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Research Article

Evaluation of Physical Activity and Diet Among Type 2 Diabetics in Libreville

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Abstract

Background: Physical activity and healthy diet can prevent or reduce risk of developing type 2 diabetes, otherwise may reduce the disease complications among diabetics. The objective of this study was to evaluate the physical activity and diet of type 2 diabetics in Libreville. Methods: It was a case-control study conducted at the Endocrinology Department of the University Hospital Centre of Libreville and at the Biochemistry Laboratory of the University of Health Sciences. Patients (n=272) recruited were divided in type 2 diabetics (n=136) and controls (n=136). Physical activity was assessed using WHO Global Physical Activity Questionnaire (GPAQ). Diet was assessed using FAO Food Consumption and Diversity Scores (FCS and DDS). Results: Diabetics had higher overall physical activity than controls (19.1% *vs.* 10.3% respectively; p= 0.0033). Then, low activity was obtained in more than half of diabetics (80.8%). Acceptable dietary intake was more frequent in controls than in cases (78.7% vs. 51.4%, p= 0.0000). Similarly, poor dietary diversity was observed in 34.6% of diabetics versus 8.8% of controls (p= 0.0000). Several variables were associated with type 2 diabetes. These were age (p= 0.0000), TyG (p= 0.0000), triglyceridemia (p=0.0000), first and second-degree relative family history of diabetes (p=0.0030 and p=0.0020 respectively) and alcohol consumption (p= 0.0060). When stepwise linear regression was performed, dietary intake and dietary diversity scores were negatively associated with diabetes. Conclusion: This study revealed that diabetics in Libreville are intensely physically active, but that this activity needs to be reinforced and accompanied by greater dietary diversity.

Keywords

Type 2 Diabetes, Physical Activity, FCS Score, DDS Score, GPAQ Questionnaire

1. Introduction

Type 2 diabetes mellitus (T2DM) is the chronic metabolic disease of the third millennium. Today, it affects 10.5% of the world's population [1, 2], which makes diabetes a public health issue. Indeed, it is one of the four priority

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non-communicable diseases targeted by world leaders, and a steady increase in prevalence of this disease has been recorded in recent decades [3]. Worldwide, an estimated 151 million adults were living with diabetes in 2000, compared with 537 million in 2021 [2]. Furthermore, the International Diabetes Federation (IDF) forecasts that the number of diabetics in Africa will increase by 129% (55 million), between 2021 and 2045 [2]. The origin of this worldwide growth is thought to be a change in lifestyle and eating habits over the last 30 years [3]. The increase in urbanization has led to a rise in sedentary lifestyles and a rise in high-calorie diets linked to obesity [1, 4]. Indeed, environmental factors have been widely incriminated in the onset of the disease. Although the benefits of dietary modifications, it can be difficult for health care providers to recommend appropriate dietary interventions for patients [5]. Especially since a low-quality diet is associated with a risk of type 2 diabetes, a quality diet is associated with adequate nutrient intake, healthy eating habits and a reduced risk of diet-related disease such as type 2 diabetes. The American Society of Cardiology, for example, recommends a diet rich in fruits, vegetables, plant proteins and fish, and a reduction in foods containing saturated fats, salt and refined cereals for the prevention of cardiovascular disease [6]. Several studies have recognized the beneficial role of a healthy diet in preventing and reducing the incidence of type 2 diabetes [7, 8]. To this end, dietary diversity scores can be used to reflect nutrient intake in diets [9]. Several food quality evaluation indices based on recommendations for healthy eating have been developed [10, 11]. These include the Food and Agriculture Organization's (FAO) Healthy Eating Index (HEI), Healthy Lifestyle Score (HLS), Women Dietary Diversity Score (WDDS) and Households Dietary Diversity Score (HDDS), and the Global Diet Quality Score (GDQS) [12-14]. However, there is no worldwide standard measure for monitoring the quality of food in populations [12]. Moreover, physical inactivity is a burden on diabetes, as it increases the risk of metabolic syndrome, cardiovascular disease and contributes to death among diabetic subjects [15]. It is a modifiable risk factor and a key element in the therapeutic approach for subjects with type 2 diabetes. Physical inactivity is assessed through the estimation of physical activity. According to the WHO, physical activity is defined as any bodily movement produced by skeletal muscles, responsible for an increase in energy expenditure above the resting level [16]. It reduces weight, body mass index, cardiovascular disease and glycated haemoglobin levels, and improves glucose tolerance, insulin sensitivity and the cardio-respiratory system [17]. Current recommendations for type 2 diabetics are 150 minutes of moderate-intensity physical activity every day of the week [17, 18]. The prevalence of diabetes in Gabon was 6.5% in 2021, demonstrating the importance of this pathology in this region [2] that poses the problem of its management. The aim of this study was therefore to assess the quality of diet and physical activity among subjects with type 2 diabetes.

