

Apo B/Apo A1 Ratio: A Risk Marker in Patients with Cardiovascular Disease

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ABSTRACT

BACKGROUND AND OBJECTIVES: Cardiovascular disease (CVD) is a broad term encompassing diseases of the heart and blood vessels. The lipid and lipoprotein cholesterol levels have failed to explain the increased prevalence of CVD in normolipidemic patients. Recently ApoA1 and Apo B have been proposed as markers for assessing the risk of CVD and its treatment regimen. The purpose of this study was to determine whether the Apo B/Apo A1 ratio was superior to the conventional lipid parameters in predicting the risk of a CVD. **METHOD:** A total of 45 subjects were included in the study. The plasma levels of Apo A1, Apo B and the lipid parameters were determined on VITROS 4600 Chemistry System. The Apo B/Apo A1, LDL-C/HDL-C and total cholesterol/HDL-C ratio were then calculated. **RESULTS:** After analysing the data obtained and comparing the data with control group in whom the Apo B/Apo A1 ratio was below 0.6 patients with Apo B/Apo A1 ratio exceeding 0.9 were included in the high risk group and patients with Apo B/Apo A1 ratio between 0.6-0.9 were included in the average risk group. **CONCLUSION:** According to the results obtained it was concluded that subjects with Apo B/Apo A1 ratio exceeding 0.9 were at an increased cardiovascular risk as compared to subjects with Apo B/Apo A1 ratio less than 0.6 who were at a lower risk of developing a cardiovascular event. The Apo B/Apo A1 ratio was thus found to have better predictive value than that of classical lipid parameters in cardiovascular assessment.

Key words: Cardiovascular, lipoprotein, Apo B, Apo A1

INTRODUCTION

Cardiovascular disease (CVD) is a broad term encompassing diseases of the heart and blood vessels, including heart attack, coronary artery disease, congestive heart failure and stroke. Since CVD is the number-one killer of both men and women worldwide. The results of the lipid profile are considered along with other known risk factors of heart disease to develop a plan of treatment and follow up. Depending on the results and other risk factors, treatment options may involve life style changes such as diet and exercise for lipid lowering medications such as statins.¹ The lipid and lipoprotein cholesterol levels have failed to explain

The increased prevalence of CVD in normolipidemic patients. It is well known that apolipoproteins A1 and B are associated with cardiovascular diseases. Apolipoproteins have therefore emerged as key risk markers to predict and diagnose CVD and techniques measuring apolipoproteins are important tools of today's clinical work and research^{2,3}. Recently ApoA1 and Apo B have been proposed as relatively better markers for assessing the risk of CVD and its treatment regimen.

Atherosclerosis is a pathologic process affecting blood vessels, which leads to the development of cardiovascular disease⁴. On the whole, the subjects with Apo B /Apo A1 >0.9 had a more atherogenic lipid profile. Thus the Apo B/Apo A1 ratio can be considered as a sensitive marker of atherogenic risk. The Apo B/Apo A1 ratio can be considered as an effective marker for myocardial infarction⁵. The Apo B/Apo A1 ratio has a stronger correlation with myocardial infarction than the total cholesterol/HDL-C ratio. The concentration of lipid parameters can be

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changed through meals. But the concentration of the apolipoproteins is not affected by meals⁶. The study showed that Apo B/Apo A1 ratio have highest sensitivity, specificity and diagnostic efficiency. The study thus supports the concept that Apo A1, Apo B and Apo B/Apo A1 ratio can be used as the predictors of stroke and myocardial infarction along with the traditional lipid profile measurements.

The aim of this study was to evaluate whether the Apo B/Apo A1 ratio is a better predictor of the occurrence of future CVD events compared to traditional lipid measurements.

MATERIALS AND METHODS

The present study was conducted at Breach Candy Hospital on 45 subjects that included 15 subjects in the control group. Institutional Ethics Committee approval was taken before publishing this research paper. Apolipoproteins were measured and computed using Micro Tip Method on VITROS 4600 Chemistry System.

The instrument is fully automated and thus human errors are reduced. Following are the tests that are performed. Apolipoprotein A1, Apolipoprotein B, Total Cholesterol, Triglycerides, HDL-C, LDL-C, VLDL, Total Cholesterol/HDL-C, LDL-C/HDL-C are calculated from the results of total Cholesterol, triglycerides and HDL-C. 3ml-5ml of blood is drawn and collected in ready-made green top Sodium Heparin vacutainer (BD Ltd India) after which it is centrifuged in ROTOFIX 32 A centrifuge machine. The parameters i.e. Apolipoprotein A1, Apolipoprotein B, cholesterol, triglycerides, HDL-C are measured and computed using VITROS 4600 clinical analyser of Ortho Clinical Diagnostics. If the specimen has to be stored the plasma is separated and transferred in a tube after which it is kept in the refrigerator at 2^oC-8^oC.

