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Original Article

Biochemistry Section

# Role of Apo B and Apo A1 Levels in Relation to Conventional Lipid Profile in Patients of Ischaemic Heart Disease with or without Type II Diabetes Mellitus

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## ABSTRACT

**Introduction:** Ischaemic Heart Disease (IHD) or Coronary Artery Disease (CAD) is the most prevalent chronic disease and the main leading cause of death in the world, with more than half a million newly diagnosed IHD patients each year. Central to this are disorders of lipoprotein metabolism. Apolipoprotein B (Apo B) and Apolipoprotein A1 (Apo A1) are structural and functional components of lipoprotein particles that serve as transporters of cholesterol. Apo B and Apo A1 are among the emerging markers for Cardiovascular Diseases (CVD). Routine conventional lipid profile does not incorporate these markers.

**Aim:** To determine the level of Apo A1 and Apo B in patients of IHD with or without Type II Diabetes Mellitus (T2DM) and analyse the significance of these parameters over the conventional lipid profile.

**Materials and Methods:** The case-control study was conducted at Government Medical College, Bhavnagar, Gujarat, India from July 2013 to December 2013. The study consists of 100 participants including 50 having IHD only (Group I), 50 having IHD with T2DM (Group II) as study groups and 50 healthy individuals (Group III) as control. Various biochemical parameters including Apo B and Apo A1 were analysed and statistically evaluated to come to conclusion.

**Results:** The demographic details of the participants which shows no significant different in age and gender among groups I, II and III. Apo B and A1 were elevated in group I and II and were found highly significant (p-value <0.0001) as compared to the group III. There was positive correlation of serum Apo B levels with total cholesterol (r=0.495, p-value <0.0001), Low-Density Lipoproteins (LDL-C) (r=0.526, p-value <0.0001) and Apo A1 (r=0.685, p-value <0.0001) in group I and LDL-C (r=0.468, p-value=0.001) and Apo A1 (r=0.754, p-value <0.0001) in group II. Similarly, Apo A1 levels were positively correlated with Apo B (r=0.685, p<0.0001) in group I and LDL-C (r=0.305, p-value=0.031) and Apo B (r=0.754, p-value <0.0001) in group II.

**Conclusion:** As the Apo B and Apo A1 cover both atherogenic and antiatherogenic lipid parameters respectively, it can be used as a better predictor of development of IHD with and without T2DM in comparison to conventional parameters of lipid profile.


**Keywords:** Antiatherogenic compounds, Atherogenic compounds, Coronary artery disease, Cardiovascular diseases, Novel markers

## INTRODUCTION

The Ischemic Heart Disease (IHD) or Coronary Artery Disease (CAD) mainly occurs due to an inadequate supply of blood and oxygen to a portion of the myocardium which leads to imbalance between myocardial oxygen supply and demand [1]. In India, IHD has increased more than six-fold in the last five decades and has reached prevalence of 10% among persons in the 35-65 years age group in the last decade. Ischaemic heart disease is the most frequent cause of Cardiovascular Diseases (CVD) and is expected to account for 40% of all deaths by 2021 and has become a global problem with the increasing prevalence of obesity, metabolic syndrome and Diabetes Mellitus (DM) [2].

Coronary risk factors, which have been found to be related to dyslipidemia include obesity, smoking, DM, hypertension and physical inactivity [3]. Among the risk factors, DM and specifically, Type II Diabetes Mellitus (T2DM) have a distinctive association with IHD. Those with DM have two to four-fold higher risk of developing IHD than people without DM, and CVD accounts for an overwhelming 65-75% of deaths in people with DM [4].

An early assessment of IHD using valuable predictors can delay the onset of disease and improve the quality of life. In the pre-era, the estimation of serum lipids like cholesterol and triglycerides were used to assess the risk of IHD. But, with these parameters it is observed that there is inconsistency in the correlation between serum lipid profile and IHD, which has ultimately led to the development of better indicators. New data are accumulating in favour of measurement of non traditional lipid factors specially Apo B and Apo A1 as they are more informative to assess patients potentially at risk [5].

