ORIGINAL ARTICLE

Evaluation of Apolipoprotein B / Apolipoprotein A Ratio as an Alternate of Lipid Profile for Cardiovascular Risk Assessment in a Tertiary Care Hospital

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ABSTRACT

Objective: To compare the predictive utility of serum Apo B/Apo A ratio with serum lipid profile in evaluation of cardiovascular disease (CVD) risk assessment**.**

Study Design: Cross sectional study.

Place and Duration of Study: Research was done at Department of Chemical Pathology & Endocrinology, Armed Forces Institute of Pathology (AFIP), Rawalpindi from 1st January 2021 to 31st March 2022.

Materials and Methods: A total of 204 patients were enrolled from a tertiary care hospital admitted for recent cardiac events and were compared with 96 healthy individuals. A serum sample was taken from all the members of both groups. Their lipid profile, Apo A, and Apo B were analyzed. Apo B/ Apo A ratio was calculated. The data was analyzed using SPSS version 21.

Results: Means of patient group for total cholesterol, LDL-cholesterol, HDL-cholesterol, VLDL-cholesterol, triglycerides, and Apo B/Apo A ratio were 4.18±1.21, 2.52±1.06, 0.83±0.34, 0.71±0.31, 1.66±0.86, 0.96±0.60 respectively, whereas means for control group were 3.99±0.54, 2.31±0.56, 1.00±0.31, 0.59±0.15, 1.22±0.33 and 0.70±0.18 respectively. Independent t-test was applied to compare means between two groups, which showed statistically significant difference between Apo B/Apo A ratio, HDL, and TG (*p* value <0.001). Chi-square test was applied for comparison of two groups which was statistically significant (*p* value <0.001).

Conclusion: Apo B/Apo A ratio is a better indicator for evaluation of cardiovascular disease as compared to lipid profile suggesting it to be a new and robust marker for CVD risk evaluation in our population.

Key Words: *Apo A, Apo B, Apo B/Apo A Ratio, Cardiovascular Disease, Lipid Profile.*

Introduction

Cardiovascular disease (CVD) is a foremost risk to the health globally, which attributed to approximately 30% of the appraised 20.5 million demises worldwide every year.[1] World Health Organization (WHO) has reported that CVD is second most significant cause of death in Pakistan accounting to approximately 29%. Whereas, a local study done in Pakistan showed prevalence of CVD of approximately 17.5%.[2]

Dyslipidemia has been one of the fundamental perpetrators for atherosclerosis leading to cardiovascular related diseases.[3] People with inactive lifestyles, positive family and medical history or obesity need to be carefully evaluated for early identification of ischemic heart disease (IHD). The elevating concentration of LDL-C is by and large acknowledged as being the most central risk factors for atherosclerosis in CVD.[4]

Atherosclerosis is a protracted inflammatory process which leads to atheroma plaques development resulting in thrombus formation. However, with advancement in diagnostics, many smaller lipoproteins and apolipoproteins have emerged as causes of atherosclerosis. Of these, Apolipoprotein A (Apo A) is supplemented with cardioprotective HDL-C while Apolipoprotein B (Apo B) is allied with atherogenic LDL-C.[5] The Main instigator in the atherogenic process is the excessive number of Apo B-containing particles, because the ApoB molecule in these particles is the trail blazer to trap the atherogenic lipoproteins in the arterial wall. Contrasting to Apo B, Apo A is a foremost apolipoprotein of cardioprotective lipid that helps

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the conveyance of cholesterol from peripheral cells to liver, thus dropping the risk of growth of inflammatory plaques.[6]

Several studies have shown that in people with CVD, changes in serum Apo A and Apo B levels are similar to those for HDL and LDL, respectively.[7] Apo B values increase and Apo A values decrease in people with CVD compared with those without CVD.[8] Furthermore, these two apolipoproteins have shown better correlation with the coronary stenosis than LDL and HDL.[9]

The Apo B/Apo A ratio denotes the equilibrium between atherogenic particles, containing Apo B, and the antiatherogenic ones, rich in Apo A. Thus, in spite of the lipids, lipoproteins and lipid ratios Apo B/ Apo A ratio is displayed to be a superior consideration for CVD risk assessment.[10] Epidemiological studies have indicated that the higher the Apo B/Apo A ratio, the greater is the CVD risk, and ≥0.9 and ≥0.8 cut-off value of ApoB/Apo A ratio have been suggested to express a high CVD risk for gender specified as males and females, respectively.[11]

For ages lipid profile is being used for evaluation of CVD risk which has now become obsolete in most of the world due to its low specificity as deranged lipid profile can occur due to various other medical health conditions and may appear at a much-delayed time when it is not that significant in assessment of CVD risk. In this study, we aimed on the utilization of Apo B/Apo A ratio for CVD risk assessment in population of Pakistan. As previously no study was done to assess its significance and relation to CVD. So, there is a need for a marker which can specifically be used for CVD risk and can help in its diagnosis at a time way earlier than the development of symptoms, making it easier for clinicians as well as patients to make lifestyle modifications at an earlier time to avoid the risk of a cardiovascular event.

