

The Effect of Different Lipoproteins on the Severity of Coronary Atherosclerosis and Relation between them in Patients in Kurdistan

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Abstract

Background and objectives: Lipoproteins mainly LDL-C and Non HDL-C are among important risk factors for coronary atherosclerosis, Coronary angiography is the standard diagnostic investigation for obstructive coronary vascular disease. Finding a lipoprotein index for severity of coronary atherosclerosis which can be estimated by many score systems is matter of debate among many studies. The objective of the study is to assess the effects of different lipoproteins on severity of coronary atherosclerosis and the relation among them. **Methods:** From 1-4-2017 to 28-2-2018, 125 patients collected in Cardiac Center in Erbil were included in this case control study, the patients were collected on daily base by systematic sampling, for all patients basic demographic data collected including age, gender, ethnic group, if he used statin for more than 3 weeks, the risk factors of atherosclerosis, then standard diagnostic coronary angiography done and fasting total serum cholesterol, low density lipoprotein-C, high density lipoprotein-C, serum triglyceride and non-high density lipoprotein-C were estimated, the severity of coronary atherosclerosis were estimated by Syntax score available on line (<http://syntaxscore.com/calculator/start.htm>), patients were divided to three groups according to their score levels, the data analyzed by SPSS program. **Results :** The study showed that there were no significant differences in the demographic data among the three groups apart from the risk factors, mean ages were (57 ± 11 , 59 ± 10 and 61 ± 9 year respectively p-value 0.152), male/female ratio were (20/20, 36/8 and 31/10 respectively p-value 0.558), The study showed that statins significantly reduced cholesterol (p-value 0.03) and low density lipoprotein (p-value < 0.001) (albeit above target levels) but they did not reduce significantly the non-high density lipoprotein level (p-value 0.07) nor they reduced the score values significantly (p-value 0.32). There was significant positive correlation between high density lipoprotein level and the severity of coronary atherosclerosis in all arms. **Conclusions:** Serum level of non-high density lipoprotein is more important than low density lipoprotein as far as severity of coronary atherosclerosis is concerned and target LDL level was not achieved

Keywords: Non high density lipoprotein; Syntax score; Coronary atherosclerosis.

Introduction

Coronary atherosclerosis is the main cause behind coronary heart diseases; although there are other causes like congenital anomalies of the coronary arteries and vacuities, but these are rare causes¹.

Coronary atherosclerosis as pathology is an inflammatory process, started when oxidized low density lipoprotein (LDL) enters the intimal layer of the arteries, leading to infiltration of the area by mononuclear inflammatory cells and macrophages the last will engulf the oxidized LDL leading to formation of the foam cells, when the cells are destructed the lipid content released to the intima

leading to production of cytokines and growth factors by the macrophages, smooth muscle fibers migrate to the intimal layer in an attempt to stabilize the atherosclerotic plaque²⁻⁴.

Severity and extension of coronary atherosclerosis are among important factors that have influence on the management strategy in patients with IHD, coronary angiography is a reliable method for assessing the coronary atherosclerosis severity, extension, and functional sequelae³.

Dyslipidimia indicates abnormal lipid levels, that can be hyperlipidimia, or even low level of some of the

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lipoproteins is regarded as dyslipidemia⁴. There are many types of lipoproteins in the body; chylomicron, low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), very low and intermediate density lipoprotein cholesterol (VLDL-C and IDL-C) and LDL-C subtypes^{5,6}. Although dyslipidemia especially high LDL-C and/or low HDL-C is having a well-known relation with incidence and prevalence of coronary heart disease but its relation to the severity and extension of coronary atherosclerosis is still not clear, so the level of different lipids as an index for severity of coronary heart disease is not well established^{7,8}. Some studies showed that the triglyceride (TG) to HDL-C ratio is an index for presence of small LDL-C particles which are regarded as the most atherogenic subclass of LDL-C and it's shown to be one of the non-invasive parameters that are most strongly associated with the extent of coronary disease, as assessed by the Friesinger index from conventional coronary angiography⁹. Another study by Jung L G et al showed relation between coronary heart diseases (CHD) and free fatty acid levels (FFAs) the study showed that FFAs levels were positively and independently associated with the severity of CAD¹⁰.

