High Density Lipoprotein Cholesterol: A New Protective Function of Cardiac Structure and Function of Idiopathic Dilated Cardiomyopathy

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ABSTRACT:

BACKGROUND:

There is a suggestion that abnormal coronary physiology may be exist early in the course of idiopathic dilated cardiomyopathy (IDC), and is likely to play an important role in the pathogenesis and progression of the myopathic state in such patients. With regard to lipid profile, high-density lipoprotein cholesterol (HDL-C) particle enhances NO production and improves endothelium relaxation.

METHODS:

This study included 50 patients aged 19-72 years (13 females and 37 males) with IDC and 23 healthy controls aged 29 to 60 years (9 females and 14 males). Lipid profile, should be at least 12 hours fasting, including serum total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and triglyceride (TG) were evaluated in these two groups. Measurements of some of echocardiographic parameters including left ventricular (LV) systolic and diastolic diameters, and LV ejection fraction (LVEF) in IDC patients, and correlate its values with each one of the above lipid parameters in order to define the more predictor lipid parameter in evaluating the structure and function of the heart.

RESULTS:

The mean values of serum total cholesterol and LDL-C were insignificantly higher in patients with IDC patients than in controls. The mean of serum HDL-C was significantly low in IDC group against controls ($P< 0.001$). The mean (± SEM) serum triglyceride TG levels in patients with IDC was significantly increased when they were compared to that of normal controls ($P< 0.05$). An important inverse relation was observed between serum levels of HDL-cholesterol and LV diastolic diameter values ($r= - 0.29$, $P< 0.039$) as well as between HDL-cholesterol levels and LV systolic diameter values ($r= - 0.33$, $P< 0.02$). A borderline significant positive correlation between serum concentrations of HDL-cholesterol and the values of EF % was also shown in the IDC patients ($r= 0.28$, $P< 0.05$).

CONCLUSION:

The result of this study may point to the role of HDL-C in contribution to the LVdilatation and myocardial dysfunction (heart failure) in IDC.

KEY WORDS: Idiopathic dilated cardiomyopathy; lipid profile; HDL-C; Echocardiographic parameter.

INTRODUCTION:

Idiopathic dilated cardiomyopathy (IDC) is a disease of unknown cause that results in an enlarged heart that does not pumps properly [(1)]. It refers to congestive cardiac failure secondary to dilatation and systolic (and/or diastolic) dysfunction of the ventricles (predominantly left) in the absence of congenital, valvular, or coronary artery disease or any systemic disease known to cause myocardial dysfunction [(2)]. In 1998, Mathier and colleagues [(3)] Conducted their study on patients with IDC, and with normal coronary angiograms and no other Known causes of heart failure.

Their results confirmed both an impaired coronary microvascular vasodilator response and an epicardial vasoconstrictor response [(3)]. It has been observed that eighteen patients (82 %) of twenty-two consecutive patients with chronic stable IDC revealed both endothelial and myocardial cell damage. The observations also included an inverse statistically significant relationship between the myocardial damage and the magnitude of the coronary diameter changes [(4)]. Recently, it has been demonstrated that a significant impairment of myocardial perfusion at rest, hyperemic perfusion, and an impairment of perfusion reserve in patients with IDC [(5)]. High-density lipoprotein-cholesterol

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(HDL-C) is a heterogeneous class of lipoproteins with diverse functions and antiatherogenic effect [6]. HDL-C also exhibits numerous beneficial properties, including antioxidant, anti-inflammatory, and anti-thrombotic effects on the vasculature [7]. The anti-oxidant properties of HDL may be important in maintaining normal endothelial function [8]. HDL may influence endothelial function by antagonizing low-density lipoprotein-cholesterol (LDL-C) oxidation [9]. More recently, it has been reported that HDL-particle enhanced nitric oxide (NO), a major coronary endothelial vasodilator, production and improved endothelial dependent relaxation [10].

PATIENTS AND METHODS:

