Original Article

Cardiovascular Disease in Type 2 Diabetes

Non-HDL Cholesterol as a Predictor of Cardiovascular Disease in Type 2 Diabetes

Hafiz Abdul Kabir and Kashif Ali Hashmi

ABSTRACT

Objective: To analyze the role of non-HDL-Cholesterol as an indicator for the development of CVD in Pakistan's population with type 2 diabetes mellitus (T2DM).

Study Design: Cross-sectional analytical study

Place and Duration of Study: This study was conducted at the department of Cardiology diabetic Centre at Ch. Pervaiz Elahi Institute of Cardiology Multan from June 2020 to June 2021 for a period of one year.

Materials and Methods: The study included 90 subjects, 50 cardio paths with T2DM and 40 control. Standard enzymatic procedures were used to establish biochemical balance. A questionnaire was used as a means of collecting information about pathologies.

Results: The logistic model showed two levels of non-HDL-C: 130 mg/dl < non-HDL-C ≤ 160 mg/ dl (OR = .12, P=.002, 95% CI = .02-0.48) and 160 mg/dl < non-HDL-C ≤ 190 mg/dl (OR = 5.03, P =.036, 95% CI = 1.2-22.88) and smoking (OR= 19.28, P = .00295% CI = 3.38-109.64), inbreeding (OR = 3.66, P = .032,95% CI = 1.13-11.86) and 2 age groups 60-70 years (OR = 2.37, P<0.05,95% CI = 1.33-4.3) and those of 70 years or above (OR = 2.27, P<0.0595% CI = 1.18-4.28).

Conclusion: Non-HDL-C is a potential risk factor for the development of CVD in patients with T2DM in Pakistan.

Key Words: Non-HDL cholesterol, T2DM, cardiovascular diseases

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INTRODUCTION

One of the main causes of death in diabetic patients is cardiovascular complications. The risk of cardiovascular complications is two to more times more in type 2 diabetics as compared to people without diabetes [1]. According to various studies value of non-HDL cholesterol (non-HDL-C) is an predictor for cardiovascular problems in various communities[2]. In the American ethnic population affected by diabetes non-HDL-C is one of the various risk factors of Cardiovascular disease (CVD)[3]. In diabetics, non-HDL-C is a more valuable indicator for CVD as compared to triglycerides or low-density lipoprotein cholesterol (LDL-C), as it is strongly related to atherogenic lipoprotein[4].

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In diabetes, lipid abnormality is commonly characterized by low HDL cholesterol level, increase in triglyceride level, and increased occurrence of small dense particles of LDL[5]. During the disease composition of LDL changes because of which becomes very atherogenic [6]. When the level of triglycerides becomes higher than 100 mg/deciliter, particles of minute dense atherogenic LDL become predominant. In a prospective study conducted on the ethnic diabetic community (Indian community in the USA) which is at high risk of cardiovascular disease, it was established that non-HDL cholesterol has an important predictive value for clinical parameters[7]. Thus, non-HDL-C is a reproducible and simple index for assessing cardiovascular risk, its indicative value is equal, if not more as compared to, LDL cholesterol. This study aims to conduct multivariate analysis to access the role of non-HDL cholesterol in CVD in the diabetic population in Pakistan.

MATERIALS AND METHODS

A cross-sectional comparative study was conducted at the Diabetic Center of Cardiology at Ch.Pervaiz Elahi Institute of Cardiology Multan for 1 year from 22nd June 2020 to 22nd June 2021. The study included 90 subjects, controls (40), and cardio paths with T2DM (50). Both male and female patients, diagnosed with diabetic heart disease were included in the study. Whereas, control were healthy subjects who visited the

hospital for temporary illness. All patients were informed of the study objective and consent was taken. Participants of the study were excluded if they had refused to give their consent. Similarly, ethical approval was taken from the ethical committee of the hospital. For every control and case subject following were noted: name, age, diabetes, knowledge of CVD, height, weight, blood glucose levels, and family history of diabetes, total cholesterol, LDL-C, HDL-C, triglycerides, creatinine, and urea. Cultural and genealogical data of parents of each control and diabetic subject, socio-professional status, and educational level were also considered. Diagnosis of diabetic condition was based on World health organization (WHO) criteria 1985: moderate fasting hyperglycemia designated to fasting sugar levels between 1.1-1.25 g/l whereas diabetes is attributed to patients with fasting glucose levels exceeding from 1.26 g/l. Moreover, BMI was measured by dividing weight in kilogram by square of height in meters. After a fasting condition of minimum 10 hours, 5 ml venous blood was collected for biochemical analysis in a heparin tube. Blood glucose, urea, triglycerides, and total cholesterol were analyzed through standardized enzymes measuring protocols. The non-HDL-C was measured using the formula:

