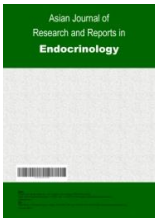

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Non High-Density Lipoprotein Cholesterol in Type2 Diabetic Patients

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Authors' contributions

This work was carried out in collaboration among all authors. Author ME designed the study. Authors HC and SM wrote the first draft of the manuscript and managed the literature searches. Authors WS, KB and KEA performed the statistical analysis. Authors DBS and FHK managed the analyses of the study. Authors FM, MM, NC and MA reviewed the final draft. All authors read and approved the final manuscript.

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ABSTRACT

Aims: To study the relationship between non high-density lipoprotein cholesterol (non-HDL-C) and metabolic disorders in type2 diabetic patients and to prove the incrimination of non-HDL-C in the genesis of chronic complications of diabetes.
Study Design: Retrospective study.
Place and Duration of Study: Endocrinology-Diabetology Department of Hedi Chaker University Hospital of Sfax for a period of two months, January and February 2020.
Methodology: We included80 type2 diabetic patients (34 men and 46 women; age range: 22-72 years) with metabolic syndrome. Each patient had undergone a complete clinical examination and biochemistry test, then, the non-HDL-C was calculated.
Results: Out of 80 patients, 57 suffered from diabetic complications like micro vascular and macro vascular complications. Unbalanced diabetes was identified in 73.75% of the patients. All the patients had a high level of non-HDL-C.

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No significant positive correlation was confirmed between non-HDL-C with body mass index, glycemic parameters, triglycerides, or total cholesterol.
Correlation between the level of non-HDL-C and coronary artery disease, myocardial infarction (MI), and stroke was identified with p values of 0.016, 0.05, and 0.04, respectively.
Patients with microvascular complications had higher levels of non-HDL-C but a positive correlation was only relevant with diabetic nephropathy (p=0.026).
Conclusion: Our study confirmed that non-HDL-C is a simple and reliable indicator of the overall risk of cardiovascular disease, thus, it may be equivalent, if not superior, to low-density lipoprotein cholesterol (LDL-C). Therefore, it should be our primary lipid treatment target for diabetic patients.

Keywords: Non-high-density lipoprotein cholesterol; diabetes; diabetic complications; metabolic syndrome.

1. INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of death worldwide. The risk of CVD must always be assessed in diabetic patients who are often classified as having a high or very high cardiovascular risk. In these patients, low-density-lipoprotein cholesterol (LDL-C) is the main therapeutic target [1,2]. In fact, many authors had incriminated the role of non-high-density lipoprotein cholesterol (non-HDL-C), thus, making it a probable new biological entity for assessing cardiovascular risk.

The objectives of this work were, first, to study the relationship between non-HDL-C and metabolic disorders in type2 diabetic patients, and secondly, to prove the incrimination of non-HDL-C in the genesis of chronic complications of diabetes.

2. MATERIALS AND METHODS

It was a cross-sectional study including 80 type2 diabetic patients with metabolic syndrome (MS). MS was defined according to the International Diabetic Federation (IDF) word wide definition. All patients were followed in the Endocrinology-Diabetology Department of Hedi Chaker University Hospital of Sfax for a period of two months, January and February 2020.

The diabetic patients presenting metabolic syndrome during follow up visit were selected in our study. Each patient had undergone a complete clinical examination, an impact assessment in search of micro- and macrovascular complications, and a metabolism assessment including a complete lipid check-up.

The non-HDL-C was calculated by the following formula:

Total cholesterol (mmol/L) - HDL cholesterol (mmol/L); it was considered high if it was ≥ 4.3 mmol/L according to the Canadian Cardiovascular Society‘s dyslipidemia guidelines.

To assess the role of non-HDL-C on type 2 diabetic patients, we proceed with the following steps.

As a first step, clinical and biological characteristics of our study population were described. The second step consisted of looking for correlations between non-HDL-C and the metabolic parameters–in particular, blood glucose and lipid findings. The third step was the comparison of non-HDL-C levels between patients with and without chronic complications of diabetes.

For the statistical study, all the data were processed using SPSS software (version 20). Quantitative variables were presented as a mean/ standard deviation and qualitative variable as an absolute number and its percentage. For the correlations, the Chi-square test was used with measurement of the Spearman coefficient.

3. RESULTS

Our population consisted of 34 men (42.5%) and 46 women (57.5%). The average age of the patients was 60.2 years with extremes ranging from 22 to 72 years. Personal history was dominated by hyperlipidemia and hypertension, followed by coronary insufficiency and obliterating arteritis of the lower limbs.

