



# Impact of Gender Differences and Glycated Haemoglobin on Atherosclerosis Risk in Type 2 Diabetic Patients from North Western Algeria

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## ABSTRACT

In type 2 diabetic patients, blood lipids and lipid ratios have been proven to be associated with atherosclerosis risk; however, results about the effect of gender differences had not been fully conclusive. In this transversal comparative study, a total of 129 adult type 2 diabetic patients (54 men and 75 women), from north western Algeria, was included to highlight the impact of gender differences on atherosclerosis risk (assessed by lipid ratios) according to their diabetic profile. Comparing between the two genders, no significant differences ( $p > 0.05$ ) were noted on diabetes duration, central obesity, body mass index and blood pressures. Moreover, the basic biochemical parameters of both glycaemic and lipid metabolism were not meaningfully divergent. However, higher significant values ( $p < 0.05$ ) of body weight, height, HbA1c levels, HDL and lipid ratios (TC/HDL, LDL/HDL and TG/HDL) were observed in male patients comparing to females. According to the HbA1c levels ( $\text{HbA1c} < 7\%$  vs.  $\text{HbA1c} \geq 7\%$ ); notable higher CT/HDL, LDL/HDL and TG/HDL in male patients comparing to women were found. The rates of these three lipid ratios were often higher in both classes of HbA1c. The consideration of gender differences is very important for prevention, diagnosis, treatment and management of atherosclerosis and CVD. The disparity in atherogenic risk, in both genders, estimated by lipid ratios need to be critically examined. Further, interventional studies are needed to determine how sex can modulate the impacts of diabetes control parameters on atherosclerosis risk.

**Keywords:** lipid ratios, atherosclerosis, type 2 diabetes, gender difference, diabetes control.

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## 1 Introduction

Globally, an upsurge in number of people dying from cardiovascular disease (CVD) is expected to reach 23.3 million by 2030 [1], [2]. The prevalence of atherosclerosis, which is the dominant cause of cardiovascular disease (CVD), is significantly higher in diabetic people comparing to those without the diabetic disease. The clinical associations between diabetes and atherosclerosis are now well established. Several observational studies suggest that damages on vascular homeostasis are due to the impact of chronic hyperglycaemia. Likewise, higher levels of the mediators of inflammation, such as C-reactive protein (CRP), interleukin-6 (IL-6), plasminogen activator inhibitor 1 (PAI-1), are observed in diabetic patients suggesting a positive correlation between diabetes and atherosclerosis [3]. Type 2 diabetes is, however, more associated to cardiovascular co-morbidities and mortality comparing to the other types of diabetes mellitus [4, 5]. As of 2016, the American Diabetes Association “ADA” has focused specifically in its treatment guidelines in type 2 diabetic disease on "atherosclerotic cardiovascular disease" and suspected peripheral arterial disease of atherosclerotic origin [6]. However, increasing evidence indicates that risk of atherosclerosis in type 2 diabetic patients is different in women and men [7], [8].

Dyslipidaemia, defined by elevated serum lipids, is one of the most significant risk factors for atherosclerosis [9]. There is contradictory data on the role of serum lipids and their ratios such as total cholesterol (TC)/high density lipoprotein (HDL), triglycerides (TG)/HDL, and low-density lipoprotein (LDL)/HDL in the promotion of atherosclerosis [10]. Though, several factors such as age, gender differences, anthropometric parameters, glycosylated haemoglobin level (HbA1c) and diabetes mellitus have been long-established to be associated with the atherosclerosis risk. The objective of this study was therefore to assess the risk of atherosclerosis (estimated using serum lipid ratios) by comparing men and women with type 2 diabetes, from the north western Algeria, according to their HbA1c level.

