

# Role of Apo-lipoprotein A1 as cardiac biomarker for severity of coronary atherosclerosis

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**Objective** Coronary heart 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 CAD patients each year. The development of atherosclerosis involves the interaction of multiple metabolic and cellular processes. Central to this are disorders of lipoprotein metabolism. Apolipoprotein A-I is the major protein component of high-density lipoprotein (HDL) in plasma. Chylomicrons secreted from the intestinal enterocyte also contain Apo A-I, but it is quickly transferred to HDL in the blood stream. The aim of this study is to determine if Apo-A1 can be used as indicator to severity and extent of CAD.

**Methods** This study was conducted in cardiac catheterisation unit at Al Hussein Medical city from November 2014 to September 2015. It included 76 patients (49 males and 27 females) who presented with signs and symptoms of CAD and have undergone angiography. Control group consisted of 20 healthy subjects (14 males and 6 females) matched for age and BMI. Serum levels of Apo-A1 were measured in both groups. After coronary angiography was done for all patients, the extent and severity of CAD was correlated with serum levels of Apo-A1. The extent of CAD was determined by angiography, according to number of coronary arteries involved and degree of narrowing in coronary artery diameter.

**Results** The angiographic finding in patient group was normal in 22 patients (28.9%), single vessel involvement in 15 patients (19.7%), two vessels disease in 15 patients (19.7%) and three vessels disease in 18 patients (23.8%). The left main stem disease (LMD) was found in 6 patients (7.9%). There was no significant difference in the serum level of Apo-A1 between patient with CAD and control group ( $P = 0.147$ ). There was no significant correlation between serum level of Apo-A1 and the extent CAD ( $r = 0.004$ ,  $P = 0.975$ ).

**Conclusion** There was no significant difference in serum level of Apo-A1 between the patients group and the control group. Also, there was no significant correlation between serum level of Apo-A1 and the extent of CAD.

**Keywords** coronary artery disease (CAD), Apolipoprotein A1, left main stem disease (LMD)

## Introduction

Globally, cardiovascular diseases (CVDs) which include coronary heart disease (CHD), strokes, rheumatic heart disease (RHD), cardiomyopathy and other heart diseases represent the leading cause to death.<sup>1</sup> CVDs refer to any disease which affects the cardiovascular system, especial CHD, vascular disease of brain, kidney and peripheral arterial disease.<sup>2</sup>

Beside endothelial dysfunction leading to inflammatory reaction, lipid metabolism disorders represent the second key event in the initiation and rapid development of atherogenesis.<sup>3</sup> The development of atherosclerosis involves the interaction of multiple metabolic and cellular processes.<sup>4</sup> Central to this are disorders of lipoprotein metabolism.<sup>5</sup> Apolipoprotein A-I is the major protein component of high-density lipoprotein (HDL) in plasma. Chylomicrons secreted from the intestinal enterocyte also contain Apo A-I, but it is quickly transferred to HDL in the bloodstream.<sup>6</sup>

There is considerable interest in the potential value of measuring circulating concentrations of apolipoproteins to assist in the assessment of the risk of CAD, as well as in their potential aetiological relevance to the disease.<sup>7</sup> Apolipoproteins are important components of lipoprotein particles, and there is accumulating evidence that the measurement of various forms of apolipoproteins may improve the prediction of the risk of CVD.<sup>8-10</sup>

There is abundant evidence that the risk of coronary atherosclerotic CVD is directly related to plasma lipid and apolipoprotein levels, but the relationships between the serum apoA-I levels and the extent of CAD have not been consistently shown. To investigate the possible relationship of the serum

levels of apoA-I, lipids and other lipoproteins with the severity of coronary lesions and number of vessels diseased, these parameters were examined in angiographically defined CAD patients and in a group of control subjects with no angiographical or clinical evidence of CAD.

Increased LDL-C concentration levels are a well-established risk factor for CAD and are currently recommended as the primary target for lipid-lowering therapy for the prevention and treatment of CVD, although its unique superiority over other circulating predictors of CAD is unclear.<sup>11</sup>

Our aim in this study is show if can use the serum level of apo-A1 as indicator to severity and extent of coronary atherosclerosis disease.

## Methods

This project was conducted at Department of Medicine (Angiographic Department) in Al Hussein Teaching Hospital / Holy Kerbala city-Iraq and in the Department of Biochemistry, College of Medicine, University of Kerbala from November 2014 to September 2015.

In this cross-sectional study, 76 patients (49 males and 27 females) were studied who had undergone angiography and were found to have CAD. Control group consisted of 20 healthy subjects (14 males and 6 females) matched for age and BMI. The demographic data, family history and results of the coronary angiography were obtained from patients' files and filled in specially designed data collection form.

