

Evaluation of the Factors Associated with Lipid Metabolism and the Response to Treatment in Type 2 Diabetic Patients Monitored at CHD-Atacora (Benin)

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Received October 18, 2019; Revised November 26, 2019; Accepted December 17, 2019

Abstract Non-insulin-dependent diabetes mellitus (NIDDM) is a multifactorial disease resulting from the interaction of genetic and environmental factors. The aim of this study was to evaluate the factors associated with lipid metabolism and treatment response in type 2 diabetic patients monitored at CHD-Atacora (Benin). A total of 200 diabetic patients were included in the study. 121 women and 79 men into two groups; namely 132 had hyperglycemia and 68 in normoglycemia. Diabetics had a mean BMI of 27.95 kg / m² while normoglycemic subjects had a BMI of 24.84 kg / m². In addition, diabetic subjects had an average triglyceride level of 2.28 mmol / L whereas subjects with normoglycemia had an average triglyceride level of 1.04 mmol / L. Oral antibiotics did not have a significant effect on lipid metabolism and glycemic control. Eating habits were similar in both groups and did not respond to a balanced diet. The results of our study reveal that triglyceride levels and BMI are a factor influencing the glycemic status of diabetic subjects. Low levels of BMI and triglyceride levels promote good glycemic control in diabetic patients monitored in the diabetic department of CHD-Atacora.

Keywords: type 2 diabetes, dyslipidemia, metformin, glibenclamide, Atacora, Benin

Cite This Article: Tinéponanti B.T. Véronique, Chabi Nicodème Worou, Sognigbé G. Basile, Adam Alassane, Akpovi D. Casimir, Sina Haziz, Kohonou N. Arnaud, and Baba-Moussa Lamine, "Evaluation of the Factors Associated with Lipid Metabolism and the Response to Treatment in Type 2 Diabetic Patients Monitored at CHD-Atacora (Benin)." *American Journal of Biomedical Research*, vol. 7, no. 2 (2019): 38-43. doi: 10.12691/ajbr-7-2-3.

1. Introduction

Type 2 diabetes is characterized by hyperglycemia resulting from a lack of insulin secretion associated with a lack of action of this hormone on its target tissues [1]. The secretion of insulin normally leads to the inhibition of lipolysis in adipocytes and therefore to the decrease of the plasma concentration of free fatty acids. The presence of free fatty acids in high concentration in plasma is implicated in the development of insulin resistance [2]. In insulin-resistant patients, lipolysis of triglycerides in adipocytes and myocytes is not controlled, resulting in a flow of fatty acids back to the liver [3,4]. The increased return of fatty acids in the liver stimulates the increase in liver VLDL production [5]. The increase in plasma concentrations of free fatty acids leads to an increase in lipid synthesis in the hepatocytes responsible for

dyslipidemia. Dyslipidemia is the set of clinical and biological manifestations related to the increase or decrease of one or more blood lipid compounds [6]. It is characterized by high circulating levels of triglyceride-rich particles, reduced synthesis of HDL lipoproteins and increased production of atherogenic LDL particle [7]. Several factors contribute to dyslipidemia and contribute to the development of vascular complications in diabetic patients. In order to limit these complications and to ensure good glycemic control, the treating physician uses oral anti-diabetics, nutritional advice, etc. Two oral hypoglycemic drugs for the management of diabetes mellitus are used. (Glibenclamide and metformin). Glibenclamide (in the sulfonylurea class) is a well-established oral hypoglycemic agent, while metformin (in the biguanide class) is a relatively new addition to the current regimen [8]. Metformin belongs to the family of antidiabetic agents insulin sensitizers and the class Biguanides [9]. It lowers gluconeogenesis by slowing

hepatic glucose production and glycogenolysis. decreases glucose absorption at the intestinal level, and also has favorable effects on lipoprotein metabolism [10,11]. Metformin promotes the reduction of LDL cholesterol as well as triglyceride levels in the blood and could therefore protect against the effects of dyslipidemia [12,13]. It would have anti-cancer. cardioprotective and same neuroprotective [14]. Glibenclamides are recent hypoglycemic sulfonamides belonging to the class of sulfonylureas. They are used either in dual therapy (metformin + sulfonylurea hypoglycemic) or in monotherapy in case of contraindication / intolerance to metformin. They allow not only the reduction of microvascular (glomerular) complications. but also of glycemia [11].

The objective of this study is therefore to evaluate the factors associated with lipid metabolism and the response to treatment in type 2 diabetic patients monitored by CHD-Atacora (Benin).

