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Original Article

# Non-HDL cholesterol predictive factor of type 2 diabetes in the city of Tlemcen

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ABSTRACTS

*Background:* type 2 diabetes mellitus (T2DM) is associated with disorders of lipoprotein metabolism mixed dyslipidemia. The purpose of this study is to verify whether non high density lipoprotein cholesterol (non-HDL-C) can contribute to the development of T2DM in a population in the extreme western Algeria.

*Methods:* The study was conducted in Tlemcen region on a sample of 1852 subjects,1059 with T2DM and 793 controls, these were evaluated for biochemical parameters, measured using standard enzyme procedures (SFBC or IFCC recommendations) on the Beckman CX7® PLC (Beckman-Coulter®, NY, USA). All the information related to the disease were collected from the patients and recorded using predesigned questionnaire.

*Results:* The logistic model retained, the two levels of non-HDL-C: 130 mg/dl < non-HDL-C≤160 mg/dl (OR = 0,69; 95% CI = 0,49–0,97, P = 0,033) and non-HDL-C>190 mg/dl (OR = 2,22; 95% CI = 1,31–3,76, P = 0,003), inbreeding (OR = 1,71; 95% CI = 1,44–2,04, P = 0,000) and the two age groups 60–70 years (OR = 2,14; 95% CI = 1,47–3,1, P ≪ 0,001) and 70 years and over (OR = 2,26; 95% CI = 1,51–3,38, P ≪ 0,001).

*Conclusions:* The logistic model shows that non-HDL-C contributes to the development of type 2 diabetes in our population.



## 1. Introduction

T2DM is associated with disorders of lipoprotein metabolism, including mixed dyslipidemia combining hyper production of very low density lipoproteins (VLDL), low levels of high density lipoprotein cholesterol (HDL-C) and small and dense low density lipoprotein cholesterol (LDL-C).

Many experimental studies have investigated the effects of different classes of lipoproteins on cell function and survival.

Their measurement in clinical practice is not a new concept. The Helsinki Heart Study 3 used non-HDL-C levels for the management of dyslipidemia [1].

On this basis, non-HDL-C was added as a secondary treatment target in patients with high triglyceride levels (>200 mg/dL) [2].

In an analysis of combined data from 68 studies [3], non-HDL-C was the best predictor of all cholesterol measurements, both for coronary heart disease and stroke [4].

Similarly, T2DM is frequently associated with mixed dyslipidemia, as well as lipotoxicity characterized by an increase in triglyceride content at the β-pancreatic cell level.

New data suggests a link between cholesterol metabolism and cell function β, thus the accumulation of cholesterol in the pancreatic islets alters insulin secretion.

Indeed, the increase in plasma lipid concentration, as well as their accumulation in tissues, contributes to the development of hepatic and muscular insulin resistance and to beta cell dysfunctions [5,6], in part via the induction of metabolic stress, involving in particular oxidative stress, endoplasmic reticulum (ER) stress and the disruption of calcium homeostasis [7].

Finally, the different classes of lipoproteins have their own effects on apoptosis and cell proliferation of β-pancreatic cells (protection of HDL-C and deleterious effect of LDL-C).

Knowing that HDL-C also has a protective effect on the beta cells, the purpose of this study is to verify whether non-HDL-C can contribute to the development of T2DM in a population in the extreme western Algeria.

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## 2. Methods

This was a case-control study that included 1852 subjects, type 2 diabetics (1059), and controls (793).

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

Patients were recruited by health specialists. Only individuals known to have type 2 diabetes were considered.

For each case and control subject, we noted: identification, age, knowledge of 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 WHO criteria in 1985 [8]: 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 tests. Blood glucose, total cholesterol, HDL-C, LDL-C and triglycerides were 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. This study protocol is approved by an Ethics Committee of the National Agency for the Development of Health Research Algeria.

### 2.1. Statistical analysis

Data processing was performed using Minitab 16 software. A binary logistic regression study [9] was conducted to determine a predictive model of type 2 diabetes using the measured factors (the response variable is noted here as Y, which counts type 2 diabetes patients (D) and controls (T), with (D) 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 of ≤0,05.

