Correlation between Serum Nitric Oxide Levels and Lipid Profile in Several Types of Arterial Occlusion in Atherosclerosis Cardiovascular Patients

Ali Manhal Ibrahim[1*], Prof. Dr. Raid M.H. Al-Salih[2] and Prof. Dr. Adnan Taan[3]

1. Department of Chemistry, College of Sciences, University of Thi-Qar, Iraq. 2. Department of Chemistry, College of Sciences, University of Thi-Qar, Iraq. 3. College of Medicine, University of Thi-Qar, Iraq.
[2]raidstry@gmail.com
[3]adnan.t@utq.edu.iq
Correspondence author: Ali Manhal Ibrahim
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Abstract

Objective: Cardiovascular disease(CVD) or Heart atherosclerosis is a chronic disease of the arterial wall associated with inflammation and an imbalance in lipid metabolism, CVD increased with risk factors including high cholesterol, low-density lipoprotein (LDL) in the blood, low levels of high-density lipoprotein (HDL) in the blood, high blood pressure (hypertension), tobacco smoke, diabetes, Obesity, lifeless lifestyle, age - family history of heart disease is also a risk factor and uncontrollable factor. The study was designed to identify and compare lipid profile levels, NO in Atherosclerosis disease and healthy individuals.

Materials and Methods: Nitric Oxide levels and Blood lipid profile were determined in 114 CVD divided into [38 of single vessel disease] (SVD), [38 of (2 vessel disease)](2VD) and [38 of (3 vessel disease or complex)](3VD),and 114 healthy subjects, and comparing the concentration of (NO) with the rest of the biochemical parameters.

Results: Nitric Oxide and high-density lipoprotein(HDL) levels in the blood showed a significant decrease in CVD patients as compared to control group ($P \leq 0.05$).. while shown biochemical markers of blood lipid profile (serum TG, TCH, LDL, VLDL) were showing significant increase in CVD patients as compared to control group ($P \leq 0.05$), and the results indicate a significant decrease in the concentration of nitric oxide (NO) and HDL in (3 vessel disease or complex) (3VD) compared to (2 vessel disease)(2VD), which in turn less than (single vessel disease)(SVD) compared to the control groups. The results showed a significant increase in the levels of lipid profile (TG , TCH , LDL, VLDL) in (3VD) compared to (2VD), which in turn higher than (SVD).We also identified the correlation between (NO) and lipid profile and the results showed a negative correlation between (NO) and (TG,TCH.LDL.VLDL) .and positive correlation between (NO) and HDL.

Conclusion: In atherosclerosis, we find a significant reduction in levels of nitric oxide, and a significant rise in cholesterol levels, triglycerides, LDL and VLDL during atherosclerosis and significant decrease in HDL level. Especially when the type of occlusion increases (3VD), (2VD) and (SVD).

Keywords: Atherosclerosis Disease, Cardiovascular Disease (CVD), Nitric Oxide and Lipid Profile.

Introduction

Cardiovascular disease (CVD) and Heart Atherosclerosis is a chronic disease of the arterial wall associated with inflammation and an imbalance in lipid metabolism. Dysfunction of the endothelial layer results in the infiltration of LDL particles into the arterial wall, which in turn promotes infiltration of inflammatory cells and smooth muscle cell proliferation.[1,3].

Elevated low-density lipoprotein (LDL)-cholesterol (LDL-C) is a well known risk factor for atherosclerotic cardiovascular disease (ASCVD) [4-6]. and a person's chances of developing atherosclerosis increase with the number of risk factors they have - most risk factors can be controlled and atherosclerosis can be prevented or delayed - these include high Cholesterol(Total Cholesterol) and low-density lipoprotein (LDL) in the blood, low level of high-density lipoprotein (HDL) in the blood, Hypertension (high blood pressure), tobacco smoke, Diabetes Mellitus, Obesity, inactive lifestyle, age - a family history of heart disease is also a risk factor and the one which cannot be controlled [7, 8].

One prevalent hypothesis is that it is caused by damage to the endothelium .Healthy endothelium releases nitric oxide; Nitric oxide (NO) is a small gaseous signaling molecule that has important biological effects [9].

Nitric oxide (NO) is involved in several physiological functions, including vasodilation, neurotransmission and immune response [10,11]. NO is produced from the conversion of the amino acid L-arginine to L-citrulline by one of a family of enzymes, the nitric oxide synthases (NOS) [12]. Nitric oxide can both promote and inhibit lipid peroxidation. By itself, nitric oxide acts as a potent inhibitor of the lipid peroxidation chain reaction by scavenging propagatory lipid peroxyl radicals.