2. Material and Methods

2.1. Patients and Ethical Aspect

The present study involved 200 diabetic participants recruited comprehensively on the basis of the patient admission register in the diabetic department of CHD-Atacora in Natitingou. The written informed consent of each patient was solicited and obtained before winding up in the study and confidentiality was ensured. The study protocol has been validated by the ethics committee of the University of Abomey-Calavi. The participants were submitted to a pre-validated structured questionnaire. It relates to the sociodemographic characteristics of patients. the collection of anthropometric data. lifestyle and personal and family history. Patients were stabilized on metformin alone or in combination with glibenclamide. Blood samples were also taken from these patients.

Included in this study are all patients diagnosed with type 2 diabetes for at least 4 years. of both sexes, aged 30 years and over and regularly monitored by the center's diabetology department for at least 12 months. Patients with edema and pregnant women are not included.

2.2. Dependent Variable

The dependent variable is glycemic status.

The sample size was determined by the following formula:

SCHWARTZ formula

$$n = \frac{z^2 X p X q}{i^2}$$

With $z = 1.96$ for a risk of 5%

p : according to the STEPS survey carried out in 2008 on MNT. the prevalence of diabetes is 2.6% [11] in Benin

$$q = 1 - p \text{ et } i = 0.03.$$

$$n = \frac{1,96^2 X 0,026 X 0,974}{0,03^2} = 108.09.$$

3. Methods

Samples were taken from individuals fasting for at least 12h. From a 5 ml sample of venous blood. sterile on a dry tube. Glucose levels were determined by the glucose oxidase method using commercial kits provided by ELITech Clinical Systems. The results made it possible to constitute two groups of diabetic patients: patients with hyperglycemia and those with normoglycemia. The determination of the other biochemical parameters namely. total cholesterol. triglycerides. HDL cholesterol. proteins. was performed with Elitech Clinical Systems kits to evaluate dyslipidemia in our diabetic patients monitored by CHD-Atacora (Benin) . The instructions in the package leaflet of each kit were strictly followed for the assay.

3.1. Statistical Analyzes

The data was analyzed by the R version i386 3.5.2 software.

A descriptive analysis was performed on the entire study population according to the glycemic status of the subjects monitored (diabetic subjects versus subjects with normoglycemia). The Pearson Chi-2 statistical tests (or Fisher's exact test according to the variable distribution) for the qualitative variables and the Student's t-test for the quantitative variables were performed. The relative risk associated with the genotype was estimated by calculating the odds ratio (OR) and its 95% confidence interval. Finally. a logistic regression analysis was performed to identify the factors associated with the subjects' glycemic status.

4. Results

Body mass index and triglyceride levels were significantly different in both groups. Diabetics have an average BMI of 27.95 +/- 5.65 kg / m² (overweight). while subjects with normoglycemia have a BMI of 24.83 ± 5.34 kg / m² (normal body size). diabetic patients had an average triglyceride level of 2.28 ± 0.37 mmol / L while normoglycemic subjects had an average triglyceride level of 1.04 ± 0.35 mmol / L. The dietary habits of both groups were similar and have no significant effect on glycemic status.

Table 1. Lipid metabolism and dietary habits of T2DM patients versus subjects with normal blood glucose

Characteristic of the sample	T2DM	Subjects with normal blood sugar	p-value ^a
Total number (Female / Male)	132(76/56)	68(45/ 23)	0.28 ^b
Age (years)	55.86 ±10.83	56.17±11.44	0.85
BMI (kg / m ²)	27.95±5.65	24.83±5.34	0.02*

Characteristic of the sample	T2DM	Subjects with normal blood sugar	p-value ^a
Waist size			
Women	98.42±11.53	96.51±12.73	0.41
Men	92.37±11.03	95.56±10.07	0.22
Total cholesterol	1.62±0.43	1.54±0.35	0.13
HDL cholesterol	0.64±0.19	0.63±0.18	0.57
LDL Cholesterol	0.93±0.47	0.89±0.36	0.61
triglycerides	2.28±0.37	1.04±0.35	0.04*
protein	68.02±8.44	66.04±5.72	0.49
Breakfast			0.35 ^b
porridge	45(34.35)	19(30.15)	
Cereals	21(16.03)	13(20.63)	
tubers	13(9.92)	11(17.46)	
Fruits	2(1.52)	1(1.58)	
Pasta	33(25.19)	16(25.39)	
Tea	17(12.99)	3(4.79)	
Lunch			0.63 ^b
porridge	3(2.32)	0(0.00)	
Cereals	44(34.10)	18(27.69)	
tubers	14(10.85)	9(13.84)	
Fruits	5(3.87)	5(7.69)	
Pasta	63(48.86)	33(50.78)	
collation			0.27 ^b
porridge	23(21.49)	14(22.58)	
Cereals	38(35.51)	21(33.87)	
tubers	34(31.77)	17(27.41)	
Fruits	8(7.47)	4(6.45)	
Pasta	4(3.76)	6(9.69)	
Having dinner			0.35 ^b
Cereals	10(7.81)	6(9.52)	
tubers	9(7.03)	8(12.69)	
Fruits	3(2.34)	2(3.17)	
Pasta	106(82.82)	47(74.62)	

