Research Article

C-reactive protein and Apo B as better predictor of STEMI than lipid profile

Preshant Shrivastava[1]*, Anshul Agrawal[2]

[1]Department of Medicine, People's College of Medical Sciences and Research Centre, Bhopal, Madhya Pradesh, India
[2]Department of Medicine, Maharani Laxmibai Medical College, Jhansi, Uttar Pradesh, India

*Correspondence:
Dr. Preshant Shrivastava,
E-mail: dr_dada1@yahoo.com

ABSTRACT

Background: Total cholesterol, triglycerides, high density lipoprotein and low density lipoproteins are the recommended lipid variables for diagnosis and treatment of coronary artery disease. However, recent information shows the importance of apolipoprotein B and CRP as risk predictors of suspected CAD. Inflammation plays a major role in atherothrombosis and measurement of inflammatory markers such as CRP may provide a promising novel biochemical indicator for detecting individuals at high risk of plaque rupture.
Methods: A total number of 43 cases of acute myocardial infarction with ST elevation myocardial infarction were included in this study. In this study CRP was elevated in more patients than LDL/HDL ratio (60.5% vs 20.9% respectively). Similarly, Apo B was elevated in more number of patients than LDL (72.1% vs 39.5% respectively). Also, Apo B/Apo A1 ratio was elevated in more number of patients than LDL/HDL ratio (51.2% vs 20.9% respectively).
Results: In our study maximum incidence of ST elevation MI was present in age group 56-65 years with youngest of age 28 years and oldest of age 75 years. Out of 43 patients who suffered from STEMI 72.1% were males and only 27.9% were females. Out of 43 cases, 46.5% of cases had anterior wall MI, and 46.3% of the cases had inferior wall MI and only 9.3% of the cases developed anteroseptal wall MI. In our study death was encountered in only 9.3% (N – 4) of the cases.
Conclusions: The results of the current study support the concept that the levels of apolipoprotein B, Apo B/Apo A1 ratio and CRP are strongly related to Coronary artery disease in addition to the conventional lipid profile.

Keywords: CRP, Apo B, STEMI, Lipid profile

INTRODUCTION

Coronary Artery Disease remains an important health problem, and merits continued attention from basic and clinical researchers, epidemiologists and practicing physicians. The inter heart case-control study reported that nine established risk factors (high APOB/APOA1 ratio, smoking, hypertension, diabetes, obesity, psychosocial stress, low fruit and vegetables intake, low alcohol intake and sedentary lifestyle), explained more than 90 per cent of acute myocardial infarction. While smoking and APOB/APOA1 ratio alone accounts for 66 percent of risk factor for CAD.[1] Apolipoproteins are the protein components of lipoproteins.[2]

Apolipoproteins serve both as enzymatic co factors and as recognition elements that bind to specific receptors on the peripheral tissues.[3] Apolipoprotein A1 (apoA1) is the protein constituent of high density lipoprotein cholesterol (HDL-C) whereas Apolipoprotein B (apoB) is the protein constituent of low density lipoprotein cholesterol (LDL-C).[4] LDL-C and apoB are atherogenic whereas HDL-C

and apoA-1 are anti-atherogenic. Each of the atherogenic particles in plasma {Very Low density lipoprotein cholesterol (VLDL-C), Intermediate density lipoprotein (IDL), Low density lipoprotein cholesterol (LDL-C) and lipoprotein (a)} contains one molecule of apoB and therefore, measurement of plasma apoB represents the total number of atherogenic particles.[4]

It is becoming increasingly clear that inflammation is an important factor in acute myocardial infarction. With inflammation, there will be release of inflammatory Cytokines from the inflamed tissue, which stimulates liver to synthesize a number of acute phase proteins, including the prototypical acute phase reactant, C Reactive Protein.

In clinical studies, it is shown that, circulating levels of CRP were found to correlate with total infarct size and with prognosis in acute myocardial infarction. Thus CRP is an indicator of underlying coronary inflammation as well as extent of myocardial necrosis.

The present study was carried out to evaluate the relationship between ApoB, CRP and Lipid profile in patients with IHD.