The structural and functional components of lipoprotein particles are Apo B and Apo A1 which serves as transporters of cholesterol. One molecule of Apo B is present in all Low, Intermediate and Very Low-Density Lipoproteins (LDL-C, IDL-C and VLDL-C, respectively) that helps in transfer of cholesterol and triglycerides from sites of production to tissues where they are utilised for various cellular purposes. On the other hand, Apo A1 which is major apolipoprotein associated with High Density Lipoprotein (HDL-C) plays an important role in the reverse cholesterol transport by transferring cholesterol from tissues back to the liver [6].

If we can define risk factors more accurately and timely, then primary prevention of CVD will be more cost effective and efficient. Assay of apolipoproteins are standardised, simple, inexpensive and can be performed with random blood sample.

Various reports suggest that raised Apo B concentrations and lower Apo A1 concentrations are positively correlated with IHD risk. Apolipoprotein biomarkers are promising as predictors for future cardiovascular events in IHD and Acute Coronary Syndrome (ACS) as their levels remains stable even in non fasting states compare to LDL-C [7].

The present study was designed to compare the novel markers Apo B and Apo A1 with conventional lipid profile parameters in IHD patients with or without T2DM.

## MATERIALS AND METHODS

The case-control study was conducted at Government Medical College, Bhavnagar, Gujarat, India for a duration of six months (July 2013 to December 2013). The approval for the study was taken from the Institutional Human Ethics Committee {Ref No.-IRB (HEC) 249/2012 Biochemistry no.10/2012}. Informed consent was taken from all the participants. The study consisted of 100 Acute Coronary Syndrome (ACS) cases admitted to intensive cardiac care units of hospital as study group (Group I and II) and 50 healthy individuals as control group (Group III) selected randomly having same demographics. All admitted study group participants had a history of chest pain with Electrocardiography (ECG) changes or raised Creatine Kinase-MB (CK-MB) as evidence of ACS.

**Inclusion and exclusion criteria:** Patient with age more than 30 years from both genders, with symptoms of IHD having ECG changes and elevated cardiac biomarkers were included in group I. In addition to this, patients diagnosed with T2DM for more than five years and taking oral hypoglycaemics were included in group II. Patients having history of chronic alcohol consumption, hepatobiliary disorders, hepatitis, congestive heart failure, stroke, transient ischaemia, intermittent claudication, Peripheral Vascular Disease (PVD), atrial fibrillation or patients with history carotid surgery, coronary artery bypass graft surgery, PTCA or patients on pacemaker, on insulin therapy and on lipid lowering agents were excluded from the study.

To find out the significance of Apo A1 and Apo B over conventional lipid profile parameters, subjects underwent the following investigations:

Serum Apo A1 and Apo B by Immunoturbidimetric method; Total cholesterol by Cholesterol Oxidase- Peroxidase method; Triglycerides by Glycerol Phosphate Oxidase- Phenol Amino Antipyrine method;

Serum LDL-C and HDL-C by Direct Enzymatic method; Glycated haemoglobin (HbA1c) by Immunoturbidimetric latex method and; Fasting Blood Sugar (FBS) levels by Glucose Oxidase Peroxidase method [8-10]. All parameters were measured by standardised test kits on fully automated biochemistry analyser (IL-650 by Instrumentation Laboratories, UK) at National Accreditation Board for Testing and Calibration Laboratories (NABL) accredited Clinical Biochemistry Laboratory, Sir T. Hospital, Bhavnagar. Internal Quality Control and External Quality Assessment Score (EQAS) were within normal range for all these parameters during study period.

## STATISTICAL ANALYSIS

In data analysis, comparison of all parameters between control and study groups was carried out by applying one-way Analysis of Variance (ANOVA) test. Collected data were slightly deviated from normal distribution. So we have used Post-hoc Analysis for obtaining the true difference between study groups. Pearson correlation coefficient was used to find out correlation of Apo A1and Apo B with conventional lipid profile parameters. Regression analysis was done. The p-value <0.05 was considered as statistically significant. All statistical analysis was done on Statistical Package for the Social Sciences (SPSS) version 23.0 (IBM, Chicago, IL, USA) software.

