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International Journal of Clinical Biochemistry and Research

Journal homepage: https://www.ijcbr.in/

Original Research Article

Cardiometabolic profile of type 2 diabetic subjects in Libreville

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ARTICLE INFO

Article history:
Received 09-03-2021
Accepted 26-03-2021
Available online 30-04-2021

Keywords:
Type 2 diabetes
Cardiovascular risk factors
Metabolic syndrome
Cardiometabolic
Framingham

ABSTRACT

Type 2 diabetes is the chronic metabolic disease associated with cardiovascular, renal and neurological complications, responsible for morbidity and mortality. In addition, the incidence of cardiovascular disease was 10.3 out of 1000 type 2 diabetics per year in low-income countries like Gabon. Thus, this work was setup to determine the cardiometabolic profile of type 2 diabetic subjects in Libreville.

Materials and Methods: This was a cross-sectional analytical study, which took place at the Endocrinology Department of the University Hospital Center of Libreville (CHUL) and at the Biochemistry Laboratory of Health Sciences University (USS). 210 subjects were enrolled, including 95 diabetics and 115 controls. Their anthropometric values were recorded and biochemical parameters obtained by spectrophotometric methods. Metabolic syndrome was defined according to NCEP ATP III criteria, and 10-years cardiovascular risk was assessed using Framingham and American Heart Association (AHA) / ACC risk scores.

Results: The metabolic syndrome was found among 75.8% of diabetics against 24.2% among controls (p = 0.000). In all, 42.1% of diabetics had a high cardiovascular risk by the Framingham equation versus 6.1% for the controls and 41.1% with the AHA / ACC score versus 4.3% for the controls. Diabetic women were more affected than men (54.6% against 13.8% p = 0.000).

Conclusion: Type 2 diabetics should undergo intensive management of cardiovascular risk factors in order to reduce the level of cardiovascular risk. Thus their life shall be improved by reducing morbidity and mortality.

1. Introduction

Type 2 diabetes is the chronic metabolic disease of the 3rd millennium. Therefore, it is a significant public health problem around the world. In fact, an estimated 108 million adults were living with diabetes in 1980, up from 422 million in 2014 and 463 million in 2019. According to the International Diabetes Federation (IDF) estimation in 2019, this pathology would increase by 51% worldwide, while it would almost triple in Africa with 143% in 2045. This chronic pathology is associated with cardiovascular, renal and neurological complications,[1] responsible for its morbidity / mortality. Mortality occurs by type 2 diabetes is mainly due to vascular complications leading to term by serious events such as myocardial infarction, stroke and even heart failure.[2–5] The atheromatous process is promoted by various factors, through inflammation, endothelial dysfunction, glucotoxicity and insulin resistance.[6] In 2018, IDF stipulated that two out of three type 2 diabetics have cardiovascular risk factors or have already experienced a

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https://doi.org/10.18231/j.ijcbr.2021.004

cardiovascular event.[7] Likewise, Anjana et al. have shown that, mortality from cardiovascular disease in low-income countries was five times higher than that of subjects living in high-income countries. In addition, the incidence of cardiovascular disease was 10.3 out of 1000 type 2 diabetics per year in those low-income countries like ours.[8] The latest IDF estimates show that the age-corrected prevalence of diabetics in Gabon ranges between 6 and 7%, one of the African countries with the highest prevalence. All this justifies the evaluation of cardiometabolic risk factors among type 2 diabetics in this region.

2. Materials and Methods

2.1. Subjects and recruitment

This cross-sectional and analytical study was carried out in 2019 from September 9 to December 13. It took place at the Biochemistry's laboratory of Health Sciences University (USS) and at the Endocrinology Department of Hospital University Center of Libreville (CHUL), after validation of the protocol by the national ethics committee. The study population was made up of known diabetics, coming for consultation, for their regular follow-up at the endocrinology department of the CHUL and control subjects with normal blood sugar levels, who came to USS for routine check-ups. Patients under 20 years of age, other types of diabetes, and pregnant or breastfeeding women were not included.