Non-HDL-C = total cholesterol - HDL-C

Minitab 16 software was used to process data. A predictive model of CVD related with T2DM was determined through a binary logistic regression study[8]. The forecast capacity of the logistic model was determined by calculating the area under the curve (AUC) and plotting receiving operating characteristics (ROC) curve. P-value < 0.05 for any variable was considered statistically significant.

RESULTS

According to the Table 1, level 0 represents a non-HDL-C level below 130 mg/dl. If this is considered in logistic model, level 1 subjects (130 mg/dl < non-HDL-C ≤ 160 mg/ dl) indicates that risk of exposure toT2DM and CVD is lowered when contrasted with patients with non-HDL-C below 130 mg/dl (OR = .12; P=.002, 95% CI = 0.02-0.48). On the other hand, those with higher non-HDL-C levels (160 mg/dl < non-HDL-C ≤ 190 mg/dl) are at 5 times greater risk of T2DM and CVD (OR = 5.03; P =.036, 95% CI = 1.2-22.88) as compared to subjects with non-HDL-C level 1 (130 mg/dl < non-HDL-C≤ 160 mg/dl).

About smoking, smokers are at 19 times higher risk of T2DM and CVD as compared to non- smokers (OR= 19.28; P = .002, 95% CI = 3.38-109.64).

About inbreeding, result (OR = 3.66; P = .032, 95% CI = 1.13-11.86) indicate the risk of CVD and T2DM is three and a half times more in those with related parents as compared to those from non-breeding ones.

Those aging from 60-70 years are also used in our model, such subjects are at two times higher risk of CVD and T2DM as compared to those less than younger subjects (OR = 2.37; P<0.01 95% CI = 1.33-4.3).

Nevertheless, the probability of occurrence of T2DM in those above 70 years (OR = 2.27; P<0.05, 95% CI = 1.18-4.28) is two times higher than in those with age between 60 to70 years.

Table 2 represents that adequacy tests by using the deviance method, the Pearson method, Brown methods (symmetrical alternative and general alternative), and Hosmer-Lemeshow method accepts the model with P value more than 0.05.

Table 3 indicates the predictive value of the used model. The percentage of matching pairs is very high (82%). Moreover, the results of table of discordant and matching pairs were shown by Tau-aof Kendall, Gamma of Goodman-Kruskal, and D of Somers. The measurement is usually ranged in between 0-1. The highest value indicates a significant predictive value of the model. The first 2 measurements of .72 and .78 indicate a very significant predictive capability. Similarly, the Kendall Tau-a suggests a considerable predictive capability.

Table No.1: Logistic regression model results

Predictors	Coefficient	Z (Wald)	P-Value	OR	CI (95%)
Constants	-1.10267	-1.61	.008		
Non-HDL-C 1	-2.2052	-1.99	.002	.12	.02-.48
Non-HDL-C 2	1.61404	1.10	.036	5.03	1.2-22.88
Smoking	2.95859	3.35	.002	19.28	3.38-109.64
Consanguinity	1.2945	2.16	.032	3.66	1.13-11.86
Age (60-70 years)	.85685	2.92	.005	2.37	1.33-4.3
Age (> 70 years)	.814497	2.48	.012	2.27	1.18-4.28

Table No.2: Adjustment Adequacy Tests

Methods	K-squire	DF	P-value
Pearson	8718	18	.94
Some of the difference squares	10.6654	18	.87
Hosmer-Lemeshow	.4183	6	.99
Brown:			
General alternative	.4394	3	.80
Symmetrical alternative	.0264	2	.872

DF: degree of freedom

The ROC curve associated the rate of false-positive (FPR) to that of true positive (TPR) through a graph. Generally, p (w) is compared to a threshold S= 0.5 for drawing a prediction. Therefore, the confusion matrix is constructed and the 2 indicators discussed above are extracted.

