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Research Article

NON-HDL$_C$ AND AIP COMPARED TO HS-CRP IN HYPERTRIGLYCERIDEMIC DIABETICS – A BETTER CARDIOVASCULAR RISK MARKER?

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ABSTRACT

Diabetic dyslipidemia is a modifiable risk factor of cardiovascular disease, characterized by elevated triglycerides, presence of small dense LDL-C particles and decreased HDL-C. Non-HDL-C is considered to be a measure of apo B containing atherogenic lipoproteins and a better predictor of CVD in type 2 DM. The aim of this study is to compare Non-HDL-C and Atherogenic Index of Plasma (AIP) in 120 type 2 diabetic subjects and correlate with hs-CRP, a low grade systemic inflammatory marker to assess the cardiovascular risk.
On comparison, Non-HDL-C an easily calculated parameter than AIP showed a statistically significant value ($P < 0.05$) and correlated more significantly with hs-CRP ($r = +0.86$) in hypertriglyceridemic type 2 diabetic subjects. Thus, Non-HDL-C is considered to be a simple, cost-effective calculated tool and a better representative of triglyceride rich lipoprotein that can assess diabetic dyslipidemia and considered to be a better predictor of adverse cardiovascular events.

Keywords: Non-HDL-C, Atherogenic Index of Plasma (AIP), high sensitive - C Reactive protein.

INTRODUCTION

India, a developing country is labeled as the Diabetic capital of the World. It is estimated that approximately 69.9 million people will have Diabetes Mellitus by 2025. Cardiovascular disease is the main cause of death in diabetes patients. It is projected that 40 million Indians will have CHD by the year 2020 [1]. The elevated CVS risk in diabetes is because of unnoticed dyslipidemia with elevated triglycerides (TG), TG rich remnant lipoprotein, apo B, LDL-C and decreased HDL-C [2, 3]. Apolipoprotein B represents the atherogenic particle which includes the triglyceride rich VLDL, IDL and LDL. Measurement of apo-B is useful for atherogenic risk assessment in dysglycemic patients [4].The lipid abnormality of high TG is very common in diabetic patients. Studies have reported that high TG levels are independently associated with development of CVS risk in obese population[5].

National Cholesterol Education Program (NCEP) had recognized that hypertriglyceridemic patients have increased risk for cardiovascular disease. Studies have demonstrated that Non-HDL-C acts as a strong predictor of CVS risk in individuals of all ages, males, females and patients with or without diabetes [2]. American Diabetes Association has considered the reduction of Non- HDL-C as target goal for diabetic patients (< 130 mg/dL) in addition to lowering LDL-C [6].

Atherogenic Index of Plasma (AIP) is calculated as Log (TG / HDL-C); with TG and HDL-C expressed in molar concentration. It also predicts the cardiovascular risk in diabetic patients, as it considers the levels of TG as an important risk factor [7]. Thus any changes in the lipid profile make the individuals more risky to develop endothelial dysfunction. C- reactive protein (CRP) is a low grade non-specific inflammatory marker that predicts cardiovascular risk. Studies have established the role of CRP in the evolvement of atheromatous lesions and are useful in diagnosing and assessing the different inflammatory stages of atherosclerotic lesions [8]. It is considered as a prominent marker of subclinical vascular inflammation and thus quantified with highly sensitive assays. The reference range of hs-CRP in adult population is categorized as low risk < 1 mg/L, average risk 1 – 3 mg/L and high risk > 3 mg/L [9].

The aim of the present study was to determine and compare AIP and non-HDL-C in type 2 diabetic patients with hs- CRP to identify the high risk lipid profile leading to adverse cardiovascular outcomes.

MATERIALS AND METHODS

A comparative and cross-sectional study was conducted among 120 type 2 diabetic patients. Institutional Ethical Committee approved the study and informed consent was obtained from the subjects.

