



## Effect of Gender and Body Weight on Postprandial Glucose and Lipid Metabolism in Adults with Type 2 Diabetes

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### ABSTRACT

**Introduction:** The magnitude of the healthcare problem of type-2-diabetes increases according to its association with several risk factors for cardiovascular diseases such as obesity and dyslipidemia.

**Methods:** This study took place in the north-western region of Algeria. We aimed to assess the effect of body weight and gender on postprandial lipid and glucose in type-2-diabetes patients. 93 diabetic patients (age 55.65±13.81 years) were studied. Anthropometric parameters and body mass index (BMI) were measured. Fasting and postprandial (PP) glucose and lipid (total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides, apo A-I and apo B) profiles were evaluated.

**Results:** There were a positive correlation between postprandial glucose and BMI in women ( $r^2 = 0.041$ ). Negative correlation with BMI was noticed for PP TG in both males ( $r^2 = 0.011$ ) and females ( $r^2 = 0.021$ ). A significant difference ( $p = 0.019$ ) was observed for PP HDL-c in women ( $0.39 \pm 0.10$  g/L vs. men  $0.33 \pm 0.12$  g/L) and also for PP apo A-I (women:  $1.33 \pm 0.27$  g/L vs. men:  $1.09 \pm 0.34$  g/L;  $p = 0.0003$ ). According to gender and weight groups, our results indicated that female gender and overweight are associated with elevated PP HDL-c and PP apo A-I levels. However, obesity in women is related to high concentration of PP TG.

**Conclusions:** The present study suggests that gender difference and weight classes are important factors that contribute to determining the postprandial responses, both for glucose and lipids, in type 2 diabetic patients.

**Keywords:** *gender difference; postprandial dyslipidemia; type 2 diabetes; weight groups.*

### INTRODUCTION

In nearly the whole developed and developing countries through the world, type 2 diabetes is continuing to be an increasing public health burden. The worldwide prevalence of diabetes among adults (aged 20-79 years) will increase from 6.4% in 2010 to 7.7% by 2033.<sup>1</sup>

Higher vascular disease risks, including cardiovascular diseases (CVD), atherosclerosis, myocardial infarction,

stroke and peripheral vascular disease are commonly associated with type 2 diabetes in adults.<sup>2,3</sup> Patients with type 2 diabetes were seen to manifest symptoms

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of hypertension, abnormal lipemia, obesity, lack of physical exercise and blood sugars which were not properly controlled. By systematic control of these risk factors, diabetic patients may protract the development of heart disease. Change of lifestyle is paramount in CVD strategies in diabetes management.<sup>4, 5</sup> The exceeding of body weight associated with glucose intolerance and/or type 2 diabetes is characterized by hyperinsulinaemia, peripheral resistance to the action of insulin, hypertriglyceridaemia, decreased high-density lipoprotein cholesterol (HDL-c) and other lipid and carbohydrate changes.<sup>6, 7</sup> While a significant association between coronary artery disease and fasting hypertriglyceridaemia has been found in diabetes mellitus according to several studies,<sup>8, 9</sup> and considering that we are spending the most part of the day in the postprandial phase, it was about thirty years ago, when Zilvermit suggested that postprandial lipemia may have a role in atherogenesis and other cardiovascular problems.<sup>10</sup>

Currently, both type 2 diabetes and obesity have been associated with exaggerated postprandial lipemia and glycaemia. Postprandial lipid and glucose metabolism states have been investigated under some standardized circumstances, such as standardized fatty meal or an oral glucose tolerance test, which may not reflect exactly the free-living daylong situation.<sup>11, 12</sup>

However, direct comparison study between groups according to their body weight with or without diabetes based on the normal daily diet are scarce.<sup>13, 14</sup>

Hence, the major aim of our study was to investigate the effects of body weight and gender difference on postprandial lipid and glucose responses in adult patients with type 2 diabetes.

## METHODS

### Patients and Study Design

Our study was carried out during five months, from March to July 2013, and covered a total of 93 adult diabetic patients (35 men and 58 women). This work took place in two cities located in the North-western region of Algeria; Sidi-Bel-Abbès city: Public Establishment of Proximity Health (diabetes centre of Ex Gambetta and Mostefa Ben Brahim polyclinic) and Mascara city (Meslem Tayeb Hospital). Informed consent was obtained from each participant before initiating the study protocol.

The average of diabetes duration was  $5.15 \pm 3.53$  years ( $5.31 \pm 3.11$  years for males vs.  $5.11 \pm 3.78$  years for females). All adult patients with type 2 diabetes, following an oral and/or dietary treatment and free from

any degenerative health complication were solicited to take part in our study. Patients treated with insulin and pregnant women were excluded from this study.