2.2. Anthropometric parameters assessment

The Anthropometric parameters such as blood pressure (mmHg), weight (kg), height (m), age (years) and sex, were noted. The body mass index (BMI) was calculated, from the formula BMI = Weight (kg) / $(\text{Height})^2$ (m^2). Thus, intervals used were: below 18.5 kg/m^2 patients were in underweight range, between 18.5 and 24.9 kg/m^2 they were in healthy weight range, between 25 and 29.9 kg/m^2they were overweight range and between 30 and 39.9 kg/m^2 they were in obese range.[9] Waist circumference (WC) was measured using a flexible but non-stretchy graduated tape with an accuracy of 0.1cm. The measurement was taken halfway between the last rib and the iliac crest. The WC cut-off values used were those of the National Cholesterol Education Program, Adult Treatment Panel III (NCEP ATP III) for the diagnosis of Metabolic Syndrome.[10] Blood pressure was obtained using a sphygmomanometer for patient who had been at rest for at least 5 minutes. Two measurements were carried out and the mean result was considered, in relation to the thresholds of harmonized definition of ACC / AHA to define arterial hypertension (systolic BP> 130 mm Hg or diastolic BP> 80 mm Hg).[11]

2.3. Biochemical assessment

Glucose, creatinine, total cholesterol and triglycerides were determined using the Mindray BS 200® spectrophotometer by colorimetric and enzymatic methods with BIOLABO reagent kits. HDL cholesterol was obtained after precipitation of the other fractions with phosphotungstic acid. Then LDL cholesterol was calculated using Friedwald's formula for triglyceride concentration less than 4 mmol / L.[12] LDL hypercholesterolemia has been defined by the European Society of Cardiology / European Society of Atherosclerosis (< = 100 mg / dL (2.6 mmol / L).[13] Above 2.6 mmol / l of LDL -C plasma, individual is considered to have LDL hypercholesterolemia. Chronic Kidney Disease Epidemoliogy collaboration (CKD-EPI) equation was used to estimate the glomerular filtration rate.[14] Insulinoresistance was calculated by using triglyceride index with formula: IR = ln [(TG * GLY (mg / dl)) / 2], with a threshold of 8.18.[15] The metabolic syndrome has been defined according to the criteria of NCEP ATP III.[10]

2.4. Cardiovascular disease risk scoring

The Framingham equation and that of the American Heart Association (AHA) / ACC (American College Cardiology), were used to evaluate the cardiovascular risk over 10 years. Therefore, for subjects whom metabolic syndrome was demonstrated, the result of the Framingham equation was multiplied by 1.5. Equations used in the study by Genest et al. in 2009 made it possible to determine the different levels of risk.[16] Thus, for the Framingham equation, the risk was low for a probability less than 10%, moderate for probability between 10 and 20% and finally high for probability greater than 20%.[16] On the other hand, for the AHA / ACC, the risk was low for probability less than 5%, moderate if this probability was between 7.5 - 20% and high for probability greater than 20%.[17]

2.5. Statistical analysis

Data were entered and analyzed using Excel 2013, Epi info and Minitab software. Descriptive and analytic analysis were made. The quantitative variables were expressed by the mean and its standard deviation, while the qualitative variables were expressed as a percentage with 95% CI. Analysis of variance (ANOVA) was used to compare the means of quantitative variables between two groups, while the χ^2 test compared the qualitative variables between two groups. The difference was considered significant for a probability less than 0.05.

3. Results

3.1. Sociodemographic parameters

In total, the study involved 210 individuals including 95 type 2 diabetics and 115 controls. Thus, 71.9% of the population were women and no difference was found between the patients and the controls (p = 0.272). Moreover, the diabetic subjects were aged 55.0 ± 10.9 years versus 39.0 ± 11.8 years for control (p = 0.000). Waist circumference was 100.6 ± 18.3 cm versus 90, 6 ± 13.9 cm for diabetic and controls respectively (p = 0.000). Systolic blood pressure averaged were 142.5 ± 24.9 mmHg among diabetic patients and 129.4 ± 24.5 mmHg among control group (p = 0.000). In addition, 22.1% of diabetic subjects consumed alcohol, compared to 33.9% for controls (p = 0.041). A family history of diabetes was recorded for 41.1% of diabetic subjects versus 24.3% for controls (p = 0.007). Likewise, family history of hypertension was reported in 43.2% of diabetic subjects and in 31.3% of controls (Table 1).

3.2. Biological parameters

Triglyceride concentration was 0.9 ± 0.5 mmol / L among diabetics, compared to 0.6 ± 0.3 mmol / L among controls (p = 0.004). Likewise, the glomerular filtration rate was estimated at 85.7 ± 29.3 ml / min / 1.73 m^2 for the diabetics against 99.4 ± 33.4 ml / min / 1.73 $m^2$for the control group (p = 0.003). The glucose triglyceride index was on average 6.8 ± 0.7 among diabetics and 6.1 ± 0.5 among control group (p = 0.000). The mean cardiovascular risk was 19.5 ± 13.3% for diabetics versus 4.9 ± 6.5% for controls (p = 0.000), with the Framingham equation, while the equation of AHA / ACC gave 20.5 ± 17.0% versus 4.3 ± 10.7% (p = 0.000). The metabolic syndrome was demonstrated in 75.8% of diabetics versus 20.0% of controls (p = 0.000) (Table 2).