Fifty patients with IDC aged 47.22 ± 1.91 years as (mean ± SEM) (13 females and 37 males) were encountered at cardiology unit, Ibn-Albitar hospital-Baghdad. Diagnosis of IDC was based on the WHO/ ISFC criteria [11]. It was made when the echocardiogram showed a left ventricular ejection fraction (LVEF) of less than 50 % in the absence of angiographic coronary artery disease. Patients were excluded from study if they had a history of primary valvular disease, severe hypertension, heavy alcohol abuse or other known causes of dilated cardiomyopathy (DCM). Twenty-three healthy subjects aged 43.39 ± 1.84 years (9 females and 14 males) were included as control group. Clinical characteristics of patients and controls are seen in Table 1. Fasting total cholesterol, high density lipoprotein-cholesterol (HDL-C), low density lipoprotein-cholesterol (LDL-C), and triglyceride (TG) were measured in serum of all IDC patients and healthy controls. Total serum cholesterol concentration was determined according to the enzymatic colorimetric method of Allain et al. [12]. Serum HDL-C was assayed according to the enzymatic method of Demacker et al [13]. Serum LDL-C was estimated by using the Friedwald et al formula [14]. Serum TG was determined according to the enzymatic method of Bucolo and David [15]. Echocardiographic parameters including left ventricular end-diastolic diameter (LVEDD), septal thickness diastolic diameter (DD), LV end-systolic diameter (LVESD), septal thickness systolic diameter (SD) and LV ejection fraction (LVEF %) were measured in all IDC patients by consultant cardiologists in order to evaluate the structure and function of the heart. **Statistical Analysis:-** Statistical significance was assayed by ANOVA and student t-test. The linear regression test was applied for the correlation between different parameters and the significance of the r-values were checked using t-test. P-values of less than (0.05) were considered significant.

RESULTS:

The mean (± SEM) value of age of patients with IDC (47.22 ± 1.91 year) are comparable to the age of controls (43.39 ± 1.84 year). Table 2 revealed the mean (± SEM) value of the measured echocardiographic parameters including LVEF %, LVEDD, spetal thickness DD, LVESD and septal thickness SD in patients with IDC. Table 3 showed the results of lipid profile parameters in IDC and control groups. The mean (± SEM) values of the serum total cholesterol and serum LDL-cholesterol were insignificantly higher in IDC patients (4.37 ± 0.16 mmol/L; 3.19 ± 0.14 mmol/L, respectively) than in control group (4.29 ± 0.18 mmol/L; 3.06 ± 0.19 mmol/L, respectively), see figures 1 and 2. There was a significantly low serum mean (± SEM) HDL-cholesterol level in patients with IDC against controls (0.84 ± 0.03 mmol/L, 0.99 ± 0.03 mmol/L; $P < 0.001$, respectively, figure 3). The mean (± SEM) serum TG levels IDC patients (1.82 ± 0.14 mmol/L) was significantly increased when they are compared to that of the normal controls (1.25 ± 0.14, $P< 0.05$, figure (4) of the most important result of the present study in IDC group is the presence of a statistically significant inverse relation between serum levels of HDL-cholesterol and LV diastolic diameter values ($r= - 0.29$, $P< 0.039$) as well as between serum HDL-cholesterol concentrations and LV systolic diameter values ($r= - 0.33$, $P< 0.02$), see figures 5 and 6 respectively. In the same group (IDC) a borderline significant positive correlation between serum HDL-cholesterol levels and the ejection fraction (EF %) values ($r= 0.28$, $P < 0.050$) was also shown (figure 7).

Table (1) : Echocrdiographical data with Idiopahtic Dilated Cardiomyopathy.

	Idiopahtic Dilated Cardiomyopathy. (n=50)
LVEF(%)	34.46±1.17
LVEDD(mm)	68.27±1.29
Septal thickness DD(mm)	8.44±0.38
LVESD(mm)	55.61±1.38
Septal thickness SD (mm)	8.88±0.39

. Results expressed as mean (± SEM). . LVEF (left ventricular ejection fraction), LVEDD (left ventricular end-diastolic diameter), septal thickness DD (septal thickness diastolic diameter), septal thickness SD (septal thickness systolic diameter).

Table (2): Mean (± SEM) serum values of Total Cholesterol, LDL-Cholesterol, HDL-Cholesterol and Triglyceride in controls and patients with IDC.

	Total cholesterol(mmol/L)	LDL-C(mmol/L)	HDL-C(mmol/L)	TG(mmol/L)
Controls n = 23	4.29 ± 0.18	3.06 ± 0.19	0.99 ± 0.03	1.25 ± 0.14
IDC n = 50	a 4.37 ± 0.16	3.19 ± 0.14	B 0.84 ± 0.03	C 1.82 ± 0.14

a. ANOVA tests: No significant differences between controls and IDC group
.b. ANOVA tests between controls and IDC group: P< 0.001.
c. ANOVA test between controls and DC group: P< 0.05.

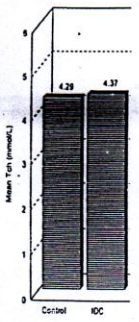

Figure (1)
Mean (± SEM) Serum Values of Total Cholesterol in Controls and Patients with IDC.

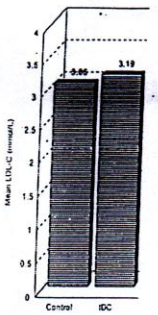

Figure (2)
Mean (± SEM) Values of Serum Low- Density Lipoprotein Cholesterol (LDL-C) in Control, IDC.