For diabetes, the average duration was 11.53 years with extremes ranging from 1 to 27 years. Micro vascular complications were present in 57 patients (71%) and Macro vascular complications in 46 patients (29%) (Figs. 1, 2).

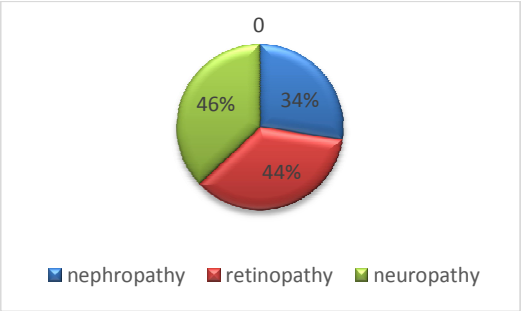

Fig. 1. Micro_vascular complications

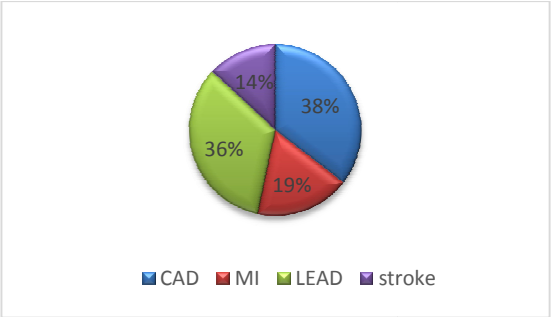

Fig. 2. Macro_vascular complications

The average body mass index (BMI) was estimated at 31.3 kg / m², with extremes ranging from 21 to 99 kg / m². Normal BMI was noted in 23 patients, overweight in 18 (22.5%), and obesity in 39 (48.8%). A waist circumference (WC) above 102 cm was noted in 20% of the male patients. It was more than 88 cm in 50% of the female patients.

The average value of fasting blood glucose was 9.29 mmol/L. The median glycated hemoglobin A level was 9.5% with extremes between 5 and 17%. It was over 7% in 73.75% of the patients. Cholesterol levels ranged from 3.6 to 8.75 mmol/L. Hypercholesterolemia was noted in 55% of the patients. The mean level of LDL-C was 5.35mmol/L, with extremes between 0.2 and 5.17mmol/L. The mean level of non-HDL-C was 4.76 mmol/L, with extremes between 2.6 and 6.82 mmol/L. It was elevated in all patients.

Our results did not show a correlation between non-HDL-C and BMI. However, a statistically significant positive correlation was confirmed with WC. Moreover, non-HDL-C was not correlated with glycemic parameters, triglycerides, or total cholesterol. However, a statistically significant positive correlation was found with LDL-C (P = 0)

Patients with macrovascular complications had higher levels of non-HDL-C than those without cardiovascular disease. This was noted in all types of macrovascular disease.

Mean non-HDL-C was 4.65 mmol/L [2.6_7.18] in patients with myocardial infarction (MI) vs 4.1 mmol/L [2.6-6.18] in those without MI (P = 0.05). It was also noted that the mean level of non-HDL-C in coronary artery disease (CAD) was 4.75 [2.6-6.18] mmol/L versus 4.6 [2.7-6.18] mmol/L in those free of CAD (P = 0.016).

The mean non-HDL-C in patients with lower extremity arterial disease (LEAD) was 4.30 [2.9-6.18] mmol/L versus 4.16 [2.6-6.18]in those without LEAD (P = 0.06). The average non-HDL-C was 5.89 [5.6-6.18] mmol/L in patients with transient ischemic attack (TIA) versus 4.17 [2.6-6.18] mmol/L in those without TIA (P = 0.026). The mean level of non-HDL-C in patients with stroke was 4.21 [2.6-6.18] mmol/L versus 4.2 [2.78-5.93] mmol/L in those without stroke (P = 0.04).

The statistical study also showed that patients with microvascular complications had higher levels of non-HDL-C (Table 1). This was verified with all types of microvascular complications.

4. DISCUSSION

Non-HDL cholesterol includes all lipoproteins containing atherogenic apolipoprotein B (apoB), very low-density cholesterol lipoproteins (VLDL), intermediate-density lipoproteins (IDL), lipoproteins (a), chylomicrons and their triglyceride-rich remnants [3,4]. Non-HDL-C refers to total cholesterol value minus HDL cholesterol.