3.3. Cardiovascular risk levels

Regardless of the cardiovascular risk score considered, the diabetics were more at moderate and high risk than the controls with values of p = 0.000 (Table 3). Moreover, among diabetics, Framingham score gave a high risk for 54.6% of women, against 13.8% of men. Similarly, 22.7% of women in this group had a moderate risk versus 48.3% of men (p = 0.000). However, the AHA score gave a similar distribution of risk in women and men (p = 0.237). In fact, the risk was high for 40.9% of women and for 41.4% of men, while it was moderate for 34.9% of women and for 48.3% of men. In the control group, the risk was low for 86.1% of individuals, with the Framingham or AHA / ACC score. This proportion was similar for men and women (p = 0.859 and p = 0.692), for the 2 scores studied.

4. Discussion

Cardiovascular diseases represent a public health problem due to their prevalence and their socio-economic impact. For people with diabetes, they are the most common cause of morbidity and mortality.[18] Duration of diabetes among this population was around 5 years in previous study suggesting high mortality of this population in Gabon.[19]

In addition, in its 2018 publication, IDF stated that two out of three diabetics have cardiovascular risk factors or have already experienced a cardiovascular event.[7] The results in Africa are even more startling. In fact, while 55% of diabetics were under 60 years old, and 45% had diabetes for less than six years, 47% still thought they were spared of cardiovascular risk and 16% were at low risk.[20]

So to improve the care of diabetic patients, it is important to assess the level of cardiovascular risk of these individuals. This work therefore set out to assess the cardio-metabolic risk among people with type 2 diabetes in Libreville. For that, a case-control study was carried out with 95 diabetics who came in consultation for the control of their diabetes. Ignoring subjects with decompensated or hospitalized diabetes resulted in an underestimation of the cardiometabolic risk factors assessed. The equations used in this study were Framingham's and AHA / ACC's. None of these equations have been developed in Africa. They were therefore used in this study by default. Other equations were used in relation with the specificities of populations such as the European SCORE. For this study, the Framingham equations and that of the AHA / ACC were chosen and used, as the first is the basic equation from which all the others have been derived, while the second was established taking into account an appreciable proportion of black American subjects, quite close to Africans. The present study has shown that 4 to 5 times more people with diabetes have an elevated 10-year cardiovascular risk compared to the control population, regardless of the equation used to assess this risk.

Likewise, this work has shown that the average risk was higher among women than men with diabetes, but also more than 40% of this population had a high cardiovascular risk, whatever the equation used against 4 to 6% for the control group. These results are in line with those of other authors in Africa, using the Framingham equation.[21] Large meta-analyzes have confirmed that type 2 diabetes affects cardiovascular risk differently between the two sexes and the most affected are women.[22] Our results point in the same direction. This difference between women and men is thought to be due to a distribution of central adiposity, lipid profile and hormones. It is true that women tend to be more obese than men, being overweight favored by estrogen during pre-menopause.[23] The risk level found in this population of diabetics requires multimodal and intensive management of these patients in order to improve their morbidity and mortality. This multimodal care concerns the

Table 1: Comparison of socio-demographic parameters between diabetic subjects and controls

Variables	Total	Diabétics	Controls	P
Effective	210	95 (45,2)	115 (54,8)	
Sex N, (%)				0,272
Men	59 (28,1)	29 (30,5)	30 (26,1)	
Women	151 (71,9)	66 (69,5)	85 (73,9)	
Age (ans) Mean value ± standard deviation	46,2±13,9	55,0±10,9	39,0±11,8	0,000
weight (kg) Mean value ± standard deviation	73,4±15,1	75,6±16,0	71,5±14,1	0,050
Waist(m) Mean value ± standard deviation	1,6±0,1	1,6±0,1	1,6±0,1	0,350
Waist size (cm) Mean value ± standard deviation	95,1±16,7	100,6±18,3	90,6±13,9	0,000
BMI (kg/m2) Mean value ± standard deviation	27,7±7,7	29,1±9,6	26,6±5,6	0,020
Systolic blood pressure(mm Hg) m ±SD	135,3±25,5	142,5±24,9	129,4±24,5	0,000
Diastolic blood pressure(mm Hg) m ± SD	78,8±23,7	82,9±20,8	75,4±25,5	0,020
Alcohol consumption N (%)				0,041
No	150 (71,4)	74 (77,9)	76 (66,1)	
Yes	60 (28,6)	21(22,1)	39 (33,9)	
Tobacco consumption N (%)				0,128
No	198 (94,3)	92 (96,8)	106 (92,2)	
Yes	12 (5,7)	3 (3,2)	9 (7,8)	
Family history of diabetes N (%)				0,007
No	143 (68,1)	56 (58,9)	87 (75,7)	
Yes	67 (31,9)	39 (41,1)	28(24,3)	
Family history of high blood pressure (%)				0,051
No	133 (63,3)	54 (56,8)	79 (68,7)	
Yes	77 (36,7)	41 (43,2)	36 (31,3)	

