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Type 2 Diabetes and Complications at a Diabetes Tertiary Care Center of Libreville - Gabon

Aude Syntia Mbang Bengone[1], Rosalie Nikiéma-Ndong[2], Guy Roger Ndong Atomo[3], Alvine Sibylle Batou[4], Eudine Tsouka[5], Felix Ovono Abessolo[6], Edouard Ngou-Milama[7]

[1, 2, 4, 5, 6, 7]Department of Chemistry - Biochemistry, Faculty of Medicine, University of Health Sciences, P.O. Box 4009 Libreville – Gabon

[3]Laboratory of Research in Biochemistry (LAREBIO), University of Sciences and Technology of Masuku, P. O. Box 913 Franceville, Gabon

Corresponding author
Mbang Bengone Aude Syntia, E.mail : haudess[at]yahoo.fr

Abstract: ***Aim: Evaluate diabetes management and its complications at a diabetes tertiary care center. Patients and methods: This was a cross-sectional and descriptive study, conducted from April 2018 to July 2020 at a diabetes tertiary center. Type 2 diabetes patients received during the study period and following all criteria were enrolled. After a clinical exam, venous blood sample were taken for measuring concentrations of lipids, glucose, glycated hemoglobin, creatinine and microalbuminuria. Based on their medical records, we noted treatment modalities and diabetic complications. Results: Of the 609 patients enrolled, 57% had diabetes that had evolved since less than 5 years. More than half (56%) of patients were treated with oral antidiabetic drugs. Otherwise, 43.9% of patients had not achieved the objectives of glycated hemoglobin. LDL cholesterol was high among 38.0% of our patients and 16.0% of them were treated with statins. Microalbuminuria was present among 44.8% of patients and 22.3% of patient had low estimated glomerular filtration. Systolic blood pressure was high among 43.7% of patients and 54.0% of them were treated, especially by enzyme converting inhibitors. Conclusion: Diabetes monitoring and its complications is sub-optimal. This should be improved by the management of drugs and by strengthening educational and nutritional aspects.***

Keywords: angiotensin converting enzyme inhibitors.- Complications- dyslipidemia- Metformin- Type 2 diabetes

1. Introduction

In 2019, the International Diabetes Federation (IDF) estimated people living with diabetes worldwide at 463 million and aged from 20 to 79 years, of which 9.3% were adult's.[1]Low- and middle-income countries account for 79.4% of these diabetes cases. Projections lead to 578.4 million adult people with diabetes in 2030 and 700.2 million in 2045.[1]The most significant increases will be for countries beginning the transition from low- income to middle-income. This is the case in Africa, where the number of people living with diabetes will increase by 48% within 2030 and 143% within 2045. However, Africa has 59.7% of cases of undiagnosed diabetes, which represent approximately 11.6 million of people. The number of deaths due to diabetes and its complications was estimated in 2019 at 4.2 million.[1]

In Africa, the estimated percentage of diabetes-related deaths was 73.1% among people under the age of 60 years wich is the most active age group.[1]In Gabon, the comparative prevalence, adjusted for age, is 6-7%, compared to 4.7% for all of Africa. It's therefore a real health problem. Mortality due to diabetes, in particular type 2 diabetes, is mainly linked to its chronic complications, such as micro and macro angiopathies, closely related to atherosclerosis.[2]Numerous studies have shown an increased risk of death from cardiovascular disease and all causes in subjects with and without diabetes.[3,4,5]Reducing cardiovascular disease has therefore become an imperative, and diabetes management is no longer limited to lowering blood sugar. Indeed diabetes management involves controlling cardiovascular risk factors[6], without forgetting the acute complications, because these risk factors lead to an explosion of cardiovascular disease and chronic kidney disease in this population.[7]

In this setting where Gabon is among the African countries with the highest prevalence of diabetes, it is useful to assess the cardiovascular risk factors and complications of diabetes among this population, in relation to their treatment.

2. Patients, Material and Methods

Ethical Clearance

The National Committee on Ethics for Research (CNER) of Gabon reviewed and approved the study.. All paticipants were informed of the study objectives before being freely enrolled. Thus, questionnaires were submitted to participants after written inform consent obtained. No names were recorded on the questionnaires. Adequate training data collectors took place to ensure confidentiality and all questionnaires were kept safe.

Patients

This cross-sectional, descriptive and hospital based study was carried, from April 2018 to July 2020 at the Department of Endocrinology of the University Hospital of Libreville and in the Laboratory of Biochemistry, Faculty of Medicine and Health Sciences. This structure was the unique tertiary care center dealing with diabetics in Libreville, Gabon. Patients with type 2 diabetes for at least one year, over the age of 30 years and regularly monitored for the management of their diabetes were recruited. Children, pregnant women, inpatients and patients with type 2 diabetes followed at the *CHUL* who had a modification of their antidiabetic

treatments during the year and those who refused to be part of the study, were not included.

A questionnaire provided information on socio-demographic data (age, sex, occupation, marital status, and residence), duration of diabetes, current treatment (confirmed by physicians or the presence of medication initiated by the patient), general antecedents (personal or family history of diabetes and/ or hypertension and/ or other heart conditions), lifestyle (alcoholism, smoking).

Clinical examination measured weight, height, and waist circumference, lying and standing blood pressure. We defined hypertension as systolic blood pressure (SBP) ≥ 140 mmHg and / or diastolic blood pressure (DBP) ≥ 90 mmHg,[6] or antihypertensive drug use. The Body Mass Index (BMI) was calculated for each patient from the following formula: BMI= weight (Kg)/Height(m)². Abdominal obesity was determined for men by waist circumference greater than or equal to 94 cm, and for women at 80 cm.

