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THE ANALYSIS OF THE SUB-FRACTIONS OF HIGH-DENSITY LIPOPROTEIN (HDL) CHOLESTEROL IN THE GROUP WITH AND WITHOUT DIABETES

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ABSTRACT

Background and objectives: It is HDL2 that is primarily responsible for mediating the protective effect of HDL against CAD. Both coronary heart disease and type 2 diabetes mellitus have been linked to elevated total cholesterol levels, as well as elevated triglyceride and lower HDL cholesterol levels. a comparison of HDL subfractions in diabetic and non-diabetic populations is the focus of this research.

Methods: Case-control research blood from 33 healthy subjects without diabetes and 28 people with diabetes who have just been detected. Sample was taken from Department of Biochemistry, Mediciti Institute of Medical Science, Hyderabad, Telangana, India between January 2015 to June 2015. The homogeneity of HDL-C was measured using a colorimetric enzymatic test. HDL3-C was measured using the simple precipitation method1 by adding Heparin/Mn/DS reagent. The statistical significance of the differences in means was determined using unpaired t-tests.

Results: HDL 2 levels were significantly higher in non-diabetic group compared to the diabetic group, there is no significant difference between Diabetic and Non- Diabetic groups in HDL 3 levels. Total cholesterol, LDL, and Triglycerides are significantly higher in Diabetics compared to non-Diabetic group.

Conclusion: The research demonstrated that the method for calculating HDL-C fractions was straightforward and economical.

Keywords: HDL, Cholesterol, Lipoprotein, Diabetes.

INTRODUCTION

In observational studies, an elevated low-density lipoprotein cholesterol (LDL-C) level is related with an increased risk of coronary heart disease (CHD), and this connection persists after controlling for other risk factors. There is now strong evidence of its causative significance in CHD from randomized controlled trials of medicines that decrease LDL-C. However, triglycerides' involvement in CHD remains unclear [1,2,3]. Higher triglycerides and lower high-density lipoprotein cholesterol (HDL-C) are both associated with coronary heart disease (CHD), according to observational data from a large meta-analysis of prospective studies, but the associations between the two are attenuated to the null after

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adjustment for confounders. However, the results of the REDUCE-IT trial and other recent Mendelian randomization trials have provided some evidence for a causal relationship between triglycerides and CHD.

Different triglyceride-containing lipoprotein sub-fractions contribute to the total circulating triglyceride concentration, which is not commonly tested in clinical practice. Very low-density lipoproteins (VLDLs) transport triglycerides from the liver, whereas chylomicrons transport fatty acids from the gut after a meal. Varied lipoprotein sub-fractions may have different relationships with CHD risk since the concentration of triglycerides generally decreases when the lipid content of these lipoproteins is hydrolyzed [3,4]. Recent advances in high-throughput technology have made it possible to measure triglyceride-containing lipoprotein sub-fractions in serum nuclear magnetic resonance spectroscopy in addition to other lipoprotein subclasses and metabolites (NMR). This platform was used in a prospective cohort research in China, and the results suggested that the kind of triglyceride-containing lipoprotein sub-fraction may influence the correlation of triglycerides with CHD [4,5,6]. The same methodology was then applied to the populace of Finland in separate research. To the best of our knowledge, however, no research has looked at whether or not lipoprotein sub-fractions containing triglycerides are linked to an increased risk of coronary heart disease or stroke in groups other than Caucasians [5,6].

MATERIAL AND METHODS

The research including cases and controls. samples taken while fasting from 33 subjects without diabetes and 28 individuals with a recently diagnosed case of diabetes at Department of Biochemistry, Mediciti Institute of Medical Science, Hyderabad, Telangana, India between January 2015 to June 2015. An enzymatic colorimetric approach was used in order to carry out a homogenous HDL-C test.

In order to quantify HDL3-C, a straightforward precipitation method1 was carried out by including the Heparin/Mn/DS reagent. The difference between HDL-C and HDL3 was the starting point for the production of HDL2. In order to evaluate the statistical (Med CalC software; PC Version 12.7.0. Belgium) differences between the mean values, unpaired t-tests were used.

RESULT

Table 1. Lipid profile parameters among the study groups.

GROUPS		AGE (yrs)	FBS (mgl)	T. CHOLE (mg/dl)	TG (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)	HDL (mg/d)	HDL2 (mg/dl)	HDL3 (mg/dl)
DIABETIC	MEAN ± SD	48.5 (7.12)	193.96 (64.20)	255.56 (37.04)	255.73 (41.89)	198.59 (49.17)	117.64 (18.59)	47.02 (11.59)	8.66 (9.5)	38.64 (8.01)
	95 % CI	(45.73-51.26)	(169.06-218.60)	(241.19-269.92)	(239.48-271.97)	(179.52-217.66)	(110.46-124.81)	(42.52-51.51)	(4.97-12.34)	(35.53-41.75)
NONDIABETIC	MEAN ± SD	41.727 (8.02)	100.12 (4.63)	161.98 (26.95)	135.21 (26.74)	107.93 (21.7)	60.77 (14.03)	57.52 (12.93)	11.86 (9.18 0)	46.11 (10.56)
	95 % CI	(38.88-44.57)	(98.47-101.16)	(152.26-171.70)	(125.73-144.70)	(100.24-115.63)	(55.794-65.74)	(52.93-62.10)	(8.60-15.11)	(42.36-49.85)
	P VALUE	P = 0.0009	P = 0.0015	P < 0.0001	P < 0.001	P < 0.0001	P < 0.0001	P < 0.0001	0.0060	0.0033

