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Original Article

Predictive value of non-HDL cholesterol for cardiovascular disease in a population in far western Algeria with type 2 diabetes

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ABSTRACTS

Background: Non high density lipoprotein cholesterol (non-HDL-C) is a risk factor for cardiovascular disease (CVD) in people with type 2 diabetes. The aim of our study is to estimate the relative multivariate risk of non-HDL-C in the occurrence of CVD in a population in the extreme western Algeria with type 2 diabetes mellitus (T2DM).

Methods: Our study was carried out in western Algeria on a population of 1111 subjects, 371 cardiopaths with T2DM and 740 controls. The biochemical balance was established using standard enzymatic procedures (SFBC or IFCC recommendations) on the Beckman CX7® PLC (Beckman-Coulter®, NY, USA). Information on the pathologies was collected by means of a questionnaire.

Results: The logistic model retained the two levels of non-HDL-C: 130 mg/dl < non-HDL-C≤160 mg/dl (OR = 0.11; 95% CI = 0.03−0,47, P = 0.003) and 160 mg/dl < non-HDL-C≤190 mg/dl (OR = 5.02; 95% CI = 1.1−22.87, P = 0.037) and smoking (OR = 19.27; 95% CI = 3.39−109.63, P = 0.001), inbreeding (OR = 3.65; 95% CI = 1.12−11,85, P = 0.031) and the two age groups 60−70 years (OR = 2.36; 95% CI = 1.32 −4.2, P<<0.01) and 70 years and over (OR = 2.26; 95% CI = 1.19−4.29, P<<0.05).

Conclusions: Non-HDL-C is a powerful risk factor for the occurrence of cardiovascular disease in type 2 diabetics in the extreme western Algeria.

1. Introduction

Cardiovascular complications are the leading cause of death in people with diabetes. Indeed, type 2 diabetics have a two to four times higher risk of cardiovascular events than adults without diabetes [1,2].

Many studies have shown that the value of non-HDL-C can be an indicator of cardiovascular risk in different populations, including Europeans [3].

Non-HDL-C appears to follow the multiple risk factors for CVD among American ethnic minorities disproportionately affected by diabetes [4,5].

In diabetic patients, non-HDL-C may be a more potent predictor of CVD than low density lipoprotein cholesterol (LDL-C), or triglycerides, because it has a strong correlation with atherogenic lipoproteins [6].

The common lipid abnormality of diabetes is characterized by high triglyceride levels, low HDL cholesterol levels and an increased presence of small dense LDL particles [7]. Changes in the composition of LDL-C that can accompany the disease make LDL-C exceptionally atherogenic [8]. In fact, once the triglyceride level exceeds 100 mg per deciliter (mg/dl), small dense atherogenic LDL-C particles predominate [9].

In this regard, Lu et al. established, in a prospective study, the predictive value of non-HDL-C for clinical parameters in an ethnic diabetic population (Indian communities in the United States) at high cardiovascular risk [10]. Non-HDL-C is therefore a simple, reliable and reproducible index of the overall risk of cardiovascular risk, which may be equivalent to, if not higher than, LDL cholesterol [11].

Most of the available data, which studies the extension of risk factors for CVD in the Maghreb [12], and in particular in Algeria [13], are of a descriptive nature.

It is proposed to estimate the relative multivariate risk of non-HDL-C in the occurrence of cardiovascular pathologies in a

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diabetic population in extreme western Algeria.

2. Methods

This was a case-control study that included 1111 subjects, cardiopaths with T2DM (371), and controls (740).

The participants, both male and female, were admitted to the University Hospital in Tlemcen.

Patients are recruited by health specialists. Only individuals known to have diabetic heart disease are considered.

For each case and control subject, it was noted: identification, age, knowledge of cardiovascular disease, diabetes, weight, height, family history of diabetes, and respective levels of blood glucose, total cholesterol, HDL-C, LDL-C, triglycerides, urea and creatinine. Genealogical and cultural data were also collected on the parents of each diabetic and control subject (degree of inbreeding of the parents) as well as the educational level and socio-professional situation of each individual.