accentuation of patient education regarding cardiovascular risk factors, lifestyle modification and drug interventions. However, few diabetics admit discussing cardiovascular disease with their treating physician.[24] It is therefore necessary, especially in Africa, to accentuate the therapeutic education of diabetic subjects, with a strong emphasis on cardiovascular diseases. They are not only common in type 2 diabetes but they also exist in type 1 diabetes.[25] This makes it a significant burden of morbidity and mortality.

Each of these modalities would have an impact on one or more cardiovascular risk factors that were identified in this study. This is the case for blood pressure, systolic or diastolic, body mass index, triglyceride glucose index or glomerular filtration rate, which are more disturbed among diabetic subjects compared to controls. The glucose triglyceride index, used as a marker of insulin resistance and metabolic disorder, has also recently been considered as a predictive marker of cardiovascular events for diabetic subjects.[26,27] Several studies have indeed proven an association between the control of cardiovascular risk factors and the development of diabetes.[28,29] Glycated hemoglobin has not been evaluated in this work, although its value is associated with the increased prevalence of acute or chronic renal failure, and therefore with cardiometabolic risk.[30] There is thus a multitude of markers that can be used as prognostic factors for cardiovascular complications in type 2 diabetics, and all of these markers lead to practically the same conclusions because they are associated with each other, as reported by Naka et al.[31] Thus improving the morbidity and mortality of our diabetic subjects would result by reducing the overall cardiovascular risk.

This support should therefore target all modifiable risk factors, which have an impact on the overall risk. However, the probability of reaching the target values of a combination of several risk factors taken individually is often very low among diabetic subjects, as shown by other studies,[32] whereas it is precisely this association of risk factors that accounts for the high overall cardiovascular risk among this population. In this study, the concentration of LDL-cholesterol was not significantly different from that

Table 2: Comparison of biological parameters between women and men in diabetics and controls, then in the 2 groups

Variables	Diabétics				Controls				Total	p**
	Women	Men	p*	Sous total		Men	p*	Sous total		
Glycemia (mmol/L) m±SD	7,9±3,2	8,7±4,4	0,000	8,2±3,6	4,9±1,4	4,5±0,8	0,000	4,8±1,3	6,3±3,1	0,000
Total Cholesterol (mmol/L) m±SD	4,6±0,9	4,3±0,8	0,305	4,5±0,9	4,4±1,1	4,7±1,2	0,309	4,5±1,1	4,5±1,0	0,813
Triglycerides (mmol/L) m±SD	0,8±0,5	0,9±0,5	0,742	0,9±0,5	0,6±0,3	0,7±0,3	0,567	0,6±0,3	0,7±0,4	0,000
HDL-C (mmol/L) m±SD	1,3±0,9	1,2±0,6	0,010	1,3±0,9	1,2±0,7	0,9±0,5	0,016	1,2±0,7	1,2±0,8	0,525
LDL-C (mmol/L) m±SD	2,7±1,4	2,8±0,8	0,862	2,7±1,2	2,9±1,1	3,5±0,9	0,019	3,1±1,1	2,9±1,2	0,075
Creatinine (μmol/L) m±SD	80,3±22,5	89,9±22,6	0,058	83,2±22,8	74,7±18,4	98,4±30,3	0,000	80,9±24,4	81,9±23,6	0,396
CKD-EPI (mL/min/1,73m2) m±SD	88,9±28,1	78,6±31,1	0,040	85,7±29,3	107,3±33,3	76,9±21,6	0,000	99,4±33,4	93,3±32,2	0,003
TriglyceridesIndex glucose TyGm±SD	6,8 ±0,7	6,9±0,7	0,458	6,8±0,7	6,1±0,5	6,1±0,4	0,880	6,1±0,5	6,4±0,7	0,000
Metabolic syndrome N (%)			0,004				0,426			0,000
No	10 (15,1)	13(44,8)		23 (24,2)	66 (77,6)	26 (86,7)		92 (80,0)	115 (54,8)	
Yes	56 (84,9)	16(55,2)		72 (75,8)	19 (22,4)	4 (13,3)		23 (20,0)	95 (45,2)	
Framingham (%) m±ET	23,4±13,8	16,6±15,6	0,037	19,5±13,3	4,7±6,7	5,8±6,9	0,453	4,9±6,5	11,5±12,5	0,000
Score American Heart Association (%) m±ET	20,4±18,5	20,2±13,2	0,045	20,5±17,0	4,4±11,9	4,0±6,6	0,838	4,3±10,7	11,6±16,0	0,000