In addition, nitric oxide can also inhibit many potential initiators of lipid peroxidation, such as peroxidase enzymes.

However, in the presence of superoxide, nitric oxide forms peroxynitrite, a powerful oxidant capable of initiating lipid peroxidation and oxidizing lipid soluble antioxidants.[13,16].

Recent studies have shown that cholesterol-lowering therapy improves endothelium-dependent vasodilation in coronary[17,18] and systemic [19] arteries due to an increased bioavailability of nitric oxide (NO) [20], the most important endothelium derived vasodilating substance. Apart from vasodilating effects, NO has been found to be a principal factor involved in the antiatherosclerotic properties of the endothelium [21].

Material and Methods

This study conducted at AL-Nasiriyah Heart Center ,and AL-Rabea Hospital especially, Biochemistry Laboratory, the Hormones and immunes Laboratory and specialist clinics. It included (114) subjects, control (114).

A bout (5mL)of blood samples of Atherosclerosis patients and controls were taken and allowed to clot at room temperature in empty disposable tubes centrifuge to separate it in the centrifuge at 3000 rotor per minute (rpm)for 10min,the serum samples were separated and stored at (-30ºC) until analyzed Lipid Profile and Nitric Oxide (NO).

Serum cholesterol(TCH) was analyzed by enzymatic colorimetric method by UV/VIS spectrophotometer, kits supplied by Biolabo, France .Serum triglyceride (TG) was analyzed by enzymatic colorimetric method by UV/VIS spectrophotometer, kits supplied by Biolabo, France. Serum high density lipoprotein (HDL) was analyzed by enzymatic colorimetric method by UV/VIS spectrophotometer, kits supplied by Biolabo, France. Serum low density lipoprotein (LDL) is calculated through the following equation

LDL = Total Cholesterol - (HDL + VLDL) Serum very low density lipoprotein (VLDL) is calculated through the following equation: VLDL = Triglyceride/5 Serum Nitric Oxide (NO) was measured by using the colorimetric method recommended, The researcher's method (Dervisevic, A. et al., 2012)[22] was used to estimate the concentration of nitrogen oxide (NO).The results were expressed as mean ± standard deviations (mean ± SD). One way ANOVA-test was used to compare parameters in different studied groups. P-values ($P \leq 0.05$) were considered statistically significant.

Results

In this work, we identified the effect of CVD on body fat (TG) and (TCH), lipoprotein (HDL), (LDL), (VLDL) and we determined its effect on oxidation status through mensuration lipid peroxidation and its effect on concentrations of lipid peroxide (Nitric oxide) (NO).

The levels of biochemical markers of body fat (TCH, TG, LDL, VLDL) showed a significant increase in CVD patients compared to the control group, while HDL showed a significant decrease in CVD patients compared to the control group. And nitric oxide showed a significant decrease in CVD patients compared to the control group.

We also identified the effect of type of arterial occlusion (single vessel disease) (SVD), (2vessel disease) (2VD) and (3vessel disease or complex) (3VD) on those parameters biochemical, and the results indicate a significant decrease in the concentration of nitric oxide(NO) in (3VD) compared to (2VD), which in turn less than (SVD) compared to the control groups.

As shown a significant decrease in the concentration of HDL in (3VD) compared to (2VD and SVD).

The results showed a significant increase in the levels of lipid profile (TG, TCH, LDL, VLDL) in (3VD) compared to (2VD), which in turn higher than (SVD).

We also identified the correlation between (NO) and lipid profile and the results showed a negative correlation between (NO) and (TG, TCH.LDL.VLDL). and positive correlation between (NO) and HDL.

Table- 1: Serum Nitric Oxide(NO) concentrations in control with CVD

Groups	No.	NO concentration(µmol/mL)mean± SD
Control	**114**	7.52 ± 0.93^{a}
Patient	**114**	5.20 ± 1.21^{b}
Lsd		0.24

* Each value represents mean ± SD values with non-identical superscript (a,b or c…etc.) were considered significantly differences ($P \leq 0.05$).