The diagnosis was made according to world health organization (WHO) criteria in 1985 [14]: diabetes from 1.26 g/l, moderate fasting hyperglycemia from 1.10 to 1.25 g/l. The body mass index was estimated by weight (kg) divided by the square of height (m). Venous blood is collected after a fast of at least 10 h 5 ml of blood was collected on a heparin tube for the biochemical test. Urea, blood glucose, total cholesterol and triglycerides are measured using standard enzyme procedures (SFBC or IFCC recommendations) on the Beckman CX7® PLC (Beckman-Coulter®, NY, USA). The non-HDL-C has been calculated by the following formula: non-HDL-C = total cholesterol - HDL-C.

Subjects will only be eligible for the study after obtaining their consent, or parental consent if they are under 18 years of age. This study protocol is approved by the ANDRS (Ethics Committee of the National Agency for the Development of Health Research in Algeria).

2.1. Statistical analysis

Data processing was performed using Minitab 16 software. A binary logistic regression study [15] was conducted to determine a predictive model of heart disease associated with type 2 diabetes using the measured factors (the response variable is noted here as Y, which counts diabetic heart disease (C) and controls (T), (C) being the reference value).

The Area under curve (AUC) was calculated and the receiving operating characteristics (ROC) curve was plotted to determine the forecast capacity of our logistics model. The results are considered statistically significant from a P-value ≤ 0.05.

3. Results

Non-HDL-C levels were categorised according to the National Cholesterol Education Program-Adult Treatment Panel-III (NCEP-ATP-III) [16]. From our results in Table 1, level 0 indicates an non-HDL-C level <130 mg/dl taking this factor into account in the logistic model, it appears in level 1 (130 mg/dl < non-HDL-C≤160 mg/dl) that the risk of occurrence of CVD and T2DM is reduced once compared to subjects with an non-HDL-C level <130 mg/dl (OR = 0.11; 95% CI = 0.03–0.47, P = 0.003). While subjects with high non-HDL-C levels (160 mg/dl < non-HDL-C≤190 mg/dl) are five times more exposed to CVD and T2DM (OR = 5.02; 95% CI = 1.1–22.87, P = 0.037) than those with an non-HDL-C level 1 (130 mg/dl < non-HDL-C≤160 mg/dl).

Regarding smoking, smokers are 19 times more exposed to CVD and T2DM than non-smokers (OR = 19.27; 95% CI = 3.39–109.63, P = 0.001).

Table 1
Results of the logistic regression model study.

Predictors	Coefficients	Z (Wald)	P-value	OR	CI (95%)
Constant	−1,10269	−2,62	0,009		
Non HDL-C 1	−2,2051	−2,98	0,003	0,11	0,03–0,47
Non HDL-C 2	1,61403	2,09	0,037	5,02	1,1–22,87
Smoking	2,95858	3,34	0,001	19,27	3,39–109,63
Consanguinity	1,2944	2,15	0,031	3,65	1,12–11,85
Age (60–70 years)	0,85684	2,91	0,004	2,36	1,32–4,2
Age (>70 years)	0,814499	2,49	0,013	2,26	1,19–4,29

Key: Non HDL-C 1: (130 mg/dl < non-HDL-C≤160 mg/dl), **Non HDL-C 2:** (160 mg/dl < non-HDL-C≤190 mg/dl), **OR:** odds ratio, **CI:** confidence interval.

Table 2
Adjustment adequacy tests.

Methods	K-squire	DF	P-value
Pearson	8717	17	0,949
Sum of the difference squares	10,6653	17	0,873
Hosmer-Lemeshow	0,4182	5	0,995
Brown:			
General alternative	0,4393	2	0,803
Symmetrical alternative	0,0263	1	0,871

Key: DF: degree of freedom.

For inbreeding, the result is (OR = 3.65; 95% CI = 1.12–11.85, P = 0.031), which shows that the risk of exposure to CVD and T2DM in subjects with related parents is three and a half times higher than in subjects from non-inbreeding marriages.

