

EVALUATE OF NON-HDL-C AND CALCULATED LIPID PROFILE RATIOS AMONG PRE-DIABETIC INDIVIDUALS

ABSTRACT

INTRODUCTION:

Diabetes mellitus, a non-communicable disease is increasing in prevalence worldwide. The disease as such does not cause mortality but, its complications do. One among the complications is dyslipidaemia which leads to atherosclerotic diseases. Pre-diabetes is a mid-state between non-diabetes and diabetes mellitus. They have a greater chance of progressing into the disease. Dyslipidaemia, a major aetiological factor for atherosclerosis, is also noted in pre-diabetic stage, report studies.

AIM:

To evaluate of non-HDL-C and calculated lipid profile ratios among pre-diabetic individuals

Objectives:

1. To analyse the lipid profile among non-diabetics, pre-diabetes individuals and diabetic patients.
2. To compare the calculated lipid profile parameters and ratios like Non-High Density Lipoprotein-Cholesterol (Non-HDL-C), Total cholesterol / HDL-C (TC/HDL-C), Low Density Lipoprotein-Cholesterol / HDL-C (LDL-C/HDL-C) among non-diabetics, pre-diabetes individuals and diabetic patients.
3. This would guide the clinician in early prediction of atherosclerotic events like myocardial infarction.

MATERIALS AND METHODS

This study was a cross-sectional study involving 26 non-diabetic controls, 26 prediabetic and 26 diabetic cases. The participants were of 18-45 years of age. The data was collected over a duration of three months. The groups were classified based on their HbA1c concentration. The blood samples were analysed for fasting lipid profile. The parameters, Non-HDL-C, TC/HDL-C and LDL-C/HDL-C by their respective methods.

RESULTS

The calculated lipid profile parameters, Non-HDL-C, TC/HDL-C and LDL-C/HDL-C were found to be increased in pre-diabetic subjects and diabetic subjects when compared to the healthy non-diabetic controls. The parameters also showed a positive correlation and was statistically highly significant among the three groups.

CONCLUSIONS

There was a positive association observed among the groups for the calculated lipid profile parameters, Non-HDL-C, TC/HDL-C and LDL-C/HDL-C and were found to be increasing with their HbA1c. The values were found to be high in pre-diabetics when compared to the control group. Therefore Non-HDL-C, TC/HDL-C and LDL-C/HDL-C should be monitored in pre-diabetic individuals along with their glycaemic status to avoid atherosclerotic complications.

Keywords: Non-HDL-C, Total cholesterol / HDL-C, LDL-C / HDL-C and pre-diabetes.

INTRODUCTION

Diabetes mellitus is one of the diseases familiar to human beings since the ancient ages. The disease has a heterogeneous aetiology like genetic predisposition, lifestyle and the environmental factors. In the recent times the prevalence and incidence of diabetes mellitus has increased among the developing countries as well.

As per International Diabetes Federation (IDF) around 415 million diabetes mellitus patients were confirmed worldwide in 2015 and is feared to rise to 592 million cases in 2035 [1]. Diabetes mellitus cases in India was around 69.1 million and in Tamil Nadu it was 10.4 million in 2010, reports ICMR-INDIAB study [2].

Diabetes mellitus (DM) on a long-term basis results in the malfunction and irreversible damage to various organs [3]. The disease itself is preceded by a condition called as pre-diabetes. The condition is between the normoglycemic and hyperglycaemic levels of diabetes mellitus. There is a 50% chance for pre-diabetics to develop diabetes mellitus, reports a study [4].

Among the complications of diabetes mellitus, Cardio vascular disease (CVD) is the most common with around 80% of all-inclusive death in diabetes mellitus [5]. The risk is equally shared by pre-diabetes as well [6].

The major predisposing factor of CVD in diabetes mellitus is considered as dyslipidaemia which leads to the quickening of atherosclerosis. The importance of lipid profile ratios like Total cholesterol / HDL-C (TC/HDL-C) and Low Density Lipoprotein-Cholesterol / HDL-C (LDL-C/HDL-C) had been illustrated in various studies conducted [7]. Another parameter which gained clinical importance in the recent years is the Non-High Density Lipoprotein-Cholesterol (Non-HDL-C) in dyslipidaemic complications [8]. LDL-C/HDL-C and TC/HDL-C ratio can also be considered as potential markers for predicting glycaemic control in diabetes mellitus patients, reports a study [9]. Hence, this study was aimed at studying the lipid profile derived parameters like Non-HDL-C, TC/HDL-C and LDL-C/HDL-C among pre-diabetes and to compare the same with diabetes and non-diabetes.

MATERIALS AND METHODS

The data was collected retrospectively from the Clinical laboratory of the Department of Biochemistry at Sree Balaji Medical College Hospital over a period of three months. Group-B and Group-C had 26 pre-diabetics and 26 diabetics between the age group 18-45 included in the cross-sectional study. The participants were attending General Medicine out-patient departments. The participants with HbA1c values between 5.7 – 6.4 % were grouped together in Group-B and HbA1c $\geq$ 6.5 % were grouped under Group-C. Equal number of men and women (13 each) were involved in Group-B and Group-C. Group-A were age and sex matched controls with normal HbA1c (< 5.7 %) concentration.

