Association of Apolipoprotein B and Triglyceride Levels with Coronary Artery Disease

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ABSTRACT

Objective: To find the association of Apolipoprotein B and triglycerides with coronary artery disease.

Study Design: Cross-sectional study.

Place and Duration of Study: Department of Chemical Pathology and Endocrinology, Armed Forces Institute of Pathology, Rawalpindi, in collaboration with HITEC Institute of Medical Sciences, Taxila Pakistan, from Mar 2019 to Mar 2020.

Methodology: Four hundred and forty-four individuals of either gender and 18-70 years were included in the study. According to CT angiography, participants were differentiated into those with coronary artery disease and without coronary artery disease. In addition, serum triglycerides were analysed by glycerol phosphate enzymatic endpoint method on ADVIA 1800R Clinical Chemistry Auto analyzer, and apolipoprotein B was analysed on BT1500 Clinical Chemistry analyzer.

Results: The sample population had 144(32.0%) females and 300(68.0%) males. 164(37.0%) patients had coronary artery disease. 120(27.0%) participants were between 35 and 45 years of age, and 96(22.0%) were between 56 and 65 years. 126(30.0%) patients had hypertension, 352(79.3%) had apolipoprotein B levels >130 mg/dl. Positive Pearson’s correlation was found between apolipoprotein B and triglycerides with coronary artery disease.

Conclusion: There is a strong association between apolipoprotein B and non-fasting triglyceride levels with coronary artery disease. The apolipoprotein B can be used as a routine biomarker for screening and treatment monitoring coronary artery disease along with other lipid profile parameters.

Keywords: Apolipoprotein B, Body Mass Index, Coronary Artery Disease, Hypertension, Risk factor, Triglycerides.


INTRODUCTION

Coronary artery disease (CAD) is the narrowing of the lumen of blood vessels of the heart due to gradual plaque formation leading to obstruction to blood flow to cardiac musculature. CAD is a major cause of death and disability in western civilization. Even though its mortality has slowly decreased over the last many years in western countries, it is still the cause of one-third of the deaths in adults over 35 years of age.1 CAD can be prevented, but lack of exercise, smoking and consumption of fatty foods are causing greater mortality due to CAD worldwide.2

It has been established for the past three decades that high total blood cholesterol, specifically LDL cholesterol (LDL-C), is a major risk factor leading to coronary artery disease (CAD).3 Smaller LDL-particle size is associated with triglyceride (TG) metabolism disorders, often leading to atherogenesis.4,5 However, many research studies have indicated that more efficient risk prediction can be achieved by measuring serum ApoB levels.6 Single best approach to provide precise measurement of the serum lipoprotein content is to measure the apolipoprotein B (Apo B) concentration, which provides a direct measurement of the concentration of particles that lead to atherogenic plaque formation,7 because both VLDL and LDL particle possess one molecule of apoB as well. Apolipoproteins are a vital functional and structural component of lipoproteins. As there is only one apoB molecule per lipoprotein particle, apoB corresponds to the combined number of VLDL, IDL, and LDL particles, thus giving the most accurate concentration of proatherogenic particles.8

Triglycerides are the fraction of lipids acquired from diet and synthesized in the body by the liver. Their plasma concentration is dependent on dietary intake.9 TGs are transported primarily in chylomicrons and LDL-C. In the past, many studies have been conducted that showed higher plasma TGs levels associated with a greater risk of CAD; however, the individual role of TGs still not clear as a causative factor in CAD.9,10 There is evidence in different studies suggesting that higher triglycerides are a marker of CAD risk.

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METHODOLOGY

It was a cross-sectional study conducted at the Armed Forces Institute of Pathology (AFIP) from March 2019 to March 2020. This study was conducted on 444 patients visiting AFIP for their laboratory investigation through convenient sampling. Ethical approval was obtained from the Institutional Review Board (IRB) of AFIP vide no FC-CHP18-5/READ-IRB/21/090. The sample size was calculated by the WHO sample size calculator with a 95% confidence level and a 5% margin of error, taking the disease prevalence of Coronary Artery Disease in the Islamabad Rawalpindi area as 6.2%.11

Inclusion Criteria: Individuals between the ages of 18-70 years, of either gender were included in the study. Participants were differentiated into those having CAD and without CAD based on history and CT angiography.

Exclusion Criteria: People with known co-morbid conditions like diabetes mellitus, chronic liver disease, chronic kidney disease and congestive cardiac failure were excluded from our study.

