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Association between LDL, Apolipoprotein-B Apolipoprotein A-I and Lipoprotein(a) and Severity of Coronary Artery Disease Based on Coronary Angiography

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Abstract

Atherosclerosis is the most important contributor to increasing burden of coronary artery disease (CAD). Growing evidence suggests that the ratios of Apo B/Apo A-I and Lp(a) are better indexes for risk assessment of CAD. Elevated plasma levels of lipoprotein(a) in humans represent a major inherited risk factor for atherosclerosis. Thus, a study was performed to determine the association betwwen serum Apo B, Apo A-I, and lipoprotein(a) levels, and severity of CAD in patients with CAD confirmed on coronary angiography findings. An analytical case control study was carried out with 85 patients (58 males and 27 females) 40 - 60 years of age confirmed as having CAD on coronary angiography and 85 age and sex matched healthy volunteers as controls. Serum samples were analyzed for Apo A-1 LDL, Apo B, Apo A-I, and lipoprotein(a) concentration and the severity of CAD was assessed using coronary angiography scoring method. Patients with CAD had significantly high serum LDL-C, Apo B and Lp(a) levels compared to control subjects. However, serum Apo A-I level did not show a significant difference between two groups. Subjects with a positive family history of CAD with increased serum Lp(a) ≥ 17.3 mg/dL have high risk for development of CAD. Present study suggests that serum Lp(a) cut-off value of 17.3 mg/dL may be an important predictor in ruling out major vessel disease and luminal narrowing by atheroma.

Keywords

Coronary Artery Disease, Apo B, Apo A-I, LDL-C, Lp(a), Coronary Angiography Score

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1. Introduction

Atherosclerosis is the most important contributor to increasing burden of coronary artery disease (CAD). Although the precise mechanisms involved in the pathogenesis are not clear, it has been postulated that the reactive oxygen species (ROS) formation in vascular endothelial cells can promote conversion of low density lipoprotein cholesterol (LDL-C) to atherogenic oxidized LDL (oxLDL). This oxLDL and the subsequent generation of lipidperoxidase accelerate the development of atherosclerotic plaque [1] [2].

Several mechanisms by which high density lipoprotein (HDL) protects against development of CAD have now been identified. The reverse cholesterol transport (RCT) is one of the well established antiatherogenic functions of HDL. This cardioprotective effect of HDL is largely due to Apo A-I mediated cellular cholesterol efflux, Lecithinecholesterol acyl transferase (LCAT) mediated maturation of HDL particles and several antioxidative processes. Thus, the Apo A-I is the main structural protein of antiatherogenic lipoprotein which is more important than estimation of total HDL content for biochemical pathways that make HDL antiatherogenic. However, these studies did not address the crucial question of whether the Apo A-I levels predicted the severity of CAD which was independent of traditional lipid based variables [3].

The ratio of LDL/HDL cholesterol conventionally represents the balance of pro atherogenic and anti-atherogenic lipids. However, growing evidence supports the idea that the ratios of Apo B/Apo A-I and Lp(a) are better indexes for risk assessment of CAD [4]. Hence, the investigation the association of the above markers may have future benefits in management of patients with CAD in Sri Lanka

Epidemiologic studies have identified Lp(a) as a risk factor for atherosclerotic diseases such as coronary artery disease and cerebrovascular accidents. The structure of lipoprotein(a) is similar to plasminogen and tPA (tissue plasminogen activator) and it competes with plasminogen for its binding site, leading to reduced fibrinolysis. Also, because Lp(a) stimulates secretion of PAI-1, it leads to thrombogenesis. Lp(a) also carries cholesterol and thus contributes to atherosclerosis [4]. In addition, Lp(a) transports the more atherogenic pro inflammatory oxidized phospolipids which attract inflammatory cells to vessel walls, and leads to smooth muscle cell proliferation. Few studies have shown that the Apo B/Apo A-I ratio, Apo B and Lp(a) are independent risk factors for CAD and are superior to any of the cholesterol ratios. Elevated plasma levels of Lp(a) in humans represent a major inherited risk factor for atherosclerosis. Lp(a) consists of a LDL-like particle with an additional glycoprotein, apolipoprotein(a) (apo(a)), linked to apolipoprotein B100 [5] [6].