The Group-B participants were found to have pre-diabetic HbA1c incidentally and the Group-C participants were known Type-2 Diabetes mellitus patients on treatment visiting the General Medicine department for follow up. Patients with known dyslipidaemia and on treatment for the same were excluded from the study.

Serum samples from the study participants and the non-diabetic controls were collected by following the institutional ethical guidelines. Informed and written consent were obtained in the local language. Strict aseptic measures were followed in the sample collection procedure. The collected samples were analysed for HbA1c and lipid profile parameters like Total Cholesterol, HDL-C and LDL-C. The lipid profile parameters were analysed in BS 480

Mindray and HbA1c was measured in BS 390 Mindray by their respective methods [Table 1]. Both are fully automated Biochemistry analysers.

The Non-HDL-C was calculated from the formula:

$$\text{Non-HDL-C} = \text{Total Cholesterol} - \text{HDL-C}.$$

The lipid profile ratios like TC/HDL-C and LDL-C/HDL-C were calculated from the lipid profile parameters. The normal ranges of Non-HDL-C, TC/HDL-C and LDL-C/HDL-C were obtained from the laboratory reference range.

Table 1: Parameters with their methods of estimation.

Parameter	Method
HbA1c in %	Immunoturbidimetry
Total Cholesterol (mg/dl)	CHOD-POD
HDL-C (mg/dl)	Direct
LDL-C (mg/dl)	Direct

All the three groups, Group-A, Group-B and Group-C had their means and standard deviations (SD) calculated. Statistical Package for the Social Sciences (SPSS) version 17 software was used to perform the statistical analysis. Analysis of variance (ANOVA) waste method of comparison used to find the statistical significance and correlation of Non-HDL-C, TC/HDL-C and LDL-C/HDL-C among the three groups (non-diabetics, pre-diabetics and diabetics). $P \leq 0.05$ was considered significant.

RESULTS

HbA1c had a mean of 5.4 in control Group-A. The pre-diabetic individuals in Group-B had a mean HbA1c of 6.05 whereas, Group-C diabetic subjects had 8.09 as mean HbA1c [Table 2]. The HbA1c values were used to divide the subjects into two groups namely, pre-diabetes and diabetes respectively as Group-B and Group-C.

Table 2 : The HbA1c values were used

Parameters	Normal range	Group - A	Group - B	Group - C	P value
HbA1c	< 5.7 %	5.40 ± 0.25	6.05 ± 0.26	8.09 ± 1.26	<0.01*
NON-HDL-C	< 130	125.57 ±	144.10±	161.60 ±	<0.01*

	mg/dl	29.35	40.35	32.59	
TC/HDL	3-5	3.32± 0.96	4.11 ± 0.92	5.32 ± 1.45	<0.01*
LDL/HDL	1.5-3.5	2.10± 0.57	2.43 ± 0.86	3.76 ± 0.78	<0.01*

Values of Non-HDL-C, TC/HDL-C and LDL-C/HDL-C are expressed in mean ± standard deviation. The values are statistically significant based on the 'P' value. *P-value < 0.01

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The parameters Non-HDL-C, TC/HDL-C and LDL-C/HDL-C were calculated from the lipid profile parameters for all the participants of the three groups.

The mean and SD of Non-HDL-C was 125.57±29.35 in Group-A controls. 144.10± 40.35 and 161.60 ± 32.59 were the means and SD for Group-B and Group-C respectively. An increase in Non-HDL-C levels was observed in pre-diabetic and diabetic patients than the control group.

TC/HDL-C had a mean of 4.11 among pre-diabetics and 5.32 among diabetes patients, which shows an increase when compared to the non-diabetics with a mean of 3.32. The same trend was also noted with the LDL-C/HDL-C, with a mean of 2.1, 2.43 and 3.76 among non-diabetics, pre-diabetics and diabetics respectively.

Statistical analyses by ANOVA and Pearson's correlation were performed to determine the relationship between the parameters. P value < 0.01 was considered as highly significant. The results obtained clearly show increased Non-HDL-C, TC/HDL-C and LDL-C/HDL-C to a greater extent in Diabetes mellitus patients, lesser extent in Pre-diabetes group when compared to the non-diabetic controls, with a highly significant p < 0.01. [Table 2]

DISCUSSIONS

The study included three groups, non-diabetics, pre-diabetics and diabetics based on the HbA1c values. Lipid profile parameters were estimated from the fasting samples. Non-HDL-C, TC/HDL-C and LDL-C/HDL-C were calculated from the lipid profile. The means of the calculated lipid profile ratios showed a positive correlation among the groups and was found to be statistically highly significant in ANOVA study.

Another study reported TC/HDL-C ratio as the major predictor of vascular complications like atherosclerosis. The ratio was considered as the Hazard ratio [7]. In diabetes mellitus, Non-HDL-C can be considered as a better predictor of CVD, reports a study [8]. These studies concurred with the current study as the Non-HDL-C and TC/HDL-C were found to be increased in pre-diabetes and diabetes. Triglyceride/HDL-C ratio was also associated with the risk of diabetes mellitus among elderly in China, a recent study reports [10]. The advantage of the current study is that, TC/HDL-C does not require a fasting sample.