In our study, our aim was to evaluate the Apo B/Apo A ratio in comparison with lipid profile in patients with recent cardiac events and compare it with the normal healthy individual.

Materials and Methods

A cross-sectional study was carried out in the Chemical Pathology & Endocrinology Department, AFIP Rawalpindi from 1st January 2021 to 31st March 2022 after getting ethical approval from the Institute with *IRB # FC-CHP-26/READ-IRB/21/658*. Sample size calculation was performed using a World Health Organization sample size calculator, with confidence interval of 95%, margin of error 5% and *p* value at less than 0.05 considered to be significant, and our sample size came out to be 300. Participants were selected through non-probability convenient sampling and divided into two Groups; Group I comprised of patients and Group II comprised of age matching healthy individuals. Patients were taken from the AFIC with the positive Trop-I results and healthy individuals coming for routine checkup at AFIP were selected. Informed consent was taken from both groups.

In group I (n=204), patients with recent history of myocardial infarction having serum Trop-I values > 0.06nmol/l were included. For group II (n =96), healthy individuals with no previous history of any cardiac, renal or any other chronic disease were selected. 5 ml venous blood was withdrawn by aseptic technique in clot activator gel tubes. Serum was immediately separated by centrifugation at 3500 revolutions per minute (RPM) for 5 minutes and analyzed.

Lipid Profile was analyzed on Advia 1800 using photometric technique, Apo A and Apo B were analyzed on Roche Cobas c501 using turbidimetric technique.[12] Statistical Package for Social Sciences (SPSS) program version 21.0 was used for data analysis. Results were articulated as mean ± SD. Descriptive statistics, independent-sample student t-test and chi-square test used to compare mean of lipid profile and Apo B/Apo A ratio between both groups. Apo B/ Apo A ratio of >0.7 was considered as significant for development of CVD while value <0.7 was considered as healthy.[13]

Results

Mean age for group I was 57±9 years whereas, mean age of group II was 52±11 years. In Group I, 60% (122) of patients were males while 40% (82) was female. However, gender percentages in Group II were 70% (66) for males and 30% (28) for females. For statistical analysis, SPSS 21 software was used. The Shapiro-Wilk test used to check distribution of data and found to be Gaussian. Means of patient group for total cholesterol, LDL-cholesterol, HDL-cholesterol, VLDL-cholesterol, triglycerides and Apo B/Apo A ratio were 4.18±1.21 (<5.2 mmol/l),

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2.52±1.06 (<3.2mmol/l), 0.83±0.34 (>1.04mmol/l), 0.71±0.31 (<0.78mmol/l), 1.66±0.86 mmol/l (0.4-1.6mmol/l), 0.96±0.60 (<0.70) respectively, whereas, means for control group were 3.99±0.54 (<5.2mmol/l), 2.31±0.56 (<3.2mmol/l), 1.00±0.31 (>1.04mmol/l), 0.59±0.15 (<0.78mmol/l), 1.22±0.33 (0.4-1.6mmol/l) and 0.70±0.18 (<0.70) respectively (Fig.1).

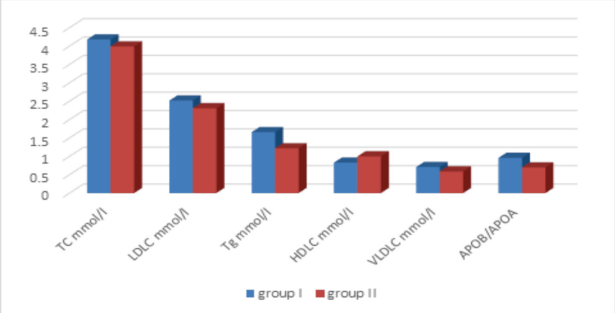

Fig. 1: Results of participants Group wise (n=300)

Independent t-test was applied for comparison of means between Group I & II, which showed significant difference between Apo B/Apo A ratio, HDL, VLDL, and TG, whereas total cholesterol and LDL-cholesterol, did not indicate any noteworthy difference between the two groups, shown in Table 1. For comparison of the difference between the two groups, a Chi-square test was performed, while taking cutoff of 0.7 as significant for Apo B/Apo A ratio in patients and control group, as shown in Table 2. The *p* value <0.05 was considered as significant for the comparison of the two groups.

Table I Comparison of means between Case Group I and Control Group II.