### Anthropometric Measurements

The measurements were taken in the morning for weight, height and waist circumference (WC) according to the recommendations of the World Health Organization (WHO).<sup>15</sup> The body weight (in kilograms) was measured using an electronic balance (TS-2003A: 360 lb, Capacity: 180 Kg, Graduations 0.1Kg). The body height was measured with a body meter (Seca 206, Germany; Measuring range: 0 - 220 cm, Graduation Length: 1 mm) then the body mass index (BMI) was defined as follow:  $BMI (kg/m^2) = \text{weight (kg)}/\text{height}^2 (m^2)$ .

The WC was measured with a measuring tape (Maximum: 150 cm, Graduation Length: 1 mm), we gently tightened the tape around the patient's abdomen roughly in line with the navel without depressing the skin.

### Blood Pressure Measurement

The blood pressure was taken precisely in the morning using OMRON M3 Digital Automatic Blood Pressure Monitor (Omron Healthcare., Ltd. Kyoto, Japan).

Each patient was seated in a congruous position for at least five minutes, with good back support and arms being folded at the level of the heart. The feet should touch the floor and legs should not be crossed. The procedure was explained to each patient with specific instructions not to talk prior or during the procedure.

### Biological Parameters

For the fasting period, blood samples were drawn from each patient 12 h after an overnight fast for glucose and lipid profile measurement. However, concerning the postprandial metabolism, blood samples were taken 2h after the beginning of breakfast for glucose and 3-4 h for total cholesterol (TC), HDL-c, low density lipoprotein cholesterol (LDL-c), triglycerides (TG), apolipoproteins A1 (apo A-I) and apolipoproteins B (apo B).

According to the proposal for standardization of postprandial studies established by Lairon et al. 2007 the morning is the ideal time sampling.<sup>16</sup> The postprandial peak of lipids is around 3h after the beginning of meals.<sup>17</sup>

To determine the serum concentration of glucose, total cholesterol, HDL-c and triglycerides, both in the fasting state or the postprandial state, the enzymatic colorimetric methods (Spinreact Reagents, Spain)

were used.<sup>18</sup> Direct determination of serum LDL-c level was performed without the need for any pre-treatment or centrifugation steps. However, the HbA1c concentration value was determined using an ion exchange resin separation.

For the measurement of apo A-I and B in human serum, turbidimetric tests (Spinreact Reagents, Spain) were used. Insoluble complexes occur after specific reaction between apo A-I and apo B antibodies and serum sample containing apo A-I and apo B, which induce a change in the absorbance that can be quantified by comparison with known calibrators for the concentration of apo A-I and apo B.

### Other Information

A questionnaire for gathering socio-professional data, lifestyle and eating behaviour was done by patients with a three days food diary.

Drugs prescribed and pharmacological measures followed by our adult diabetic patients were collected from their medical records.

According to information derived from the medical reports of each patient, metformin alone (38.70%) or in combination with glimepiride (55.91%), followed by sulfonylureas (5.37%) were the most common anti-diabetic agents prescribed for our patients. However, the most commonly prescribed drugs for cardiovascular co-morbidities were Statins (54.83%), precisely Fluvastatin & Atorvastatin and then lastly antiplatelet drugs. Patients who continue to use Statins during the period of our study were excluded from our sample. Patients are informed not to use oral medications during the day of sampling both for the fasting glucose and postprandial glucose.

### Statistical Analysis

All data were processed and analyzed through SPSS 20.0 (Statistical Package for the Social Sciences, IBM Corporation; Chicago, IL. August 2011). 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  $p = 0.05$ . BMI and waist girth were correlated with some postprandial and fasting lipid and glucose levels using the simple linear regression with a confidence interval of 95%.

## RESULTS

### Patient's Characteristics

A total of 93 adult diabetic patients were included in our study, the majority of the participants was females (62.36% vs. 37.64% males). The prevalence of normal weight, overweight and obesity was 32.25 %, 41.93% and 25.81 %, respectively (Table 1).