## RESULTS

[Table/Fig-1] shows demographic details of the participants which shows no significant different in age and gender among groups-I, II and III. [Table/Fig-2] shows significant statistical difference among groups-I, II and III with regards to the various biochemical parameters measured.

| Variables | | Group I (n=50) | Group II (n=50) | Group III (n=50) |
|---|---|---|---|---|
| Age (years) | Mean±SD | 51.4±9.39 | 52.96±9.26 | 48.92±9.23 |
| | Range | 32-75 | 37-70 | 32-68 |
| Gender | Male | 35 | 28 | 26 |
| | Female | 15 | 22 | 24 |

**[Table/Fig-1]:** Demographic details of study subjects.

| Parameters | Group I (n=50) | | Group II (n=50) | | Group III (n=50) | |
|---|---|---|---|---|---|---|
| | Mean±SD | Range | Mean±SD | Range | Mean±SD | Range |
| FBS (mg/dL) | 91.4± 8.98 | 64-110 | 170.96± 71.30 | 110-420 | 86.90± 6.46 | 74-99 |
| HbA1c (%) | 5.54± 0.39 | 4.6-6.3 | 7.29± 1.36 | 5.7-12.2 | 4.38± 0.52 | 3.8-5.7 |
| Total Cholesterol (mg/dL) | 174.2± 45.64 | 103-275 | 189.76± 55.12 | 99-447 | 159.52± 22.91 | 107-191 |
| Triglycerides (mg/dL) | 115.9± 57.85 | 52-359 | 125.20± 63.29 | 44-407 | 115.50± 33.89 | 58-186 |
| HDL-C (mg/dL) | 50.16± 11.60 | 27-77 | 50.82± 13.78 | 24-83 | 48.76± 11.09 | 32-78 |
| LDL-C (mg/dL) | 99.38± 33.05 | 51-185 | 115.36± 35.17 | 53-205 | 79.88± 19.87 | 47-119 |
| Apo A1 (mg/dL) | 109.22± 28.95 | 55-163 | 126.42± 36.75 | 65-240 | 138.14± 21.87 | 78-172 |
| Apo B (mg/dL) | 124.58± 37.34 | 59-234 | 136.26± 42.28 | 47-235 | 95.82± 20.31 | 53-138 |

**[Table/Fig-2]:** Descriptive data of biochemical parameters.
FBS: Fasting blood sugar; HbA1c: Glycated haemoglobin; LDL-C: Low density lipoproteins; HDL-c: High density lipoprotein

The comparison of the various biochemical parameters between study groups (Groups-I and II) and control group (Group III) is shown in [Table/Fig-3,4]. Values of FBS, HbA1c, total cholesterol, LDL-C, Apo B and Apo A1 are statistically significant (p-value <0.05) in the patients compared to the controls.

| ANOVA | | | | | | | |
|---|---|---|---|---|---|---|---|
| No. | Parameter | | Sum of squares | df | Mean square | F | p-value |
| 1 | FBS | Between groups | 675.0 | 2 | 337.500 | 4.986 | 0.008 |
| | | Within groups | 9950.5 | 147 | 67.690 | | |
| 2 | HbA1c | Between groups | 214.564 | 2 | 107.282 | 141.149 | <0.001 |
| | | Within groups | 111.729 | 147 | 0.760 | | |
| 3 | Total cholesterol | Between groups | 22867.893 | 2 | 11433.947 | 6.076 | 0.003 |
| | | Within groups | 276637.600 | 147 | 1881.888 | | |
| 4 | Triglycerides | Between groups | 2988.813 | 2 | 1494.407 | 0.527 | 0.591 |
| | | Within groups | 416503.480 | 147 | 2833.357 | | |
| 5 | HDL-C | Between groups | 110.653 | 2 | 55.327 | 0.371 | 0.691 |
| | | Within groups | 21917.220 | 147 | 149.097 | | |
| 6 | LDL-C | Between groups | 31574.013 | 2 | 15787.007 | 17.391 | <0.001 |
| | | Within groups | 133440.580 | 147 | 907.759 | | |
| 7 | Apo A1 | Between groups | 21159.413 | 2 | 10579.707 | 11.902 | <0.001 |
| | | Within groups | 130664.780 | 147 | 888.876 | | |
| 8 | Apo B | Between groups | 43315.893 | 2 | 21657.947 | 18.081 | <0.001 |
| | | Within groups | 176079.180 | 147 | 1197.818 | | |