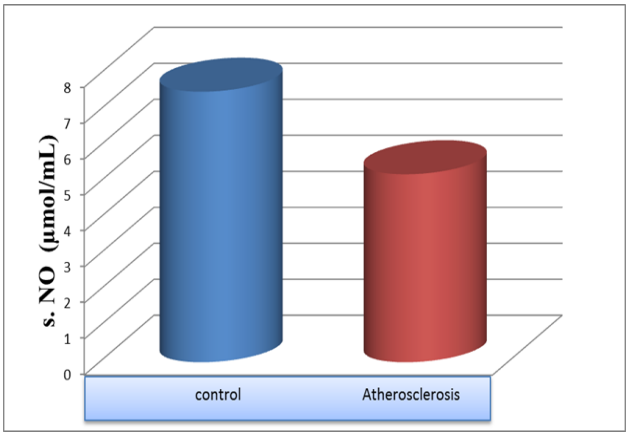

Figure- 1: Serum NO levels of control and CVD groups

Table- 2: Serum Lipid Profile concentrations of (control) and (Atherosclerosis patients) groups

Group	NO	T CH (mg/dL)	T G (mg/dL)	HDL (mg/dL)	LDL (mg/dL)	VLDL (mg/dL)
con	114	**162.28 ±46.97 b**	**105.45 ± 45.38 b**	**50.73± 7.54 a**	**97.20 ± 19.31 b**	**20.05 ± 5.08b**
AS	114	**252.57 ±57.98a**	**161.59 ± 39.47 a**	**35.25 ± 6.88 b**	**185.01 ±59.17a**	**32.32 ± 7.89a**
LSD		**11.55**	**9.04**	**1.58**	**9.60**	**1.46**

- Legend as in table (1)

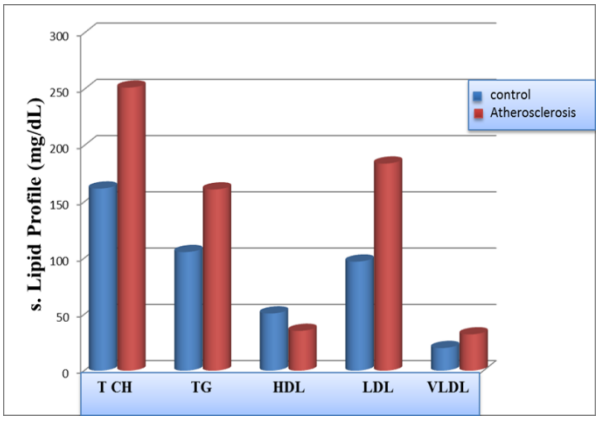

Figure - 2: Serum Lipid Profile levels of control and CVD group

Table -3: Serum NO concentrations in control And the type of vessel occlusion

Group	NO	NO concentration(g/dL) mean± SD
control	**38**	**7.57± 1.07 a**
1 vessel	**38**	**6.27± 0.98 b**
2 vessel	**38**	**5.20 ± 0.65 c**
3 vessel	**38**	**4.24 ± 0.95 d**
LSD	**38**	**0.24**

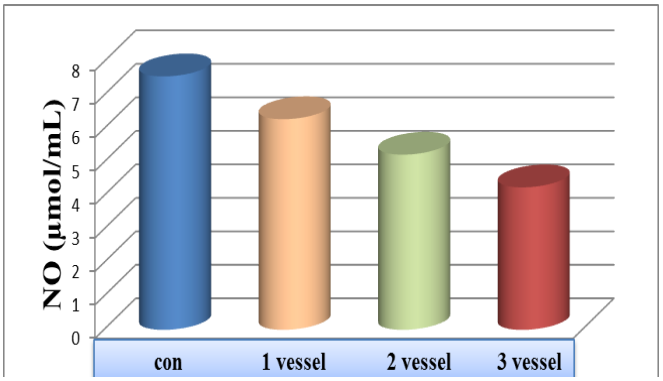

Figure- 3: Serum no levels of control And the type of vessel occlusion

Table- 4: Serum Lipid Profile concentrations of control And the type of vessel occlusion

Group	NO	T CH (mg/dL)	T G (mg/dL)	HDL (mg/dL)	LDL (mg/dL)	VLDL (mg/dL)
con	**38**	**161.56± 23.97 d**	**105.08 ±24.97 d**	**50.30 ± 6.51 a**	**90.25±18.69 d**	**21.02 ± 4.99 d**
1vessel	**38**	**209.71± 37.55 c**	**135.56 ±30.2 c**	**41.18 ±4.58 b**	**141.41± 28.18c**	**27.11 ± 6.05 c**
2vessel	**38**	**256.99 ±32.86b**	**160.44 ±36.78 b**	**34.82 ± 4.02 c**	**190.08± 23.1 b**	**32.09 ±7.28 b**
3vessel	**38**	**292.89± 38.83a**	**188.47 ±32.5 a**	**29.62 ± 6.29 d**	**225.57± 41.1 a**	**37.69 ±6.50 a**
LSD		**10.68**	**7.90**	**1.43**	**10.54**	**1.58**