The relationship between lipoprotein levels and the degree of coronary atherosclerosis is less consistent and depends on the method of assessment on patient. Sullivan *et al.* [7] has introduced an angiographic score to measure the extent of coronary atherosclerosis. This score has designed to reflect the proportion of the coronary endothelial surface area affected by atheroma. Although few studies have reported the association between apolipoprotein levels and the severity of CAD to our knowledge, these studies have only concentrated on the traditional stenosis or vessel score rather than the severity of atheroma quantified in best reflection of the atherosclerosis process. Therefore, this study was performed to determine the association between Apo B and Apo A-I and Lp(a) cholesterol levels and the severity of CAD based on three coronary angiography scoring systems viz. vessel, stenosis and extent score using coronary angiography reports and the compact disc recordings of angiograms.

2. Materials and Methods

2.1. Subjects

An analytical case control study was carried out with 85 patients (58 males and 27 females) 40 - 60 years of age confirmed as having CAD on coronary angiography findings at Cardiology Unit, National Hospital and Nawaloka Hospitals PLC, Colombo Sri Lanka during 2013 and 2014. Subjects with a history of cardiovascular, renal, hepatic disease, malignancy and on hypolipidemic therapy and oral anticoagulants that could interfere with the present study were excluded from the study. A total of 85 age and sex matched healthy volunteers who had normal exercise ECG and estimated Glomerular Filtration Rate (eGFR) more than 60 ml/min/1.73 m^2 attending a routine health screening program at Family Health Care Centre, University of Sri Jayewardenepura, Nugegoda, Sri Lanka were recruited as controls to compare the lipoprotein parameters with patients. The sample size of the study was calculated for a matched case control study with a power of 80%; ratio of cases to controls 1:1; exposure in controls 30%; expected odds ratio of 2.6 and an alpha error of 5%.

2.2. Collection of Samples and Biochemical Investigations

Blood samples (5 ml) were drawn after overnight fast (8 - 10 hrs) from antecubital vein, from both patients and controls. Clotted blood samples were centrifuged for 10 minutes at 3500 rpm to separate serum and stored at −20˚C pending analysis. LDL, Apo B, Apo A-I, and lipoprotein(a) activity was measured by using Biosystems S.A (Barcelona, Spain) assay kits on Konelab 20XT Clinical Chemistry Analyzer (Thermo, Finland).

Assay principle of LDL based on solubility of cholesterol from HDL, very low density lipoproteins (VLDL) and chylomicrons. The cholesterol esters are broken down by cholesterol esterase and cholesterol oxidase in a non-colour forming reaction. Then, solubilizes cholesterol from LDL in the sample and ultimately produces H_2O_2. The LDL cholesterol is then spectrophotometrically measured at 540 nm wavelength by using peroxidase [8].

Apo A-1 in the sample precipitates in the presence of imidazole buffer, sodium azide and Goat anti-human Apo A-1 antibodies. The light scattering of the antigen-antibody complexes is proportional to the Apo A-1 concentration and can be measured by turbidimetrically at 340 nm wavelength [9]. In the same way, Apo B in the sample precipitates in the presence of glycine buffer, sodium azide and Goat anti-human Apo B antibodies. The light scattering of the antigen-antibody complexes is proportional to the Apo B concentration and can be measured by turbidimetically at 340 nm wavelength [9].

The Lp(a) level measure by reaction gives an insoluble aggregate that causes turbidity in presence of glycine buffer, sodium azide and anti-human lipoprotein(a) antibodies. The degree of turbidity can be measured optically at 600 nm wavelength and it is proportional to the amount of Lp(a) in the sample.

2.3. Assessment of Severity of Coronary Artery Disease

Coronary angiography reports and the compact disc recordings of angiograms were independently reviewed by an interventional cardiologist, who was blinded to the patients' clinical and laboratory findings. Angiogram findings were then evaluated using three different score systems—vessel score, stenosis score, and extent score. The angiograms were scored according to a method described by Sullivan *et al.* in 1990 [7]. Identified coronary arteries were Main Left Coronary Artery, Left Anterior Descending Artery, Main Diagonal Branch, First Septal Perforator, Left Circumflex Artery, Obtuse Marginal and Posterolateral Vessels, Right Coronary Artery, Main Posterior Descending Branch. The scoring system is described below

2.3.1. Vessel Score

This was calculated as the number of vessels with a significant stenosis (70% or greater reduction in lumen diameter). Depending on the number of vessels involved, vessel score ranged from 0 to 3. The left main coronary artery stenosis was scored as single vessel disease.

