The Libyan International Medical University

Faculty of Basic Medical Science

Dyslipidemia and Risk of Cardiovascular Disease

Mahmoud Moftah Alhaddad

2125

Supervised by: Dr. Osama Othman

Assisted by: Dr. Marwa Yousef

Report Submitted to fulfill the requirements for Scientific Research Activity

Date of Submission: 9 / 3 / 2020

Abstract

Background: Dyslipidemia (or dyslipoproteinemia) : refers to abnormal concentrations of serum lipoproteins**,** means An increased serum concentration of low density lipoprotein (LDL) and low levels of high density lipoprotein cholesterol (HDL- C) .

objectives: describe the role of high density lipoprotein and low density lipoprotein in the development of cardiovascular disease.

method: In 2006, the Lithuanian High Cardiovascular Risk Primary Prevention Program was initiated in Lithuania to recognize patients at high risk of cardiovascular disease. The research recruited men between 40 and 50 years of age and women between 50 and 65 years**,** 83,376 patients was taken for analysis divided into two group extream dyslipidemia group and control group .

Result: A total of 83,376 patients have been analyzed, from 2009 to 2015. The study found that people with extreme dyslipidemia were twice as likely as those in the control group to have three or more risk factors.

conclusion: High level of LDL and low level of HDL can lead to atherosclerosis and many cardiovascular diseases .

Introduction

Dyslipidemia (or dyslipoproteinemia) : refers to abnormal concentrations of serum lipoproteins. it is estimated that nearly half of the U.S population has some form of dyslipidemia, especially among white and Asian populations. dyslipidemia means An increased serum concentration of low density lipoprotein (LDL) and low levels of high density lipoprotein cholesterol (HDL- C) . LDL is responsible for the delivery of cholesterol to the tissues. so the serum levels of LDL are normaly controlled by hepatic receptors for LDL that bind LDL and limit liver synthesis of this lipoprotein, HDL is responsible for "reverse cholesterol transport" which returns excess cholesterol from the tissues to the liver, where it binds to hepatic receptors (including the LDL receptor) and is processed and eliminated as bile or converted to cholesterol – containing steroids.

LDL is a strong indicator of coronary risk. however, high dietary intake of cholesterol and fats, often in combination with a genetic predisposition to accumulations of LDL in the serum (e.g., dysfunction of the hepatic LDL receptor), results in high levels of LDL in the bloodstream . the term LDL actually describes several types of LDL molecules, the "small dense" LDL particles are the most atherogenic. LDL oxidation that migration into the vessel wall, and phagocytosis by macrophages are key steps in the pathogenesis of atherosclerosis. LDL also plays a role in endothelial injury, inflammation, and immune responses that have been identified as being important in atherogenesis. Aggressive reduction of LDL with diet and cholesterol-lowering drugs, such as the statins and ezetimibe, is associated with a dramatic decrease in risk for coronary artery disease (CAD) .

low levels of high density lipoprotein cholesterol (HDL- C) also are a strong indicator of coronary risk, and high levels of HDL may be more protective for the development of atherosclerosis than low levels of LDL. HDL also participates in endothelial repair and decreases thrombosis. it can be fractionated into several particle densities (HDL-2 and HDL-3) or sizes (large, medium, small) that have different effects on vascular function. HDL-2 is most effective at reverse cholesterol transport and its selective measurement is a better indicator of cardiovascular risk than total HDL levels. it has been found that inflammation in early atherogenesis results in the production of toxic oxygen radicals that can reduce or eliminate the protective function of HDL . Exercise

, weight loss , fish oil consumption , and moderate alcohol use can result in modest increases in HDL . other lipoproteins associated with increased cardiovascular risk include elevated serum VLDL and increased lipoprotein (a) . Triglycerides (TG) are associated with an increased risk for CAD , especially in combination with other risk factors such as diabetes . [(1)]

Aim of study : the study objectives were to evaluate the Risk of CV events in patients with low level of HDL and high level of LDL.