## 3. Results

Non-HDL-C levels were categorised according to the National Cholesterol Education Program-Adult Treatment Panel-III (NCEP-ATP-III) [10], the logistic model (Table 1) retained the level 1 of non-HDL-C (130 mg/dl < non-HDL-C≤160 mg/dl) with (OR = 0,69; 95% CI = 0,49–0.97, P = 0,033). It can be seen that subjects with a rate of non-HDL-C close to ideal are less exposed to T2DM compared to subjects with an non-HDL-C level <130 mg/dl.

The risk of exposure to T2DM in subjects with high levels of non-HDL-C between 160 mg/dl and 190 mg/dl) is about half that of subjects with levels close to the ideal of non-HDL-C (OR = 1,53; 95% CI = 0,96–2,46, P = 0,075).

Subjects with very high levels of non-HDL-C (non-HDL-C>190 mg/dl) are twice as exposed to T2DM as in the previous class (OR = 2,22; 95% CI = 1,31–3,76, P = 0,003).

Taking into account the smoking factor in the logistic model, it appears (OR = 1,54; 95% CI = 0,97–2,44, P = 0,069) that the risk of exposure to T2DM in smokers is multiplied by 1,54 compared to non smokers.

With respect to inbreeding (OR = 1,71; 95% CI = 1,44–2,04, P = 0,000), which shows that subjects with related relatives have a 1,71 risk of developing T2DM compared to subjects from non-inbreeding marriages.

For the age factor, the age group [60–70 years] is twice as exposed to T2DM as subjects under 60 years of age (OR = 2,14; 95% CI = 1,47–3,1, P ≪ 0,001). While subjects over 70 years of age also have twice the risk of developing T2DM in relation to the age group [60–70 years] (OR = 2,26; 95% CI = 1,51–3,38, P ≪ 0,001).

We kept the variables non-HDL-C 2 (160 mg/dl < non-HDL-C≤190 mg/dl) and smoking although they are not significant in the forecast model because they favor significance and the adequacy tests are more favorable to their retention than to their withdrawal.

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).

The predictive capabilities of this model (Table 3) reveal a very high percentage of matching pairs (65%). Somers' D and Goodman-Kruskal's Gamma values of 0,35 and 0,37 imply a good predictive capability, Kendall's Tau-a gives a relatively low predictive capability.

### 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)

**Table 2**
Adjustment adequacy tests.

| Methods | K-squire | DF | P-value |
|---|---|---|---|
| Pearson | 66,3701 | 58 | 0,211 |
| Sum of the difference squares | 73,8582 | 58 | 0,078 |
| Hosmer-Lemeshow | 12,4744 | 6 | 0,052 |
| Brown: | | | |
| General alternative | 1,7371 | 2 | 0,42 |
| Symmetrical alternative | 0,0164 | 1 | 0,898 |

**Key: DF:** degree of freedom.

**Table 1**
Results of the logistic regression model study.

| Predictors | Coefficients | Z (Wald) | P-value | OR | CI Min (95%) | CI Max (95%) |
|---|---|---|---|---|---|---|
| Constant | −0,503762 | −3,56 | 0,000 | | | |
| Non-HDL-C 1 | −0,367995 | −2,13 | 0,033 | 0,69 | 0,49 | 0,97 |
| Non-HDL-C 2 | 0,428116 | 1,78 | 0,075 | 1,53 | 0,96 | 2,46 |
| Non-HDL-C 3 | 0,798425 | 2,97 | 0,003 | 2,22 | 1,31 | 3,76 |
| Smoking | 0,42968 | 1,82 | 0,069 | 1,54 | 0,97 | 2,44 |
| Consanguinity | 0,536299 | 6,01 | 0,000 | 1,71 | 1,44 | 2,04 |
| Age (60–70 years) | 0,759953 | 4,01 | 0,000 | 2,14 | 1,47 | 3,1 |
| Age (>70 years) | 0,814721 | 3,97 | 0,000 | 2,26 | 1,51 | 3,38 |

**Key: Non HDL-C 1:** (130nmg/dl < nonHDL-C≤160 mg/dl), **Non HDL-C 2:** (160 mg/dl < non-HDL-C≤190 mg/dl), **Non HDL-C 3**: (non-HDL-C>190 mg/dl), **OR:** odds ratio, **CI:** confidence interval, **mg/dl:** milligram per deciliter.