Serum triglyceride levels were analyzed (non-fasting state) on ADVIA 1800R Clinical Chemistry Random Access Auto analyzer using Glycerol-3-Phosphate Oxidase enzymatic endpoint method. Serum Apolipoprotein B was analyzed on BT1500 Clinical Chemistry Turbidometric Analyzer using the immuno-turbidimetry technique. Internal quality control was run before the analysis of samples.

All parameters were analyzed according to standard operating procedures. Informed consent was taken from study participants. TGs levels were stratified into three groups; 0.4-1.6 mmol/l were categorized as desirable, 1.7-2.2 mmol/l as borderline and 2.3-5.6 mmol/l as high risk for CAD. ApoB levels were categorized into two groups; <130 mg/dl and >130 mg/dl.12 Participants were categorized into three groups according to their BMI. BMI 18-25 was categorized as normal, BMI of 26-30 was categorized as overweight, and BMI >30 was categorized as obese. Statistical Package for Social Sciences (SPSS) version 20.0 was used for the data analysis. Descriptive data were analyzed and presented in the form of percentage graphs. The Chi-square test was carried out, and the *p*-value ≤0.05 was considered statistically significant. Pearson’s correlation was applied to determine the relationship between different variables of interest.

RESULTS

A total of 444 subjects participated in the study. The mean age was 50.6±16.6 years. Three hundred (68.0%) were males, and 144 (32.0%) were females. Out of 444 participants, 164 (36.9%) had CAD. In addition, 136 (31.0%) participants had hypertension. In the sample population majority of the participants belonged to two age groups 35-45 years, 120 (27.0%) and 56-65 years, 96 (22%) (Figure).

Eighty-eight out of 92 (98.5%) participants with Apolipoprotein B <130 mg/dl were found to have no CAD. Participants with >130 mg/dl of Apolipoprotein B had a greater proportion of CAD, which showed that deranged Apolipoprotein B significantly affects CAD. The *p*-value was significant, as shown in Table-I.

<table>
<thead>
<tr>
<th>Coronary Artery Disease</th>
<th>Apolipoprotein B n(%)</th>
<th><em>p</em>-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes (n=164)</td>
<td>&gt;130 mg/dl 76 (46.3)</td>
<td>88 (53.7)</td>
</tr>
<tr>
<td>No (n=280)</td>
<td>276 (98.5)</td>
<td>4 (1.5)</td>
</tr>
</tbody>
</table>

The relationship between CAD and Triglycerides levels was found to be equivocal. 220 out of 292 (75.4%) patients within the desirable range of Triglycerides level (0.4-1.6 mmol/l) were found to have no CAD. Participants with high-risk levels of TGs (2.3-5.6 mmol/l) had the highest number of CAD-positive cases, (64, 69.6%) (Table-II).

<table>
<thead>
<tr>
<th>Triglycerides (mmol/l)</th>
<th>Coronary Artery Disease n(%)</th>
<th><em>p</em>-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.4-1.6 (n=292)</td>
<td>72 (24.6)</td>
<td>220 (75.4)</td>
</tr>
<tr>
<td>1.7-2.2 (n=60)</td>
<td>28 (46.6)</td>
<td>32 (53.4)</td>
</tr>
<tr>
<td>2.3-5.6 (n=92)</td>
<td>64 (69.6)</td>
<td>28 (30.4)</td>
</tr>
</tbody>
</table>
Results showed that with increasing levels of triglycerides, susceptibility to CAD proportionally increased. 208(81.2%) individuals with normal BMI (18-25) were found to have no CAD. However, participants with BMI in the range of 26-30 showed a higher risk of having CAD 84(53.8%). While 100% of the patients with BMI>30 had CAD. The p-value of 0.001 was found to be significant, showing that with increasing BMI risk of CAD has proportionately increased. CAD and hypertension were also found to be significantly associated. 252(81.8%) of the patients without hypertension had no CAD. On the other hand, 108 (79.4%) participants with hypertension had CAD, which showed that hypertension significantly affects CAD (Table-III).

<table>
<thead>
<tr>
<th>Body Mass Index (kg/m²)</th>
<th>Coronary Artery Disease n(%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-25 (n=256)</td>
<td>Yes 48(18.8) No 208(81.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>26-30 (n=156)</td>
<td>Yes 84(53.8) No 72(46.2)</td>
<td></td>
</tr>
<tr>
<td>&gt;30 (n=32)</td>
<td>Yes 32(100.0) No 0(0.0)</td>
<td></td>
</tr>
</tbody>
</table>

A positive Pearson correlation was found between Apolipoprotein B and TGs with CAD with a p-value <0.001 (Table-IV).