For every configuration, the confusion matrix was constructed and TPR and FPR were calculated.

The value of the area under curve was .89, thus the model adopted in subjects with CVD and T2DM was found to be quite predictive (Fig I).

Table No.3: The measure of association (between probability previsions and response variables)

Pairs	Number	%tage	Measure recapitulative	
Concordant	2098	83	D of Sommers	.72
Discordant	277	9.9	Gamma of Goodman-Kruskal	.78
Ex aequo	182	7.1	Tau-a of Kendall	.33
Total	2557	100		

DISCUSSION

In diabetic patients with cardiovascular complications, results reveal that risk of the relation between CVD and type 2 diabetes mellitus (T2DM) in both genders is associated with both levels of non-HDL-C (130 mg/dl < non-HDL-C160 mg/dl and 160 mg/ dl < non-HDL-C190 mg/dl), inbreeding, smoking, individuals aging between 60 and 70 years and above. In this study, the potential of association between CVD and T2DM is less in cases having a non-HDL-C level between 130 mg/ dl and 160 mg/dl as compared to the one with non-HDL-C levels less than 130 mg/dl.

While there is five times more risk of this association in subjects having a non-HDL-C value between 160-190 mg/dl than those with the non-HDL-C value between 130 mg/dl-160 mg/dl. Multiple researches reveal that in both diabetics and non-diabetics non-HDL-C is associated with cardiovascular complications. A study shows that diabetic patients with non-HDL-C levels> 130 mg/dl are more exposed to pre-process myocardial injury than those having non-HDL-C < 100 mg/dl[9].

It is also observed that diabetic patients with non-HDL-C levels in between 111.9-134.7 mg/dl are at greater risk of coronary heart disease (with CI =1.09-1.39, HR=1.23) than those with non-HDL-C level less than 11.97mg/dl [10]. A Chinese cohort study with 27020 participants revealed that in individuals with a non-HDL-C more than 190 mg/dl, there is an elevated risk of CVD (with CI =1.50-2.47, HR=1.93) when contrasted with those having non-HDL-C level less than 130 mg/dl who are further categorized based on diabetic status: greater risk of CVD in diabetes patients (CI=1.50-1.42, HR=1.22) as compared to non-diabetics (CI=1.04-1.19, HR=1.11)[11].

In another study, out of 25639 subjects about 2066 developed cardiovascular disease. The risk of development of cardiovascular complications increased with increase in non-HDL-C, when compared to normal non-HDL-C level subjects[12]. Likewise, there is 3 times greater risk of development of CVD (CI=1.58-6.21, HR=3.13) in subjects with non-HDL-C level more than 180 m/dl compared to those with non-HDL-C level less than 100 mg/dl [13].

Considering smoking as a variable, according to our logistic model there is 19 times more risk of the relation between CVD and T2DM in the smoker as compared to a nonsmoker, and our results match with those of Kitamura[14]. Whereas, another study concluded that there is no relation between various levels of non-HDL-C and smoking, as the P-value of .84 was found[11].

There is a lack of careful research on inbreeding and the role of non-HDL-C in CVD and in T2DM. In this study, this factor is used to access its involvement. This model demonstrates that there is three and a half times more risk of association between two diseases because of inbreeding. This is in line with the potent correlation found between cardiovascular profile and inbreeding in 587 patients[15]. Age factor is also used in this model. Results reveal that subjects under 60 are less exposed to both these diseases as compared to those aged 60 and 70, who have two times higher risk of developing these. Those over 70 also have two times higher risk of developing these diseases. A Chinese study containing a sample of 351 patients with heart disease showed the average age to be 58.6 ± 10 years16, which approaches the age of developing T2DM and CVD found in our study.

CONCLUSION

Non-HDL-C carries a potential risk for exposure to CVD in T2DM in Pakistan. Other significantly associated factors studies are age, inbreeding, and smoking.

Author's Contribution:

Concept & Design of Study:	Hafiz Abdul Kabir
Drafting:	Kashif Ali Hashmi
Data Analysis:	Kashif Ali Hashmi
Revisiting Critically:	Hafiz Abdul Kabir, Kashif Ali Hashmi
Final Approval of version:	Hafiz Abdul Kabir

Conflict of Interest: The study has no conflict of interest to declare by any author.

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