**[Table/Fig-3]:** Analysis of Variance between biochemical parameters of group I, II and III.
p-value <0.05 was considered as statistically significant; FBS: Fasting blood sugar; HbA1c: Glycated haemoglobin; LDL-C: Low density lipoproteins; HDL-c: High density lipoprotein

| Post-hoc | | | | | | |
|---|---|---|---|---|---|---|
| Groups | | Mean Difference (I-J) | Standard error | Sig. | 95% CI | |
| | | | | | Lower | Upper |
| **FBS** | | | | | | |
| Group III | Group I | -4.50000 | 1.64548 | 0.019 | -8.3960 | -0.6040 |
| | Group II | -4.50000 | 1.64548 | 0.019 | -8.3960 | -0.6040 |
| **HbA1c** | | | | | | |
| Group III | Group I | -1.16200 | 0.17436 | 0.001 | -1.5748 | -0.7492 |
| | Group II | -2.91000 | 0.17436 | 0.001 | -3.3228 | -2.4972 |
| **Total cholesterol** | | | | | | |
| Group III | Group I | -14.68000 | 8.67615 | 0.212 | -35.2225 | 5.8625 |
| | Group II | -30.24000 | 8.67615 | 0.002 | -50.7825 | -9.6975 |
| **Triglycerides** | | | | | | |
| Group III | Group I | -0.48000 | 10.64586 | 0.999 | -25.6861 | 24.7261 |
| | Group II | -9.70000 | 10.64586 | 0.634 | -34.9061 | 15.5061 |
| **HDL-C** | | | | | | |
| Group III | Group I | -1.40000 | 2.44210 | 0.835 | -7.1822 | 4.3822 |
| | Group II | -2.06000 | 2.44210 | 0.677 | -7.8422 | 3.7222 |
| **LDL-C** | | | | | | |
| Group III | Group I | -19.50000 | 6.02581 | 0.004 | -33.7673 | -5.2327 |
| | Group II | -35.48000 | 6.02581 | 0.001 | -49.7473 | -21.2127 |
| **Apo A1** | | | | | | |
| Group III | Group I | 28.92000 | 5.96280 | 0.001 | 14.8019 | 43.0381 |
| | Group II | 11.72000 | 5.96280 | 0.124 | -2.3981 | 25.8381 |
| **Apo B** | | | | | | |
| Group III | Group I | -28.76000 | 6.92190 | 0.001 | -45.1489 | -12.3711 |
| | Group II | -40.44000 | 6.92190 | 0.001 | -56.8289 | -24.0511 |

**[Table/Fig-4]:** Post-hoc Analysis of biochemical parameters of Group III.
p-value <0.05 was considered as statistically significant; FBS: Fasting blood sugar; HbA1c: Glycated haemoglobin; LDL-C: Low density lipoprotein; HDL-C: High density lipoprotein

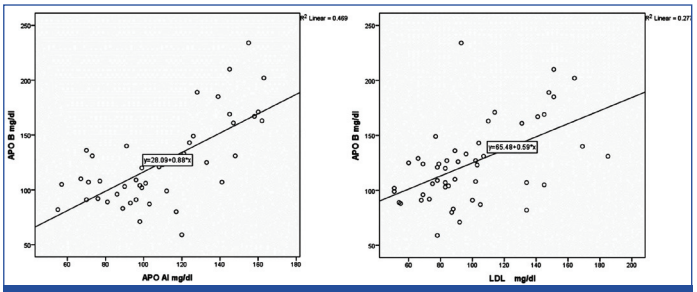
Serum Apo B levels were positively correlated with Total Cholesterol (r=0.495, p-value <0.0001), LDL-C (r=0.526, p-value <0.0001) and Apo A1 (r=0.685, p-value <0.0001) in Group I and LDL-C (r=0.468, p-value=0.001) and Apo A1 (r=0.754, p-value <0.0001) in Group II [Table/Fig-5]. Serum Apo A1 levels were positively correlated with Apo B (r=0.685, p-value <0.0001) in Group I and LDL-C (r=0.305, p-value=0.031) and Apo B (r=0.754, p-value <0.0001) in Group II [Table/Fig-6]. [Table/Fig-7,8] depicts the same.