The average of age was  $55.65 \pm 13.81$  years. Males and females had approximately similar age ( $p = 0.0700$ ). Men had significantly a higher weight ( $p = 0.001$ ) and height ( $p = 0.0002$ ) (Table 2). However, the body weight was sharply higher compared to the ideal body weight (Lorentz formula) both in male ( $81.87 \pm 11.86$  Kg vs.  $66.84 \pm 4.49$  Kg) and in female ( $74.07 \pm 9.78$  Kg vs.  $59.12 \pm 4.96$  Kg). The gender had no significant effect ( $p = 0.963$ ) on the mean BMI between male ( $27.45 \pm 5.54$  Kg/m<sup>2</sup>) and female ( $27.49 \pm 3.86$  Kg/m<sup>2</sup>). Five patients (3 men and 2 women) had morbid obesity BMI  $\geq 35$  Kg/m<sup>2</sup>. Android obesity has been studied using the waist circumference, which was higher in both genders compared to standards although the difference between genders was not significant ( $p = 0.381$ ).

The Systolic blood pressure was observed to be slightly high in all participants without a significant difference ( $p = 0.995$ ) between male and female. Furthermore, results of Diastolic blood pressures were not significantly related to the patient's gender.

### Plasma Concentrations in the Fasting State

The blood concentration in HbA1c indicated that no significant difference existed between male and female ( $p = 0.865$ ) nonetheless, the levels of HbA1c were high for all the participants reveal abnormal results levels in blood sugar rates over a period of weeks or months (Table 2).

**Table 1. Frequency of normal weight, overweight and obesity among the study sample (n = 93).**

		Gender (frequency)		Total
		Male	Female	
Weight classes	Normal Weight	13 (13.97%)	17 (18.27%)	30 (32.25%)
	Overweight	12 (12.90%)	27 (29.03%)	39 (41.93%)
	Obese	10 (10.76%)	14 (15.05%)	24 (25.81%)
Total		35 (37.64%)	58 (62.36%)	93 (100.0%)

**Table 2. Anthropometric and biological characteristics of the participants.**

Parameters	Men (35) mean±Std.	Women (58) mean±Std.	P values for t-test
Age (year)	56.37±15.87	55.22±12.53	0.700
Diabetes Duration (year)	5.31±3.11	5.11±3.78	0.792
Weight (Kg)	81.87±11.86	74.07±9.78	0.001
Height (cm)	173.02±6.11	164.43±5.85	0.000
Ideal Body Weight (Kg)*	66.84±4.49	59.12±4.96	0.000
Waist Circumference (cm)	98.38±9.52	96.47±10.48	0.381
BMI (Kg/m <sup>2</sup> )	27.45±4.54	27.49±3.86	0.963
Systolic Pressure (mmHg)	13.04±1.86	13.04±1.69	0.995
Diastolic Pressure (mmHg)	7.62±0.97	7.47±0.98	0.462
Heartbeat	82.94±9.90	73.24±5.82	0.000
HbA1c (%)	7.45±1.65	7.50±1.14	0.865
F glucose (g/L)	1.66±0.70	1.46±0.53	0.131
F TC (g/L)	1.67±0.37	1.63±0.33	0.663
F HDL-c (g/L)	0.37±0.11	0.38±0.09	0.372
F LDL-c (g/L)	1.02±0.33	1.01±0.31	0.841
F TG (g/L)	1.30±0.55	1.42±0.65	0.387
PP glucose (g/L)	2.28±1.07	2.19±0.73	0.637
PP TC (g/L)	1.79±0.53	1.78±0.39	0.970
PP HDL-c (g/L)	0.33±0.12	0.39±0.10	0.019
PP LDL-c (g/L)	1.15±0.47	1.09±0.34	0.465

PP TG (g/L)	1.69±1.10	1.53±0.69	0.394
PP apo A-I (g/L)	1.09±0.34	1.33±0.27	0.000
PP apo B (g/L)	0.89±0.31	0.96±0.41	0.413

**BMI: Body Mass Index; F TC: Fasting Total Cholesterol; F HDL-c: Fasting HDL Cholesterol; F LDL-c: Fasting LDL Cholesterol; F TG: Fasting Triglycerides; PP TC: Posprandial Total Cholesterol; PP HDL-c: Posprandial HDL Cholesterol; PP LDL-c: Posprandial LDL Cholesterol; PP TG: Posprandial Triglycerides; PP apo A-I: Posprandial apo A-I; PP apo B: Posprandial apo B**

\* Lorentz formula

During the fasting period there were no significant differences for glucose or any lipid parameters (TC, HDL-c, LDL-c and TG) between male and female.

#### Plasma Concentration in the Postprandial State

We observed some postprandial lipid abnormalities in the investigated patients particularly of HDL-c and apo A-I. Postprandial (PP) HDL-c was significantly higher among women than men ( $0.39 \pm 0.10$  g/L vs.  $0.33 \pm 0.12$  g/L;  $p = 0.019$ ) and also a significant high concentration of PP apo A-I in women ( $1.33 \pm 0.27$  vs.  $1.09 \pm 0.34$  in men). Contrariwise, there was no inter-gender variability for postprandial glucose or other postprandial lipid parameters.