The classification of atherosclerotic patient depended on the extent of CAD. There are 4 main coronary arteries: left main

coronary artery, left anterior descending artery (LAD), left circumflex (LCX) and right coronary arteries (RCA) were assessed. All patients underwent coronary angiography and the result collected from the catheterisation laboratory according to the patient's name and file number. The angiographic results concern the presence of significant (lesions more than or equal to 70% diameter stenosis for coronary arteries and more than or equal to 50% diameter stenosis for left main coronary artery by visual estimation)<sup>12</sup> coronary artery lesion and the numbers of arteries involved by a significant lesion and classified as follows:

- Normal (no significant lesion).
- LMS (left main stem) disease.
- One vessel involvement.
- Two vessels involvement.
- Three vessels involvement.

None of the patients had any contraindication for coronary angiography. The angiographic result subscribed by authorised interventional cardiologists at the Iraqi Center for Heart Diseases. Coronary angiography is performed under local anaesthesia. As the procedure was sterile, all potential access sites had to be disinfected, shaved and sterilised. The patient was asked to lie down in supine position on the cardioangiograph table at the beginning of the procedure, and prepared for the procedure in sterile conditions. Coronary angiography was performed with the patient in the fasting state.

Blood samples were collected after overnight fasting, about 5 ml venous blood was withdrawn and placed in plain tube and serum was separated after 15 min at room temperature by centrifugation at 300 rpm for 15 min.

The Apo-A1 measured by turbidimetric monoreagent for the quantitative determination of Apo-A1 wavelength: (Fig. 1)

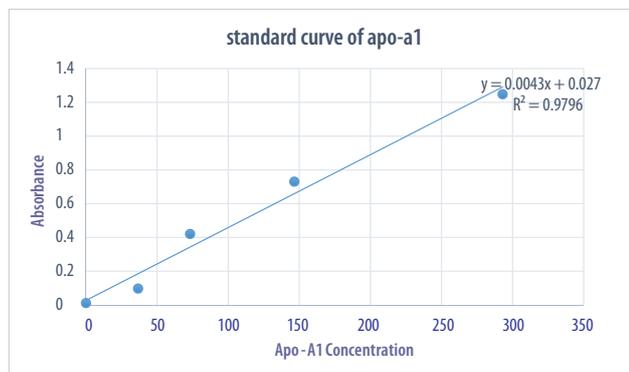


Fig. 1 Standard curve of apo-A1 obtained by spectrometer at 340 nm by EXEL program 2013.

Table 1. Angiographic findings of the studied group (n = 76)

Angiographic Findings	No.	%
Normal	22	28.95
One vessel	15	19.74
Two vessel	15	19.74
Three vessel	18	23.68
LMD	6	7.89
Total	76	100

340 nm, Hg 334/365 nm. The Apo-A1 concentration in the sample is calculated by interpolation of its absorbance (A) from the calibration curve. The result measured by turbidimetry with absorbance reading at 340 nm shown on the y axis against Apo-A1 and concentration shown on the x axis was obtained by Excel Program 2013.

## Results

There were 76 patients included in this study, with a mean age of  $57.76 \pm 9.69$  years (range 32–79 years), of which 49 patients were males (64.4%) and 27 patients were females (35.6%) and a control group of 20 healthy people with no significant disease (presence of disease was ruled out by history, physical examination and biochemical tests) with mean age of  $43.9 \pm 4.03$  years were selected.

Regarding the angiographic finding in patient group, it was normal in 22 patients (28.9%), single vessel involvement in 15 patients (19.7%), two vessels disease in 15 patients (19.7%) and three vessels disease in 18 patients (23.8%). LMD was found in 6 patients (7.9%), while the remaining 70 patients (92.1%) were free of LMD. These findings are shown in Table 1.

The Apo-A1 had non-significant differences between coronary atherosclerosis disease patient and control group ( $P = 0.147$ ). The lipid profile compared between coronary atherosclerosis disease patient and control group is shown in Table 2.

The coronary atherosclerosis disease patients had significantly higher S.TG ( $P = 0.007$ ) and significantly lower S.HDL ( $P = 0.0001$ ) levels compared with control people. Also there was significant difference in serum level of VLDL ( $P = 0.008$ ) between two groups.

Regarding other lipid, there are no significant difference in serum cholesterol and serum LDL-C between coronary atherosclerosis disease patients and control group. All mention above shows in Table 2.

Table 3 shows the correlations between extent of coronary atherosclerosis (angiographic finding), Apo-A1 and lipid profile in patients group.

No significant differences were observed between the serum levels of lipids or routinely measured lipoproteins A1 (Fig. 2). There was significant relation between LDL-C and the number of involved coronary artery vessels or the severity of coronary lesions ( $r = 0.264$ ) ( $P = 0.021$ ).