2.3.2. Stenosis Score

The stenosis score was calculated by a modified Gensini score as described by Reardon *et al.* in 1985 [10] and Hamsten *et al.* in 1986 [11], which places emphasis on the severity of stenosis while including some measure of the extent of coronary artery disease. Briefly, the most severe stenosis in each eight coronary segments was graded according to severity, that is; a grade of 1 for 1% - 49% reduction in luminal diameter, 2 for 50% - 74%, 3 for 75% - 99% and 4 for total occlusion. The scores for each of the eight segments were added together to give a total score out of a theoretical maximum of 32.

2.3.3. Extent Score

The extent score was calculated according to the method described by Sullivan *et al.* in 1990 which indicates the proportional of the coronary artery tree involved by angiogrphycally detectable atheroma. The proportion of each vessel involved by atheroma, identified as luminal irregulartity was multiplied by a factor for each vessel: left main artery, 5; left anterior descending artery, 20; main diagonal branch, 10; first septal perforate, 5; left circumflex artery, 20; obtuse marginal and postero-lateral vessels,10; right coronary artery, 20; and main posterior descending branch,10. When the major lateral wall branch was a large obtuse marginal on intermediate vessels, this was given a factor of 20 and the left circumflex artery a factor of 10. When a vessel was occluded and the distal vessel not fully visualized by collateral flow, the proportion of vessel not visualized was given the mean extent score of the remaining vessels. The scores for each vessel or branch were added to give a total score

out of 100, being the percentage of the coronary intimal surface area involved by atheroma.

2.3.4. Data Processing and Statistical Analysis

Reference intervals for LDL, Apo B, Apo A-I, and Lp(a) levels in control subjects were determined using 95% confidence intervals (Cl's). Owing to the skewed distribution of LDL, Apo B, Apo A-I, and Lipoprotein(a) levels, logarithmic transformations of these data were performed using SPSS software version 16.0 (Chicago, Illnois).

Continuous variables were analyzed using independent sample t test, Analysis of variance (ANOVA) and Spearman correlations were calculated to determine the correlation between the coronary angiogram scores and LDL, Apo B, Apo A-I, and Lp(a) levels. Furthermore, categorical variables were presented as absolute frequencies and percentages, whilst analyzed using chi square, Fisher's exact test, where appropriate. Multivariate logistic regression was performed and Odds Ratio was calculated to assess risk of CAD in population. A p value $\leq$ 0.05 was considered statistically significant. The accuracy of detecting the severity of CAD in patients using LDL, Apo B, Apo A-I, and lipoprotein(a) levels were determined by measuring the area under the Receiver Operating Characteristics (ROC) curve, 95% confidence interval, sensitivity, specificity and positive and negative predictive values and likelihood ratio based on the coronary angiography findings.

2.3.5. Ethical Consideration

Informed written consent from all participants was obtained prior to enrolment to the study. The study protocol was approved by the Ethics Review Committee of the Faculty of Medical Sciences, University of Sri Jayewardenepura, Nugegoda, Sri Lanka and the experiment was conducted in conformity with guideline of Helsinki declaration. An interview-administered questionnaire was made for all subjects recruited in the study. Informed written consent was obtained from all participants.

3. Results

3.1. Association between Apo B, Apo A-I and Lp(a) between Patients with CAD and Control Subjects

Lipid parameters of patients and controls are given in **Table 1**. These results indicate that except serum Apo A-I, other lipid parameters were significantly higher in patients than that of control subjects indicating that LDL, Apo B and Lp(a) appeared to as potential atherogenic markers of CAD.

3.2. Association between ApoB, Apo A-I and Lp(a) with CAD

Multivariate logistic regression analysis was performed to eliminate the influences of confounding factors for CAD. Among the risk factors assessed, patients with a family history of premature heart disease showed a significant association with CAD when compared to controls [OR 7.13 (95% CI 2.24 - 22.68), p = 0.001]. Furthermore, results also revealed that patients with CAD had significantly high serum Apo B [1.03 (95% CI 1.01 - 1.06) p = 0.006] and Lp(a) [1.02 (95% CI 0.98 - 1.07) p = 0.009] levels compared to control subjects. However, when considering the correlation coefficient values associated with vessel and stenosis scores, it was more evident that the Lp(a) would be the better indicator of assessing the severity of CAD in patients. Thus, the positive family history of CAD and increased serum Lp(a) levels appeared to be the most significant predictors for development of CAD (**Table 2**).