2. Materials and Methods

2.1. Patients and Period of Study

This cross-sectional study took place from October 17, 2018 to January 17, 2019 at the biochemistry laboratory of the University of Health Sciences (*USS*) and at the Endocrinology Department of the University Hospital of Libreville (*CHUL*). This study was validated by the National Ethics Committee of Gabon under the reference: PROT N°015/2018/PR/CNE according to Declaration of Helsinki [19], with written informed consent from the participants for their participation and the use of patient data for research. Diabetics were individuals who came at the Endocrinology Department for a consultation to monitor their disease. Control subjects with normal blood glucose levels came to the Biochemistry Laboratory of the *USS* for a routine checkup. Patients under 20 years old, other forms of diabetes, and pregnant or breast-feeding women were excluded. Anthropometric parameters such as blood pressure (mmHg), weight (kg), height (m), age (years) and sex, were recorded. Body mass index (BMI) was calculated using the formula BMI = Weight (kg)/Height2 (m^2). The following ranges were used: patients with BMI ≥ 25 kg/m^2, were considered overweight, and those with BMI < 18.5 kg/m^2 were considered lean. BMI values between 18.5 and 24.9 kg/m^2 were considered normal [20]. Waist circumference (WC) was measured using flexible but non-stretchable graduated tape measure, to an accuracy of 0.1cm. The WC cut-off values used were those of the IDF, whose African cut-off values were ≤ 94 cm in men and ≤ 80 cm in women [20]. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured twice on the left arm using a blood pressure monitor (Beurer), among patient who had been seated and at rest for at least 5 minutes. The mean of the two measurements was reported.

2.2. Methods

Biological analysis

Glucose, creatinine, total cholesterol and triglycerides were determined on Mindray's BS200® spectrophotometer by colorimetric and enzymatic methods using BIOLABO protocol reagent. HDL-C (Low Density Lipoprotein-Cholesterol) was obtained after precipitation of the other fractions with phosphotungstic acid [21]. LDL-C (High Density Lipoprotein-Cholesterol) was then calculated using the Friedwald formula, after ensuring that the serum triglyceride concentration was below 4 mmol/L [22]. The CKD- EPI (Chronic Kidney Disease Epidemiology collaboration) equation was used to assess glomerular filtration rate [23]. Insulin resistance was assessed using the triglyceride index (TyG), whose formula is: TyG= ln [(Triglyceridemia*Glycemia (mg/dl)) / 2]. An index value greater than 8.18 indicated insulin resistance [24].

Physical activity

Physical activity was assessed using the WHO Global Physical Activity Questionnaire (GPAQ) [25]. It comprises 16 questions (P1-P16) and collects information on physical activity in three different situations: at work, when moving from one place to another, and during leisure time. To analyze the questionnaire data, the metabolic equivalent (MET), which expresses the ratio between metabolic rate during physical activity and metabolic rate at rest, was used. It is estimated that the caloric expenditure of a moderately active person is four times higher than that of a person at rest. While that of a very active person is eight times higher than the caloric expenditure of a person at rest. So, energy expenditure of 4 METs was attributed to time spent in moderately intense physical activity, and 8 METs to time spent in intense physical activity. Thus, the total physical activity score was calculated as the sum of all METs per week in work, commuting and leisure respectively. Finally, physical activity levels were classified into 3 classes: intense (MET / min / week ≥ 3000), moderate (600 ≤ MET / min / week ≤ 2999) and low (MET / min / week < 600 [25].

