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Alterations in biochemical parameters of hyperlipidemia in coronary artery disease patients

Siddiqua Jamall, Mohammad Ishaq and Kanwal Abbasi*
[1]Department of Biochemistry, University of Karachi, Karachi, Pakistan

Abstract: An interaction between modified lipoproteins, monocytes derived macrophages, T-cells and normal cellular elements of the arterial wall results in the formation of atherosclerotic plaque. High levels of serum lipids and lipoproteins are a major risk factor for atherosclerosis. In this study, lipid profiles of hyperlipidemic patients with coronary artery disease were determined. The mean values of plasma total lipids (861.18±126.29 mg/dL), triglyceride (221.26±110.05 mg/dL), total cholesterol (219.68±51.64 mg/dL) and LDL-cholesterol (134.3±41.70 mg/dL) were found to be significantly higher in hyperlipidemic patients as compared to normal individuals. In contrast, the plasma HDL-cholesterol was observed to be significantly reduced in the hyperlipidemic patients (37.5±9.37 mg/dL) as compared to normal individuals (51.3±7.9 mg/dL). Individuals with hyperlipidemia with increased LDL-cholesterol and reduced HDL-cholesterol are highly susceptible to atherosclerosis.

Keywords: HDL-cholesterol, LDL-cholesterol, Total lipids, lipoproteins, triglycerides, atherosclerosis, coronary artery disease
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***Author for Correspondence:** sidjam@hotmail.com

INTRODUCTION

Coronary artery disease (CAD) is characterized by atherosclerosis in the cardial coronary arteries. The plaques formed as a result of atherosclerosis progressively narrow the lumen of coronary artery and impair myocardial blood flow. The atherosclerotic plaques are formed due to the interactions between modified lipoproteins, monocytes derived macrophages, T-cells and normal cellular elements of the arterial wall[1-3]. High levels of total lipids and lipoproteins are considered as major risk factors for atherosclerosis[4,5]. Studies have shown a strong direct correlation between the total lipid and cholesterol levels and the development of ischemic heart disease[4,6-9]. The merit of lowering total cholesterol levels has been recognized for some years now, but to our best knowledge, the role of increasing high-density lipoprotein (HDL) values in patients at risk for cardiac disease has not received much attention. The protective features of HDL have been attributed primarily to its function of removing cholesterol from peripheral tissues and transferring it to the liver in a process known as reverse cholesterol transport (RCT), that results finally in the excretion of cholesterol in the bile[10,11]. Other attributed function of HDL is to impede the oxidation of LDL[12] since it is reported to inhibit the migration of monocytes through endothelial cells, thereby halting further oxidation of LDL and inflammatory reaction[13-15].

The apoAI–mediated delivery of cholesteryl esters from HDL to hepatocytes occurs through high affinity cell membrane scavenger receptors of class B member I (SR-BI)[16,17]. Despite detailed understanding of HDL and RCT, the mechanisms by which HDL and apoAI are atheroprotective remain complex and are not fully understood. Certain studies have indicated that circulating levels of HDL and apoAI, do not regulate RCT but rather it is regulated by cholesterol efflux from the peripheral tissues[18,19]. Homozygous deficiency of cholesteryl ester transferase protein in the plasma has been found to enhance HDL cholesterol delivery to the liver thereby decreasing the risk of CAD[20].

The significance of HDL-cholesterol becomes more clarified in clinical settings, where patients with low HDL receiving gemfibrozil treatment had shown a 6% increase in HDL and a 31% decrease in triglycerides without significant changes in LDL cholesterol levels when compared with patients given a placebo. Most significantly, coronary events were reduced by 22% in the gemfibrozil group[21].

Keeping in view the role of HDL-cholesterol, the present study was carried out to explore the relationship between low HDL concentrations and hyperlipidemia in coronary heart diseases.

MATERIALS AND METHODS

Collection of samples

The blood samples were collected from 50 patients of coronary artery disease and from 40 age and sex matched healthy individuals with their prior consent. The plasma was prepared and then stored at -20°C.