Michael F et al studied the lipoproteins in both genders and their relation with severity of coronary atherosclerosis in term of extent of the disease angiographically, they found that there is marked differences in male and female patients, in male the severity of atherosclerosis was strongly related to the level of LDL-C and apo lipoprotein B levels, while in female patients it was related to STG, IDL-C and LDL-C concentration¹¹.

Jan J. et al studied the relation between Coronary atherosclerosis extend and five different subtypes of HDL-C, they found strong inverse relation between atherosclerosis and large particle HDL-C subtype, in patient whom were having normal STG, such finding was not detected in patients with high STG¹². Such inverse relation was noted by Jenkins P j et al, regardless of STG, the same study showed positive relation between TSC, LDL-C and Non HDL-C with coronary atherosclerosis severity¹³.

Li and colleagues studied 1757 patients whom were not receiving lipid lowering therapy, for all of them coronary angiography done, and lipid profiles estimated, the severity

of coronary atherosclerosis assessed by Gensini score system, they found Non HDL-C level was more related to the score system compared to LDL-C levels though both of them were related¹⁴. Ji and colleagues studied 365 Chinese patients with coronary atherosclerosis; they found that TSC, LDL-C and Non HDL-C concentration are well related to the number and severity of coronary lesion, a meta-analysis among patients treated with statins showed that levels of Non HDL-C were superior to LDL-C in relation to the risk of future major cardiovascular events; a large participant-level analysis showed Non HDL-C was superior to LDL-C or total cholesterol¹⁴.

The LDL-C target level depends on the risk group, for patients with very high risk the target LDL-C is to be below 70 mg/dl or at least 50% reduction of base line LDL-C, patients with high risk level their LDL-C level to be less than 100 mg/dl. All the other patients LDL-C need to be reduced below 115 mg/dl¹⁵.

The effects of statins are the result of their capacity to reduce cholesterol biosynthesis, mainly in the liver, where they are selectively distributed, as well as to the modulation of lipid metabolism, derived from their effect of inhibition upon HMG-CoA reductase¹⁶. There are many ways of assessing severity of coronary atherosclerosis, the most common one is Syntax score system which depends on the anatomical location of the lesion, severity of stenosis, and the type of the lesion, there is special calculator for assessing the Syntax score^{3,17}. Such kind of research hasn't been done in Kurdistan and the results of the research will help the health system to improve the treatment of patients with coronary heart disease. The aim of the study was to assess the effects of different lipoproteins on severity of coronary atherosclerosis and the relation between them.

Patients and methods

125 patients collected in Erbil Cardiac Center were included in the study from 1-4-2017 till 28-2-2018, the patients were chosen randomly on daily bases by systematic sampling. The study was a case control study. Patients whom included in the study were patients who were indicated for coronary angiography, patients who could not perform coronary angiography because of

any reason including patient wish or coronaries cannot be assessed because of inability to perform complete coronary angiography and cases of primary coronary angiography were excluded.

All ethical aspects regarding the angiography and blood sampling were taken in consideration. Results of the coronary angiography were analyzed by team of interventional cardiologists. Basic data were taken from each participant including, age, ethnic group, gender, the risk factors (hypertension, smoking, diabetes, family history of IHD) if any patient had more than one risk factor, he had entered group of multiple risk factors, drug history mainly statins, patient receiving statin for more than three weeks were considered statin users³.

Standard coronary angiography were done after preparation of the patients by premedication and mostly by Judkin catheters of left and right types of different sizes unless other types of catheters were needed, through femoral or radial artery approaches^{18,19}. Two types of angiography devices were used, one from Phillips Company and the other from General Electronic Company.