Aim

To compare between CRP, APOB/APOA1 ratio, LDL, and HDL as a better predictor of coronary artery disease.

METHODS

The study was carried out on patients presenting with first attack of acute ST Elevation myocardial infarction and admitted to Peoples Hospital, PCMS & RC, Bhopal, Madhya Pradesh, India.

A total number of 43 cases of acute myocardial infarction with ST elevation myocardial infarction were included in this study. All the patients were subject to ECG and Echocardiography.

In all the subjects, the concentration of total cholesterol, triglycerides, high density lipoprotein, very low density lipoprotein, low density lipoprotein, CRP, apolipoprotein A-1 and B and the ratio of ApoB/ ApoA1 were estimated.

The patients also underwent investigations for complete blood counts, liver function tests, kidney function tests and urine routine & microscopic examination.

Table 1: Risk categories for Apo B/ Apo A1 ratio and LDL/HDL ratio.[5,6,7]

Ratio	Men	Women
Apo B/Apo A1 ratio	>1.0	>0.9
LDL/HDL ratio	>3.5	>3.0

Table 2: ADA and ACC recommended values for ApoB.[8]

Risk	Apo B
Highest-risk patients: Known CVD or DM plus ≥1 additional major CVD risk factor	<80 mg/dL
High-risk patients: ≥2 CVD risk factors but no DM or known CVD or DM but no other major risk factors	<90 mg/dL

C- reactive protein[9]

The median baseline level of CRP for young adults is 0.8 mg/L.

RESULTS

In our study maximum incidence of ST elevation MI was present in age group 56-65 years with youngest of age 28 years and oldest of age 75 years. Out of 43 patients who suffered from STEMI 72.1% were males and only 27.9% were females. Out of 43 cases, 46.5% of cases had anterior wall MI, and 46.3% of the cases had inferior wall MI and only 9.3% of the cases developed anteroseptal wall MI. In our study death was encountered in only 9.3% (N - 4) of the cases.

Table 3: Comparison of lipid profile parameters.

	N	Minimum	Maximum	Mean	SD
TC	43	100.00	272.00	165.5349	31.37511
TG	43	50.00	229.00	130.5814	38.22753
VLDL	43	11.00	161.00	32.5116	23.27104
LDL/HDL	43	1.07	5.40	2.5674	0.92320
APOA1	43	70.00	133.00	107.1860	14.61124
APOB/APOA1	43	0.50	1.40	0.9670	0.24826
CRP	43	0.60	2.40	1.1023	0.55613

The mean value of total cholesterol in 43 cases who suffered from MI was 165.5±31.3, triglycerides were 130.5±38.2, VLDL was 32.5±23.2, LDL/HDL was 2.5±0.93, APOA1 was in the range of 107.18±14.16, APOB/APOA1 was in the range of 0.967±0.248 and CRP was in the range of 1.10±0.55.

Table 4: Comparison between CRP and LDL/HDL

		Count	Column N %
LDL/HDL	Elevated	9	20.9%
	Normal	34	79.1%
CRP	Elevated	26	60.5%
	Normal	17	39.5%

LDL/HDL ratio was elevated in 20.9% and CRP level was elevated in 60.5% of the cases. LDL/HDL ratio was compared to CRP, CRP was elevated in more patients than LDL/HDL ratio (60.5% v/s 20.9% respectively) and it was of statistical importance with a p-value of 0.0002 (95% CI) which was statistically significant.

Table 5: Comparison between LDL and CRP.

		Count	Column N %
LDL	Elevated	17	39.5%
	Normal	26	60.5%
CRP	Elevated	26	60.5%
	Normal	17	39.5%

LDL was elevated in 39.5% and CRP level was elevated in 60.5% of the cases. LDL was compared to CRP, CRP was elevated in more number of patients than LDL (60.5% v/s 39.5% respectively) but it was not of statistical importance with a p-value of 0.051.

Table 6: Comparison between LDL and APOB.

		Count	Column N %
LDL	Elevated	17	39.5%
	Normal	26	60.5%
APOB	Elevated	31	72.1%
	Normal	12	27.9%

Table 7: Comparison between LDL/HDL and APOB/APOA1.