Table 1. Levels of non-HDL-C and P values by microvascular complications

	Present (mmol/L)	Absent (mmol/L)	P value
Diabetic retinopathy	4.42 [2.6-6.18]	4.04 [2.7-5.93]	0.13
Diabetic nephropathies	4.37 |2.6-6.18]	3.73 [2.7-5.93]	0.026
Diabetic neuropathy	4.23 [2.7-6.18]	4.20 [2.6-6.18]	0.91

Recently, International Atherosclerosis Society and National Lipid Association argued that the non-HDL-C value is better than the LDL-C value for predicting heart disease, thus making it a better therapeutic target [5,6].

Huang et al observed high levels of non-HDL-C in individuals with metabolic syndrome, while LDL-C levels showed no significant increase [7]. This has led to the stipulation that non-LDL lipoprotein fractions are responsible for cardiovascular disease in people with metabolic syndrome [8].

In our study, no positive correlation between BMI and non-HDL-C was identified. Similarly, this relationship was not objectified in literature. However, the waist circumference was positively and statistically correlated with non-HDL-C rates. Even though waist circumference is a simple sign of abdominal obesity, it is a powerful predictor of morbidity and mortality. Non-HDL-C is likely increased in subjects with obesity, insulin resistance, and hyperglycemia through increased TG-rich lipoproteins [9,10,11]. Thus, android obesity associated with hypertriglyceridemia greater than 2mmol/L (1.8 g/L) indicates the presence of multiple other atherogenic metabolic disturbances. No data on the relationship between waist circumference and the rate of non-HDL-C are yet available in the literature.

Hyperglycemia is also a major risk factor for patients with metabolic syndrome. A one percent increase in HbA1c corresponds to an increase in the relative risk of cardiovascular mortality of 10% over 10 years (UKPDS study) [12]. In our study, no positive correlations between glycemic parameters and non-HDL-C were found. However, a dataset of the health screening program conducted by the Yuport Medical Checkup Center in Tokyo, Japan, showed positive and significant correlations between these parameters and non-HDL-C for both men and women [13]. As dyslipidemia is an important feature of metabolic syndrome, Reiko Seki et al showed a significant correlation between non-HDL-C and triglycerides [14]. Our study showed that non-HDL-C was not correlated with TG or CT. However, a significant positive correlation was objectified with LDL-C. As expected, it was negatively correlated with HDL-C.

For diabetic patients, the role of non-HDL-C in the risk of cardiovascular disease was suggested by some authors. The results of a recent meta-analysis [15] showed that non-HDL-C was the best predictor of all cholesterol measurements for both coronary artery disease events and strokes [16]. Our results are consistent with the data from this study. Indeed, we identified higher rates of non-HDL-C in patients with macro-vascular complications versus those who were free from these complications.

Given the presence of positive correlations with several cardiovascular risk factors – such as android obesity, age, male sex, LDL-C, and kidney failure – non-HDL-C is likely associated with cardiovascular risk. The hypothesis of similarity with LDL-C, which is an atherogenic process [14] responsible for the development and progression of atherosclerotic plaques and by the accumulation of these lipoproteins in the arterial intima, could be the most plausible [17,18]. Multiple studies have shown that non-HDL-C is a better predictor of cardiovascular risk compared to LDL-C [15,19,20]. Furthermore, numerous cross-sectional and prospective studies have demonstrated the value of non-HDL-C as a risk index for coronary artery disease in different populations, including Europeans [21,22,23], Hawaiians [24], and cohorts in the United States [25,26]. The results of our study were consistent with this latest study, which showed that mean non-HDL-C was significantly higher in coronary artery patients or patients with myocardial infarction versus those free of these conditions. Thus, to reduce the risk of cardiovascular events in type 2 diabetic patients, it is necessary to correct non-HDL-C [27]. Therefore, for most diabetic patients, considered to be at high cardiovascular risk, it is recommended to maintain the level of LDL-C below 70 mg/dl and the level of non-HDL-C below 100 mg/dL. For those with a very high cardiovascular risk, LDL-C levels should remain below 55 mg/dl and non-HDL-C levels below 80 mg/dl [28].

5. CONCLUSION

Our work confirmed that non-HDL-C is a simple and reliable indicator of the overall risk of cardiovascular disease, thus, making it equivalent, if not superior, to LDL cholesterol. Non-HDL-C is easily calculated from a lipid profile (non-HDL-C = total cholesterol minus HDL-C) and, therefore, does not result in any additional analysis costs to the health care system. The non-HDL-C calculation does not rely on a triglyceride value, so, there is no need to fast, as opposed to LDL-C measurements which require fasting. Therefore, it should be our primary lipid treatment target for diabetic patients.

CONSENT AND ETHICAL APPROVAL

As per international standard or university standard guideline patients consent and ethical approval has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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