| Parameter | Pearson's correlation (r) | $R^2$ Linear regression | Two tailed p-value |
|---|---|---|---|
| **Group I** | | | |
| FBS | 0.107 | 0.011 | 0.459 |
| HbA1c | -0.195 | 0.038 | 0.175 |
| Total Cholesterol | 0.495 | 0.245 | <0.001 |
| Triglycerides | 0.216 | 0.047 | 0.131 |
| HDL-C | 0.200 | 0.040 | 0.163 |
| LDL-C | 0.526 | 0.277 | <0.001 |
| Apo A1 | 0.685 | 0.469 | <0.001 |
| **Group II** | | | |
| FBS | -0.069 | 0.005 | 0.634 |
| HbA1c | -0.015 | 2.388 | 0.915 |
| Total cholesterol | 0.159 | 0.025 | 0.271 |
| Triglycerides | 0.044 | 0.002 | 0.764 |
| HDL-C | 0.106 | 0.011 | 0.463 |
| LDL-C | 0.468 | 0.219 | 0.001 |
| Apo A1 | 0.754 | 0.568 | <0.001 |

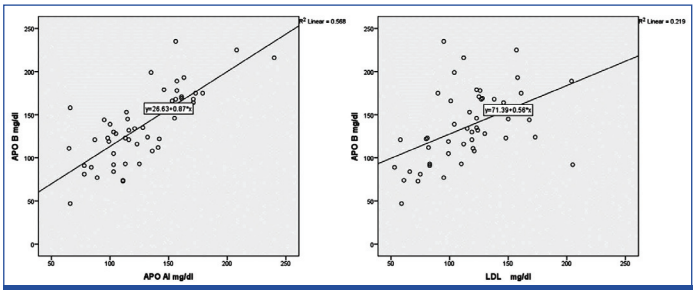
**[Table/Fig-5]:** Correlation between Apo B and other parameters.
p-value <0.05 was considered as statistically significant; FBS: Fasting blood sugar; HbA1c: Glycated haemoglobin; LDL-C: Low density lipoprotein; HDL-c: High density lipoprotein

| Parameter | Pearson's correlation (r) | $R^2$ Linear regression | Two tailed p-value |
|---|---|---|---|
| **Group I** | | | |
| FBS | -0.034 | 0.001 | 0.813 |
| HbA1c | -0.152 | 0.023 | 0.292 |
| Total cholesterol | 0.264 | 0.070 | 0.064 |
| Triglycerides | 0.079 | 0.006 | 0.587 |
| HDL-C | 0.199 | 0.040 | 0.166 |
| LDL-C | 0.176 | 0.031 | 0.221 |
| Apo B | 0.685 | 0.469 | <0.001 |
| **Group II** | | | |
| FBS | -0.017 | 2.899 | 0.907 |
| HbA1c | 0.004 | 1.79 | 0.977 |
| Total cholesterol | 0.124 | 0.015 | 0.390 |
| Triglycerides | -0.055 | 0.003 | 0.704 |
| HDL-C | 0.202 | 0.041 | 0.159 |
| LDL-C | 0.305 | 0.093 | 0.031 |
| Apo B | 0.754 | 0.568 | <0.001 |

**[Table/Fig-6]:** Correlation between serum Apo A1 and other parameters.
p-value <0.05 was considered as statistically significant; FBS: Fasting blood sugar; HbA1c: Glycated haemoglobin; LDL-C: Low density lipoprotein; HDL-c: High density lipoprotein




**[Table/Fig-7]:** Scatter Plot with Regression Line for Group I.
(Apo B vs Apo A1 and LDL-C)




**[Table/Fig-8]:** Scatter Plot with Regression Line for Group II.
((Apo B vs Apo A1 and LDL-C)

## DISCUSSION

The IHD is a condition which is caused by insufficient oxygen delivery to meet the metabolic demands of heart muscle. It can be caused by a failure to adequately perfuse cardiac myocytes with oxygenated blood (failure of supply) and/or to increase myocyte oxygen demand. Primary cause for this chain of events is considered to be atherosclerosis [11].