## 2 Patients and Methods

This is a transversal comparative study performed during four months, from November 2019 to February 2020, and covered a total of 129 adult type 2 diabetic patients (54 men and 75 women) aged 30 to 80 years ( $64.17 \pm 10.77$  years). This work took place in the Public Establishment of Proximity Health (diabetes centre Larbi Ben M'hidi; Ex Gambetta) in Sidi-Bel-Abbes, North-western Algeria. The source of information is based on medical records of diabetic patients. Data analysis were processed and performed manually using the Statistical Package for Social Sciences® (SPSS, version 24.0) and the Microsoft Excel 2013 program. Results are expressed as means  $\pm$  standard deviations, the paired student *t*-test for independent samples was used for comparing this means values with statistical significance set at  $p=0.05$ . Lipid ratios indicating the atherogenic risk were compared between the two genders according the glycated haemoglobin level using box plots.

## 3 Results

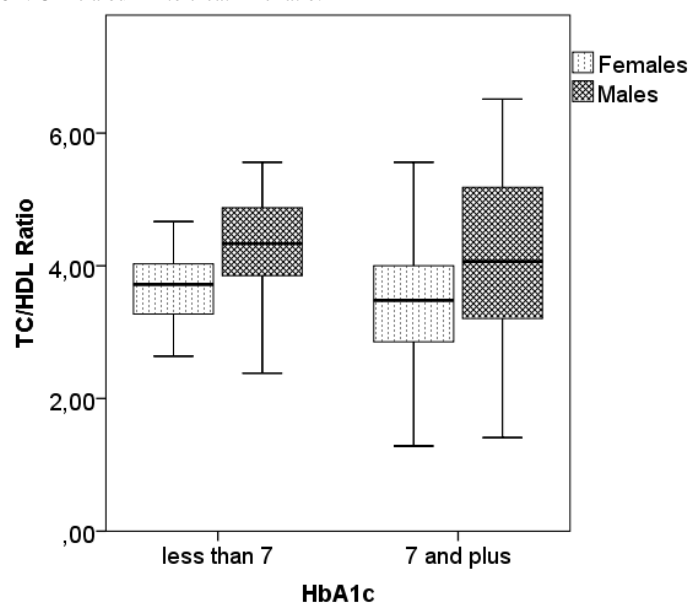
Table 1 summarizes the comparison of basic characteristics between males and females type 2 diabetic patients involved in our study. No significant differences were highlighted for diabetes duration, waist circumference, body mass index (BMI) and blood pressures. Furthermore, biochemical parameters did not show any significant differences when comparing between the two genders, namely for; fasting glycaemia, main lipid parameters, albuminuria, creatinuria, urea and creatinine. However, higher significant values ( $p<0.05$ ) of body weight, height, HbA1c levels, HDL and lipid ratios (TC/HDL, LDL/HDL and TG/HDL) were observed in male patients comparing to females.

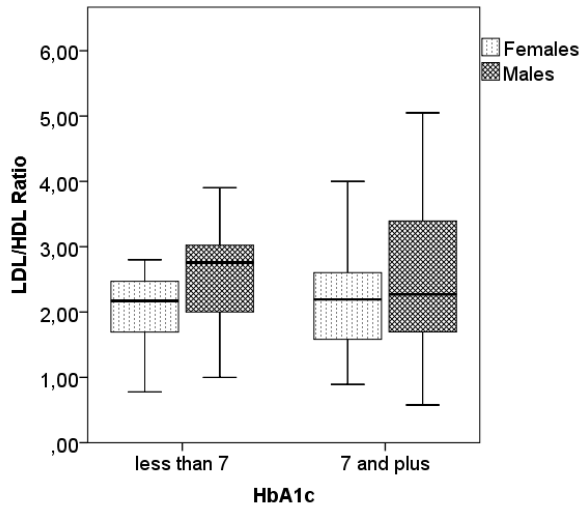
**Table 1:** Comparison of basic characteristics between male and female patients