Inclusion criteria

Type 2 Diabetic subjects aged 25 to 75 years of both sexes who visited the Diabetic clinic of our hospital were included in the study. The patients with duration of history of DM more than 1 year and less than 5 years were recruited and divided into 2 groups: Group A (n = 46) with triglyceride ≤ 150 mg/dL and Group B (n = 74) with triglyceride > 150 mg/dL. The triglyceride level was defined as per NCEP ATP III.

Exclusion criteria

Diabetic patients with infection, chronic illness, thyroid disorders and obstructive liver disease were excluded.

For lipid profile, fasting serum sample was collected and analyzed in Olympus AU400 auto analyzer for the following parameters. Fasting blood glucose, total cholesterol, triglyceride and HDL-C was measured by enzymatic method. LDL-C measured by direct immunoturbidimetric method. Non-HDL-C was calculated (TC – HDL-C) and expressed in mg/dL. AIP was calculated by using the formula AIP = log (TG/HDL-C); with TG and HDL-C expressed in molar concentration.

Statistics

The results were statistically analyzed with students't' test. The results are expressed as Mean ± Standard deviation (S.D.); $P < 0.05$ was considered statistically significant. To correlate between various parameters, Pearson's correlation coefficient was used.

RESULTS

As depicted in table (1), type 2 diabetic subjects were divided as per the triglyceridemic status. Prevalence of hypertriglyceridemia in type 2 diabetes is 62%. The atherogenic lipid profile parameters LDL-C, Non-HDL-C and AIP were studied and the results as per in table (2) showed a significant increase in type 2 Diabetics with hypertriglyceridemia on comparison with normotriglyceridemic

diabetic subjects. As shown in table (3), hs-CRP had a positive correlation with TG, Non-HDL-C, AIP and LDL-C.

Table 1: Biochemistry lipid profile parameters characterized by DM patients triglyceridemic status

Parameters	Normal triglycerides < 150 mg/dL (n= 46)	Borderline high triglycerides: 150 – 199 mg/dL (n= 57)	High triglycerides: 200 – 499 mg/dL (n= 16)	Very high triglycerides: ≥ 500 mg/dL (n= 1)
Total cholesterol mg/dL	169.5 ± 23.32	227.3 ± 37.76	259.65 ± 13.6	301.5
Triglycerides mg/dL	132.0 ± 16.01	172.01 ± 14.28	286.21 ± 33.5	627.3
HDLc mg/dL	45.0 ± 5.6	34.28 ± 4.8	30.17 ± 2.98	22.48
LDLc (Direct) mg/dL	85.72 ± 16.07	147.21 ± 14.67	164.67 ± 17.05	237.09
Non-HDLc mg/dL	124.5 ± 17.72	193.02 ± 32.78	229.48 ± 17.8	279.02
AIP*	< 0.11	> 0.21	> 0.21	> 0.21

Values are expressed in Mean ± Standard Deviation *AIP < 0.11 – low risk, 0.11- 0.21 – intermediate risk, > 0.21 – high risk

Table 2: Comparison of Non-HDLc and other cardiovascular risk markers in Normo and Hypertriglyceridemic type 2 DM

Parameters	Group A Type 2 DM (n= 46) Triglyceride < 150 mg/dL	Group B Type 2 DM (n=74) Triglyceride > 150 mg/dL	P value
Non-HDLc mg/dL	124.5 ± 17.72	233.8 ± 24.37	< 0.05
LDLc mg/dL	85.12 ± 16.07	182.96 ± 15.49	< 0.05
HDLc mg/dL	37.23 ± 4.9	31.70 ± 6.0	NS**
FBG mg/dL	102.20 ± 9.17	138.20 ± 28.17	< 0.05
HbA1c %	6.01 ± 3.9	8.8 ± 1.29	< 0.05
TC/HDL-C	3.83 ± 0.48	8.29 ± 1.28	< 0.05
LDL-C/HDL-C	2.01 ± 0.45	5.77 ± 2.58	< 0.05
hs-CRP mg/L	0.72 ± 0.24	10.80 ± 2.16	< 0.001***