High incidence of IHD and increased cardiovascular mortality in patients with T2DM is mainly contributed by the occurrence of Hyperlipidemia [12]. From more than last three decades it has been recognised that a high level of Total Cholesterol and LDL-C are major risk factors for developing IHD, but there are many patients with IHD whose LDL-C and total cholesterol levels within the recommended range [13].

A new frontier of research is now focused to identify the novel risk factors, which promote and accelerate the atherosclerotic process and hence account for the high incidence of IHD amongst Indians. The roles of Apo B and Apo A1 as risk factors for coronary heart

disease have been the subject of concentrated investigations. As Apo B is present in LDL-C, IDL-C and VLDL-C particles, the plasma concentration of Apo B indicates the total number of potentially atherogenic particles which correlate with the non HDL cholesterol levels. The plasma concentration of Apo A1 is mainly associated with HDL-C, so its expression may be responsible for determining HDL-C plasma levels [14].

In current study, authors tried to find out role of novel markers Apo B and Apo A1 for predication of IHD in comparison of conventional lipid parameters. In the present study, mean LDL-C values were 99.38±33.05, 115.36±35.17 and 79.88±19.87 mg/dL in groups-I, II and III, respectively. In comparison to that, Apo B part of LDL-C was found to increase significantly in patients of IHD with or without T2DM (124.58±37.34, 136.26±42.28 and 95.82±20.31 mg/dL) in Groups-I, II and III, respectively. This indicates Apo B is better diagnostic marker than LDL-C which is in accordance to other studies [2,13,14]. We also observed significant decrease (p-value <0.001) in Apo A1 levels in IHD patients with or without T2DM in comparison of HDL-C which showed no significant change in both study and control groups [Table/Fig-2].

The present study generated similar results to study by Philip S et al., which showed that Apo B was significantly increased and Apo A1 was significantly decreased in patients of IHD with or without T2DM [2].

Pencina MJ et al., found that Apo B improves risk assessment of future CVD events over and beyond LDL-C or non HDL-C. In the present study, levels of Apo B and Apo A1 are significantly associated with prevalence of IHD [15]. Bodde M et al., found overall mean Apo B to be high and Apo A1 to be lower in study groups compared to control group. Similar mean value of Apo B and Apo A1 associating study group to higher risk were found in the present study [16].

The present study found similar results when compared to study by Mashayekhi N et al., which showed that Apo B was significantly elevated in patient of CAD with or without DM [17]. Review of various studies by Zhang P et al., showed that there was definite correlation of higher Apo B in patients of CVD having T2DM which collaborates with the present study findings [18].

### Limitation(s)

The patient group was small in the study. Authors suggested further prospective population based research in this path for finding the superior role of apolipoproteins in early and accurate prediction of IHD.

## CONCLUSION(S)

Authors suggested that finding risk factors more accurately and timely in IHD patients will lead to more cost effective and efficient treatment. The present study provides straight forward support to the hypothesis that Apo B and Apo A1 should be introduced into clinical practice for the assessment of CVD risk factors in comparison to conventional lipid parameters. To conclude, out of all the lipid parameters Apo B and Apo A1 were significantly increased in patients of IHD with or without T2DM. The present study is a pointer in the direction of utility of apolipoproteins as markers for risk assessment of CVD.

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**PLAGIARISM CHECKING METHODS:** [Jain H et al.]
- Plagiarism X-checker: Jun 24, 2021
- Manual Googling: Jul 13, 2021
- iThenticate Software: Aug 24, 2021 (17%)

**ETYMOLOGY:** Author Origin

**AUTHOR DECLARATION:**
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

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