Data expressed as mean ± SD or frequency (%); * Statistically significant; Student's t-test; b Fisher's exact test.

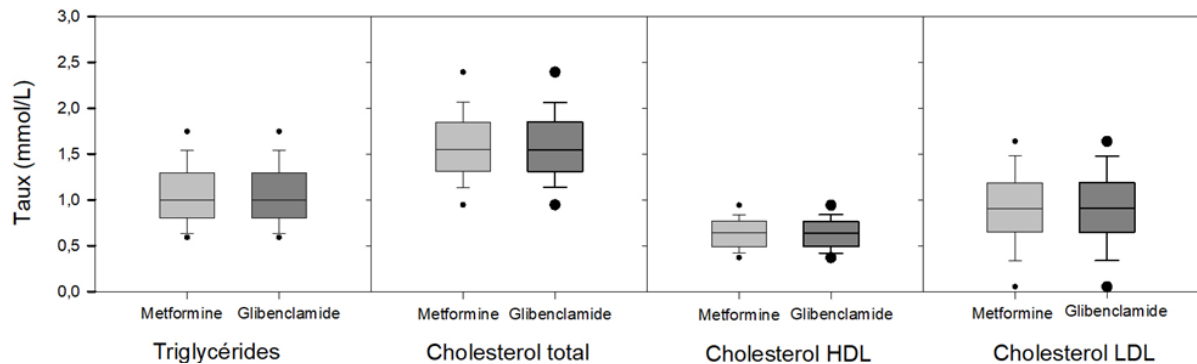


Figure 1. Medication and Lipid Metabolism in the Population (Lipid metabolism is similar in subjects taking Metformin and those taking Glibenclamide)

Table 2. Correlations between lipid metabolism, eating habits and glycemic status of subjects

	Glycemic status	
	R	P-value
Sex	0.08	0.24
Age	-0.01	0.85
BMI	-0.09	0.03*
Waist size	0.20	0.07
Total cholesterol	0.10	0.15
HDL cholesterol	-0.04	0.59
LDL Cholesterol	-0.03	0.63
triglycerides	-0.55	0.04*
protein	0.12	0.08
Breakfast	0.01	0.87
Lunch	-0.07	0.32
collation	0.02	0.79
Having dinner	0.09	0.2

BMI is significantly associated with glycemic status. More subjects have a high BMI plus they have diabetic hyperglycemia.

The triglyceride level is significantly correlated with the glycemc status of the subjects. High triglyceride levels are significantly associated with diabetic status.

Table 3. Logistic Regression by Glycemc Status as a Dependent Variable

	β	SE	P
T2DM versus normoglycemia			
Age (years)	0.01	0.01	0.97
Sex	0.01	0.41	0.69
BMI (kg / m ²)	-0.08	0.05	0.15
Waist size	0.01	0.02	0.54
Total cholesterol	0.12	0.49	0.80
HDL cholesterol	0.37	1.21	0.75
triglycerides	1.59	0.61	0.03*
protein	0.02	0.02	0.44
Breakfast			
Cereals	-0.04	0.57	0.93
starchy	-0.72	0.62	0.24
Fruits	14.33	100.9	0.98
Pasta	-0.49	0.51	0.33
Tea	0.59	0.74	0.42
Lunch			
starchy	-0.36	0.68	0.59
Fruits	-1.14	1.02	0.26
Pasta	-0.32	0.43	0.46
Collation			
Cereals	0.12	0.53	0.81
starchy	0.43	0.57	0.45
Fruits	0.11	0.78	0.88
Pasta	-0.89	0.90	0.32
Having dinner			
starchy	0.26	0.90	0.76
Fruits	0.66	1.49	0.65
Pasta	0.41	0.69	0.55

Triglyceride levels are the most important factor in the glycemc status of subjects. Subjects with lower triglyceride levels are more likely to switch from diabetic status to normoglycemia status. Specifically, a difference or increase in the glyceride level of 1 mmol / L is equivalent to a 5-fold increase in the risk of being diabetic than having a normoglycemia.