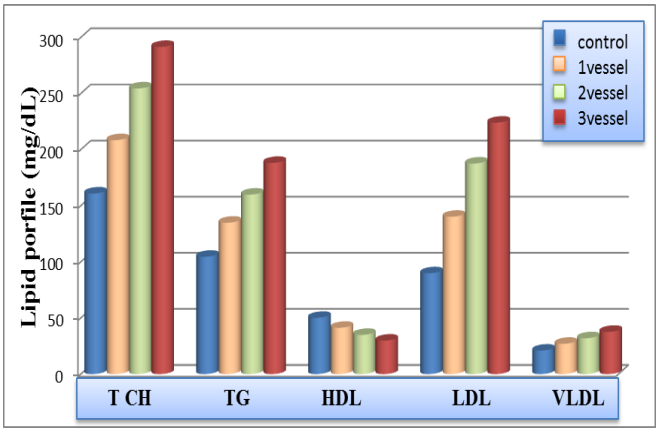

Figure -4: Serum Lipid Profile levels of And the type of vessel occlusion

There is a negative correlation between NO and T CH levels in each of 1 vessel (r = - 0.32), 2 vessel (r= - 0.31) and 3 vessel (r = - 0.33) as shown in Figure(5).

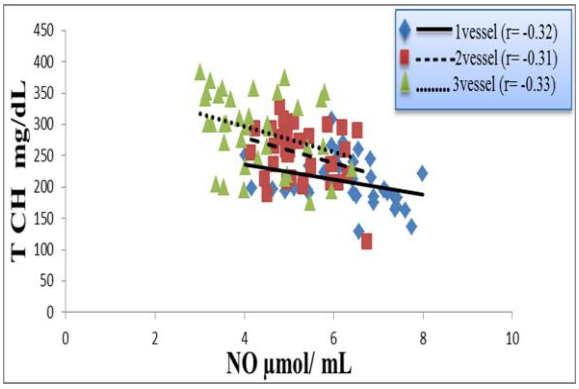

Figure- 5: Correlation between NO and serum TCH to type of vessel occlusion

There is a negative correlation between NO and TG levels in each of 1vessel (r = -0.25), 2 vessel (r= -0.36) and 3 vessel (r = -0.22) as shown in figure(6)

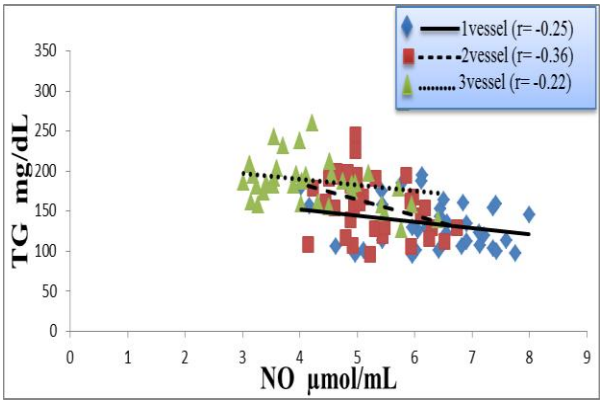

Figure -6: Correlation between NO and serum TG to type of vessel occlusion

There is a positive correlation between NO and HLD levels in each of 1 vessel (r =0.11), 2 vessel (r= 0.30) and 3 vessel (r = 0.39) as shown in Figure (7) .

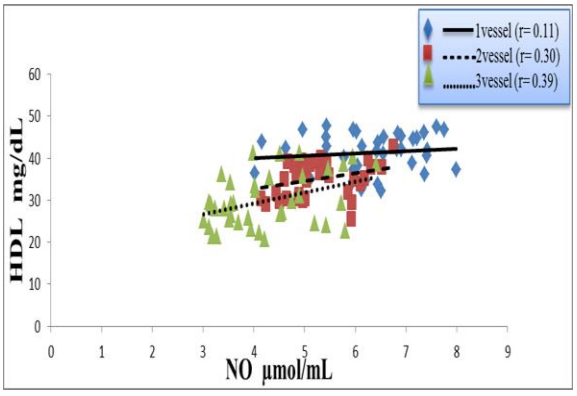

Figure -7: Correlation between NO and serum HDL to type of vessel occlusion

There is a negative correlation between NO and LDL levels in each of 1 vessel (r = -0.29), 2 vessel (r= -0.27) and 3 vessel (r = -0.33) as shown in Figure (8) .