Diet

The food consumption and diversity scores used were those of the Food and Agriculture Organization of the United Nations [26]. The food consumption survey provided information on dietary behavior over the 7 days preceding the day of sampling. The food consumption score (FCS) was calculated as the sum of the different products of the days of consumption of each food group, multiplied by its weighting [26]. Three food consumption classes were thus established. The poor consumption class, with a consumption score less than or equal to 21. The border line food consumption class comprised individuals whose score was 21 ≤ FCS ≤ 35. Finally, the acceptable food consumption class was made up of individuals whose food consumption score was greater than 35 [26]. In addition, the Dietary Diversity Score, defined on foods consumed in the 24h preceded by the day of blood sampling, was also assessed. The dietary diversity score was calculated by summing the scores for the different food groups consumed. The value of the DDS ranged from 0 to 12. Interpretation of the score gave a classification into 3 groups. When the number of food groups was less than or equal to 3, the DDS was considered low. If the number of food groups was between 4 and 5, it was considered average, and if the number of food groups was six or more, it was considered high [26].

2.3. Data Analysis

Data were entered into Excel and analyzed using SPSS software. The distribution of variables between diabetics and controls was compared using Pearson's Chi square test for homogeneity for categorical variables, and the Anova test for continuous variables. At the end of this univariate analysis, a stepwise logistic regression was performed to find the parameters associated with type 2 diabetes, using the Hosmer-Lemeshow test and the Wald test. Data analysis was finalized by plotting ROC curves using significant data from the final equation. Differences were significant for a p-value of less than 0.05.

3. Results

3.1. Socio-Epidemiological Parameters

Table 1 shows the characteristic and biological parameters of the study population. A total of 272 individuals, including 136 diabetics and 136 controls, made up the study population. The population was predominantly female, with a sex ratio of 0.36, and this observation was similar in both groups (p=0.5520). The average age of the subjects were 46.3 ±12.6 years with extremes from 20 to 73 years.

Overall, subjects with type 2 diabetes were older than controls (p=0.0000); and their blood pressure was higher (Systolic blood pressure: p= 0.0000; diastolic blood pressure: p= 0.0001). Furthermore, abdominal obesity and overweight were more prevalent in people with diabetes than in controls (p= 0.0000 and p= 0.0031 respectively). Whereas controls consumed more alcohol than diabetics (p= 0.0141).

Analysis of biological parameters showed that blood glucose levels were higher in diabetics than in controls (p= 0.0000). As for lipid levels, triglyceridemia and HDL-C were higher in diabetics than in controls, with respective values of 0.8 ±0.5 mmol/L *vs.* 0.6 ±0.3 mmol/L (p= 0.0000); 1.3 ±0.4 mmol/L *vs.* 1.1 ±0.5 mmol/L (p= 0.0183). Otherwise, LDL-C was higher in controls. In addition, mean glomerular filtration rate was significantly lower among cases than controls (86.9 ± 29.1 *vs.* 98.9 ±32.7 (p= 0.0080). The mean value of the TyG (Triglyceride Glucose Index) was higher in individuals with diabetes (p=0.0000).