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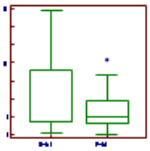

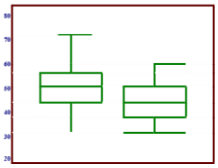

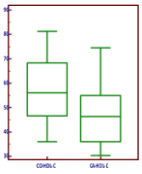

CO-HDL3 CA-HDL3

DISCUSSION

Total cholesterol levels were observed to be almost equal across all groups (NIDDM with CAD against controls and NIDDM with CAD versus CAD goup without NIDDM) in the current investigation. The prevalence of hypercholesterolaemia was about the same in diabetic and nondiabetic participants, which M.Chr. Bakogianni results corroborate with data from the Framingham research. In addition, the research found that people with type II diabetes mellitus had significantly higher triglyceride levels and only a little higher total cholesterol concentration than age-matched nondiabetic participants. Therefore, hypertriglyceridemia combined with low levels of HDL cholesterol is the predominant lipid abnormality in noninsulin-dependent diabetes mellitus rather than hypercholesterolaemia [5,6,7].

Nonetheless, our research showed that NIDDM patients with CAD had higher plasma triglyceride levels than those of nondiabetic controls and the CAD group without NIDDM. This agrees with the findings of previous researchers who found that high triglyceride levels may pose a greater threat to cardiovascular health in diabetic people than high total cholesterol levels. Higher blood triglyceride levels are associated with an increased risk of coronary artery disease, and this is especially true for individuals with non-insulin-dependent diabetes, as evidenced by the majority of prospective studies [7,8].

It is well established that insulin resistance is often seen in NIDDM patients with mild to severe hyperglycaemia. Hyperinsulinemia is the compensatory condition for insulin resistance, and it works by blocking lipoprotein lipase and boosting VLDL production. In summary, hypertriglyceridaemia in non-insulin-dependent diabetes mellitus is caused by elevated VLDL and a failure in their clearance from circulation.

It is well known that hypertriglyceridaemia is prevalent among NIDDM patients with CAD and is negatively associated to the levels of HDL cholesterol and HDL2. Plasma HDL cholesterol levels are inversely related to the risk of developing coronary artery disease (CAD), therefore a lower concentration of HDL cholesterol suggests a higher risk for CAD [8].

Although total HDL, HDL2, and HDL3 subtypes were shown to be substantially lower in NIDDM participants with CAD compared to controls, the relative drop for HDL2 was much bigger than for HDL or HDL3. HDL and HDL2 cholesterol subclass were observed to have considerably lower values than HDL3 cholesterol subclass in the second comparison between NIDDM participants with CAD and CAD patients without NIDDM.

M.Chr. Bakogianni et al. study's findings corroborate those of previous research showing a much larger HDL reduction in individuals with non-insulin-dependent diabetes. In a crosssectional research, Laakso, Voultilainen, Pyorala, and Sarlund found that the HDL and HDL2 cholesterol concentrations of non-insulin-dependent diabetics with myocardial infarction were lower than those of non-insulin-dependent diabetics without a history of myocardial infarction. In addition, Drexel et al. demonstrated that HDL2 cholesterol is the

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best predictor of CAD severity using a model of stepwise multiple regression analysis. However, the results from the Physician's Health Study found that HDL3 had a stronger association with CAD, which runs counter to M.Chr. Bakogianni et al.findings[8,9].

According to M.Chr. Bakogianni et al. findings, the presence of non-insulin dependent diabetic mellitus is related with a further reduction of HDL and HDL2 cholesterol levels even among CAD patients with already low HDL and HDL2 cholesterol concentrations.

In addition, people with NIDDM and CAD had lower concentrations of HDL and HDL subtypes HDL2 and HDL3 compared to both controls and CAD patients without NIDDM. We discovered that the "HDL2" subgroup of HDL cholesterol decreased more than the other two in NIDDM with CAD. Lower levels of both HDL2 and HDL3 cholesterol contributed to the overall decline in HDL cholesterol seen in NIDDM patients with CAD.

That's why HDL2 percentage alterations were so much more prominent than HDL3 ones. Based on M.Chr. Bakogianni et al. findings, it seems that HDL2 is a more dynamic fraction, and that changes in HDL cholesterol levels may be more reflective of shifts in HDL2 cholesterol than in HDL3 cholesterol. This agrees with the other theory who found that the alterations in "HDL2" were much bigger than those detected for HDL3 in all non-insulindependent diabetics in whose total HDL varied from normal levels. HDL2 cholesterol levels were shown to be lower in individuals with CAD than HDL3 levels, according to research by Wallentin and Sundin [9].