Estimation of total lipids, triglycerides, cholesterol, LDL-cholesterol and HDL-cholesterol.

Total lipids were estimated by colorimetric method using commercial kit (Randox Laboratories Ltd., UK). Triglycerides and Cholesterol were estimated by enzymatic colorimetric method using kits purchased from Randox Laboratories (Randox Laboratories Ltd., UK). Estimation of LDL-cholesterol was carried out by colorimetric method, while HDL-cholesterol was determined by

precipitation method using commercial kits (Randox Laboratories Ltd., UK).

Statistical analysis

The software Statistical Package for Social Sciences (SPSS) was used to perform the student's t –test. The values below 0.05 were considered as significant at the confidence interval of 95%.

RESULTS

Table 1 demonstrates that the mean values of plasma total lipids (861.18±126.29 mg/dL), triglyceride (221.26±110.05 mg/dL), total cholesterol (219.68±51.64 mg/dL) and LDL-cholesterol (134.3±41.70 mg/dL) were significantly higher in hyperlipidemic coronary artery disease patients as compared to normal individuals. Normal individuals had mean values of total lipids (666.2±80.2mg/dL), triglyceride (117.6±40.2mg/dL) and cholesterol (178±31mg/dL) and LDL-cholesterol (105.6±25.9 mg/dL). Significantly lower mean value of plasma HDL-cholesterol was found in hyperlipidemic patients (37.50±9.37 mg/dL) as compared to normal individuals (51.3±7.9 mg/dL) as shown in figure 1. Individuals with higher LDL-cholesterol and lower HDL-cholesterol are highly susceptible to atherosclerosis.

Table 1: Lipid profile of normal individuals and hyperlipidemic patients.

No	Parameters	Controls (n=40)	Hyperlipidemic Patients (n=50)
1	Total Lipids (mg/dL)	666.2 ± 80.2	861.18± 126.29
2	Triglycerides (mg/dL)	117.6 ± 40.2	221.26± 110.05
3	Cholesterol (mg/dL)	178 ± 31	219.68± 51.64
4	LDL-Cholesterol (mg/dL)	105.6±25.9	134.3± 41.70
5	HDL-Cholesterol (mg/dL)	51.3± 7.9	37.50± 9.37

Values are Mean±SD, (n) number of individuals is given in parenthesis, the normal individuals were compared with the hyperlipidemic patients, the significance of difference is indicated by p values calculated by independent t- test.

DISCUSSION

Lipids and lipoproteins studies have been done to correlate the positive relationship between total lipids, cholesterol, and low-density lipoproteins to high-density lipoproteins ratio and triglyceride to the risk of coronary heart diseases. Low HDL-cholesterol levels have been found to be a risk factor for CAD. The focus of treating hyperlipidemia has been on lowering LDL cholesterol levels. In this study the HDL-cholesterol levels in normal individuals and patients with hyperlipidemia were determined. The data showed a significant decrease in the values of HDL-cholesterol in hyperlipidemic patients as compared to normal individuals (37.5 ± 9.37 mg/dL and 51.3 ± 7.9 mg/dL) respectively. Thus, the measurement of total cholesterol alone is no longer considered adequate for screening. In addition, although a low HDL cholesterol level (< 40 mg/dL) is still considered a positive risk factor for CAD, a high HDL (> 60 mg/dL) is now considered a negative risk factor[22,23].

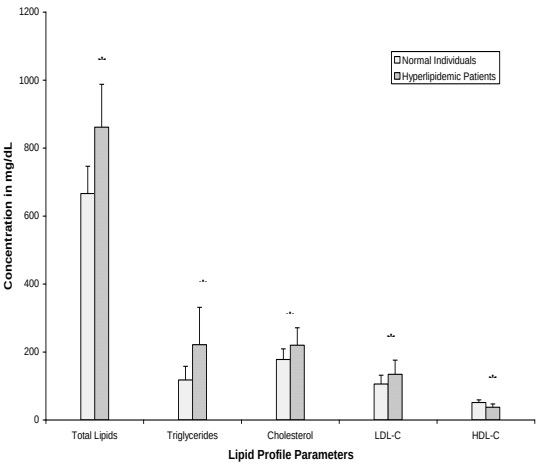

Figure 1: Comparison of lipid profile of normal individuals and hyperlipidemic patients**.** Values are Mean±SD of n=40 normal subjects and n=50 hyperlipidemic patients. The significance of difference is indicated by p values calculated by independent student's t- test. The ** denotes significance at p<0.01 and ***denotes significance at p<0.001.

