ASSOCIATION OF LIPID FRACTIONS LEVELS WITH CARDIOVASCULAR DISEASE

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ABSTRACT

Objective: The aim of this study is to analyze the association of serum lipids and lipoproteins in patients with angina pectoris.

Methods: A total of 110 patients (60 males and 50 females) with angina pectoris aged (55±5) years and 80 healthy controls (43 males and 37 females) aged (45±4) years were enrolled in this case-control study from the clinic of Al Yarmouk Hospital. Serum lipids, lipoprotein(a) [Lp(a)], apolipoprotein-A1, and apolipoprotein-B levels were measured and studied.

Results: The results of this study showed that increased odds of angina pectoris were associated with increased serum levels of Lp(a) more than serum levels of apolipoprotein-B.

Conclusions: Analysis of Lp(a) may be an important determinant of cardiovascular disease diagnosis.

Keywords: Lipoprotein(a), Apolipoprotein-A1, Apolipoprotein-B, Angina pectoris.

INTRODUCTION

Cardiovascular diseases are the most common cause of death worldwide. These facts advocated the researchers to modify the strategies used for prediction, prevention, and treatment of cardiovascular diseases.

Inflammatory mechanisms play an important role in the pathogenesis and prognosis of atherosclerosis. Many atherogenic lipoproteins play a critical role in the proinflammatory reaction such as apolipoprotein B, oxidized low-density lipoprotein (LDL), and lipoprotein(a) [Lp(a)]. Whereas anti-atherogenic lipoproteins such as high-density lipoprotein and exert anti-inflammatory function [1].

LDL cholesterol (LDL-C) is one of the most common predictors of cardiovascular diseases, but many studies suggested that apolipoprotein-B (apo-B) and non-high-density lipoprotein cholesterol (non-HDL-C) may be more precisely predict the risk of cardiovascular disease [2].

Apo-B is present as a single molecule in low-, intermediate-, and very LDL, while apolipoprotein-A1 (apo-A1) is the major apolipoprotein associated with HDL. The ratio between the concentrations of apo-B and apo-A1 (apo-B/ apo-A1) may reflect the balance between the opposing processes of arterial internalization of cholesterol and the reverse transport of cholesterol back to the liver [3,4].

Lp(a) is composed of a LDL particle and a glycoprotein molecule known as apolipoprotein (a) [apo-(a)], which is structurally homologous to plasminogen (a) [5]. Therefore, Lp(a) has a tendency to exert both proatherogenic and prothrombotic effects (impaired fibrinolysis) in multiple stages of the atherosclerosis process, some of which are apo-(a) dependent other are related to the LDL component [6].

Lp(a) does not bind to the LDL - receptor, and accordingly, its level in circulation is not determined by the particle clearance but is determined by its synthesis [7,8].

The goal of this case-control study was to measure the association (odds ratio [OR]) and the percent changes in relation to biochemical variables in patients with stable angina, focusing on serum levels of lipids, and lipoproteins.

METHODS

A total of 110 patients (60 males and 50 females), with stable angina pectoris aged (55±5) years and 80 healthy controls (43 males and 37 females), aged (45±4) years were recruited from the clinic of Al Yarmouk hospital in Iraq. All participants evaluated through collecting medical histories and routine clinical laboratory tests. Exclusion criteria included patients with diabetes, liver disease, renal failure, and heart failure.

At fasting state, laboratory analyses of serum total cholesterol (TC), HDL-C, and triglycerides (TGs) levels measured using standard methods on automated analyzer.

LDL-C (mg/dl)=TC-[(TG/5)+HDL-C]

Non-HDL-C (mg/dl)=TC-HDL-C

Lp (a), apo-A1, apo-B, and C-reactive protein (CRP) levels measured using enzyme-linked immunosorbent assay.

All eligible participants provided written informed consent to partake in this study. The study protocol conforms to the ethical guidelines and approved by the Institution's Ethics Committee.