3.3. Assessment of the Severity of Coronary Artery Disease Based on Scoring System

Severity of coronary artery disease (CAD) was assessed by the vessels score, stenosis score, and extent score by perusing the coronary angiogram reports showed a mean vessel score of 1.67 out of a maximum of 3 (95% CI 1.46 - 1.87), which indicates that most of the patients in the study population had involvement of at least two out of the main three coronary vessels (**Table 3**).

The mean stenosis score of the patients was 8.09 out of a theoretical maximum of 32 (95% CI 6.87 - 9.30), indicating that more than one third of the collective vessel diameter of the segments studied was having significant stenosis 50.96% out of a theoretical maximum of 100% (95% CI 45.82 - 56.11). Thus overall, results indicate that the severity of CAD was higher in this study population (**Table 3**).

Table 1. Laboratory lipid parameter levels between Patients and controls.

	Mean	SD	Minimum	Maximum	p value*
Apolipoprotein A1 (mg/dl)					
Patients	110.6	20.8	71	181	0.962
Controls	110.8	18.3	79	169	
LDL (mg/dl)					
Patients	85.1	34.3	19.4	154.6	0.003**
Controls	68.0	25.0	25.6	129.1	
Apolipoprotein B (mg/dl)					
Patients	95.2	25.3	41.5	152.2	0.025**
Controls	74.7	23.0	37.8	143.7	
Lipoprotein(a) (mg/dl)					
Patients	23.8	12.7	10.4	64.3	0.001**
Controls	19.2	7.9	7.2	39.2	

*Independent sample t test comparing Patients and controls. **Significant at $p \leq 0.05$.

Table 2. Associations of risk for coronary artery disease in study population by multivariate logistic regression analysis.

Variable	Odds ratio	95% confidence interval		p value
Age (Years)#	1. 01	0.96	−1.06	0.526
Gender	0.86	0.28	−2.58	0.790
Positive Family history of CAD	7.13	2.24	−22.68	0. 001*
Apo A1	0.988	0.96	−1.01	0.352
LDL	1. 00	0.98	−1.02	0.838
Apo B	1. 03	1. 01	−1.06	0. 006*
Lp(a)	1. 02	0.98	−1.07	0.009*

#Consider as continuous variable; *Significant at $p \leq 0.05$.

Table 3. Severity of CAD in patients group.

	Mean	SD	95% CI
Vessel score	1.67	0.76	1.46 - 1.87
Stenosis score	8.09	4.51	6.87 - 9.30
Extent score	50.96	19.39	45.82 - 56.11

The frequency distribution of three severity scoring systems in patients with CAD is given in **Table 4**. According to subgroups of scoring systems, almost 43% of patients had single vessel disease in vessel score. Stenosis score and extent score were classified as mild, moderate and severe disease using scoring ranges. Therefore in stenosis score 52% patients had mild disease (1 - 7) and in extent score 47% had severe disease (≥50%).

3.4. Interpretation of ROC Curves with Respect to Concentrations of Apo B, Apo A-I and Lp(a) Based on Vessel, Stenosis and Extent Score

The diagnostic accuracy of lipoproteins for CAD based was determined by measuring the area under the ROC

Table 4. Frequency distributions of the three severity-score systems in patients with CAD.

		Patients (n)	%
Vessel score	Single vessel disease	37	43
	Double vessel disease	27	32
	Triple vessel disease	21	25
Stenosis score	(1 - 7) Mild	44	52
	(8 - 15) Moderate	23	27
	(16≤) Severe	18	21
Extent score	(≥25%) Mild	13	15
	(26% - 49%) Moderate	32	38
	(≥50%) Severe	40	47

curve (AUC), 95% confidence interval, sensitivity (SE%), specificity (SP%), positive predictive value (PP%), negative predictive values (NP%), Positive likelihood ratio (PLR) and negative likelihood ratio (NLR) (**Table 5**).

According to ROC given in vessel score the AUCs for Lp(a) was 63.9% with a detectable cutoff values of 17.3 mg/dl keeping acceptable sensitivity (79%) and positive and negative predictive values of 57% and 65% suggesting that Lp(a) appeared to be an important predictive marker of ruling out CAD in the present study population (**Table 5**).

When considering the stenosis score the Lp(a) cut off value of 17.3 mg/dl showed a high sensitivity and negative predictive values (Se 71%, NPV 75%, AUC = 0.572) compared to other makers suggesting that the Lp(a) may have a value in ruling out major vessel disease and luminal narrowing by atheroma (**Table 5**).