5. Discussion

The aim of this study was to evaluate the factors associated with lipid metabolism and treatment response in patients with type 2 diabetes who were monitored by CHD-Atacora. Benin.

In our sample of diabetic subjects, we observed a female predominance with a sex ratio of 0.65. In addition, diabetic women had abdominal obesity. This sexual difference in the distribution of type 2 diabetes in our sample suggests that sex hormones may have a role in causing the onset of type 2 diabetes. It has been suggested that the difference in prevalence of T2DM between the two sexes may be related to differences in the degree of physical activity between men and women or an effect of estrogen on carbohydrate homeostasis (use of oral contraceptives and menstrual cycle phases). Evidence suggests that women are relatively protected against fatty acid-induced insulin resistance [15]. After menopause (period of significant hormonal changes), women often

have an android distribution of their fat. The average age of our patients being 55.86 ± 10.83 years, the majority of women would be menopausal and predisposed then to android-type obesity, a predictive factor for type 2 diabetes.

We showed in our study that the majority of our diabetic patients about 2/3 or 66% had poor glycemc control. This finding could probably be explained by the non-observance of dietary advice, the lack of regular monitoring, the irregularity in taking antidiabetic medicines, etc. Our results are similar to those of [16,17] that showed a rate of 48.7% based on measurements of glycated hemoglobin (HbA1C) to 70.9% on fasting glucose measurements. These variations in results would be due to the assay technique used (HbA1C measurements and fasting glucose measurements) and to the diabetes management policy in each country.

We also showed in our study that body mass index (BMI) was associated with glycemc status and that subjects had a high BMI; the more they have diabetic hyperglycemia, BMI therefore has a predictive power in glycemc pathology. Our results are in agreement with the cross-sectional study conducted in Spain, which showed that the prevalence of diabetes mellitus in overweight or obese patients was 23.6% and that the higher the BMI, the higher the prevalence of diabetes. [18]. However, a survey in 49 developing countries showed that not only overweight but also underweight could be involved in the pathogenesis of diabetes [19].

We also showed in our study that dyslipidemia was correlated with glycemic status. In particular the triglyceride level is significantly correlated with the glycemic status of subjects. Our results are consistent with the study conducted by Kannel *et al.*, [20] who established dyslipidemia as a consistent feature of type 2 diabetes. The study found a significantly higher prevalence of dyslipidemia in patients with diabetes mellitus. report to non-diabetic individuals

Logistic regression based on glycemic status as a dependent variable showed that triglyceride levels were the most important factor in the subjects' glycemic status. In other words, subjects with lower triglyceride levels are more likely to switch from diabetic status to normoglycemia status. Specifically, a difference or increase in the glyceride level of 1 mmol / L is equivalent to a 5-fold increase in the risk of being diabetic than having a normoglycemia. Our results are superimposable to that of Yonas *et al.*, [21] which showed that patients with poor glycemic control had higher serum TG than those with good glycemic control. Abdel-Gayoum, [22] also showed in his study that improved glycemic control in patients with T2D resulted in a decrease in serum TG Guerci *et al.*, [23] observed a positive and significant correlation ($r = 0.28$, $P < 0.05$) between serum TG and HbA1c levels in his study and concluded that poor glycemic control appeared to be directly associated with hypertriglyceridemia. Moreover and Hirano [24] showed that although the increase of free fatty acids released by insulin-resistant tissues is a major factor of diabetes lipidus, acute hyperglycemia also increases plasma TG by stimulating secretion hepatic TG, independently of plasma insulin or free fatty acid levels.

The results of our work showed that taking antidiabetic drugs (metformin or metformin + glibenclamide) had no significant effect either on the glycemic status or the lipid metabolism of our diabetic patients. Our results are in agreement with those of [25,26] who also showed that there is no change in the lipid profile with the taking of metformin. However, the study conducted by Mooradian [7], showed a combination of metformin with an improvement in lipid profile even in non-diabetic patients. Another study conducted by Srivastava *et al.* [27] shows that antidiabetic drugs improved the glycemic state blood pressure, lipid profile and renal status of all patients included in the study. Yonas *et al.*, [21] has also shown that metformin added to other hypoglycemic drugs provides additional benefit in the form of reduced glycemic load and improved lipid profile.

6. Conclusion

Triglyceride levels and BMI would be a factor influencing the glycemic status of diabetics. Low levels of BMI and triglyceride levels promote good glycemic control in diabetic patients monitored in the Atacora CHD diabetology department.

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