The LDL-C/HDL-C ratio is termed as the Atherogenic index. The ratio was found to be positively correlated with the cardio vascular risk factors in two different populations, Malaysia and Iran [11,12]. This was in concordance with the current study as it showed a gradual increase in pre-diabetes and diabetes with a high statistical significance. There were various other studies conducted in other parts of India which showed similar results [13,14].

The LDL-C/HDL-C ratio showed no significant increase in prediabetics when compared to the non-diabetic controls, reports a study [15]. This contrasted the current study.

Hence, there shall be further studies conducted on a larger population to understand the correlation of the lipid profile ratios with the complications of diabetes mellitus.

CONCLUSION

The study concludes with an increase in lipid profile calculated parameter and ratios like, Non-HDL-C, TC/HDL-C and LDL-C/HDL-C among diabetes mellitus compared to those with pre-diabetic range of HbA1c and controls. The parameters shall be used as predictors for atherosclerosis among pre-diabetes individuals during their follow-up visits to avoid major complications of diabetes mellitus.

Ethical standards

The ethical standards of the health care institution were strictly adhered to during the conduct of the study.

Limitations of the study

The study population shall be enlarged as it was relatively less.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

REFERENCES

1. International Diabetes Federation. IDF Diabetes Atlas 7th edition. 2015; IDF;13.
2. Pradeepa R, Anjana RM, Joshi SR, Bhansali A, Deepa M, Joshi PP, et al. Prevalence of generalized & abdominal obesity in urban & rural India - the ICMR-INDIAB study (Phase-I) [ICMR-INDIAB-3]. Indian J Med Res 2015; 142: 139-50.
3. Shi Y, Hu FB. The global implications of diabetes and cancer. Lancet 2014; 383:1947-8.
4. Danaei G, Finucane MM, Lu Y, et al. National, regional, and global trends in fasting plasma glucose and diabetes prevalence since 1980: systematic analysis of health examination surveys and epidemiological studies with 370 country-years and 2. 7 million participants. Lancet. 2011;378:31–40.
5. Animaw W, Seyoum Y. Increasing prevalence of diabetes mellitus in a developing country and its related factors. PLoS One 2017;12:e0187670.
6. Bhowmik B, Siddiquee T, Mujumder A, Afsana F, Ahmed T, Mdala IA, et al. Serum lipid profile and its association with diabetes and prediabetes in a rural Bangladeshi population. Int J Environ Res Public Health 2018;15:1944.
7. Gimeno-Orna JA, Faure-Nogueras E and SanchoSerrano MA. Usefulness of total cholesterol/HDLcholesterol ratio in the management of diabetic dyslipidaemia. Diabet Med 2005; 22: 26-31.
8. Lu W, Resnick HE, Jablonski KA, Jones KL, Jain AK, Howard WJ, et al. Non-HDL cholesterol as a predictor of cardiovascular disease in type 2 diabetes: the strong heart study. Diabetes Care 2003; 26: 16-23.
9. Artha IMJR, Bhargah A, Dharmawan NK, et al. High level of individual lipid profile and lipid ratio as a predictive marker of poor glycemic control in type-2 diabetes mellitus. Vasc Health Risk Manage. 2019;15:149-157.

10. Zheng D, Li H, Ai F, Sun F, Singh M, Cao X, Jiang J, He Y, Tang Z, Guo X. Association between the triglyceride to high-density lipoprotein cholesterol ratio and the risk of type 2 diabetes mellitus among Chinese elderly: the Beijing Longitudinal Study of Aging. *BMJ Open Diabetes Res Care*. 2020 Mar;8(1):e000811.
11. Bo MS, Cheah WL, Lwin S, New TM, Win TT, Aung M. Understanding the relationship between atherogenic index of plasma and cardiovascular disease risk factors among staff of an University in Malaysia. *J Nutr Metab* 2018;2018.
12. Kazemi T, Hajihosseini M, Moossavi M, Hemmati M, Ziaee M. Cardiovascular risk factors and atherogenic indices in an Iranian population: Birjand East of Iran. *Clin Med Insights Cardiol* 2018;12:1-6.
13. Mahat R, Singh N, Rathore V, Gupta A, Shah R. Relationship between atherogenic indices and carotid intima-media thickness in prediabetes: A cross-sectional study from Central India. *Med Sci* 2018;6. doi: 10.3390/medsci6030055.
14. Ranjit PM, Guntuku GS, Pothineni RB. Comparison of lipid profile and new atherogenic indices among the coronary artery disease (CAD)-negative and -positive diabetic dyslipidemia subjects. *Int J Med Sci Public Health* 2015;4:1574-9.
15. Miyazaki Y, Furugen M, Akasaka H, Saitoh S, Miura T. Atherogenic lipids profile relates to postprandial hyperglycemia and hyperinsulinemia due to whole body insulin resistance in prediabetic subjects. *J Diabetes Mellitus* 2012;2:272-8.