The result of coronary angiography was reported by specialist interventional cardiologists, for all chosen patients 12 hours fasting total serum cholesterol (TSC), LDL-C, TG, HDL-C, and Non HDL-C lipoproteins were estimated from blood samples taken from the inserted arterial sheath once its inserted and put in non-heparinized tubes, centrifuged to separate the plasma then lipid panels estimated by Cobas lipid panel⁹. Severity of

coronary atherosclerosis were assessed by Syntax score 1 calculator which is available online from the website <http://syntaxscore.com/calculator/start.htm>.

According to the Syntax score the patients were divided into three groups 3 patients with score of zero (normal coronary angiography), these patients were used as control group (group 1), patients with score value to less than 22 (mild to intermediate severity atherosclerosis) (group 2), and patients with score of 22 or higher (severe atherosclerosis) (group 3).

The data were inserted in SPSS program version 23 and the differences were analyzed by t test for numerical variables, and Chi-square for categorical data, statistical analysis was done at significance level of ≤ 0.05 , the correlation assessed by Pearson Correlation Coefficient, its significance assessed by t-test, at level of significance of ≤ 0.05 .

Results

The three groups show no significant differences regarding the demographic features apart from the risk factors. The three groups contain both genders and the difference in male/female ratio were not statistically significant, as well as there were no significant differences in the number of patients using statins, it's shown that the most important risk which significantly leads to severe atherosclerosis is when multiple risk factors for atherosclerosis are collectively present in the same patient, Table 1.

Table (1): Demographic data of the three groups

Groups/demographic variables	G1(40)	G2 (44)	G3 (41)	p-value
Mean age \pm SD	57 \pm 11	59 \pm 10	61 \pm 9	0.152
Risk factors				
Hypertension	13	11	6	
Smoking	15	1	4	
Diabetes	0	0	4	0.003
Family history	0	2	0	
Multiple risks	3	12	27	
No risks	9	1	0	
Gender				
Male/Female	20/20	32/12	27/14	0.112
Ethnic groups				
Kurdish/Non Kurd	28/12	36/8	31/10	0.588
Stain				
Using/Not using	14/26	24/20	24/17	0.09

The study showed that statins significantly reduced TSC, and highly significantly reduced LDL-C but no significant reduction in Non HDL-C was achieved by statins, despite that the mean Syntax score value was not significantly different between patients using statins (17±3) and those not using statins (15±2). Most of the patients were having coronary atherosclerosis, (groups 2 and 3) despite that the mean LDL level among the statin users was more than the target LDL for such patients (less than 70 mg/dl) (Table 2).

Table (2): The effects of statins on the different lipid parameters of the patients.

±SD dl	Patients using statins (61)	Patients not using statins(64)	p-value
	17±3	15±2	0.32
	135.6±77.9	154.5±61	0.131
	76.5±31.3	101.9±29.5	<0.001
	34.7±12.3	36.3±8.9	0.39
LDL	105.6±54	135±61	0.07

The statin which were used by the patients were atorvastatin 20 mg daily in (40%) of the cases, rosuvastatin 10 mg daily (25%), rosuvastatin 20 mg daily (15%), atorvastatin 40 mg daily (15%), the others were receiving simvastatin in different doses(5%). By Paerson correlation coefficient , it has been shown that both TSC and Non HDL-C lipoprotein and STG are positively and significantly correlated with the Syntax score values, HDL-C was negatively related to the score values but not significantly (Table 3).

Table (3): The correlation between different lipoproteins and Syntax score values and their significance.

Lipoproteins	Correlation Coefficient	p-value
TSC	0.323	0.03
LDL	0.192	0.78
HDL	-0.13	0.23
Non HDL	0.363	0.01
STG	0.343	0.03

In sub analysis of the patients who were not using statins, TSC, LDL-C, STG and Non HDL-C showed significant positive correlation with score values, HDL-C showed negative correlation but not significant one, Table 4.

Table (4): The correlation between different lipoproteins and Syntax score values and their significance in cases whom were not receiving statins.