#### Correlations

Among adult male diabetic patients, BMI was positively correlated to HbA1c values ( $r^2 = 0.077$ ) but negatively to PP glucose ( $r^2 = 0.013$ ). In the opposite, in women, BMI is inversely correlated to HbA1c ( $r^2 = 0.046$ ) and

positively to PP glucose ( $r^2 = 0.041$ ) (Figure 1).

Concerning the postprandial lipid parameters, PP HDL-c is linked to the BMI in both gender groups particularly in men ( $r^2 = 0.099$  vs.  $r^2 = 0.009$  in women) (Figure 2). However, inversely relations were noticed between PP TG and BMI ( $r^2 = 0.011$  in male vs.  $r^2 = 0.021$  in female).

As indicated in figure 3. Correlation between PP TG and waist girth, which represents a good indicator of android obesity, was positive in men ( $r^2 = 0.026$ ) and negative in women ( $r^2 = 0.044$ ).

Taking into consideration the gender and weight groups (normal weight, overweight and obese), our results indicated that female gender and overweight are associated with elevated PP HDL-c and PP apo A-I levels. However, obesity in women is related to high concentration of PP TG (Figure 4).

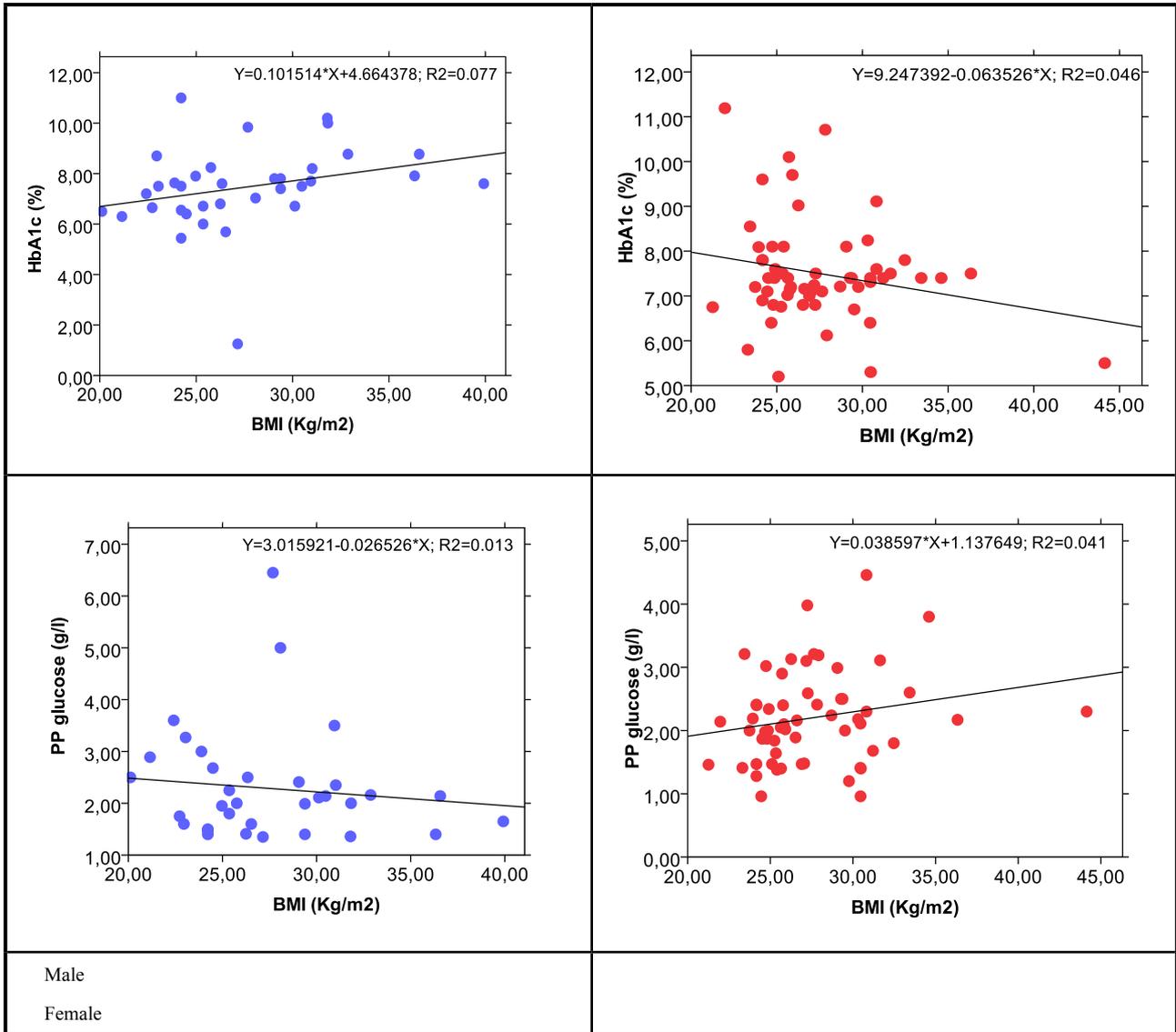


Figure 1. Effect of BMI on HbA1c and postprandial glucose among males and females.

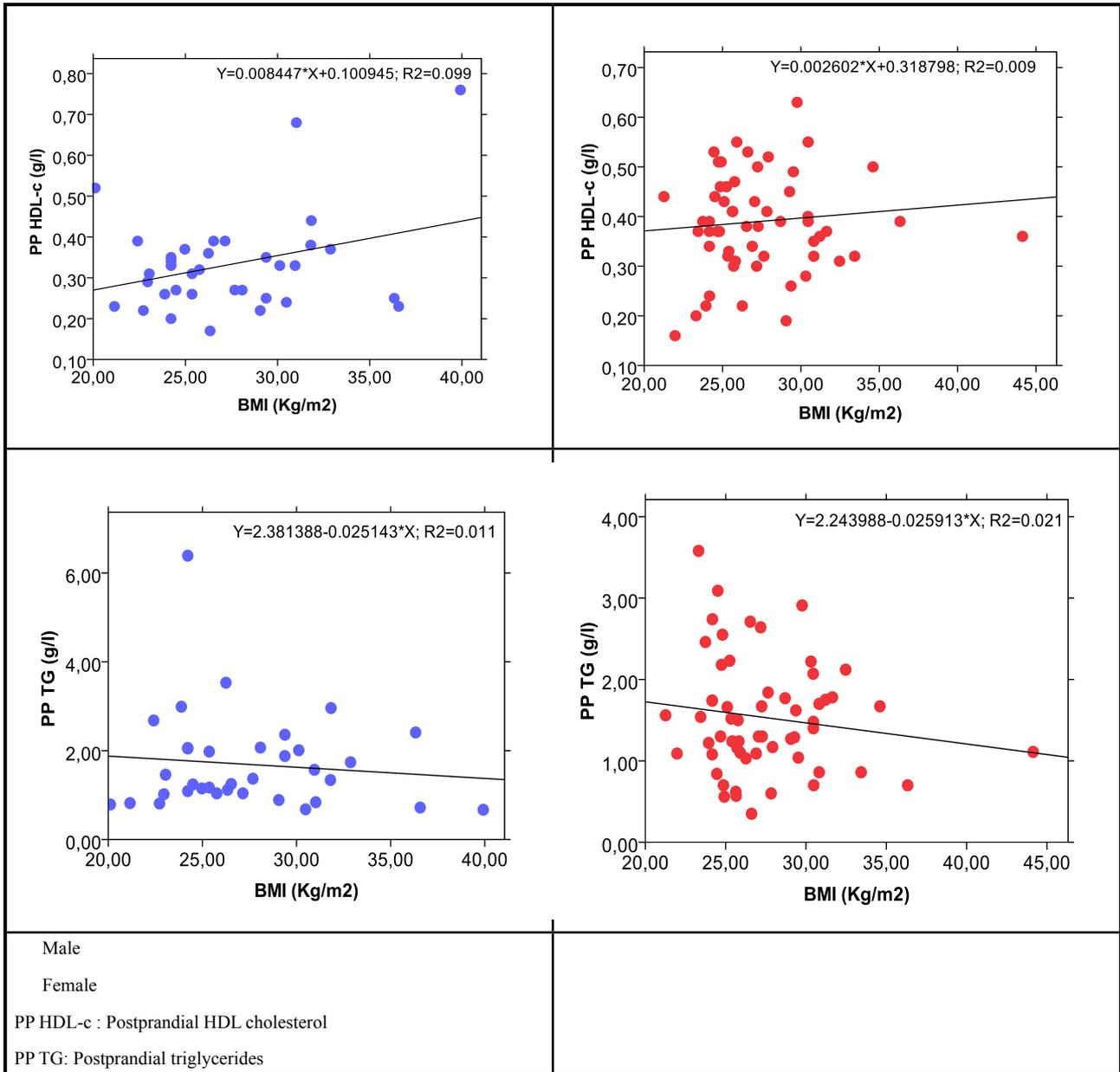


Figure 2. Effect of BMI on postprandial HDL cholesterol and triglycerides among males and females.