All numerical data gave as mean ± standard deviation with 95% confidence interval (CI). Comparisons of continuous variables were assessed by Student's t-test, p values of (0<0.05) were regarded to be statistically significant. All statistical analyses performed using Microsoft excel and SPSS version 18.0 for windows.
**RESULTS**

The demographic and biochemical data of the studied participants are listed in Table 1.

Notably, the mean serum levels of lipids and lipoproteins that included TC, TG, LDL-C, non-HDL-C, apo-B and Lp(a) were considerably higher in patients with angina pectoris than in control subjects. Conversely, the mean serum levels of HDL-C and apo-A1 were substantially lower in cases as compared with control subjects (Table 1).

In Fig. 1, the plotted bar graph of the percent changes in lipids fractions and lipoproteins for patients with stable angina as related to healthy control showed high percent elevation in Lp(a) level and low percent elevation in apo-B level (+133.88 %, +9.32%), respectively. As well there was a high percent elevation noted in CRP level (+167.5%) which is an inflammatory biomarker.

The association or correlation between the presence of angina and the increased levels of most interested lipids and lipoproteins more than normal levels were estimated using OR as shown in Table 2, in which high significant positive correlation was found between the selected variables and the presence of angina.

Moreover, the odds of increased level of Lp(a) was 2.2 times among cases than control (OR=2.2; 95% CI=1.53-3.22, p<0.001), while the odds of increased level of apo-B was 1.87 times among cases than control (OR=1.87; 95% CI=1.16-2.36, p<0.001).

**DISCUSSION**

Low-density lipoprotein-cholesterol is a well-known risk factor for cardiovascular diseases, physicians in worldwide direct first-line of treatment toward lowering LDL-C.

Table 1: The demographic and clinical data of the studied participants

| Variables          | Control   | Angina pectorispaints |
|--------------------|-----------|-----------------------|
| Number             | 80        | 110                   |
| Gender (male/Female)| 43/37     | 60/50                 |
| Age (year)         | 45±4      | 55±5                  |
| CRP (mg/L)         | 1.54±1.03 | 4.12±1.15***          |
| TC (mmol/L)        | 3.77±0.525| 5.13±0.53***          |
| LDL-C (mmol/L)     | 1.92±3.04 | 2.91±2.52***          |
| HDL-C (mmol/L)     | 1.25±0.272| 0.92±0.33***          |
| TG (mmol/L)        | 1.53±0.21 | 2.33±0.278***         |
| Non-HDL-C (mg/dl)  | 2.46±0.321| 4.15±0.39***          |
| Apo-A1 (mg/dl)     | 155±10.3  | 143.7±15.5***         |
| Apo-B (mg/dl)      | 96.4±12.6 | 105.38±18.4***        |
| Lp(a) (mg/dl)      | 12.28±4.8 | 28.72±8.46***         |

Data are presented as mean±SD (standard deviation) for continuous variables, ***High significant difference p<0.001 versus control, mg/L: Milligram per liter, mg/dl: Milligram per deciliter, mmol/L: Millimole per liter, Number: Sample size of the participants, CRP: C-reactive protein, TC: Total cholesterol, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, Non-HDL-C: Non-high density lipoprotein cholesterol, TG: Triglyceride, Apo-A1: Apolipoprotein-A1, Apo-B: Apolipoprotein-B, Lp(a): Lipoprotein(a)

Table 2: Association between the presence of stable angina and the increased levels of lipids and lipoprotein

| Parameters          | OR (95% CI)   | p value |
|--------------------|---------------|---------|
| Apo-B              | 1.87          | (1.16-2.36) | *** |
| LDL-C              | 2.05          | (1.22-2.52) | *** |
| Non-HDL-C          | 2.12          | (1.4-2.87)  | *** |
| Lp(a)              | 2.2           | (1.53-3.22) | *** |

Sample size (n)=80 for control subjects, (n)=110 for angina pectoris patients, OR; Odds ratio, ***High significant correlation p<0.001, CI: Confidence interval, Apo-B: Apolipoprotein-B, LDL-C: Low-density lipoprotein cholesterol, Non-HDL-C: Non-high density lipoprotein cholesterol, Lp(a): Lipoprotein(a)

This study denoted that increased serum levels of non-HDL-C, LDL-C, apo-B, and Lp(a) were comparably and consistently associated with increased odds of angina attack, but the odds of increased level of Lp(a) were more than the odds of increased level of apo-B; this may lead to suggest that the level of Lp(a) may be more useful for diagnosis and prognosis of angina than apo-B level.