Our studies concurred with previous studies which positively correlated low levels of HDL-cholesterol with incidence of CAD[22-23,24]. The PROCAM study concluded that the major risk is determined by the levels of plasma HDL-cholesterol and marked reduction in its concentration increases risk of CAD. Among the various risk groups, the highest incidence of CAD occurs in the subjects suffering from mild to moderate hypertriglyceridaemia in combination with a low level of HDL-cholesterol[22,23].

Epidemiological and intervention studies have also demonstrated the inverse relation between serum HDL and coronary artery disease[25]. Other studies established the therapeutic role of HDL after

raising its levels by treatment with Gemfibrozil[26]. Another study concluded that bezafibrate elevated HDL-C levels and lowered triglycerides, and also reduced the cardiovascular events[27]. In accordance with all these studies our results of the lipid profiles of subjects with high Total lipid, Triglyceride, Cholesterol and LDL –cholesterol and low level of HDL have a high risk for coronary artery disease.

REFERENCES

1. Ross R. Atherosclerosis: an inflammatory disease. *N. Engl. J. Med*., 1999; 340: 115–126.
2. Davies MJ. Stability and instability: two faces of coronary atherosclerosis. The Paul Dudley White Lecture 1995. *Circulation*,1996; 94: 2013–2020.
3. Fishbein MC and Siegel RJ. How big are coronary atherosclerotic plaques that rupture? *Circulation*, 1996; 94: 2662–2666.
4. Kannel W B, Castelli W P, Gordon T and McNamara P M. Serum cholesterol, lipoproteins, and the risk of coronary heart disease. The Framingham Study. *Ann. Intern. Med.*, 1971; 74: 1-12.
5. Schaefer JR, Hufnagel B, Maisch B and Krieglstein J. "Why is it always the heart which suffers from myocardial infarction?" The "Marburg hypothesis" of the pathogenesis of atherosclerosis. *Herz*, 2010; 35: 192-197.
6. Castelli WP, Garrison RJ, Wilson PW, Abbott RD, Kalousdian S and Kannel WB Incidence of coronary heart disease and lipoprotein cholesterol levels. The Framingham Study. *JAMA*., 1986; 256: 2835-2838.
7. Lu H, Zeng L, Liang B, Shu X and Xie D. High prevalence of coronary heart disease in type 2 diabetic patients with non-alcoholic fatty liver disease. *Arch. Med. Res*., 2009; 40: 571-575.
8. Natarajan P, Ray KK and Cannon CP. High-density lipoprotein and coronary heart disease: current and future therapies. *J. Am. Coll. Cardiol*., 2010; 55: 1283-1299.
9. Tsuneto A, Hida A, Sera N, Imaizumi M, Ichimaru S, Nakashima E, Seto S, Maemura K and Akahoshi M. Fatty liver incidence and predictive variables. *Hypertens. Res*., 2010; [Epub ahead of print].
10. Kwiterovich PO Jr. State-of-the-art update and review: clinical trials of lipid-lowering agents. *Am. J. Cardiol*., 1998; 82: 3U-17U; discussion 39U-41U.
11. Kwiterovich PO Jr. The antiatherogenic role of high-density lipoprotein cholesterol. *Am. J. Cardiol*., 1998; 82: 13Q-21Q.
12. Tall, AR. An overview of reverse cholesterol transport. *Eur. Heart. J*., 1998; 19: A31-35.
13. Toth PP. Should we target HDL cholesterol level in lowering cardiovascular risk? *Pol. Arch. Med. Wewn*., 2009; 119: 667-672.