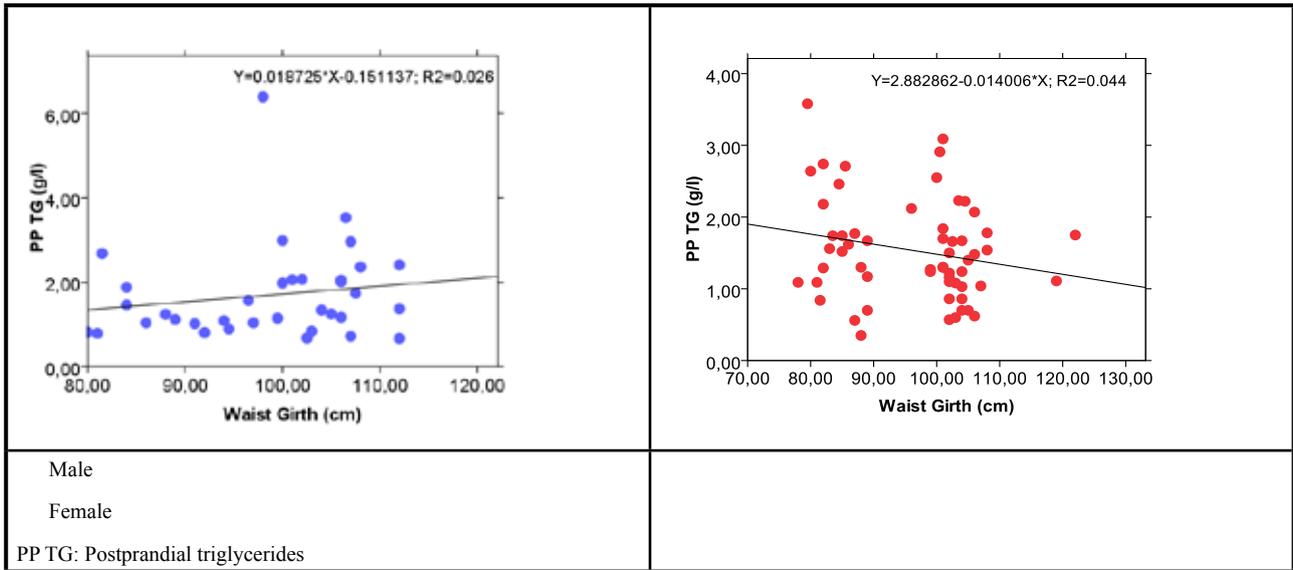


Figure 3. Effect of waist circumference on postprandial triglycerides among males and females.