However, Lp(a) has shown a moderate but significant sensitivity and negative predictive values of 70% and 55% respectively (AUC 0.504) with a moderate accuracy for predicting severity of CAD for extent score compared to stenosis score (**Table 5**). Thus, when considering severity of CAD, the Lp(a) cut off value of 17.3 mg/dL may be an important predictor in ruling out major vessel disease and luminal narrowing by atheroma.

4. Discussion

The traditional risk factors like hypertension, dyslipidemia, diabetes mellitus, obesity, smoking, family history of heart disease etc. have been long recognized as the major risk factors for development of CAD [12] [13]. However, according to the distribution of risk factors of our study population, the family history of heart disease was the most significant risk factor associated with CAD (odd ratio of 7.13) compared to age and gender. In addition, the elevated serum levels of Apo B and Lp(a) in patients seem to be act synergistically with the standard risk factors of the development of CAD [13] [14] suggesting that these parameters in our study population may exacerbate the onset and severity of CAD.

The atherogenic dyslipidemic profile appears to accelerate the progression of atherosclerosis. Thus, measurement of different forms of apolipoprotein may improve cardiovascular risk prediction [15] [16]. Among these risk factors Apo A-I has been reported to be better predictor of cardiovascular events than non HDL cholesterol and HDL cholesterol, even in subjects taking lipid modifying therapy [17]. Although several study reports the association between dyslipidemia and cardiovascular events, their association with coronary atherosclerotic burden have shown variable results. Thus, these findings raise questions about the conventional risk assessment in patients.

Recently, several meta-analyses have provided evidence on the association between the atherogenic lipoproteins and the severity of CAD. However, these studies have reported inconsistent results due to differences in the methods of assessment of atherosclerosis burden [18] [19]. Majority of these studies have only concentrated the traditional stenosis or vessel score than the severity and extent of atheroma which quantifies in best reflection of the atherosclerosis process [7] [20]. The vessel score as described before in other studies is a traditional method of assessing the severity of ischemia compared to stenosis and extent scores. Therefore, we used a different angiographic scoring method to measure the extent of coronary atherosclerosis namely, the vessel, stenosis and the extent score [7] [10] [11]. Therefore we believe that this is the most recent study has made an attempt

Table 5. Receiver operating characteristic curves generated optimum cut-off values for coronary artery disease risk markers with severity of CAD scoring systems.

Cut-off values	(%) SE 95%CI	(%) SP 95%CI	(%) PPV 95%CI	(%) NPV 95%CI	PLR 95% CI	NLR 95% CI	AUC 95% CI	p value
Vessel score								
Apo A-1 112.5 (mg/dl)	64 44 - 81	55 35 - 74	58 40 - 76	62 41 - 80	1.43 0.8 - 2.4	0.65 0.4 - 1.2	0.370 0.223 - 0.517	0.092
LDL-C 73.2 (mg/dl)	72 51 - 87	31 15 - 51	50 34 - 66	53 28 - 77	1.04 0.7 - 1.4	0.92 0.4 - 2.05	0.555 0.403 - 0.707	0.478
Apo B 68.1 (mg/dl)	79 59 - 92	7 1 - 23	45 31 - 60	25 4 - 65	0.84 0.7 - 1.0	3.11 0.7 - 14.1	0.601 0.446 - 0.756	0.191
Lp (a) 17.3 (mg/dl)	75 55 - 89	45 26 - 64	57 40 - 73	65 41 - 85	1.36 0.9 - 2.0	0.56 0.3 - 1.2	0.639 0.494 - 0.784	0.071
ApoB/ApoA1 0.61	79 59 - 92	14 4 - 32	47 32 - 62	40 12 - 74	0.91 0.7 - 1.2	1.55 0.5 - 4.9	0.634 0.482 - 0.786	0.082
Stenosis score								0.153
Apo A-1 112.5 (mg/dl)	58 34 - 78	52 36 - 69	39 22 - 58	70 51 - 85	1.20 0.7 - 1.9	0.82 0.5 - 1.5	0.379 0.227 - 0.532	
LDL-C 73.2 (mg/dl)	71 44 - 90	30 17 - 47	30 17 - 47	71 44 - 90	1.01 0.7 - 1.4	0.98 0.4 - 2.4	0.494 0.315 - 0.674	0.944
Apo B 68.1 (mg/dl)	77 50 - 93	10 3 - 24	27 15 - 41	50 16 - 84	0.85 0.6 - 1.1	2.35 0.7 - 8.3	0.542 0.356 - 0.728	0.619
Lp (a) 17.3 (mg/dl)	71 44 - 90	38 23 - 54	32 18 - 50	75 51 - 91	1.13 0.8 - 1.7	0.78 0.3 - 1.8	0.572 0.395 - 0.749	0.393
ApoB/ApoA1 0.61	77 50 - 93	15 6 - 30	28 16 - 43	60 26 - 88	0.90 0.7 - 1.2	1.57 0.5 - 4.9	0.607 0.423 - 0.792	0.203
Extent score								
Apo A-1 112.5 (mg/dl)	60 41 - 77	52 32 - 71	58 39 - 75	54 33 - 73	1.25 0.8 - 2.0	0.77 0.4 - 1.4	0.393 0.243 - 0.544	0.167
LDL-C 73.2 (mg/dl)	67 47 - 83	26 11 - 46	50 34 - 66	41 19 - 67	0.90 0.6 - 1.3	1.29 0.6 - 2.90	0.487 0.293 - 0.597	0.867
Apo B 68.1 (mg/dl)	77 58 - 90	4 0.6 - 19	47 33 - 62	13 2 - 53	0.80 0.6 - 1.0	6.3 0.8 - 47.9	0.445 0.293 - 0.597	0.477
Lp (a) 17.3 (mg/dl)	70 51 - 85	41 22 - 61	57 40 - 73	55 32 - 77	1.18 0.8 - 1.8	0.74 0.3 - 1.5	0.504 0.351 - 0.656	0.962
ApoB/ApoA1 0.61	77 58 - 90	11 3 - 29	49 34 - 64	30 7 - 65	0.86 0.7 - 1.1	2.10 0.6 - 7.32	0.491 0.337 - 0.646	0.911