As well high percent of increased level of Lp(a) among other lipids and lipoprotein in patients with stable angina may confirm the above suggestion.

There were many controversial opinions focuses on the superiority of the measurement of LDL-C, non-HDL-C, apo-B and Lp(a) that are consistent with the results of this study or contrasted.

First, LDL cholesterol calculated using Friedewald’s formula’s that is accurate only when serum triglyceride levels lower than 400 mg/dl, so this equation is particularly inaccurate once the patients have triglycerides levels higher than 400 mg/dl or have type III hyperlipoproteinemia [11].

Second, non-HDL-C calculated to provide an estimate of cholesterol levels in the atherogenic particles including low-, intermediate-, and very LDL Arsenault et al., in 2009, suggested that non-HDL-C was associated with coronary heart disease risk independent of their plasma LDL-C levels [12].

Moreover, the National Cholesterol Education Program Adult Treatment Panel III guideline in 2001 mentioned that non-HDL-C is not a novel concept and recommended as a secondary target for patients with triglycerides levels >200 mg/dl, i.e., non-HDL-C is useful for estimating LDL-C atherosgenicity in patients with triglycerides levels outside of Friedewald’s formula’s range [13].

Third, the measurement of apo-B level in some study suggests being superior to non-HDL-C level and should be introduced into routine care [14], while others do not support routine measurement of apo-B [15].

Likewise, the Joint European Society of Cardiology/European Atherosclerosis Society guidelines on the management of dyslipidemias recommended the measurement of apo-B as a better index of adequacy of LDL-lowering therapy than measurement of LDL-C. If the measurements of apo-B are not available, the guidelines consider the use of non-HDL-C [16].

Fig. 1: Percent changes in lipids, lipoproteins, and C-reactive protein for patients with angina pectoris as compared with control subjects. Sample size (n)=80 for control subjects, (n)=110 for angina pectoris patients, HDL-C: High-density lipoprotein cholesterol, Non-HDL-C: Non-high density lipoprotein cholesterol, Apo-A1: Apolipoprotein-A1, Apo-B: Apolipoprotein-B, TC: Total cholesterol, TG: Triglyceride, LDL-C: Low density lipoprotein cholesterol, Lp(a): Lipoprotein(a), CRP: C-reactive protein.
Fourth, the elevated level of Lp(a) was strongly correlated with the degree of coronary atherosclerosis as suggested by Batalla et al. [17] and with the restenosis after revascularization as mentioned by Miyata et al. [18]. However, Skinner et al. not confirmed the prognostic value of Lp(a) levels in patients with coronary artery disease [19].

Moreover, the guideline’s of treatment toward lowering Lp(a) in patients with cardiovascular diseases may be controversial; some study revealed that the reduction of Lp(a) level using niacin treatment lack its efficacy for lowering vascular risk [20]. Another study mentioned the safety of lowering Lp(a) levels in patients with coronary heart disease using acetrapib, a cholesterol ester transfer protein inhibitor [21].

Another drug like statin [22] or plant like blend of Moringa oleifera could be used for lowering blood levels of cholesterol and triglyceride either by inhibiting the de novo synthesis or by inhibiting the intestinal absorption of cholesterol [23].

CONCLUSION

Among lipids and lipoproteins variables, although Non-HDL-C and LDL-C measurements provide a convenient, valuable, and clinically plausible end point but the measurement of Lp(a) is more accurate than others for the diagnosis and prognosis of atherosclerosis-related diseases.

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