Our model also used the age group [60–70 years], whose subjects aged 60–70 years are twice as exposed to CVD and T2DM as those under 60 years of age (OR = 2.36; 95% CI = 1.32–4.2, P<<0.01).

However, the risk of exposure to type 2 diabetes in subjects over 70 years of age (OR = 2.26; 95% CI = 1.19–4.29, P<<0.05) is twice as high as in the age group [60–70 years].

In Table 2, adequacy tests using the Pearson method, the deviance method, the Hosmer-Lemeshow method and the Brown methods (general alternative and symmetrical alternative) accept the model with (P>>0.05).

Table 3 shows the forecasting capabilities of our model. There is a very high percentage of matching pairs (82%). The summaries of the table of matching and discordant pairs are represented by D of Somers, Gamma of Goodman-Kruskal and Tau-a of Kendall, these measurements are generally between 0 and 1, where the highest values show that the model has better predictive capabilities. The first two measurements of 0.71 and 0.77 imply a very high predictive capacity, the Kendall Tau-a gives a relatively good predictive capacity.

3.1. ROC curve

The ROC curve (Fig. 1) relates the rate of true positive (TPR) to the rate of false positive (FPR) in a graph. Usually, we compare p(w) to a threshold S = 0.5 to make a prediction y(w). We can thus construct the matrix of confusion and extract the two indicators

Table 3
Measure of associations (between response variable and probability previsions).

Pairs	Number	Percentage	Measures récapitulative	
Concordant	2097	82	D of Somers	0,71
Discordant	278	10,9	Gamma of Goodman-Kruskal	0,77
Ex aequo	181	7,1	Tau-a of Kendall	0,32
Total	2556	100		

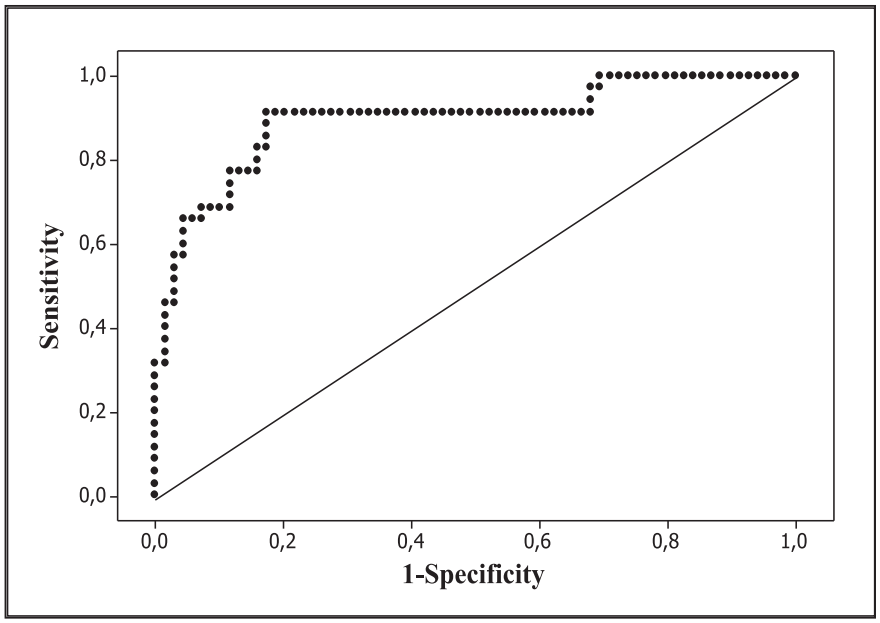

Fig. 1. ROC curve of the decision threshold, for modelling predictive values of non HDL cholesterol in the occurrence of CVD in T2DM.

mentioned above. The ROC curve generalizes this idea by varying the entire continuum of possible S threshold values between 0 and 1. For each configuration we construct the confusion matrix and calculate TPR and FPR.

The value of the AUC equal to 0.89, therefore the model used in patients with CVD and T2DM, has excellent discrimination.