variables	All patients, n=129	Males, n=54	Females, n=75	p value*
Age (years)	64.17±10.77	66.61±9.59	62.42±11.28	<b>0.029</b>
Diabetes duration (years)	13.95±8.98	12.87±8.16	14.67±9.47	0.281
<b>Anthropometric parameters</b>				
Weight (kg)	76.81±16.86	82.66±15.49	72.60±16.65	<b>0.001</b>
Height (m)	162.45±8.43	169.06±6.66	157.82±6.17	<b>0.000</b>
Waist circumference (cm)	107.31±12.14	108.75±10.88	106.34±12.93	0.353
BMI (kg/m <sup>2</sup> )	29.33±6.56	29.29±6.68	29.36±6.52	0.953
<b>Blood pressure</b>				
Systolic Blood Pressure (mmHg)	12.39±1.76	12.66±1.52	12.21±1.89	0.223
Diastolic Blood Pressure (mmHg)	6.58±0.98	6.66±0.93	6.53±1.01	0.549
<b>Biochemical parameters</b>				
Fasting glycaemia (g/l)	1.48±0.60	1.55±0.56	1.43±0.64	0.636
HbA1c (%)	7.96±1.45	8.03±1.67	7.91±1.28	<b>0.017</b>
Total cholesterol (g/l)	1.59±0.50	1.62±0.58	1.57±0.45	0.562
HDL (g/l)	0.43±0.10	0.39±0.10	0.46±0.10	<b>0.002</b>
LDL (g/l)	0.98±0.38	0.98±0.47	0.98±0.31	0.903
Triglycerides (g/l)	1.18±0.67	1.36±0.79	1.06±0.53	0.562
Urea (g/l)	0.38±0.13	0.43±0.13	0.29±0.10	0.462
Creatinine (g/l)	12.02±0.87	14.96±10.37	7.62±2.59	0.149
<b>Lipid ratios</b>				
TC/HDL	3.80±1.36	4.20±1.52	3.52±1.18	<b>0.009</b>
LDL/HDL	2.36±0.96	2.55±1.11	2.23±0.82	0.086
TG/HDL	2.94±2.22	3.58±2.70	2.51±1.71	<b>0.011</b>

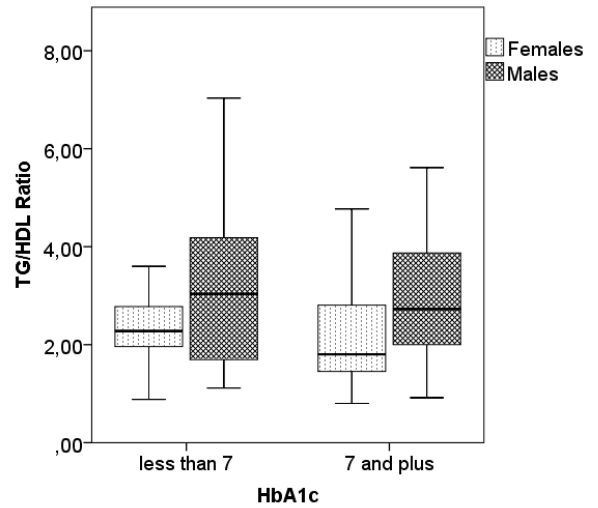
(\*) Comparison between males and females using Student's *t*-test, a  $p < 0.05$  was considered as significant; BMI: body mass index; HbA1c: glycated haemoglobin; TC: total cholesterol; LDL: low-density lipoprotein cholesterol; HDL: high-density lipoprotein cholesterol; TG: triglycerides; ACR: Urine albumin to creatinine ratio.

Our findings about the comparison of lipid ratios, between males and females with type 2 diabetes, according to the HbA1c levels (HbA1c < 7% vs. HbA1c ≥ 7%) revealed high levels of TC/HDL (figure 1. A), LDL/HDL (figure 1. B) and TG/HDL (figure 1. C) in male patients comparing to females. The rates of these three lipid ratios are often higher in both classes of HbA1c.