Methods

In 2006, the Lithuanian High Cardiovascular Risk Primary Prevention Program was initiated in Lithuania to recognize patients at high risk of cardiovascular disease and to introduce primary prevention methods. The research recruited men between 40 and 50 years of age and women between 50 and 65 years of age without cardiovascular disease (CVD) from all regions of Lithuania. A total of 83,376 individuals were surveyed between 2009 and 2015. Extreme dyslipidemia group, which was analyzed in depth, consisted of 11,265 individuals, extreme dyslipidemia if TG > 7.5 mmol /l, or LDL-C > 6 mmol /l, , patients without dyslipidemia were included in the control group if TC > 5 mmol /l, LDL-C > 3 mmol /l, TG > 1.7 mmol /l , Yet HDL-C in men > 1.0 mmol /l and in women> 1.2 mmol /l. All patients with severe dyslipidemia group were classified into 3 subgroups by blood lipid levels, moderate hypercholesterolemia group consisting of 3 smaller subgroups: high LDL-C group (6 mmol /l), possible family hypercholesterolemia group (FH group) (LDL-C=6.5–8. 4 mmol /l CVD family history) and definite FH group (LDL-C group 8.5 mmol /l). Severe hypertriglyceridemia group consisting of 2 subgroups, high TG-level group (≥ 4.5 mmol / l) and very high TG-level group (≥ 10 mmol / l) and mixed dyslipidemia group (TG ≥ 4.5 mmol / l and LDL-C ≥ 6 mmol / l in the same person).[(2)]

The predictive value of HDL cholesterol levels in 9770 patients was assessed by a post-hoc analysis of the recently completed research Treating New Targets (TNT). The primary outcome measure was the period for a first major cardiovascular event, described as death from coronary heart disease, non-fatal non-procedural myocardial

stroke, cardiac resuscitation, or catastrophic or non-fatal stroke,The predictive relationship between HDL cholesterol levels in the third month of statin treatment and the time for the first major cardiovascular event was evaluated in univariate and multivariate analysis and was also evaluated for specific LDL cholesterol strata, including subjects with LDL cholesterol levels below 70 mg per deciliter (1.8 mmol per liter).,. [3]

Results

A total of 83,376 patients have been analyzed, from 2009 to 2015. The average age was 52.3-6.18 years, 59.1% (49234) females. The study found that people with extreme dyslipidemia were twice as likely as those in the control group to have three or more risk factors, seen in (Table1) , Those with extreme dyslipidemia had significantly higher levels of blood pressure, abdominal obesity, Body mass index > 30 (kg / m2), diabetes mellitus, unbalanced diet, inadequate physical activity, a population around 5 times higher in patients with severe dyslipidemia than in the control group.[2]

In patients receiving statins, the level of HDL cholesterol was predictive of major cardiovascular events across the TNT study cohort, both when HDL cholesterol was con-sided as a continuous variable and when subjects were stratified according to HDL cholesterol level quintiles. When the study was stratified in patients receiving statins according to the amount of LDL cholesterol, Borderline importance was the association between HDL cholesterol level and major cardiovascular events (P= 0.05). Even among subjects with LDL cholesterol levels below 70 mg per deciliter, those with the highest quintile of HDL cholesterol were at lower risk of major cardiovascular events than those with the lowest quintile (P= 0.03). [3]

Table 1 : Cardiovascular risk profile of severe dyslipidemia and control group[1]