## Discussion

The prevention of coronary vessel disease has become one of the most important healthy challenges of recent times. Several

Table 2. Comparison between atherosclerotic patient and control group in the measured parameters

Variables	Control n = 20	Atherosclerotic Patient n = 76	P values
Apo_A1	167.89 $\pm$ 20.26	160.38 $\pm$ 40.10	NS
S. TC	171.70 $\pm$ 34.33	155.07 $\pm$ 42.46	NS
S.TG	137.65 $\pm$ 39.34	177.97 $\pm$ 70.29	0.007
S.HDL-C	43.20 $\pm$ 10.62	36.01 $\pm$ 6.45	0.0001
S.LDL-C	100.97 $\pm$ 34.21	83.45 $\pm$ 36.59	NS
S.VLDL-C	27.52 $\pm$ 7.86	35.48 $\pm$ 14.13	0.008
BMI	27.11 $\pm$ 1.83	28.99 $\pm$ 5.00	NS

Table 3. Correlations of Apo-A1 and lipid profile with coronary atherosclerosis disease severity

Parameters Correlated		Extent of CAD	Apo-A1	S.TC	S.TG	S.HDL-C	S.LDL-C
Apo-A 1	R	0.004					
	P	0.975					
S.TC	R	0.149	0.106				
	P	0.200	0.302				
S.TG	R	0.203-	0.113	0.484			
	P	0.078	0.274	0.0001			
S.HDL-C	R	0.077-	0.148	0.086	-0.066		
	P	0.506	0.150	0.407	0.522		
S.LDL-C	R	0.264	0.046	0.931	0.195	-0.098	
	P	0.021	0.653	0.0001	0.057	0.344	
S.VLDL-C	R	0.200-	0.117	0.487	0.997	-0.056	0.197
	P	0.083	0.256	0.0001	0.000	0.590	0.054

factors (modifiable and non-modifiable) such as HT, DM, smoking etc. are recognised as risk factors for coronary vessel disease and aggressive correction of these play vital role in coronary vessel disease prevention.

However, measuring Apo-A1 and Apo B/Apo-A1 ratio cannot be useful in laboratory tests. The findings of the current study indicated significant correlation between the LDL level and extent of coronary atherosclerosis disease. No significant correlation was observed between Apo-A1 and the severity of coronary atherosclerosis disease. The analysis of LDL showed that this variable increased with the number of vessels affected. Several studies agree that high levels of LDL are correlated with the presence and severity of coronary atherosclerosis disease<sup>13-15</sup> Korhonen et al.'s<sup>16</sup> study adds that high levels of LDL are associated with an increased risk of coronary atherosclerosis disease, and the more vessels obstructed, the higher the serum LDL level in the group, thus corroborating the findings of the present study.

The results of the present study are in agreement with the study conducted by Pischon et al. in Harvard University, demonstrating that serum Apo-A1 level is not associated with severity of coronary atherosclerosis disease.<sup>17</sup>

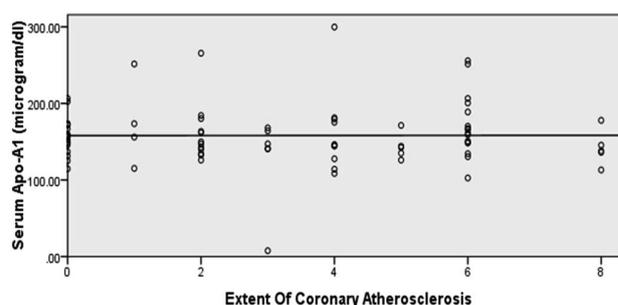


Fig. 2 Correlation between extent of CAD and level of Apo-A1.

Sabin et al. obtained similar results. They found that after adjusting the role of gender, age, smoking and hypertension, Apo-A level and Apo B/Apo-A ratio were independently correlated to peripheral atherosclerosis and brain stroke.<sup>18</sup> In a prospective study by Sweetnam et al., after adjusting the results for cardiovascular risk factors, regardless of plasma lipids, a strong correlation was found between the incidence of ischemic heart disease and low level of Apo-lipoprotein A1.<sup>19</sup>

The results of a study performed by Yazici et al. in Turkey revealed a significant correlation between the Apo-A serum level and cardiac troponins in the patients with angina pectoris. However, no significant relationship was found between the severity of coronary atherosclerosis disease and the number of diseased vessels.<sup>20</sup>

These results are in agreement with our study regarding the correlation between Apo-A1 and the severity of coronary atherosclerosis.

In a study by Habib et al., including 140 patients in Saudi Arabia, a significant correlation was observed between Apo-A1 and severity and extension of coronary arteries stenosis in the patients but not in the control group.<sup>21</sup> However, our study did not show any such result.

## Conclusion

We conclude that there is no difference in Apo-A1 level in patients with coronary atherosclerosis and in healthy people. Also, the level of Apo-A1 cannot be used as an indicator to determine the extent of CAD. ■

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