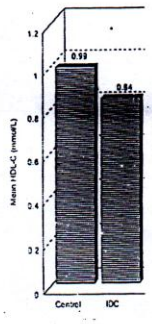

Figure (3)
Mean (±SEM) Serum Values of High – Density Lipoprotein – Cholesterol (HDL-C) in Controls and Patients with IDC.

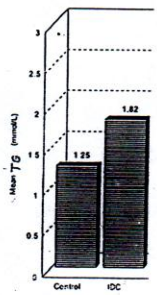

Figure (4)
Mean (± SEM) Serum Values of Triglyceride (TG) in Controls and Patients with IDC.

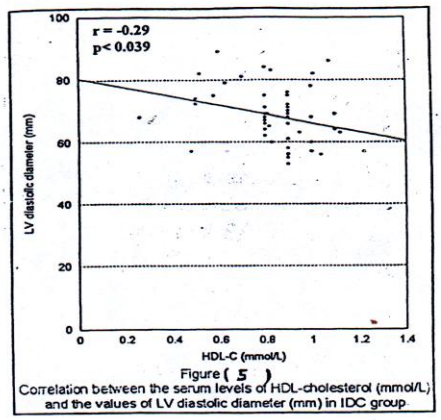

Figure (5)
Correlation between the serum levels of HDL-cholesterol (mmol/L) and the values of LV diastolic diameter (mm) in IDC group

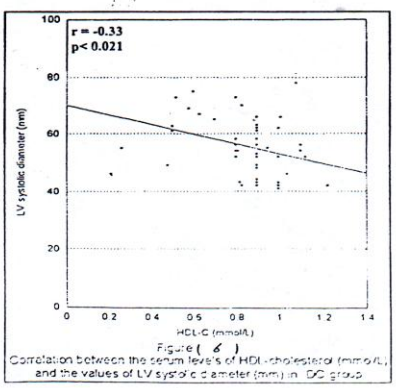

Figure (6)
Correlation between the serum levels of HDL-cholesterol (mmol/L) and the values of LV systolic diameter (mm) in IDC group

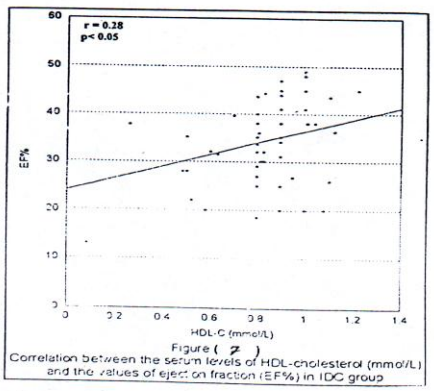

Figure (7)
Correlation between the serum levels of HDL-cholesterol (mmol/L) and the values of ejection fraction (EF%) in IDC group

DISCUSSION:

The results of serum total cholesterol and LDL-cholesterol in this study are consistent with those observed by Cooke et al(16) and Stolen et al (5) who have found no statistical differences between the serum total cholesterol and LDL-cholesterol levels of the IDC patients and that of the normal controls. Elevated serum LDL-cholesterol levels are causally related to ischemic heart disease (IHD) and reduction in these levels reduce the incidence of IHD and the associated mortality rate [17].

The finding of present study in relation to serum HDL-cholesterol is similar to that reported by Cooke et al [16] who showed that the mean HDL-cholesterol serum levels of patients with congestive heart failure (CHF) (n= 31) was significantly lower than that of eighteen normal subjects (0.86 ± 0.24 and 1.2 ± 0.31 mmol/L, respectively). HDL-cholesterol functions as an autonomous protective factor for the endothelium. It has been observed that HDL- induces activation of endothelial NO synthase, NO release, and vasorelaxatory effects [18, 19]. Interestingly, our study revealed an important relation between serum levels of HDL-cholesterol and echocardiographic parameters.

A statistically significant inverse correlation between serum HDL-cholesterol levels and the diameter values of both LV diastole (figure 5) and systole (figure 6) with a borderline significant direct correlation (figure 7) between HDL-cholesterol levels and EF % values were noted in IDC group. These latter observations may represent another recent function of HDL-cholesterol in preservation of cardiac structure and function. HDL may have a direct protective effect of the heart or may be mediated via the improvement of coronary endothelial cell. In 1998, Mathier and Coworkers (3) observed that preservation of coronary endothelial function is accompanied by subsequent improvement in LV ejection fraction in IDC patients. Spieker et al [20] deduced that intravenous HDL infusion rapidly normalizes endothelium-dependent vasodilation by increasing NO bioavailability. In conclusion, this study may point to the role of biochemical factor, HDL-cholesterol, in contribution to changes in heart structure and LV dysfunction in patients with IDC.

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