**Figure 1. A:** Comparison of total cholesterol/HDL ratio between males and females according to HbA1c level.

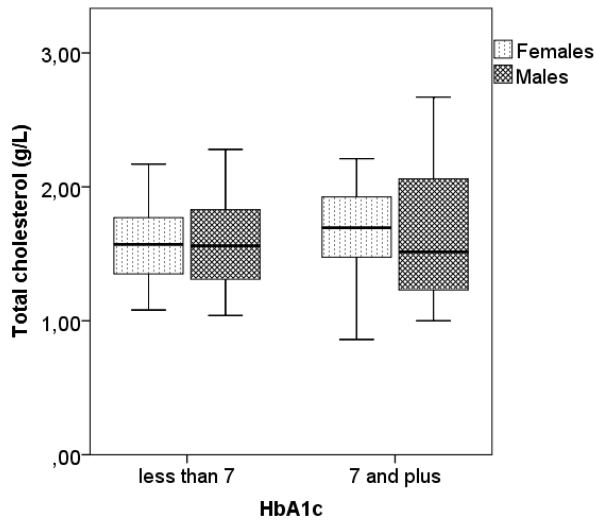


**Figure 1. B:** Comparison of total LDL/HDL ratio between males and females according to HbA1c level.

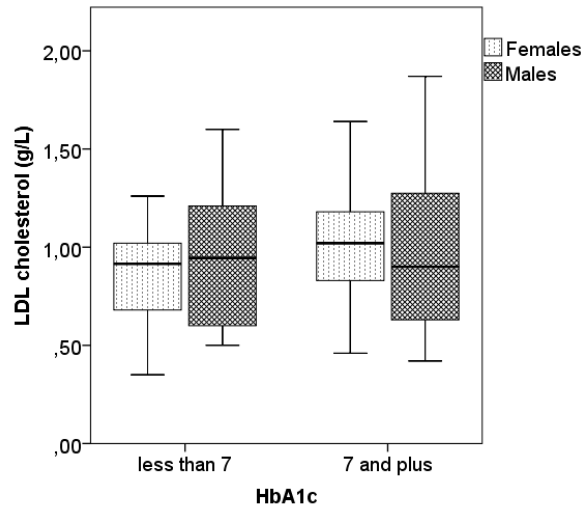


**Figure 1. C:** Comparison of triglycerides/HDL ratio between males and females according to HbA1c level.

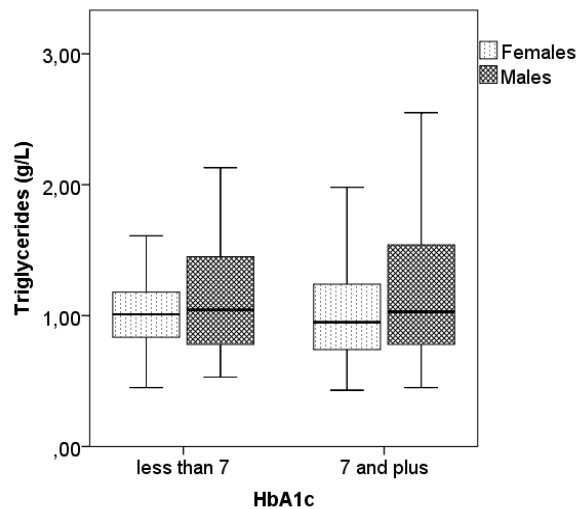
The comparison of traditional lipid parameters (TC, LDL and TG) between males and females according to the HbA1c levels indicated higher total cholesterol rates and LDL cholesterol in females with HbA1c  $\geq 7\%$  (figure 2. B). Nonetheless, total cholesterol (figure 2. A), LDL and triglycerides (figure 2. C) rates were higher in male type 2 diabetic patients with either higher or lower levels of HbA1c.



**Figure 2. A:** Comparison of total cholesterol level between males and females according to HbA1c level



**Figure 2. B:** Comparison of LDL level between males and females according to HbA1c level



**Figure 2. C:** Comparison of triglycerides level between males and females according to HbA1c level

## 4 Discussion

The number of people estimated to be affected by diabetes by 2045 is about 693 million [11]. Diabetes as a chronic non-communicable disease is one of the leading causes of death, due to a high incidence of cardiovascular complications and especially atherosclerosis as major cardiovascular disease (CVD) [12]. Atherosclerosis is considered as a leading cause of morbidity and mortality in both men and women. During recent decades, considerable research has been undergone to understand the pathophysiology of atherosclerosis [13]. Before atherosclerosis becomes apparent, it progresses silently for many years or decades. The key marker of atherosclerosis is dyslipidaemia defined by alterations of lipid parameters and more precisely of lipid ratios [14].