Variable	Group I	Group II	*p*-value
Total cholesterol (<5.2mmol/l)	4.18±1.21	3.99±0.54	0.12
LDL-C (<3.2mmol/l)	2.52±1.06	2.31±0.56	0.06
HDL-C (>1.04mmol/l)	0.83±0.34	1.00±0.31	0.001***
VLDL-C (<0.78mmol/l)	0.71±0.31	0.59±0.15	0.001***
Triglyceride (0.4-1.6mmol/l)	1.66±0.86	1.22±0.33	0.001***
Apo B/Apo A	0.96±0.60	0.70±0.18	0.001***

Asterisk (*) added for the significant *p* value i.e. less than 0.05.

Asterisk (**) added for the significant *p* value i.e. less than 0.01.

Asterisk (***) added for the significant *p* value i.e. less than 0.001.

Table II: Comparison of Apo B/ Apo A ratio between Group I and Group II (Chi-Square)

		Ratio group		Total	*p* value
		< 0.7	> 0.7		
	case	81	123	204	0.01*
	control	68	28	96	0.01*
Total		149	151	300	

Asterisk (*) added for the significant *p* value i.e. less than 0.05.

Discussion

Present study (n=300) has revealed that Apo B/A has been proven a better marker in workup of estimation of CVD risk. Apo B/Apo A ratio for Group I was 0.96±0.60 while for Group II ratio was 0.70±0.18 *p*-value (0.01) which has shown a significant difference.

DengF. *et al.,*[14] done a similar study with atherosclerotic CVD going through percutaneous coronary intervention with coronary syndrome and divided them into acute or chronic group. The data showed similar results that Apo B/Apo A ratio was considerably high in ACS patients than that in CCS patients ($p<0.001$) and was greater in cases having plaques compared to without plaques. Thus, showing Apo B/ Apo A is more significant in acute disease which supports present study.

Similarly, LiuY. *et al.,*[15] used ApoB/Apo A ratio to assess coronary heart disease in diabetics. In their study, 2563 patients having ACS previously diagnosed as diabetics were counted in. It was observed that with higher incidents of acute myocardial infarction (AMI), the Apo B/Apo A was notably increased. They concluded that the Apo B/apo A ratio in patients with diabetes alongwith ACS is an autonomous predictor for complex lesions and impending AMI. This study also supports present study.

In another study,WangX. *et al*.,[16] evaluated the use of Apo B/Apo A ratio along with SYNTAX system, an angiographic technique to grade coronary artery lesions' complexity, for acute coronary syndrome. They concluded that the combining of Apo B/Apo A with SYNTAX scoring system should be the emphasis of clinician for early treatment and long-standing follow-up observation in medium and high-risk group. Thus, showing the impact of Apo B/Apo A ratio.

Similarly, significant differences between HDL, VLDL

and TG between Group I and II was found in present study which is in accordance with earlier studies. Whereas, total cholesterol and LDL-cholesterol, does not display any momentous difference between the two groups which are considered as hall-mark of atherogenesis which is in agreement with earlier studies.[17] Thus, giving us confidence in the significance of Apo B/Apo A ratio in our population.

Results of present study clearly shows that lipid profile does not significantly change in presence of CVD, while Apo B/Apo A ratio is suggestively greater in MI patients showing that this ratio should be used at earlier time to assess the risk of myocardial infarction. Thus, it can be assumed that Apo B/Apo A ratio can be utilized to assess cardiac risk in people with family history and/or people with higher chance of having an AMI.

According to extensive literature research to this day, no study is published to rule out the significance of Apo B/ Apo A ratio in comparison to lipid profile. Thus, it can be positively said that Apo B/ Apo A ratio proves to be better cardiac disease risk predictor than the conventionally used lipid profile.

Much research for utilization of this marker for other diseases which eventually lead to CVD is also being done. A study for evaluation of diabetes risk was done which showed ApoB/Apo A as an efficient marker.[18] Another study was done to determine ApoB/Apo A ratio significance in children and young adults with Type 1 diabetes mellitus for evaluation of metabolic risk and microvascular complications which showed that this ratio can be used for determine of metabolic risk and insulin resistance. Thus, depicting its role in other conditions which can ultimately raise the CVD risk.[19]

Conclusion

Our study showed that Apo B/Apo A ratio foresee the peril towards atherosclerosis beforehand the lipid profile. Lipid profile can sometimes be misleading to the impending cardiac risk. But Apo B/ Apo A ratio indicates the risk very early and is not affected by other related factors. Thus, concluding it to be more beneficial than the routine lipid profile.

Limitation of Study

In our study, single-center data was present and was done only in patients with cardiac events already recorded. In future, study in patients even before any cardiac event and only at risk can be added to understand its variability. Furthermore, multi-center data and cohort study can be done to improve the better prediction using this marker.

Recommendation

Longitudinal study should be done to evaluate the Apo B/Apo A levels in individuals at risk of ischemic heart disease to assess its response with the progress of disease.

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CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

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DATA SHARING STATMENT

The data that support the findings of this study are available from the corresponding author upon request.