<table>
<thead>
<tr>
<th>Apolipoprotein B</th>
<th>r value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triglycerides</td>
<td>-0.698</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Table-IV: Pearson’s Correlation between Apolipoprotein B and Triglycerides level with Coronary Artery Disease (n=444)

DISCUSSION

In our study, we aimed to establish the association of serum apolipo-protein B and triglyceride levels with coronary artery disease by comparing the serum concentration of these parameters in individuals with and without coronary artery disease. Furthermore, we intended to incorporate the use of serum apolipoprotein B and triglyceride levels as individual risk factors for the development of coronary artery disease rather than the need for a complete lipid profile for this purpose.

Our study showed a significant association of apolipoprotein B with CAD. Mean apo B levels of people with CAD were calculated to be 128.24 mg/dl, significantly higher than the mean apoB levels of participants without CAD (88.23 mg/dl). The mean triglyceride levels of participants with coronary artery disease were also higher (1.919 mmol/l) than those without CAD (1.233 mmol/l).

A similar study conducted by Nayyer et al. showed that Mean Apo-B levels of patients having diabetes with myocardial infarction were higher (68.3±42.23 ng/ml) as compared to patients having diabetes without myocardial infarction (49.97±33.880 ng/ml) with a p-value <0.001. Similarly, mean triglyceride levels were higher (301.4±55.1 mg/dL) in patients with diabetes with myocardial infarction than those without MI (137.7±84.7 mg/dL). A study conducted by Smith et al. explained that high levels of apoB are associated with hypertriglyceridemia, which may increase the LDL density and particle number, ultimately increasing the risk of cardiovascular disease development due to apoB.

A study conducted by Carr et al. showed that apoB has the advantage over LDL-C and non-HDL-C as a better marker for risk assessment of coronary artery disease due to the easy availability of standardized assays at a much lower cost than LDL-C and non-HDL-C. Furthermore, serum apoB measurement does not require a fasting sample and gives the precise cholesterol particle number making it a more accurate marker for CAD risk stratification.

Past studies indicated that LDL-C was a strong predictor of coronary artery disease (CAD) with close monitoring. LDL-C levels inaccurate measurement of atherogenic lipoproteins because very low-density lipoprotein (VLDL) remnants may also contribute to atherogenic plague formation leading to coronary artery disease. However, among most recent studies, apoB is considered a stronger predictor of CAD and more helpful in monitoring therapy. Our study results suggest that apoB as a particular lipoprotein measurement is strongly associated with the incidence of CAD. This indicates that plasma concentration of atherogenic lipoprotein in the form of apoB measurement may be more indicative of the development of atherosclerosis than the amount of cholesterol (quantified by LDL-C and non-HDL-C) that the lipoprotein particles transport into the arterial wall. In a study conducted by Chan et al. showed that apolipoprotein B is a better predictor of CAD than LDL cholesterol. Apolipoprotein B measurements are convenient, cost-effective, standardized and more accurate than those for LDL cholesterol. Measurement of apolipoprotein B...
should be routinely added to the routine lipid profile (cholesterol, triglycerides and high-density lipoprotein cholesterol) for correct risk ascertainment of coronary artery disease.\textsuperscript{20}

Measurement of apoB in plasma is almost equivalent to calculating the number of apoB containing lipoproteins released by the liver because there is analytically only one apoB molecule per hepatic lipid particle.\textsuperscript{21} Although the concentration of LDL cholesterol and triglycerides calculates the concentration of lipid substances carried in circulating lipoproteins, and they do not accurately detect the number of atherogenic lipoproteins.\textsuperscript{22}

**CONCLUSION**

There is a strong association between apolipoprotein B and non-fasting triglyceride levels with coronary artery disease. The apolipoprotein B can be used as a routine biomarker for screening and treatment monitoring of CAD and other lipid profile parameters.

**Conflict of Interest:** None.

**Author’s Contribution:**

Following authors have made substantial contributions to the manuscript as under:

HH: Study design, data analysis, critical review, drafting the manuscript, critical review, approval of the final version to be published.

ZH: Critical review, drafting the manuscript, approval of the final version to be published.

MA & AB: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

HJ & SJR: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

**REFERENCES**