Table 1. *Socio-epidemiological parameters between diabetic subjects and controls.*

Variables	Total (*n*=272)	Diabetics (*n*=136)	Controls (*n*=136)	*p*-value
Gender n(%)				
Women	200 (73.5)	100 (73.5)	100 (73.5)	0.5520
Men	72 (26.4)	36 (26.4)	36 (26.4)	

Variables	Total (*n*=272)	Diabetics (*n*=136)	Controls (*n*=136)	*p*-value
Age (years) mean ±SD	46.3 ±12.6	52.4 ±9.7	40.2 ±2.3	0.0000
Weight (kg) mean ±SD	74.8 ±15.7	77.6 ±17.1	72.0 ±13.6	0.0031
Size (cm) mean ±SD	1.6 ±0.1	1.6 ±0.1	1.6 ±0.1	0.2502
WC (cm) mean ±SD	94.0 ±15.6	98.9 ±16.5	90.2 ±13.2	0.0000
BMI (kg/m^2) mean ±SD	27.5 ±5.7	28.7 ±6.0	26.3 ±5.2	0.0005
SBP (mmHg) mean ±SD	134.1 ±24.5	140.2 ±24.5	128.0 ±23.1	0.0000
DBP (mmHg) mean ±SD	85.2 ±19.5	89.6 ±20.9	80.7 ±16.9	0.0001
Alcohol consumption n(%)				
Yes	73 (26.8)	28 (20.6)	45 (33.1)	0.0141
No	199 (73.2)	108 (79.4)	91 (66.9)	
Tobacco consumption n(%)				
Yes	4 (1.5)	0(0.0)	4 (2.9)	0.0061
No	268 (98.5)	136 (100.0)	132 (97.1)	
Blood glucose (mmol/l)	6.4 ±3.0	8.1 ±3.5	4.8 ±1.0	0.0000
Total cholesterol (mmol/l)	4.5 ±1.1	4.6 ±1.1	4.5 ±1.1	0.5703
Triglycerides (mmol/l)	0.7 ±0.4	0.8 ±0.5	0.6 ±0.3	0.0000
HDL-Chol (mmol/l)	1.2 ±0.5	1.3 ±0.4	1.1 ±0.5	0.0183
LDL-Chol (mmol/l)	3.0 ±1.2	2.8 ±1.2	3.2 ±1.1	0.0044
SGOT (IU/L)	25.7 ±10.4	25.7 ±12.0	25.9 ±8.3	0.9540
SGPT (UI/L)	21.8 ±20.4	24.5 ±26.3	17.6 ±9.1	0.0077
Creatinine (µmol/l)	83.7 ±31.4	86.5 ±36.7	80.9 ±24.7	0.1498
CKD-EPI(ml/min/1.73m^2)	92.8 ±31.5	86.9 ±29.1	98.9 ±32.7	0.0080
TyG	7.9 ±0.7	8.3 ±0.6	7.6 ±0.4	0.0000

SD (Standard deviation); Serum SGOT (Glutamic Oxaloacetic Transaminase); SGPT (Serum Glutamic Pyruvic Transaminase), TyG (Triglyceride Glucose Index).

3.2. Assessment of Physical Activity and Diet

Table 2 shows that physical activity related to travel and leisure was high in 7.3% and 9.6% of diabetics *versus* 2.9% and 4.4% of controls respectively but not statically significant (p= 0.0548 and p= 0.0516. Overall physical activity was high in 19.1% of diabetics versus 10.3% of controls (p=0.0033). Analysis of the results of the dietary survey showed that acceptable food consumption score (FCS) was less frequent in diabetics than in controls (51.4% *versus* 78.7%, p= 0.0000). The dietary diversity score (DDS) was higher in controls (34.6%) than in diabetics (8.8%, p=0.0000).

Table 2*. Assessment of the study population's lifestyle habits.*

Variables n/ (%)	Total	Diabetics	Controls	OR [95% CI]	*p*-value
FCS					
Acceptable	177 (65.1)	70 (51.4)	107 (78.7)	0.3[0.2 – 0.5]	0.0000
Poor/Moderate	95 (34.9)	66 (48.5)	29 (21.3)		