	Control group ($n = 8.538$)	**Severe dyslipidemia ($n = 11.265$)**	***p* value**
	Average ± SD (95% CI)	Average ± SD (95% CI)	
Age (years)	–50.57) 6.04 ± 50.7 (50.83	(53.63–53.4) 6.21 ± 53.51	0.001 >
Waist circumference (cm)	–90.36) 13.11 ± 90.64 (90.92	(94.92–94.44) 13.02 ± 94.68	0.001 >
BMI (kg/m^2)	–26.96) 5.43 ± 27.08 (27.19	(29.2–29.02) 5.01 ± 29.11	0.001 >
SBP (mmHg)	–130.26) 15.43 ± 130.58 (130.91	(136.68–136.04) 17.21 ± 136.36	0.001 >
DBP (mmHg)	–80.99) 9.12 ± 81.19 (81.38	(84.37–84.01) 9.78 ± 84.19	0.001 >
Heart rate (beats/min)	(71.7–71.33) 8.7 ± 71.52	(72.75–72.43) 8.68 ± 72.59	0.001 >
Glucose (mmol/l)	(5.37–5.32) 1.07 ± 5.34	(5.77–5.71) 1.57 ± 5.74	0.001 >
TC (mmol/l)	(4.42–4.4) 0.44 ± 4.41	(8.09–8.06) 0.99 ± 8.08	0.001 >
LDL-C (mmol/l)	(2.43–2.41) 0.43 ± 2.42	(5.37–5.33) 1.19 ± 5.35	0.001 >
HDL-C (mmol/l)	(1.59–1.57) 0.36 ± 1.58	(1.61–1.59) 0.51 ± 1.6	0.005
TG (mmol/l)	(0.94–0.93) 0.31 ± 0.93	(2.7–2.61) 2.27 ± 2.65	0.001 >
SCORE index (points)	(1.25–1.2) 1.19 ± 1.22	(2.83–2.75) 2.26 ± 2.79	0.001 >
Arterial Hypertension (%)	(45.3–43.1) 44.2	(64.4–62.6) 63.5	0.001 >
Diabetes mellitus (%)	(8.7–7.5) 8.1	(16.7–15.3) 16	0.001 >
Abdominal obesity (%)	(31.3–29.3) 30.3	(51.9–50.1) 51	0.001 >
BMI > 30 (kg/m^2) (%)	(25–23.2) 24.1	(39.7–37.9) 38.8	0.001 >
Smoking (%)	(27.4–25.5) 26.4	(23.5–21.9) 22.7	0.001 >
Metabolic syndrome (%)	(9.9–8.6) 9.2	(48.1–46.3) 47.2	0.001 >
RF ≥ 3 (%)	(45.2–43.1) 44.1	(85.1–83.8) 84.5	0.001 >
Family history of CVD (%)	(23.6–21.8) 22.7	(30.6–28.9) 29.7	0.001 >
Diet (unbalanced) (%)	(54.5–52.4) 53.5	(67.4–65.6) 66.5	0.001 >
Physical activity (insufficient) (%)	(45.3–43.2) 44.2	(56.9–55.1) 56	0.001 >

Discussion

It has long been known that a low level of HDL cholesterol is a powerful predictor of increased cardiovascular risk,1-6 but it has not been clear whether a low HDL cholesterol level would remain a significant risk factor in people whose LDL cholesterol was reduced to very low levels. Indeed, it has been argued hypothetically that if the LDL cholesterol level were reduced sufficiently, the level of HDL cholesterol might become irrelevant. In this post hoc analysis from the TNT trial, HDL cholesterol level was a significant predictor of major cardiovascular events across the entire study cohort, even after all other baseline risk factors, including baseline LDL cholesterol level, had been taken into account. This effect was more pronounced in the analyses using HDL cholesterol level as a continuous variable than in those using quintiles of HDL cholesterol levels at month 3 of the trial, a result suggesting that outlier HDL cholesterol levels may have had an important role in the relationship we observed. The effect of LDL cholesterol levels during statin treatment on the predictive value of HDL cholesterol was examined. After adjustment for covariates, the predictive value of HDL cholesterol levels was of borderline significance, a result consistent with a suggestion that in patients with coronary heart disease, higher HDL cholesterol levels may offset the increased risk associated with higher LDL cholesterol levels. In a further analysis, we examined the rela- tionship between the quintile of HDL cholesterol level during statin treatment with risk in those patients in the lowest stratum of LDL cholesterol level (<70 mg per liter).

This analysis demonstrated that even among patients in this very low LDL cholesterol stratum, the risk of major cardiovascular events was reduced in those with higher rather than lower HDL cholesterol levels. Given that HDL and LDL cholesterol levels during statin treatment were both independently predictive of major cardiovascular events across the whole range of HDL and LDL cholesterol lev- els in this analysis, it was not surprising to find that the ratio of LDL to HDL cholesterol was also highly predictive of the risk of major cardiovascu- lar events. A similar result was observed for the ratio of total cholesterol to HDL cholesterol. These results are consistent with previous studies.[2]

In this study, the prevalence of familial hypercholesterolemia was 0.1 per cent and possible familial hypercholesterolemia was 0.5 per cent. The second cause of primary

extreme dyslipidemia-mixed dyslipidemia is prevalent in about 0.5–2% of the general population, whereas the prevalence of primary prevention in this middle-aged Lithuanian population was 0.1%. There is insufficient information on prevalence and co-morbidity of severe hypertriglyceridemia (SHTG) among adults when it comes to (SHTG).[3]

Conclusion

In this study, the bottom line is that the dyslipidemia that means High level of LDL and low level of HDL can lead to atherosclerosis and many cardiovascular diseases , also the other lipoproteins associated with increased cardiovascular risk include elevated serum very low density lipoprotein (VLDL) and increased lipoprotein (a) and Triglycerides (TG) .

References

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