The VITROS CHOL Slide method is performed using the VITROS CHOL Slides and the VITROS Chemistry Products Calibrator Kit 2 on VITROS 4600 Chemistry System.

The VITROS TRIG Slide method is performed using the VITROS TRIG Slides

and the VITROS Chemistry Products Calibrator Kit 2 on VITROS 4600 Chemistry System.

The VITROS dHDL Slide method is performed using the VITROS dHDL Slides and the VITROS Chemistry Products Calibrator Kit 25 on 4600 Chemistry System.

The quantitative measurement of LDL-C is performed using the VITROS Chemistry Products dLDL Reagent in conjunction with the VITROS Chemistry Products Calibrator Kit 19 and VITROS Chemistry Products FS Calibrator 1 on the VITROS 4600 Chemistry System.

QUALITY CONTROL MATERIAL

Performance verifiers level 1 and 2 from Ortho Clinical Diagnostics were used as internal quality control materials for cholesterol, triglycerides, high density lipoprotein and low density lipoprotein.

The VITROS Apo A1 and Apo B reagents are dual chambered packages containing stable, ready to use liquid reagents that are used in two-step reactions to quantitatively measure Apo A1 and Apo B. The VITROS Chemistry Products Calibrator Kit 21 is used to calibrate VITROS 4600 Chemistry System for quantitative measurement of Apolipoprotein A1 (Apo A1) and VITROS Chemistry Products Calibrator Kit 22 is used to Calibrate VITROS 4600 Chemistry system for quantitative measurement of apolipoprotein B (Apo B).

Special performance verifiers level 1 and 2 from Ortho Clinical Diagnostics were used as internal quality control material for Apolipoprotein A1 and Apolipoprotein B.

Table 1: Biochemical Analysis for Average Risk Patients

Parameters	Control Group(n=15) MEAN ± S.D	Average Risk Group(n=15) MEAN ± S.D	Value
Apolipoprotein A1	152.53 ±26.61	119 ± 14.21	0.0002 *
Apolipoprotein B	66.44 ± 11.19	87.63 ± 14.77	0.0001*
Apo B/Apo A1	0.50 ± 0.07	0.75 ± 0.08	0.0001*
Cholesterol	154.30 ±22.57	172.06 ±31.10	0.08 (NS)
Triglycerides	100.54 ± 29.41	141.20± 30.13	0.0008*
Dhdl	50.27 ± 13.69	37.75 ± 8.48	0.005*
Ldl	84 ± 21.83	102.35± 38.17	0.1 (NS)
Vldl	20 ± 5.97	28.20±6.00	0.0008*
Totalcholesterol/Hdl	3.21±0.72	4.71±0.85	0.0001*
Ldl Cholesterol/Hdl	1.76 ± 0.69	2.80± 0.74	0.0004*

Results were compared at 5% level of significance.

Table 2: Biochemical Analysis for High Risk Patients

Parameters	Control Group(n=15) MEAN± S.D	High Risk Group(n=15) MEAN ± S.D	p Value
Apolipoprotein A1	152.53 ± 26.61	114.66 ± 27.58	0.0007*
Apolipoprotein B	66.44 ± 11.19	128.12 ± 41.56	0.0001*
Apo B/Apo A1	0.50 ± 0.07	1.12 ± 0.27	0.0001*
Cholesterol	154.30 ± 22.57	188.47 ± 38.38	0.006*
Triglycerides	100.54 ± 29.41	254.27 ± 141.71	0.0003*
Dhdl	50.27 ± 13.69	27.73 ± 6.34	0.0001*
Ldl	84 ± 21.83	122.30 ± 52.67	0.01*
Vldl	20 ± 5.97	50.87 ± 28.27	0.0003*
Total Cholesterol/Hdl Cholesterol	3.21 ± 0.72	7.12 ± 1.79	0.0001*
Ldl Cholesterol/Hdl Cholesterol	1.76 ± 0.69	4.34 ± 1.37	0.0001*

Results were compared at 5% level of significance.

RESULTS

In 15 control subjects, the mean value of Apo B/Apo A1 was found to be less than 0.6. The mean values of the lipid parameters i.e. Cholesterol, triglycerides, LDL, VLDL, Total Cholesterol/HDL Cholesterol, LDL Cholesterol/ HDL Cholesterol are found to be in the normal range. The dHDL value was also found to be in the normal range. Hence these subjects with Apo B/Apo A1 ratio less than 0.6 have a lower risk of developing a cardiovascular risk.