SE—Sensitivity; SP—Specificity; PPV—Positive predictive value; NPV—Negative predictive value; PLR—Positive likelihood ratio; NLR—Negative likelihood ratio; AUC—Area under curve; CI—Confidence interval.

to investigate the association of lipoprotein parameters and the severity of CAD based on vessel, stenosis and extent score based on coronary angiography findings.

According to coronary angiography evaluation, it was observed that Lp(a) showed a best cutoff value of 17.3 mg/dL with significant AUC (0.69) and sensitivity and negative predictive value of 75% and 65% respectively, with the vessel score compared to LDL, Apo B, Apo A-I and even with the Apo B/Apo A-I ratio. In addition the Lp(a) also showed a high sensitivity (71%) and a negative predictive value (75%) with the stenosis score indicating that Lp(a) may have a clinical importance in ruling out major vessel disease and luminal narrowing by coronary atherosclerosis. However, when considering the extent score, Lp(a) showed a moderate accuracy with a sensitivity and negative predictive values of 70% and 55% respectively. As extent score quantify the proportion length of coronary endothelial surface area occluded by atherosclerosis, the extent score can be used as a strong and independent predictor for CAD. Thus, Lp(a) may have a moderate potential value in predicting the extent score. However, when considering the three coronary angiography scores, the serum Lp(a) cut-off value of 17.3 mg/dL has a potential in ruling out the severity of CAD. Thus, the serum Lp(a) may be an important

marker for screening patients with strong risk associated factors for CAD compared to LDL, Apo B and Apo A-I. Very few studies have reported cut-off values of Lp(a) established based on coronary angiography [18] [20]. These values show skewed distribution among different ethnic groups ranged from 20 - 32 mg/dl [18]-[21] suggesting that ethnic differences are considered to be a vital factor to produced heterogeneity. As our study has taken more precaution by assessing the severity of CAD using vessel, stenosis and extent scores, we believe that the cut-off value of 17.3 mg/dl would be more acceptable for subjects with a family history of premature heart disease.

5. Conclusion

Serum Lp(a) levels showed a significant association with the severity of CAD assessed by vessel, stenosis and extent scores which place emphasis on the number of coronary vessels involved and their luminal narrowing. Individuals possessing a cut-off value of ≥17.3 mg/dL for Lp(a) with positive family history of premature heart diseases appear to be more susceptible for CAD. However, more patient numbers need the past clinical database on prevalence of CAD. Thus, lager sample numbers may be needed as far as the cutoff values are concerned in predicting the accuracy for CAD.

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