Variables n/ (%)	Total	Diabetics	Controls	OR [95% CI]	*p*-value
DDS					
High	59 (21.7)	12 (8.8)	47 (34.6)	0.2 [0.1 - 0.4]	0.0000
Low/Moderate	213 (78.3)	124 (91.2)	89 (65.4)		
Physical activities					
Work-related					
High	10 (3.7)	5(3.7)	5 (3.7)	1.0 [0.3 - 3.5]	0.6253
Low/Moderate	262 (96.3)	131 (96.3)	131 (96.3)		
Travel-related					
High	14(5.2)	10 (7.3)	4 (2.9)	2.6 [0.8 - 8.6]	0.0548
Low/Moderate	258 (94.8)	126 (92.6)	132 (97.1)		
Leisure-related					
High	19 (7.0)	13 (9.6)	6 (4.4)	2.3 [0.8 - 6.2]	0.0516
Low/Moderate	253 (93.0)	123 (90.4)	130 (95.6)		
Global					
High	40 (14.7)	26 (19.1)	14 (10.3)	0.48 [0.24 - 0.99]	0.0033
Low/Moderate	232 (85.3)	110 (80.8)	122 (89.7)		

Furthermore, the results showed that FCS and DDS were significantly protective factors against disease, with respective odds ratios of 0.3 [0.2 - 0.5] and 0.2 [0.1- 0.4]. The same observation was made for overall physical activity (OR= 0.48 [0.24-0.99].

However, the relationships between physical activity and the two dietary scores were not gender-dependent (Table 3). In addition, a comparison of the different scores studied according to the sex of the general population showed that overall physical activity was comparable in men and women (p=0.3548) as well as dietary intake, (p=0.1488).

Multivariate analysis using binary logistic regression showed that several variables were associated with type 2 diabetes. These were age (p= 0.0000), TyG (p= 0.0000), triglyceridemia (p=0.0000) and family history of first--and second-degree relatives with diabetes (p=0.0030 and p= 0.0020 respectively), alcohol consumption (p= 0.0006), dietary intake and dietary diversity scores (p=0.0150 and p=0.0000 respectively).

With Table 4, the 2 dietary scores were found to be significantly negatively correlated with the probability of developing type 2 diabetes (B= -0.032 and B= -0.546 respectively). Whereas age and triglyceride index were positively correlated with the onset of the disease (B= 0.104, B=2.738 respectively).

***Table 3**. Assessment of the sexe's lifestyle habits.*

	Total	Women	Men	OR [95% CI]	*p*-value
Global physical activity					
High	40 (14.7)	28 (14.0)	12 (16.7)	1.2 [0.6 - 2.6]	0.3548
Low/moderate	232 (85.3)	172 (86.00)	60 (83.3)		
FCS					
Acceptable	177 (65.1)	131 (65.5)	46 (63.9)	1.1 [0.6 - 1.9]	0.4568
Poor/moderate	95 (34.9)	69 (34.5)	26 (36.1)		
DDS				1.5 [0.7 - 3.1]	0.1488

	Total	Women	Men	OR [95% CI]	*p*-value
High	59 (21.7)	47 (23.5)	12 (16.7)		
Low/moderate	213 (78.3)	153 (76.5)	60 (83.3)		

Table 4. *Variables in equation of the binary logistic regression model.*

Equation variables	B	Wald	*P*-value	Exp (B)	95% CI Lower-Upper
Age	0.104	36.664	0.0000	1.133	1.068 - 1.151
TyG	2.738	47.254	0.0000	194.969	6.368 - 37.550
Triglycerides (mmol/l)	-4.434	26.686	0.0000	0.012	0.002 - 0.064
History of first degree relative with diabetes (yes)	-1.377	8.832	0.0030	0.252	0.102 - 0.626
History of second degree relative with diabetes (yes)	-2.001	10.020	0.0020	0.135	0.039 - 0.467
Alcohol Consumption(yes)	1.174	7.597	0.0060	3.234	1.404 - 7.449
FCS	-0.032	8.019	0.0150	0.962	0.944 - 0.994
DDS	-0.546	12.772	0.0000	0.569	0.432 - 0.776
Constant	-20.240	44.807	0.0000	0.000	

