratio was highest for LDL cholesterol 7.825 (p value <0.05), then total cholesterol, 5.954 (p value <0.05) followed by HDL cholesterol 4.955 (p value <0.05) and lastly triglycerides 1.659 (p value <0.05). But when TC to HDL-C ratio considered, the Odd's ratio was 11.951 (p value <0.05) which clearly indicate that this simple measurement of TC/HDL-C ratio is a strong risk marker as Lp(a) and apo(B) apoA1 ratio. In our medical college set up where almost all the patients belong to poor socioeconomic status, the measurement of TC to HDL ratio measurement is much cost effective than Lp(a) or apoB-apoA1 ratio measurement.

Two largest studies in this field were INTERHEART study [4] and AMORIS study[5] .The INTERHEART study, which was a case control study, were all ethnic groups in both sexes were studied. The important conclusion was, the ratio of apo B – apoA1 was the most powerful marker associated with acute myocardial infarction. ApoB was better than total cholesterol, LDL cholesterol and non-HDL cholesterol. Apo-A1 was better than HDL cholesterol.

In AMORIS study[5], a cohort study also revealed that, association between the apo B – apoA1 ratio and cardiovascular risk was independent of traditional lipid variables. In AMORIS study the HDL cholesterol and LDL cholesterol were indirectly measured. Most of the increased CAD risk in South Asians can be explained by a higher prevalence of traditional risk factors, especially at a younger age. INTERHEART study (an international case-control study examining risk factors for initial MI in 52 countries, including 12,000 cases of initial MI and 14,000 controls) demonstrated that over 90% of global MI risk can be attributed to 9 modifiable risk factors (smoking, DM, lipids, central obesity, hypertension, diet, physical activity, alcohol consumption, and psychosocial factors). This was true for all populations including South Asians. However, South Asians presented with initial MI at earlier ages (53 yrsvs 58 yrs) and this can be explained by the presence of more risk factors at an earlier age. Protective factors (moderate daily alcohol consumption, regular physical activity, daily intake of fruits and vegetables) were significantly lower among South Asians. Harmful factors were significantly higher in South Asians (DM and elevated apoB/apoA-1 ratio). When compared to other risk factors, elevated apoB/apoA-1 ratio had the single highest attributable risk in South Asians. When compared to other ethnic groups, certain risk factors had higher attributable risk in South Asians: apoB/apoA-1 ratio, low daily consumption of fruits and vegetables, lack of regular exercise, and high waist hip ratios (marker of central obesity which predisposes to insulin resistance).

In INTERHEART study LDL cholesterol and HDL cholesterol were measured directly but they were not incorporated in the statistical analysis.

Data from Quebec Cardiovascular study [6] showed that apolipoprotein B level was associated with CAD independent of LDL cholesterol level but apoA1 level was not associated with CAD independent of HDL cholesterol level.

The PRIME study[7] reported that apolipoprotein A-1 level was associated with CAD independent of HDL cholesterol level.

Data from ARIC study[8] suggested that apolipoprotein A-1 and B levels no longer contributed to CAD risk prediction when considered together with traditional lipid values.

The Caerphilly study[9] corroborated the lack of a lipid-independent association between apolipoprotein level and CAD.

EPIC – Norfolk[10], a case control study showed that apo-B – apoA1 ratio was more closely associated with future CAD events than was total cholesterol-HDL ratio, but that the two measures were equivalent in their ability to discriminate between persons with and those without cardiovascular events. Thus the replacement of traditional lipid values with the apoB-apoA1 adds little to CAD risk assessment.

Parish et al [11] concluded that ratio of apoB to apoA1 encapsulated almost all the information from measurements of lipoproteins and of both cholesterol fraction.

The fasting blood sugar value was higher among cases 123.96 (SD = 39.86) than among controls 96.41 (SD = 9.46).The odds ratio is 9.418 (p value<05). This shows an impaired fasting blood sugar is a significant risk factor of acute coronary syndrome.

Considering the associated risk factors, male sex is definitely a significant risk factor. The Coronary Artery Disease in Indians (CADI) study demonstrated a CAD prevalence of 10% amongst first generation South Asian immigrants to the United States, compared to a 2.5% CAD prevalence among the general population in the Framingham study [12]. The higher prevalence is further magnified in younger South Asians. Religion occupation and socioeconomic status are not significantly associated with acute coronary syndrome (p value >0.05). The past history of diabetes and hypertension are obviously risk factors of acute coronary syndrome (p value <0.05).

In this study smoking has significant association with acute coronary syndrome. Studies have shown that 40-50% of the males in India are smokers in a prospective case control study conducted in Bangalore, 200 patients with a first myocardial infarction were compared with 200 age and sex matched controls. The adjusted Odd's ratios for smoking, hypertension and fasting blood glucose as risk factors for AMI were 3.7, 3 and 2.8 respectively. Pais et al [13] from the same group confirm these findings reiterating the importance of smoking as a risk factor in Indian context

But current alcohol use is not a significant risk factor for acute coronary syndrome (p value >0.05). Family history of diabetes, hypertension and family history of CAD in <55 years are significant risk factors for acute coronary syndrome (p value 0.05). In a study in young individuals by Dwivedi et al [14] those with ACS 18.8% subjects gave history of premature CAD in their first degree relatives.

The quantitative variables studied revealed the following findings. Mean systolic BP and diastolic BP, BMI is high in cases than control.

Among the biochemical parameters studied raised apoB-apoA1 ratio, Lp(a), fasting lipid profile are all risk factors. Comparing among these parameters, apoB-apoA1 ratio, Lp(a) and total cholesterol-HDL ratio have almost equivalent risk estimate. Among the fasting lipid profile, LDL–C has the highest odds ratio and Triglycerides the least. Apo(B)- Apo A1 ratio and Lp(a) measurement is not cost effective when compared to TC- HDL-C ratio, as they all have almost same odds ratio. In our medical college set up prefer TC-HDL-C ratio to apo(B)-apoA1 ratio and Lp(a).Apo B is more significant than LDL in acute coronary syndrome.

Conclusion

Emerging risk factors such as apoB-apoA1 ratio.Lp(a)_ are significant risk markers of acute coronary syndrome.

But this study suggest that replacement of traditional lipid values with apoB-apoA1 ratio, Lp(a) adds little to risk assessment in acute coronary syndrome. Especially in our medical college, were most of the patients belong to poor economic status, total cholesterol – HDL ratio is as efficient, as the emerging risk factors, included in this study. However, other characteristic like, the ability of apoB apoA1 ratio on non fasting samples AMI make it useful in some setting. To prevent this deadly disease, a multi pronged approach with reduction of serum lipids, blood sugar, better control of blood pressure, weight reduction and cessation of smoking is needed.

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