		Count	Column N %
LDL/HDL	Abnormal	9	20.9%
	Normal	34	79.1%
APOB/APOA1	Abnormal	22	51.2%
	Normal	21	48.8%

LDL was elevated in 39.5% of the cases and apoB was elevated in 72.1% of the cases, apoB was elevated in more number of patients than LDL (72.1% v/s 39.5% respectively) and it was of statistical importance with p-value of 0.0023 (95% CI) which was statistically

significant. LDL/HDL ratio was elevated in 20.9% of the cases and apoB/apoA1 ratio was elevated in 51.2% of the cases, apoB/apoA1 ratio was elevated in more number of patients than LDL/HDL ratio (51.2% vs 20.9% respectively) and it was of statistical importance with p-value of 0.0034 (95% CI) which is significant.

DISCUSSION

Ischemic heart disease is one of the leading causes of morbidity and mortality in most countries of the world. The debate on the value of lipids as a predictive risk factor for atherogenesis has centered for many years on total cholesterol, triglycerides and low density lipoprotein. Recently the interest has been focused on role of apolipoproteins and inflammatory marker in atherogenesis.

Elevated CRP levels have been regarded as a risk factor for CAD. The reason for this is that LDL particles are responsible for delivering cholesterol from liver to the peripheral tissues. Oxidation of LDL particles is a key process in the development of atherosclerosis. Within vascular endothelium, oxidized LDL particles induce inflammation, proliferation and apoptosis of endothelial and smooth muscle cells.[10]

Present study shows that CRP has statistically stronger correlation with STEMI as compared to LDL/HDL ratio(*p* value 0.0002). Similar results were seen in study by Kulsoom et al that High serum CRP levels rather than high LDL:HDL are associated with myocardial infarction in the patients presenting with first myocardial infarction.[11] Similar observations have also been made by Ridker et al that C-reactive protein level is a stronger predictor of cardiovascular events than the LDL cholesterol level.[12]

DeBeer et al measured CRP and creatinine kinase MB levels in patients with definite myocardial infarction.[13] They found that all individuals with infarction developed raised CRP levels and there was a significant correlation between the peak CRP and CKMB levels.[13] In our study, however CRP in comparison to LDL levels was not significantly associated with STEMI (*p* value 0.051).

In present study apoB proved to be more significant than LDL-C for the risk of MI (*p* value 0.0023). Observations made in a study by Sharma et al stated that the concentrations of apoA-1 and apoB are better predictors of CAD than the total plasma lipids or lipoproteins.[14] Similar observations have also been made in AMORIS study.[15]

In this study, by use of different multivariate analyses, apoB proved to be more significant than LDL-C and added predictive power to LDL-C for prediction of the risk of fatal MI.[15] In present study apoB was elevated in more number of patients than LDL (72.1% vs 39.5% respectively). apoB/apo A1 ratio is better than traditional

lipid ratios to predict the risk of MI. Sreenivasan and co-workers reviewed various etiological factors in the development of atherosclerosis and concluded that apolipoprotein- A and B are superior to conventional lipid profile in CAD.[16] Present study showed that apoB/apoA1 ratio is better indicator of MI as compared to LDL/HDL ratio (p value 0.0002). Similar observations were also seen in a study by Dawar et al that ApoB/Apo A1 ratio is better than traditional lipid ratios to predict the risk of MI.[17]

CONCLUSION

The results of present study support the concept that the levels of apolipoprotein B, apoB/apoA1 ratio and CRP are strongly related to coronary artery disease in addition to the conventional lipid profile. The concentrations of lipid parameters may be changed by meal whereas the concentration of apolipoprotein B is not affected, hence fasting samples are not required in case of apolipo-proteins as compared to conventional lipid profiles. Apo B, the protein part of LDL-C predicts the development of CAD better than the level of plasma LDL cholesterol. The observations in our study suggest the use of apolipoprotein B to be a more specific biomarker in the prediction of ischemic heart disease when compared to the currently used lipid profile.