4. Discussion

In diabetics with CVD, our results show that the risk of association between T2DM and CVD in both sexes is related to both levels of non-HDL-C (130 mg/dl < non-HDL-C≤160 mg/dl and 160 mg/dl < non-HDL-C≤190 mg/dl), smoking, inbreeding and the two age groups 60–70 years and over.

In our study, subjects with a non-HDL-C level between 130 mg/dl and 160 mg/dl are less exposed to the association between T2DM and CVD than those with a non-HDL-C level below 130 mg/dl. While subjects with a non-HDL-C level between 160 and 190 mg/dl are five times more exposed to this combination than subjects with a non-HDL-C level of 130 mg/dl and 160 mg/dl.

Most studies show that non-HDL-C is a factor of exposure to CVD in diabetics as well as in non diabetics.

First, Zeng and collaborators also report that patients with diabetes who are poorly balanced with a non-HDL-C >130 level have a higher risk of preprocess myocardial injury; than those with a level <100 mg/dl [17].

It has been shown that diabetics subjects with a non-HDL-C level between 111.97 and 134.75 mg/dl are more exposed to coronary heart disease with HR = 1.23; CI = 1.09–1.39 compared to those with a non-HDL-C level below 111.97 mg/dl [18].

A cohort study conducted in China on 27020 subjects showed that the risk of exposure to CVD in subjects with a non-HDL-C >190 mg/dl level is higher with (HR = 1.93; CI = 1.50–2.47) compared to those with non-HDL-C levels below 130 mg/dl with a relatively higher risk of exposure to CVD in diabetics (HR = 1.22; CI = 1.05–1.42) than in non diabetics (HR = 1.11; CI = 1.04–1.19) [19].

About 2066 subjects among 25639 develop a cardiovascular pathology, the risk of occurrence of CVD increases with non-HDL-C, it appears in the three high levels of non-HDL-C: (HR = 1.26; CI = 1.08–1.47), (HR = 1.51; CI = 1.31–1.74) and (HR = 1.87; CI = 1.62–2.15) respectively compared to those who have a normal level of non-HDL-C [20].

Similarly, subjects with a non-HDL-C level above 180 mg/dl are 3 times more exposed to CVD (HR = 3.13; CI = 1.58–6.21) than those with a non-HDL-C level below 100 mg/dl [21].

In a similar study, patients with a non-HDL-C>130 mg/dl level have a high incidence of major cardiovascular events (HR = 3.15; P = 0.003). Compared to patients with a non-HDL-C level less than 100 mg/dl [22].

As for the study on smoking, it appears in our logistic model that smokers are 19 times more exposed to the risk of association between T2DM and CVD, and our results corroborate those of Kitamura [21].

On the other hand, the study by Gu and collaborators showed that smoking is not associated with the different levels of non-HDL-C, the percentages of smokers according to the levels of non-HDL-C are between 36% and 38% with a P value equal to 0.84 [19].

Inbreeding has not been carefully researched in all studies concerning the predictive risk value of non-HDL-C in the occurrence of cardiovascular events inT2DM. We used this factor to see its involvement. The model shows that inbreeding increases the risk of association of the two diseases by about three and a half times.

This is consistent with a significant association found between inbreeding and the cardiovascular profile of 587 patients [23].

There is an undeniable age factor in this model. Our results show that subjects aged between 60 and 70 have a twice as high risk of developing both diseases compared to those aged under 60. Subjects over 70 years of age are also twice as exposed to both diseases.

The average age found in a study conducted in China on a population of 351 patients with coronary heart disease (58.6 ± 10 years) [24]. Approaching the age of exposure to CVD and T2DM found in our study population.

The age averages of two other Chinese populations were found to be significantly elevated compared to the different classes of non-HDL-C [19,21].

5. Conclusions

The results of the modelling showed that non-HDL-C is a powerful risk factor for the occurrence of CVD in type 2 diabetics in extreme western Algeria. The other factors studied, significantly related, are: smoking, inbreeding and age.

The model is very significant, there is a relationship between the explanatory values and the explained variables with good predictions.

Conflicts of interest

Have not a direct or indirect interest (financial or nature) with a private, industrial or commercial organization relationship with the subject presented.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dsx.2018.12.002.

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