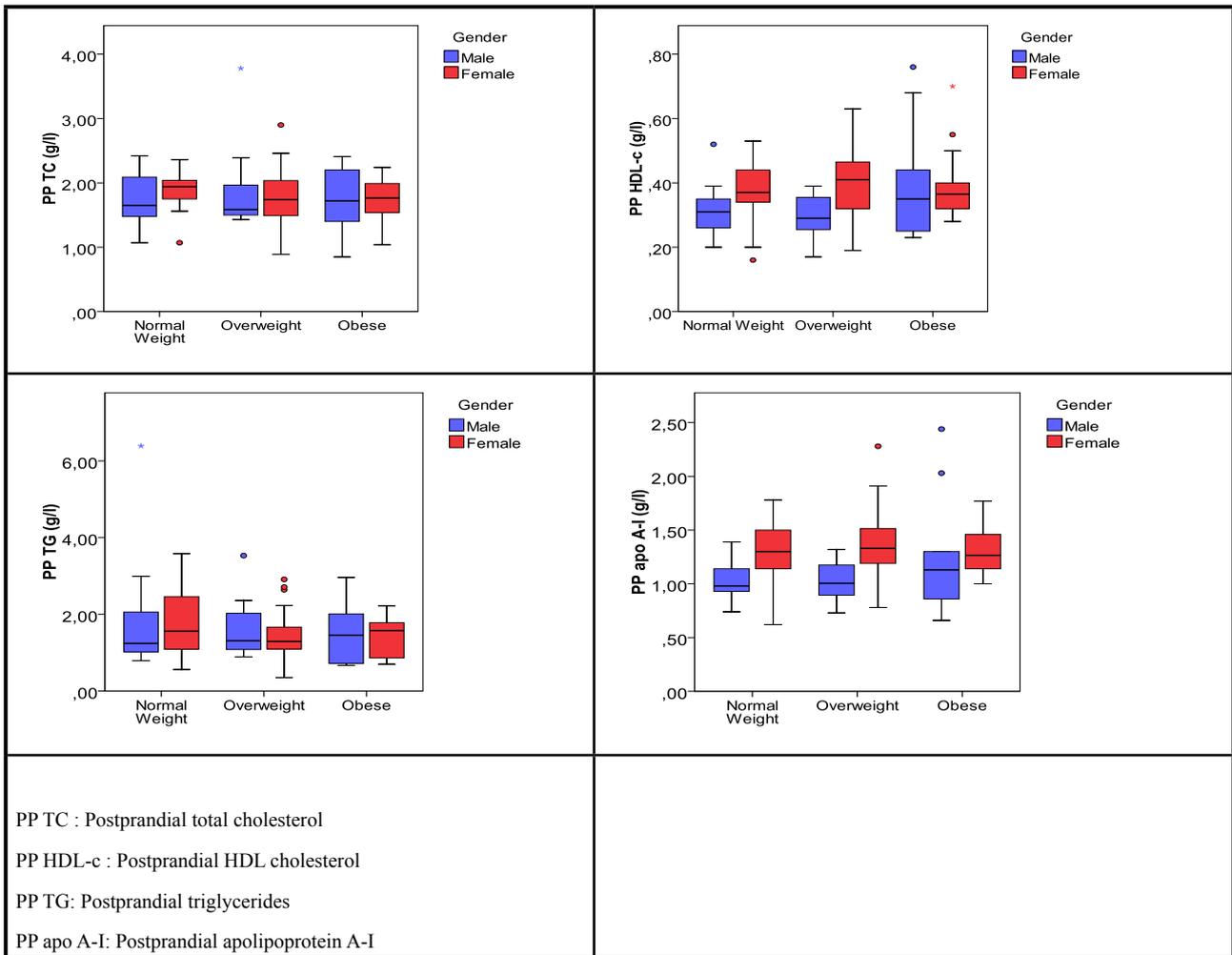


Figure 4. Postprandial lipemia according to weight classes (normal weight, overweight and obese) among diabetes patients.

## DISCUSSION

The worldwide prevalence of type 2 diabetes is genuinely increasing, the likeliest explanation is, undoubtedly, the increasing incidence of this metabolic disease, but also the better health care and the improving longevity of people with diabetes.<sup>1,2,4</sup> It is noteworthy that the increasing cardiovascular mortality and morbidity in type 2 diabetic patients stem from the association between the diabetic disease and other risk factors such as age,<sup>19</sup> diet, physical activity,<sup>20</sup> obesity, body fat distribution, hypertension and lipid abnormalities. By the time they were first diagnosed with diabetes, most of adult diabetic had already experienced these diabetic complications.<sup>21</sup>

A consistent body of data demonstrates a robust association between postprandial glucose and postprandial lipid levels, on one hand, and cardiovascular risk, coronary atherosclerosis and carotid artery intimal thickness on the other hand.<sup>10,22</sup> The importance of the postprandial state against the fasting period comes from the fact that we spend most of our waking hours in the postprandial state.

In this study we aimed to investigate the effects of body weight and gender difference on postprandial lipid and glucose responses in adult patients with type 2 diabetes.

Many studies have reported on the increasing use of HbA1c and fasting plasma glucose to monitor long-term glycemic control in diabetic patients.<sup>23-24</sup> However, according to Monnier et al., low HbA1c levels are due to the contribution of PP glucose.<sup>25</sup> With HbA1c < 7.3%, the contribution of PP glucose is 70%. Whereas, with HbA1c levels between 7.3% and 8.4%, the contribution of PP glucose is at 50%.

Our results showed no significant difference ( $p = 0.865$ ) in HbA1c levels between men and women. The same results were found by Calisti & Tognetti.<sup>26</sup> A positive correlation was observed between BMI and HbA1c level in men, conversely a negative correlation was noticed in women. A Sudanese study showed no correlation between HbA1c and BMI both in men and women.<sup>27</sup> The same results were found by Longo-Mbenza et al.<sup>28</sup> Paradoxically, there was a positive correlation between HbA1c levels and BMI in a Japanese population.<sup>29</sup>

Gender had no effect on glucose concentration neither in the fasting state ( $p = 0.131$ ) nor in the postprandial state ( $p = 0.637$ ). The same findings were obtained in many studies.<sup>13,30</sup>