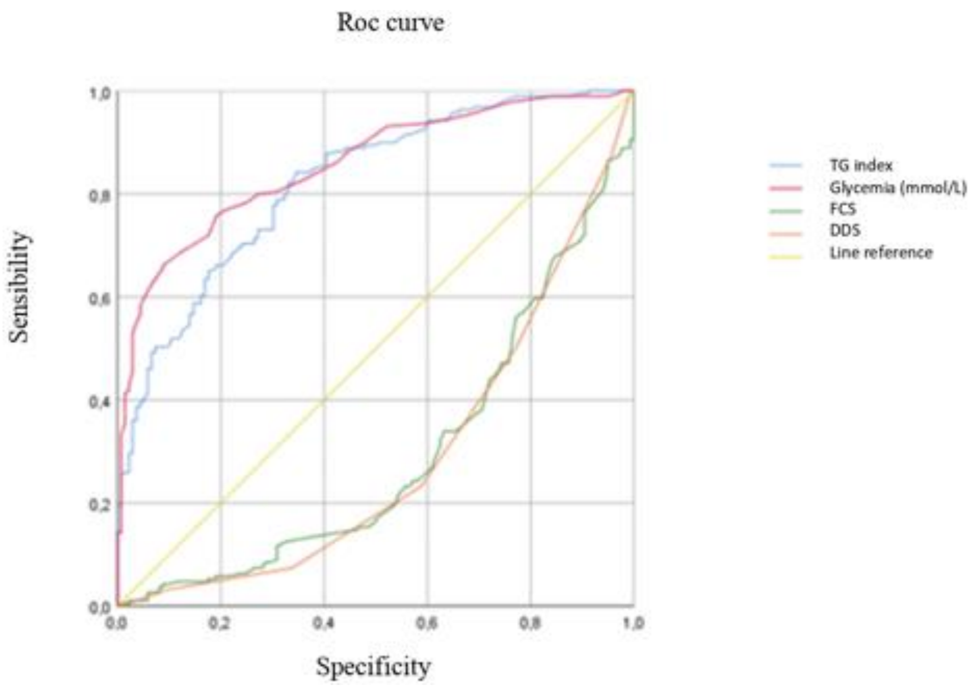

Figure 1. *Roc curve showing impact of variables (TG Index, blood glucose, FCS and DDS) in occurrence of type 2 diabetes.*

The Figure 1 of ROC curve showed that the areas of the two variables (TyG and blood glucose) were similar (0.822 and 0.856 respectively p= 0.0000). Where as those for FCS and DDS were 0.294 and 0.288 respectively p= 0.0000. Concerning the specificity and sensitivity of diagnosing the disease based on risk factors, the curve showed that for a TyG value of 7.15, the specificity of being diabetic was 13.2% and the sensitivity 98.9%. For a TyG value of 8.23, the specificity of being diagnosed with type 2 diabetes would be 91.2%, with a sensitivity of 50.3%.

4. Discussion

Assessment of the physical activity of the population in this study showed that individuals living with type 2 diabetes had better overall physical activity than controls. This result corroborates that of Miho et al, found in a Thai population [27]. However, the proportion of active diabetics found by these authors was higher than in this work. The improvement in physical activity by these patients would be due to the fact that physical exercise is recommended for their treatment. In contrast, this demonstrates the impact of physical inactivity results in an increased risk of developing type 2 diabetes among the general population, where the proportion of inactive individuals was high. Nevertheless, the majority of diabetics in this study had low levels of physical activity. This shows that compliance with the recommendations by these individuals is not optimal, hence the need to insist on the management of modifiable risk factors, as advocated by current management recommendations. Indeed, these recommendations suggest that patients engage in moderate activity every day of the week. The effect of physical activity on insulin resistance lasts between 24 and 72 hours [17]. In addition, in the areas of physical activity studied, the efforts made during travel and leisure activities were significantly more intense with diabetics than in non-diabetics. On the other hand, efforts made at work were comparable in both groups. This result identifies areas where physical activity should be more pronounced in non-diabetic subjects as part of primary prevention.