CKD-EPI(Chronic Kidney Disease Epidemiology)
p*Comparison of biological parameters between men and women in each group
p**Comparison of biological parameters in diabetic subjects and controls.

Table 3: Distribution of cardiovascular risk levels in diabetics and controls according to sex

Cardiovascularrisk score	Diabétics				Controls				p**
	Women	Men	p*	Total	Women	Men	p*	Total	
Framingham (%)			0,000				0,859		0,000
Low	15 (22,7)	11 (37,9)		26 (27,4)	74 (87,1)	25 (83,3)		99 (86,1)	
Moderate	15 (22.7)	14 (48,3)		29 (30,5)	6 (7,0)	3 (10,0)		9 (7,8)	
High	36 (54,6	4 (13,8)		40 (42,1	5 (5,9)	2 (6,7)		7(6,1)	
Score American Heart Cardiology (%)			0,237				0,692		0,000
Low	16 (24,2)	3 (10,3)		19 (20,0	74 (87,1)	25 (83,4)		99 (86,1)	
Moderate	23 (34,9)	14 (48,3)		37 (38,9)	7 (8,2)	4 (13,3)		11 (9,6)	
High	27 (40,9)	12 (41,4)		39 (41,1)	4 (4,7)	1 (3,3)		5 (4,3)	

p* Comparison of cardiovascular risk levels between men and women in each group.
p** Comparison of cardiovascular risk levels indiabetic subjects and controls.

of the controls, while the recommendations suggest values below 2.6 mmol / L. The LDL cholesterol target values were not reached in this diabetic population and therefore the cardiovascular risk is high, especially since it was a relatively young population, with an average age of 55 ± 10.9 years old, likely to live with their disease for a long time but also to develop the chronic complications linked to this disease. Other studies have shown this difficulty in correcting risk factors.[33] In addition, the glomerular filtration rate obtained by the CKD-EPI formula provided a flow rate of 85.7 ± 29.3 mL / min / 1.73m^2 among diabetics, compared to 93.3 ± 32.2 among controls. This decrease on glomerular filtration, with similar serum creatinine among 2 groups of populations, contributes to increased cardiovascular risk. The fight against cardiovascular risk factors must be generalized among diabetic subjects, such as blood sugar control.

In Conclusion, the present study, carried out among type 2 diabetics in Libreville, provided the first data on the level of cardiovascular risk on this population in Gabon. Indeed, several cardiometabolic risk factors in addition to hyperglycemia, including arterial hypertension, reduced glomerular filtration rate, metabolic syndrome and obesity were common in this population, suggesting that hyperglycemia is not the only factor leading to high cardiovascular risk. It therefore emerges from this the need to fight intensively against these cardiovascular risk factors, in order to improve the survival of these diabetic subjects. These measures should be comprehensive, taking into account the aspects of medication, physical activity and a healthy diet.

5. Abbreviations

NCEP-ATP III: National Cholesterol Education Program, Adult Treatment Panel III; **AHA:** American Heart Association; **ACC:** American College Cardiology; **IDF:** International Diabetes Federation; **BMI:** The body mass index; **WC:** Waist circumference; **BP:** Blood pressure; **HDL:** High-density lipoprotein; **LDL:** Low-density lipoprotein; **CKD-EPI:** Chronic Kidney Disease Epidemoliogy collaboration.

6. Source of Funding

This work was funded by the USS Department of chemistry-biochemistry.

7. Conflicts of Interest

Authors declare that have no potential competing interests regarding the publication of this paper.

Acknowledgments

We thank all study participants and the Department of Endocrinology of University Hospital Center of Libreville for their collaboration.

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Cite this article: MBANG BENGONE AS, NIKIEMA-NDONG R, NSAME D, NNEGUE EDZO E, NZOUGHE K, OBAME ENGONGHA C, OVONO ABESSOLO F. Cardiometabolic profile of type 2 diabetic subjects in Libreville. *Int J Clin Biochem Res* 2021;8(1):15-21.