More so, tiny HDL3 particles integrate the surface components (apolipoproteins, phospholipids, and unesterified cholesterol) of triglyceriderich lipoproteins, whereas the latter gain free cholesterol through interacting with extrahepatic cell membranes. HDL2 particles are formed when free cholesterol is converted into cholesteryl esters through lecithin:cholesterol acyltransferase (LCAT) activity (HDL2a). HDL2 particles become TG-rich via the activity of cholesteryl ester transfer protein (CETP), which mediates the exchange of cholesteryl esters and triglycerides between HDL2 particles and triglyceride-rich lipoproteins (HDL2b).

HDL2b core triglycerides are digested by hepatic lipase Patsc, Prascad, Gotto, & BengtssonOlivecrona. This results in the HDL3 particles being transformed back from HDL2 particles.

We draw the obvious conclusion that the metabolism of triglyceride-rich lipoproteins affects HDL2 and HDL3 subfractions. In NIDDM patients with poor lipoprotein lipase activity, triglyceride-rich lipoproteins are slowly digested, leading to increased HDL3 particle production. The plasma HDL2 cholesterol level has been observed to be considerably lower as a consequence. In addition, hypertriglyceridaemia is more likely to occur when lipoprotein lipase activity is low, since this hinders the clearance of plasma very low-density lipoprotein.

Together, these findings point to an unfavorable relationship between hypertriglyceridaemia and plasma HDL2 cholesterol concentrations in people with type II diabetes [9,10].

When it comes to NIDDM, the HDL2 subtype is more strongly linked to the risk of CAD, despite the fact that all HDL subclasses are crucial in ensuring that cholesterol is distributed evenly throughout the body.

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In conclusion, the reduction in total HDL may underestimate the real atherogenic potential associated with the diabetic condition, since HDL2 subfraction is believed to be more protective against CAD.

CONCLUSION

The process for the measurement of HDL-C subfractions was found to be straightforward and economical, according to the findings of the research.

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Conflict of interest:

Nil

REFERENCES:

1. Hirano, T., Nohtomi, K., Koba, S., Muroi, A., & Ito, Y. (2008). A simple and precise method for measuring HDL-cholesterol subfractions by a single precipitation followed by homogenous HDL-cholesterol assay. *Journal of lipid research*, *49*(5), 1130-1136.
2. von Eckardstein, A., Nordestgaard, B. G., Remaley, A. T., & Catapano, A. L. (2022). Highdensity lipoprotein revisited: Biological functions and clinical relevance. *European Heart Journal*, Epub-ahead.
3. Davidson, W. S., Cooke, A. L., Swertfeger, D. K., & Shah, A. S. (2021). The difference between high density lipoprotein subfractions and subspecies: an evolving model in cardiovascular disease and diabetes. *Current atherosclerosis reports*, *23*, 1-9.
4. Laakso, M., Lehto, S., Penttilä, I., & Pyörälä, K. (1993). Lipids and lipoproteins predicting coronary heart disease mortality and morbidity in patients with non-insulin-dependent diabetes. *Circulation*, *88*(4), 1421-1430.
5. Kamijo, Y., Ishii, H., Yamamoto, T., Kobayashi, K., Asano, H., Miake, S., ... & Yoshida, M. (2019). Potential impact on lipoprotein subfractions in type 2 diabetes. *Clinical Medicine Insights: Endocrinology and Diabetes*, *12*, 1179551419866811.
6. Hsu, H., Hsu, P., Cheng, M. H., Ito, Y., Kanda, E., Schaefer, E. J., & Ai, M. (2019). Lipoprotein subfractions and glucose homeostasis in prediabetes and diabetes in Taiwan. *Journal of Atherosclerosis and Thrombosis*, *26*(10), 890-914.
7. Tobey, T. A., Greenfield, M., Kraemer, F., & Reaven, G. M. (1981). Relationship between insulin resistance, insulin secretion, very low-density liporptein kinetics, and plasma triglyceride levels in normotriglyceridemic man. Metabolism, 30, 165 – 171.
8. Wallentin, L., & Sundin, B. (1985). HDL2 and HDL3 lipid levels in coronary artery disease. Atherosclerosis, 59, 131 – 136.
9. West, K. M., Ahujia, M. M. S., Bennett, P. H., Czyzyk, A., Mateo de Acosta, O., Fuller, J. H., Grab, B., Grabauskas, V., Jarrett, R. J., Kosakak, K., Keen, H., Krolewski, A. S., Miki, E., Schiak, V., Teucher, A., Watkins, P. J., Stober, J. A. (1983). The role of circulating glucose and triglyceride concentrations and their interactions with other ‘‘risk factors’’ as determinants of arterial disease in nine diabetic population samples from the WHO multinational study. Diabetes Care, 6, 361 – 369.
10. Wilson, P. W. F., Kannel, W. B., & Anderson, K. M. (1985). Lipids, glucose intolerance and vascular disease: the Framingham study. Monographs on Atherosclerosis, 13, 1 – 11.