Inflammation plays a major role in atherothrombosis, and therefore, measurement of inflammatory markers such as CRP may provide a promising novel biochemical marker for detecting individuals at high risk of plaque rupture. The observations from our study suggest that CRP has the potential to play an important role in risk assessment in ischemic heart disease.

REFERENCES

1. Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, et al, Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (The INTERHEART Study). Am Heart J. 1963;65:749-57.
2. Rifai N, Warnick GR. Lipids, lipoproteins, apolipoproteins and other cardiovascular risk factors. In: Burtis CA, Ashwood ER and Bruns DA, editors. Tietz Text Book Of Clinical Chemistry and Molecular Diagnostics, 4th ed. New Delhi: Elsevier Co. 2006:903-64.
3. Sharma R, Singh VS. Serum apolipoproteins in the patients of myocardial infarction in different age groups. Ind J Clin Biochem. 2001;16(1):122-6.
4. Lamarche B, Moorjani S, Lupien PJ, Cantin B, Bernard PM, Dagenais GR, et al. Apolipoprotein A1 and B levels and the risk of ischemic heart disease during a five-year follow-up of men in the quebec cardiovascular study. Circulation. 1996;94:273-78.
5. Gotto AM, Assmann G, Carmena R. The ILIB lipid handbook for clinical practice: Blood lipids and coronary heart disease. 2nd ed. New York: International Lipid Information Bureau; 2000;53:201.
6. Genest J, Frohlich J, Fodor G, McPherson R. the Working Group on Hypercholesterolemia and Other Dyslipidemias. Recommendations for the management of dyslipidemia and the prevention of cardiovascular disease: 2003 update. CMAJ. 2003;169:921-4.
7. Holme I, Aastveit AH, Junger I, Walldius G. Relationships between lipoprotein components and risk of myocardial infarction: age, gender and short versus longer follow-up periods in the Apolipoprotein Mortality RISk study (AMORIS). J Intern Med. 2008;264:30-8.
8. Brunzell JD, Davidson M, Furberg CD, Goldberg RB, Howard BV, Stein JH. Lipoprotein management in patients with cardiometabolic risk: consensus conference report from the American Diabetes Association and the American College of Cardiology Foundation. J Am Coll Cardiol. 2008;51(15):1512-24.
9. Casas JP, Shah T, Hingorani AD, Danesh J, Pepys MB. C-reactive protein and coronary heart disease: a critical review. J Intern Med. 2008;264(4):295-314.
10. Loidl A, Sevcsik E, Riesenhuber G, Deigner H, Hermetter A. Oxidized Phospholipids in Minimally Modified Low Density Lipoprotein Induce Apoptotic Signaling via Activation of Acid Sphingomyelinase in Arterial Smooth Muscle Cells. J Biol Chem. 2003;278:32921-8.
11. Kulsoom B, Nazrul SH. Association of serum C-reactive protein and LDL:HDL with myocardial infarction.J Pak Med Assoc. 2006;56(7):318-22.
12. Ridker PM, Rifai N, Rose L, Buring JE, Cook NR. Engl J Med. 2002;347:1557-65.
13. DeBeer FC, Hind CR, Fox KM.Measurement of serum C-reactive protein in myocardial ischemia and infarction. Br Heart J. 1982;47:239-43.
14. Sharma R, Singh VS. Serum apolipoproteins in the patients of myocardial infarction in different age groups. Ind J Clin Biochem. 2001;16(1):122-6.
15. Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, et al. Effect of potentially modifiable risk factors associated with Walldius, Jungner I, Holme I, Aastveit A, Kolar W, Steiner E. High apolipoprotein B, lowapolipoprotein A-I, and improvement in the prediction of fatal myocardial infarction (AMORIS study): a prospective study. Lancet. 2001;358:2026-33.
16. Sreenivasan RS, Kavitha A, Anush AR, Krishna MP, Renganathan NG Identification and prediction of coronary heart disease in patients with apolipoprotein levels. IJPBS. 2011;1(2):31-42.

17. Dawar R, Gurtoo A, Singh R. Apo B/ Apo A1 ratio is statistically the best predictor of Myocardial Infarction compared to other lipid ratios. Int J of Pharma and Bio Sciences. 2010;1(2):1.