In 15 average risk patients, the mean value of Apo B/Apo A1 ratio was found to be in the average risk range i.e. between 0.6-0.9. The mean values of the lipid parameters i.e. Cholesterol, triglycerides, LDL, VLDL, Total Cholesterol/HDL Cholesterol, LDL Cholesterol/HDL Cholesterol were all found to be increased as compared to control groups whereas the dHDL value was lower than the control group. Patients who have Apo B/Apo A1 ratio value higher than the control group have a higher risk of developing a cardiovascular disease as compared to the patients having values lower than the control group. Patients with dHDL value between 35-45 mg/dl and Apo B/Apo A1 ratio between 0.6-0.9 are considered to be average risk patients.

The total cardiovascular disease risk of over 20% over 10 years is defined as high risk. In 15 high risk patients, the mean value of the Apo B/Apo A1 ratio was found to be greater than 0.9. The mean value of the lipid parameters i.e. cholesterol, triglycerides LDL, VLDL,

Total Cholesterol /HDL Cholesterol, LDL Cholesterol/ HDL Cholesterol were all found to be higher than the control group whereas the dHDL value was lower than control group. Patients with dHDL values less than 35mg/dl and Apo B/Apo A1 ratio more than 0.9 are considered to be high risk patients. Abnormal blood lipid levels i.e high cholesterol,high triglycerides,high levels of low density lipoproteins(LDL-C) and low high density lipoprotein (HDL-C) all increase the risk of heart disease.

DISCUSSION

The atherogenic lipid profile is an important risk factor for cardiovascular disease (CVD). This profile is characterized by elevated levels of Total Cholesterol, LDL-C and triglycerides and lower levels of HDL-C. However, these traditional lipid risk factors are not always adequate indicators of cardiovascular disease event. In a quest to find whether apolipoproteins stand out to be better markers for CVD.

It was found that there was a significant association between high Apo B/Apo A1 ratio and increase occurrence of CVD events. The results were in agreement with the previous studies which have suggested that the ApoB/ApoA1 ratio can be considered as an effective predictor marker in myocardial infarction⁵. According to the results obtained it is seen that the Apo B/Apo A1 ratio is a promising marker for predicting the occurrence of CVD events and different studies and published data have suggested Apo B/Apo A1 ratio as a better predictor of CVD event^{4,6}. Subjects with high Apo b/Apo A1 ratio were characterized with high triglyceride levels and low dHDL levels which was in accordance to the previous study conducted⁷. Based on the findings of the current study and prospective studies, especially the studies conducted by^{8,9}, it was found that males are at a higher risk of Coronary Artery

Disease(CAD)event as compared to females owing to the raised plasma Apo B and low plasma Apo A1 levels. Apo B and Apo A1 can thus act as good candidates to act as CAD risk factor. The study suggests that the risk of CAD is increasing almost

linearly with the increasing values of Apo B/Apo A1 ratio; it thus seems logical to add Apo B/Apo A1 into clinical practice in order to simplify risk evaluation.

Patients with Apo B/Apo A1 ratio less than 0.6 and dHDL values between 40-60 mg/dL have the lowest risk of developing a cardiovascular event. Patients with Apo B/Apo A1 ratio exceeding 0.9 and dHDL below 40mg/dL have the highest risk of developing a cardiovascular risk. Thus, the Apo B/Apo A1 ratio seems to have a better predictive value than that of classical lipid parameters in cardiovascular assessment.

Apolipoproteins are simple, robust and accurate risk indicators of great value in health screening. The study thus recommends Apo B, Apo A1 and Apo B/Apo A1 ratio in assessment CVD prediction. In conclusion, the present study suggests that the measurement of Apo B, Apo A1 and Apo B/Apo A1 ratio appears to be a powerful marker to assess CVD risk and they should be routinely added to the lipid panel to assess the atherogenic potential of CVD patients.

CONCLUSION

According to the results obtained it was concluded that subjects with Apo B/Apo A1 ratio exceeding 0.9 were at an increased cardiovascular risk as compared to subjects with Apo B/Apo A1 ratio less than 0.6 who were at a lower risk of developing a cardiovascular event. The Apo B/Apo A1 ratio was thus found to have better predictive value than that of classical lipid parameters in cardiovascular assessment. Hence Apo B/Apo A1 ratio must be included in the risk stratification of the patients predisposed to cardiovascular event.

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