Concerning the fasting blood glucose levels, there was a positive but non-significant correlation between blood

glucose and BMI among male subjects ( $r^2 = 0.020$ ,  $p = 0.412$ ). However, in the postprandial state, the correlation between these variables was however negative but not significant ( $r^2 = 0.013$ ,  $p = 0.520$ ). In females, the correlation was negative in the fasting state and positive in the postprandial state. Our findings agree with those of Bakari et al.<sup>31</sup> Other studies showed mixed results.<sup>32,33</sup>

In this investigation, lipids concentrations were minimally different between men and women for the measurements performed in the fasting state. No significant difference between the two groups of gender was noticed for TC, HDL-c, LDL-c and TG levels which are not in accordance with results of many studies.<sup>34,35</sup> Somewhat, similar to the result of Mengesha.<sup>36</sup>

Despite similar fasting lipid levels, a lower but not significant PP TG response has been reported in women than men in the current study. These agree with previous results that reported higher postprandial levels of triglycerides in men than women,<sup>37</sup> and disagree with those found by Amrane & Khaled.<sup>13</sup> The postprandial lipid response is the state following the food intake but situated before the post-absorptive state. Free fatty acids, packaged into large triglyceride rich particles together with apo B, are absorbed by intestine during this phase.<sup>38</sup> In the present study, gender differences were also observed in postprandial HDL-c response. Men being characterized by a significant low postprandial HDL-c level compared with women.

In type 2 diabetes patients, there is frequently a strong interrelationship between the hypertriglyceridaemia and low HDL-c. Hypertriglyceridaemia induces an increase in lipid exchange which leads to produce triglyceride enriched HDL hydrolyzed afterwards into small dense HDL particles by hepatic lipases. The small dense HDL particles newly produced are rapidly cleared from the blood circulation.<sup>39</sup>

A significant high concentration of PP apo A-I was observed in female diabetic patients comparing to males. However, no significant difference between male and female was found about PP apo B.

Measuring apo B level, the moiety of LDL, and apo A-I concentration, the major protein found in HDL-c can play an important role in the clinical assessment and monitoring of CVD and stroke. In a recent study, including a very large sample, comparing nonfasting lipids, lipoproteins, and apolipoproteins in individuals with and without diabetes, no statistically significant differences in postprandial apo B concentrations were found.<sup>40</sup> When Jungner et al. studied apo B and A-I values in 147 576 males and females, according to the WHO standards, they found that the 95% interval for

apo A-I was between 0.99 and 1.84 g/L in males and between 1.09 and 2.04 g/L in females. However, in the same study, the median apo B concentrations in adult females were 0.92-1.38 g/L and 0.99-1.36 g/L in males, including all ages.<sup>41</sup>

The present study clearly demonstrates a high PP TG response in both males and females type 2 diabetes individuals compared to the fasting state. Comparing to some previous data,<sup>13,42</sup> a negative correlation between BMI and PP TG was observed in the present study in both genders, which agree with the result of Reznik et al.<sup>43</sup> This can be explained, if we take into account that the part of obese patients in our sample was about 25% and nearly 80% of them, had BMI < 35Kg/m<sup>2</sup> (morbid obesity) and the extensive use of Statins (Fluvastatine & Atorvastatine), in the history of our patients, which are likely to reduce triglycerides and retinylpalmitate over 30% during the postprandial state as reported by Parhofer et al.<sup>44</sup> These drugs are known to increase the number of LDL receptors and improving removal of triglyceride-rich lipoproteins remnants in the postprandial state. Statins tend to induce a modest lowering of plasma triglycerides. This is likely to be due to an inhibition of very low density lipoproteins (VLDL) synthesis.<sup>45</sup> This inhibition may also explain the proportional relation between PP HDL-c and BMI.

It is known that female gender is generally associated with an increasing activity of lipoproteins lipase which may predict the PP HDL-c accumulation as observed in

our study and this for all weight groups. This finding, concerning the relationship between female gender and PP HDL-c, can also be a good explanation for the high postprandial accumulation of apo A-I in women. But, even though the apo A-I is the major lipoproteins found in HDL-c as was cited by many authors,<sup>46, 47</sup> it has no statistically association with cardiovascular events.

## CONCLUSIONS

People with type 2 diabetes have a greater chance of developing serious complications and health problems, especially if their disease is associated with other risk factors like overweight, obesity and postprandial dyslipidemia. In the same context, there is a gender difference in postprandial metabolic responses. Avoiding postprandial responses abnormalities and diabetes as a result, requires a good mastering of body weight taking into consideration the physiological differences between males and females.

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