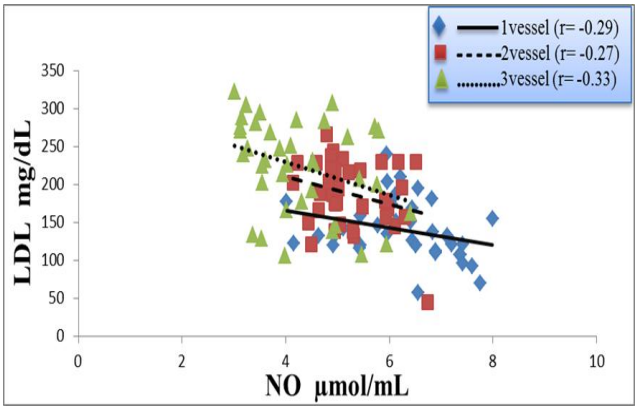

Figure- 8: Correlation between NO and serum LDL to type of vessel occlusion

There is a negative correlation between NO and VLDL levels in each of 1vessel (r = -0.24), 2 vessel (r= -0.35) and 3 vessel (r = -0.23) as shown in Figure (9) .

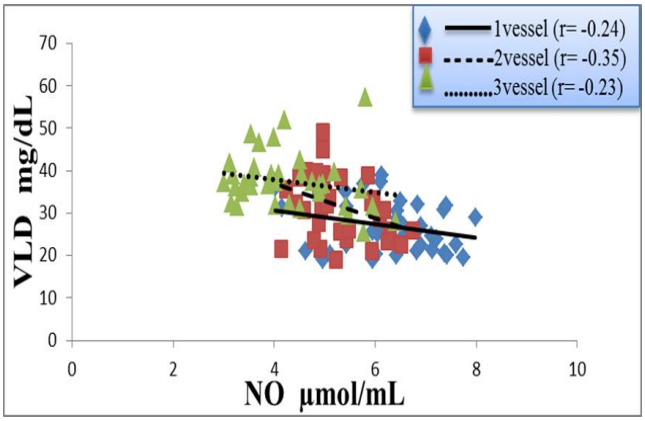

Figure- 9: Correlation between NO and serum VLDL to type of vessel occlusion

Discussion

cardiovascular disease(CVD) and Atherosclerosis is described as a chronic progressive disorder characterized by vascular sclerosis and lumen stenosis due to accumulation of lipid and platelet that triggered by lipid peroxidation, endothelial dysfunction, inflammatory mediators released by activated macrophage, and the migration and proliferation of vascular smooth muscle cell in tunica intima of artery monocytes differentiate into macrophages and engulf oxidized low-density lipoproteins (ox LDL), leading to the formation of inflammatory foam cells [23].Ox-LDL is the primary reason for which hyperlipidemia triggers Atherosclerosis . Ox-LDL brings about endothelial dysfunction via eNOS uncoupling which results in an increase in superoxide anions ($O2^{-}$) production but a decrease in NO level [24]. Low bioavailability of endothelial nitric oxide is the hallmark of vascular disease [25]. It is primarily characterized by the increase in arginase activity and eNOS uncoupling [26] .Atherosclerotic plaque is related to the accumulation of cholesterol in vascular wall. High density lipoprotein (HDL) is involved in

the reverse transport of cholesterol and increases the cholesterol efflux of macrophage. HDL-C can also resist the inhibition of ox-LDL on eNOS and can restrain oxidative stress as well as inflammation, exerting its anti atherosclerosis role and preventing endothelial dysfunction [27]. Reduced levels of HDL-C are associated with an increased risk for coronary artery disease and future cardiovascular events [28]. At least some of these anti-atherogenic effects of HDL-C may be due to its anti-inflammatory and antioxidant properties, which shows that the anti-inflammatory and antioxidant properties of HDL-C remain unquestionable in previous studies [29–32]. HDL's functional properties are predominantly anti atherogenic; the most well-studied of which is its ability to facilitate the removal of excess cholesterol from atherosclerotic plaques in a process known as reverse cholesterol transport (RCT). In addition to RCT, however, HDL has also been shown to have multiple other vascular effects which may be expected to provide additional protection; such as an ability to increase endothelial nitric oxide (NO) bioavailability, a capacity to reduce oxidative stress and inflammation, and an ability to reduce the expression of endothelial adhesion markers and transendothelial monocyte migration [33].

Conclusion

- Cardiovascular disease, we found a significant elevation in the levels of cholesterol and triglyceride during cardiovascular disease.
- Cardiovascular disease can effect on lipoproteins levels (low HDL, high LDL, and high VLDL).
- In Cardiovascular disease lipid peroxidation can clearly occur. Decrease in Nitric Oxide.
- The higher the number and type of arterial occlusion, (SVD), (2VD) and (3VD), increased the levels of (TG, TCH, LDL, VLDL) and decreased the levels of HDL and (NO).

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