Values are expressed in Mean ± Standard Deviation P value < 0.05 is considered significant. ** NS- Not significant ***Highly significant

Table 3: Correlation between hs-CRP with TG, Cardiovascular risk ratios, Non-HDL-C and AIP

Parameters	r - value	Correlation
Triglycerides mg/dL	0.79	'+'
TC/HDL-C	0.41	'+'
LDL-C/HDL-C	0.59	'+'
Non-HDL-C mg/dL	0.86	'+'
AIP	0.72	'+'

'+'- positive correlation

DISCUSSION

Laboratory diagnosis of Diabetic dyslipidemia is assessed with the plasma lipid components involved in atherogenesis. Recently, Non-HDL-C is considered to be a better indicator of cardiovascular risk. NCEP recognized hypertriglyceride as a cardiovascular risk factor and considered Non-HDL-C as one of the emerging markers of atherogenicity. Non-HDL-C can be used as a secondary target of therapy in diabetic patients with triglyceride more than 200 mg/dL.

In our study, the usual lipid profile was investigated and a significant proportion of patients had normal lipid profile. Our diabetic study group with hypertriglyceride levels had elevated LDL-C and decreased HDL-C; the cardiovascular risk ratios: TC/HDL-C and LDL-C/HDL-C which are well known risk factors for CVD were also elevated.

Interestingly, non-HDL cholesterol levels had a statistically significant increase in diabetics with hypertriglyceridemia compared to LDL-C. These results are in accordance with our previous study [10]. Though LDL-C is said to be atherogenic, it doesn't include the triglyceride rich lipoprotein (TGRLP) which are loaded with triglycerides. As the TG levels are more than 100 mg/dL the atherogenic small dense LDL particles will predominate [11]. The presence of postprandial hypertriglyceridemia is not measured correctly by the calculated LDL-C, but non-HDL-C is more reliable that can be measured in non-fasting state and thus includes the postprandial hypertriglyceridemia also [12].

Atherogenic Index of Plasma (AIP) in fact reflects the balance between atherosclerotic and protective lipoproteins, which associates TG and HDL-C. Studies have observed the significance of AIP value in assessing the CVS risk in obese patients [13]. And also AIP provides information about atherogenic plasma and quantifies the response to therapy in clinical trials of Tan et al [5].

The vascular inflammatory marker, hs-CRP was elevated in diabetic patients with hypertriglyceride levels. Increasing levels of hs-CRP indicates the chronic inflammation that leads to the progression of atherosclerosis. The present research work showed a positive correlation of hs-CRP as a cardiac marker with TG, Cardiovascular risk ratios, non-HDL-C and AIP. In fact non-HDL-C had more statistically significant correlation with hs-CRP.

David et al did a comparative study between type 2 diabetic and non-diabetic patients; classified them into low, intermediate and high risk group based on hs-CRP levels [14]. hs-CRP is considered as one of the single best predictor of future cardiovascular events and may identify patients with normal lipids but at risk for the first cardiovascular event [15]. Elevated hs-CRP levels are strong predictor of CVD; on correlating with non-HDL-C levels; it proved that non-HDL-C as the most reliable predictor of CVD. Collective information highlights that non-HDL-C is a simple, readily available, no-cost test obtained with the usual lipid profile and reflects the atherogenic risk in diabetic patients with hypertriglyceridemia and can conveniently measure CVD risk.

CONCLUSION

Non-HDL-C is more representative of all atherogenic lipoprotein which positively correlated with hs-CRP, a vascular inflammatory marker. AIP, a TG based index can significantly add value for assessing CVS risk along with other cardiovascular ratios. Easily measurable non-HDL-C is useful to clinicians to identify diabetic dyslipidemia and appropriate attention is necessary in lowering non-HDL-C especially in hypertriglyceridmic diabetic patients thereby reduces the incidence of future cardiovascular events.

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