The objective of the present study is to evaluate the effect of gender difference on atherosclerosis risk indices (lipid ratios) by comparing between well controlled type 2 diabetic patients ( $HbA1c < 7\%$ ) and less controlled ones ( $HbA1c \geq 7\%$ ).

According to literature, in type 2 diabetic population, an increase level of total cholesterol, LDL cholesterol, low HDL cholesterol level is an atherogenic lipid marker, and probably involves independent risk [15]. Whereas, when total cholesterol, HDL cholesterol, and total/HDL cholesterol ratio are compared between a healthy population and patients with atherosclerosis, the total/HDL cholesterol ratio is found to present a best atherogenic indices. This explains the best discriminatory power of total/HDL cholesterol ratio, as well as its great predictive capacity [16].

Preliminary consequences from the present study showed significant differences between the two genders regarding age, body weight, BMI, HbA1c levels and lipid ratios (TC/HDL, LDL/HDL and TG/HDL). However, the whole studied parameters were higher in male gender. All the same, according to the atherosclerosis lipid indices (lipid ratios), males have a significant higher risk. According to literature, it is often assumed that yet more men die from atherosclerosis or coronary artery disease than women [17]-[19]. One of the reasons that men are at high risk of developing atherosclerosis can be explained in part by their propensity to adopt risky behaviors such as smoking or excessive alcohol consumption [20], [21]. In addition, men and women exhibit differences in heart structure and function, sex hormones and socio-psychological characteristics [12]. However, after menopause, the risk of atherosclerosis-related diseases begins to increase in women and may even exceed that of men [13].

Our results point out that all TC/HDL and TG/HDL ratios were beyond the therapeutic target standards recognized by most authors (3.5 for TC/HDL and 3.0 for TG/HDL) [22], [23]. Likewise, the values of these ratios for men were often high compared to women.

Our findings revealed that the LDL/HDL ratio values in the study population were higher in men comparing to women, however, underneath the target level for both men (3.0) and women (2.5) as recognized by Aderibigbe et al. (2018) [24]. These outcomes are in accordance with conclusions reported from Ghana [25] and Iran [26] but different from conclusions of Ballotari et al. (2017) from Italy enlightening that diabetes constitutes a higher cardiovascular risk for women than for men [27].

The comparison of the conventional lipid parameters (TC, LDL and TG) between men and women according to the HbA1c levels indicated divergent results. While the TC and LDL rates were higher in women with  $HbA1c \geq 7\%$ , the TG values were higher in men with both levels of HbA1c. However, the majority of these traditional lipid parameters were normal.

Several studies report that diabetes increases the risk of cardiovascular disease two to three times in men and three to seven times in women [28], [29]. The causes of this superiority in women are multifactorial and can be linked to several risk factors such as a large involvement in inflammatory factors, the small size of the coronary vessels and to diabetes treatment in women who are generally less positive [7].

## 5 Conclusion

Although the number of explanatory hypotheses for the mechanisms of gender effects in atherogenesis continues to increase, the exact cellular explanation for these differences is unknown. The consideration of gender differences is very important for prevention, diagnosis, treatment and management of atherosclerosis and CVD. The differences are certainly caused by innate genes and environmental influences. However, the disparity in atherogenic risk estimated by lipid ratios need to be critically examined. There is still a long way to go in order to understand the pathophysiological basis of the difference between males and females with regard to atherosclerosis.

## 6 Declarations

### 6.1 Acknowledgments

Our gratitude is addressed to the staff of diabetes centre Larbi Ben M'hidi in which our study was conducted

### 6.2 Study Limitations

Our study is an observational investigation on patients' records in a definite area and the conclusions could not be of nationally representative or geographically diverse. However, despite these inherent limitations, we believe that our conclusions would remain unchanged in the general population.

### 6.3 Ethical Approval

Complete confidentiality of vital patient information was maintained for ethical purposes. An authorization for each student has been obtained both from the scientific council of our faculty (faculty of natural and life sciences of the University of Sidi-Bel-Abbès) and from the medical center in which our study was carried out.

### 6.4 Informed Consent

Ethical approval was obtained from institutions in which the study was performed and informed consent was taken from the participants.

### 6.5 Competing Interests

The authors declared that no conflicts of interest exist in this publication.

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