Lipoproteins	Correlation Coefficient	p-value
TSC	0.409	0.01
LDL	0.276	0.05
HDL	-0.21	0.23
Non HDL	0.4	0.01
STG	0.336	0.04

In another sub analysis including those using statins STG and Non HDL-C had positive significant correlation with score values, HDL showed significant inverse relation with the score values, Table 5.

Table (5): The correlation between different lipoproteins and Syntax score values and their significance in cases whom were receiving statins.

Lipoproteins	Correlation Coefficient	p-value
TSC	0.385	0.08
LDL	0.236	0.12
HDL	-0.359	0.01
Non HDL	0.42	0.04
STG	0.365	0.01

Genders were separately analyzed, Non HDL was the only lipoprotein that has significant positive correlation with Syntax score values in male (0.277 p-value =0.03), HDL-C was negatively related but not significantly, in female cases both STG and Non HDL-C showed significant positive correlation with score values (0.465 p-value =0.05* for STG and 0.478 p-value =0.01 for Non HDL-C).

Discussion

In this study which included 125 patients significant positive correlation detected between Non HDL-C and syntax score values this was concordant with the results of Ji and colleagues whom found that TSC, LDL-C and Non HDL-C concentration are well related to the number

and severity of coronary lesions, Li and colleagues whom found that Non HDL-C level was more related to the score system compared to LDL-C levels though both of them were related and in a meta-analysis among patients treated with statins showed that levels of Non HDL-C were superior to LDL-C in relation to the risk of future major cardiovascular events; a large participant-level analysis showed Non HDL-C was superior to LDL-C or total cholesterol¹⁴.

This study showed no significant negative correlation between HDL-C levels and syntax score values apart from male patients in whom significant negative correlation was detected, Jan J. et al found strong inverse relation between atherosclerosis and large particle HDL-C subtype, in patient whom were having normal STG, such finding was not detected in patients with high STG¹², such inverse relation was noted by Jenkins P j et al, regardless of STG, the same study showed positive relation between TSC, LDL-C and Non HDL-C with coronary atherosclerosis severity¹³.

In the present study in male patients Non HDL was the only lipoprotein that showed significant positive correlation with severity of coronary atherosclerosis, while in female patients Non HDL-C concentration and STG were significantly related to severity of atherosclerosis but Michael F et al found that in male the severity of atherosclerosis was strongly related to the level of LDL-C and apo lipoprotein B levels, while in female patients it was related to STG, IDL-C and LDL-C concentrations¹¹.

Despite that statins significantly reduced TSC, and mainly LDL-C but not Non HDL-C compared with the non-statin users, it had been shown in the present study that Non HDL level remain as the main lipoprotein that showed consistent positive relation with Syntax score values, this can indicate that statins cannot reduce significantly some of other lipoproteins included in the bulk of Non HDL-C as it can do with LDL-C levels. It had been shown in this study that using statin did not affect the score values significantly, in spite of the significant reduction in LDL-C level, since the target LDL-C level was not achieved in the statin user patients, because most of them either they were using inadequate dose of high potency statin (in 60% of cases) or they were using non potent statins

(in 15% of cases), so only 25% of cases were receiving adequate dose of high potency statins, this indicate that statins are underused in high risk patients .

Serum total triglycerides was shown in the present study to have significant positive correlation with severity of coronary atherosclerosis, and that relation was not influenced by statin use, such relation is actually the reflection of the associated hyperlipidemia that affect the other lipoproteins rather than the STG level itself, Cenk showed that high STG in a ratio to HDL is associated with high level of low particle LDL-C which is the most atherogenic subtype of LDL-C⁹.

Conclusions

It's concluded that serum level of Non HDL-C lipoprotein is more important than LDL-C as far as severity of coronary atherosclerosis is concerned; finding a reliable lipoprotein index for severity of coronary atherosclerosis is debatable, and statins were not prescribed in adequate dose in most of our very high risk patients, and target LDL level was failed to be achieved.

Conflicts of interest: The authors recorded no conflicts of interest.

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