In terms of dietary intake, acceptable consumption was more frequent in controls than in cases (p= 0.0000). In fact, this parameter is a protective factor against type 2 diabetes (OR= 0.3[0.2-0.8]). This result is supported by the odds ratio, which showed that dietary diversity was a protective factor (OR= 0.1 [0.07-0.280]) against type 2 diabetes. Other authors have found similar results [13, 28]. These researchers showed that insufficient dietary quality was a risk factor for type 2 diabetes, even though they used other types of dietary diversity scores. These results were further supported by the equation obtained from the logistic regression model; with areas under the curve of 0.294 and 0.288, respectively for the FCS and DDS scores.

In general, subjects with type 2 diabetes were older than controls (p=0.0000). Ueno et al. found the same observation in an Asian population [27]. Indeed type 2 diabetes is a disease associated with age and aging [2], which would explain this result. The population was predominantly female. This distribution was similar in each group. In addition, BMI and WC were higher in diabetics than in controls (p=0.0118 and p=0.0000 respectively). These results have been reported by other authors [27, 29] and can be explained by the fact that overweight and abdominal obesity are known risk factors associated with insulin resistance in type 2 diabetes. However, this distribution does not seem to influence the different scores studied in this work. Furthermore, analysis of the data showed that systolic and diastolic blood pressures of subjects with diabetes were relatively higher than those of non-diabetics. The results concur with those of Agyemang et al [29]. This observation may be explained by the fact that hypertension is a known risk factor for type 2 diabetes. Concerning alcohol consumption, this work showed that controls consumed more alcohol than cases (p= 0.0088). Ahmad and colleagues reported the same observation [30]. Diabetic subjects were regularly monitored, and cessation of alcohol intake was strongly recommended as part of their treatment and therapeutic education. Despite these recommendations, 20% of diabetics still drink alcohol. This suggests that the recommendations concerning alcohol consumption are not optimal and should be reinforced during information and awareness sessions. Biologically, persistent hyperglycemia was observed in diabetics. This suggests that, despite treatment and the implementation of hygienic and dietary measures, optimal management thresholds have not yet been reached. Measurement of glomerular filtration rate using the CKD-EPI formula showed that renal filtration, although normal, was lower in diabetic subjects than in controls (p= 0.000). This already suggests a disturbance in the functioning of this organ, which could lead to an accumulation of toxins and metabolic waste products from the diet. Insulin resistance was more frequent in diabetics than in controls (p=0.000). This observation may be due to the fact that this metabolic anomaly is the main pathophysiological mechanism of type 2 diabetes. This result was supported by the ROC curve obtained in this study. In addition, the lipid profile in both groups was normal. Triglyceridemia and HDL-C averages were significantly elevated in the cases (p= 0.000 and p= 0.0175 respectively). The opposite was true for LDL-C (p= 0.0149). The combination of cholesterol-lowering drugs in the treatment of diabetic subjects in this work could explain this result.

5. Conclusion

This study assessed the dietary behavior and physical activity of subjects with type 2 diabetes in Libreville, Gabon. Physical inactivity and poor diet are known risk factors for type 2 diabetes, but both are modifiable. The benefits of physical activity and a healthy diet in diabetic individuals have been demonstrated. This work revealed that subjects with type 2 diabetes in this region not only had poor dietary diversity, but more than half had low levels of physical activity. It would therefore be important to continue raising awareness in this region of the benefits of changing lifestyle of these individuals, as recommended by the WHO, in order to reduce complications and mortality rate of this disease. It would also be essential to insist on these preventive measures for non-diabetic subjects, in order to reduce the incidence of type 2 diabetes. Nevertheless a comparison of different criteria for evaluating dietary quality among subjects should be made in population. Moreover, determined the impact of physical exercise on biological parameters not through the questionnaire but by physical fitness tests in order to better appreciate the contribution of physical exercise on the prevention or on treatment of type 2 diabetes in population.

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Author Contributions

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Final approval of the manuscript: A. S. M. B, R. N- N; D. N; E. N. E, A. S. B, E. N. E, F. A. O.

Conflicts of Interest

The authors declare no conflicts of interest.

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