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

| Pairs | Number | Percentage | Measures récapitulative | |
|---|---|---|---|---|
| Concordant | 136075 | 65 | D of Somers | 0,35 |
| Discordant | 62905 | 30,1 | Gamma of Goodman-Kruskal | 0,37 |
| Ex a equo | 10220 | 4,9 | Tau a of Kendall | 0,17 |
| Total | 209200 | 100 | | |

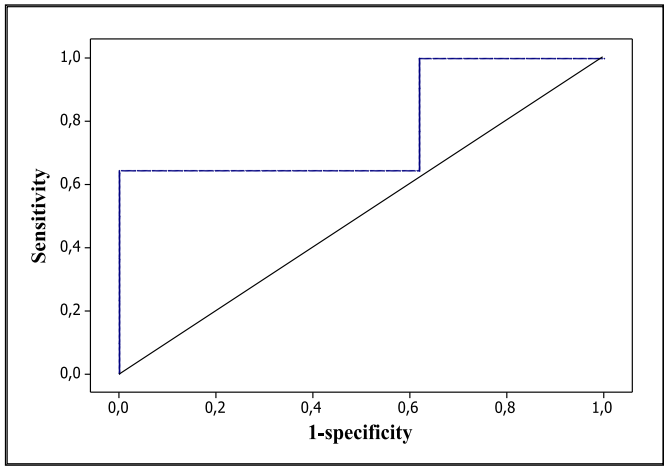


**Fig. 1.** ROC curve.

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 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 (Area under curve) equal to 0,77, which shows an acceptable discrimination of the model used in diabetics.

## 4. Discussion

In diabetics, the logistic model reveals a statistically significant association between the risk of T2DM and non-HDL-C levels (130 mg/dl < non-HDL-C mg/dl ≤ 160 mg/dl and non-HDL-C>190 mg/dl), inbreeding and the two age groups retained in diabetics with heart disease (60–70 years and over 70 years).

Subjects with a non-HDL-C level between 130 and 160 mg/dl are less exposed to T2DM than those with a non-HDL-C level below 130 mg/dl. Subjects with a non-HDL-C level between 160 and 190 mg/dl have a risk multiplied by 1,53 compared to those in class 130–160 mg/dl. However, subjects with a non HDL-C level above 190 mg/dl are twice as exposed to T2DM as subjects with a non-HDL-C level between 160 and 190 mg/dl.

For T2DM, studies performed for the prediction of T2DM by non-HDL-C are very rare.

Our results are consistent with those found in a descriptive study conducted in Taiwan on 104 type 2 diabetics and 21 controls which showed that the number of subjects with a non-HDL-C level above 130 mg/dl is significantly higher compared to those with a level below 130 mg/dl (P < 0,001) and controls (P = 0,021) [11].

According to a case control study conducted in Bangladesh on 103 type 2 diabetics and 47 non diabetics, the average non-HDL-C is significantly higher in diabetics (181 ± 40,11) than non diabetics (142,47 ± 63,27) with a p value equal to 0,000 [12].

In another study conducted in Venezuela, the mean non-HDL-C in diabetics (180,67 ± 78,99) is significantly higher than in controls (133,60 ± 18,40) [13].

From our results, smokers have a risk of exposure to T2DM multiplied by 1,54 compared to non smokers.

These results contradict those found in a study conducted in Sweden on a diabetic population, a small percentage of patients who smoke was observed (17,9%) [14].

Our logistic model shows that subjects from inbred marriages have a risk of exposure to T2DM multiplied by 1,71.

Our results are consistent with a similar study conducted in the same region that shows that inbreeding increases the risk of T2DM three times [15].

In another study in a Saudi Arabian diabetic population, fasting blood glucose levels increase with increasing degrees of inbreeding [16].

Regarding age, the result found in diabetics without heart disease is almost identical to that found in diabetics with heart disease.

This result is similar to that found in the study by Zhen et al., who showed that subjects in group A (HbA1c<7%) have a significantly higher mean age (60,17 ± 9,49) than those in group B (HbA1c>7%) with a P < 0.05) [17].

On the other hand, the age of exposure to T2DM found in a previous study (50–61 and > 60 years of age is lower than that found in the latter study [18].

In the Zabeen team study, no significant differences were found between the average age of diabetics (46,53 ± 5,43) and non diabetics (47,38 ± 7,61) [12].

## 5. Conclusions

The logistic model shows that non-HDL-C contributes to the development of T2DM in our population. Inbreeding and age are also significantly related to T2DM.

## 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.2018.11.021.

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