14. Leite JO and Fernandez ML. Should we take high-density lipoprotein cholesterol levels at face value? *Am J Cardiovasc. Drugs*, 2010; 10: 1-3.
15. Yu BL, Wang SH, Peng DQ and Zhao SP. HDL and immunomodulation: an emerging role of HDL against atherosclerosis. *Immunol. Cell Biol.*, 2010; 88: 285-290.
16. Krieger M. The "best" of cholesterols, the "worst" of cholesterols: a tale of two receptors. *Proc. Natl. Acad. Sci., USA*. 1998; 95: 4077-4080.
17. Krieger M. Charting the fate of the "good cholesterol": Identification and characterization of the high-density lipoprotein receptor SR-BI. *Annu. Rev. Biochem*., 1999; 68: 523-558.
18. Jolley CD, Woollett LA, Turley SD and Dietschy JM. Centripetal cholesterol flux to the liver is dictated by events in the peripheral organs and not by the plasma high density lipoprotein or apolipoprotein A-I concentration. *J. Lipid Res*., 1998; 39: 2143-2149.
19. Brousseau ME, Eberhart GP, Dupuis J, Asztalos BF, Goldkamp AL, Schaefer EJ and Freeman MW. Cellular cholesterol efflux in heterozygotes for tangier disease is markedly reduced and correlates with high density lipoprotein cholesterol concentration and particle size. *J. Lipid Res*., 2000; 41: 1125-1135.
20. Zhong S, Sharp DS, Grove JS, Bruce C, Yano K, Curb JD and Tall AR. Increased coronary heart disease in Japanese-American men with mutation in the cholesteryl ester transfer protein gene despite increased HDL levels. *J. Clin. Invest.*, 1996; 97: 2917-2923.
21. Rubins HB, Robins SJ, Collins D, Fye CL, Anderson JW, Elam MB, Faas FH, Linares E, Schaefer EJ, Schectman G, Wilt TJ and Wittes J. Gemfibrozil for the secondary prevention of coronary heart disease in men with low levels of high-density lipoprotein cholesterol. Veterans Affairs High-Density Lipoprotein Cholesterol Intervention Trial Study Group. *N. Engl. J. Med*., 1999; 341: 410-418.
22. Assmann G, Schulte H and von Eckardstein A. Hypertriglyceridemia and elevated lipoprotein(a) are risk factors for major coronary events in middle-aged men. *Am. J. Cardiol.*, 1996; 77: 1179-1184.
23. Assmann G, Schulte H and Cullen P. New and classical risk factors--the Münster heart study (PROCAM). *Eur. J. Med. Res*., 1997; 2: 237-242.
24. Gordon DJ, Probstfield JL, Garrison RJ, Neaton JD, Castelli WP, Knoke JD, Jacobs DR Jr, Bangdiwala S and Tyroler HA. High-density lipoprotein cholesterol and cardiovascular disease. Four prospective American studies. *Circulation*, 1989; 79: 8-15.
25. Boden WE. High-density lipoprotein cholesterol as an independent risk factor in cardiovascular disease: assessing the data from Framingham to the Veterans Affairs High-Density Lipoprotein Intervention Trial. *Am. J. Cardiol*., 2000; 86: 19L-22L.
26. Manninen V, Tenkanen L, Koskinen P, Huttunen JK, Mänttäri M, Heinonen OP, and Frick MH. Joint effects of serum triglyceride and LDL cholesterol and HDL cholesterol concentrations on coronary heart disease risk in the Helsinki Heart Study. Implications for treatment. *Circulation*, 1992; 85: 37-45.
27. Tenenbaum A, Motro M, Fisman EZ, Tanne D, Boyko V and Behar S. Bezafibrate for the secondary prevention of myocardial infarction in patients with metabolic syndrome. *Arch. Intern. Med.*, 2005; 165: 1154-1160.