Biochemical analyses

Triglycerides, total cholesterol, creatinine and fasting glucose measurements were performed using standard spectrophotometric techniques, followed by a reading with the Biomerieux Visual® spectrophotometer. LDL cholesterol was obtained by a direct method. It was based on the reaction acceleration of the cholesterol oxidase with free cholesterol non-HDL particles (chylomicrons, VLDL, LDL), and the selective separation of HDL with a specific detergent. Similarly, HDL was obtained by a direct method based on the Daiichi process.[7] The readings of these 2 direct methods were made on Mindray's BS 200® Multi Analyzer. Glycated hemoglobin was measured from capillary blood collected at the fingertip by a DCATM Systems reader from SIEMENS according to the manufacturer's recommendations. The MDRD formula gave an estimation of glomerular filtration.[9]The turbidimetric technique Microalbumin® allowed to obtain microalbuminuria, in 24-hour urine and according to the manufacturer's recommendations. We used target values of the American Diabetes Association (ADA) for biochemical parameters:[6] fasting blood glucose ≤ 7 mmol/L, glycated hemoglobin ≤ 6.5%, total cholesterol ≤ 4.5 mmol/L, HDL cholesterol ≥ 1.03 mmol/L for women and ≥ 1.0 mmol/L for men, LDL-cholesterol ≤ 2.6 mmol/L, triglycerides ≤ 1.7 mmol/L, blood creatinine of between 50 and 120 µmol/L. Renal impairment was defined as a creatinine clearance less than 60 mL/min/1.73 m².[9]

Data analysis

Data were entered and analyzed using the software Epi info and Excel. The analysis has given descriptive statistics of the study population and the different impairments in qualitative and quantitative variables.

3. Results

Epidemiological characteristics of the population

The study population size was 609 subjects, whose average age was 52±9.7 years, ranging from 32 to 65 years old. 46.0 of them were unemployed. There was 55.2% of male subjects. Furthermore, 29.9% regularly consumed alcohol and 3.4% said they were smokers. The study population was predominantly overweight with an average BMI of 27.7±17 kg/m². 56.3% of this population was hypertensive and 54.0% had a family history of diabetes (table 1).

Table I: Socio-demographic parameters of the general population

Parameters	*Values*
Age (years)	52±9.7
Men	336 (55.2%)
Weight (kg)	73.4±17
BMI mean (kg/m²)	27.2±17
Thinness	7 (1.2%)
Normal Weight	231 (38.0%)
Overweight	203 (33.3%)
Obesity	168 (27.5%)
Mean Abdominal perimeter (cm) • Men • Women	95±13.6 96±12.5 93,6±14.8
Hypertensive patients	343 (56.3%)
Employed subjects	329 (42.3%)
Alcohol consumption	182 (30.0%)
Current smoker	21 (3.4%)
Duration of diabetes (years) < 5 5 - 10 > 10	6 ± 3 350 (57.5%) 119 (19.5%) 140 (23.0%)
Family history of diabetes	329 (54.0%)

Antidiabetic treatment modalities found

The most common treatment modality was represented by oral antidiabetic drugs (OAD), used alone (56.8%) or in combination with insulin (31.5%). 9.9% of patients were treated by insulin alone and 1.8% of patients with type 2 diabetes have adopted uniquely hypocaloric regimen. Among these OAD, the most prescribed molecule was metformin alone (35.5%) or associated with sulfonylureas (table 2).

Table II: Oral antidiabetic agents used by patients

Molecules	Numbers	Percentages (%)
Metformin	189	36.0
Metformin / glibenclamid	182	34.6
Metformin / glicazide	35	6.5
Metformin / glimepirid	14	2.6
Metformin / vildagliptin	7	1.3
Glicazid / vildagliptin	7	1.3
Glibenclamid	28	5.2
Glicazid	28	5.2
Vildagliptin	21	4.0
Glimepirid	7	1.3

Main complications found

One hundred and thirty-three patients (21.8%) displayed complications in their note records. Diabetic foot was the most common complication (9.4%), followed by diabetic nephropathy (3.9%) and diabetic retinopathy 3.1% (table 3). Of the 609 patients, 525 had an electrocardiogram (86.2%). Seventy patients (11.5%) had experienced cardiac arrhythmia and 6.7% a myocardial ischemia. Ventricular hypertrophy and cardiomyopathy concerned 5.7% and 3.4% of patients respectively.

Table III: Major complications found in diabetics

Complications	Numbers	Percentages (%)
Diabetic foot	57	9.4
Nephropathy	24	3.9
Retinopathy	19	3.1
Obliterative arterial disease of the lower limbs	14	2.3
Hypoglycemia	14	2.3
Other Cardiovascular diseases	5	0.8
Total	133	21.8

Biochemical parameters

In the study population, mean blood glucose was 7.27±3.64 mmol/L with extremities ranging from 2 mmol/L to 22 mmol/L, while glycated hemoglobin values ranged from 4.6 at 14.0%, for an average of 7.6±2.2%. Mean concentration of serum creatinine was 103±80.3 µmol/L with an average creatinine clearance of 109±73.3 mL/min. Otherwise mean concentration of LDL cholesterol was 2.9±1.85 mmol/L, while that of triglycerides was 1.8±1.5 mmol/L (table 4).

Table IV: Distribution of biochemical parameters in the general population

Biochemical parameters	Mean value ± standard deviation
Glycemia (mmol/L)	7.2±3.6
Glycated hemoglobine (%)	7.6±2.3
Total cholesterol (mmol/L)	5.3±2.4
HDL Cholesterol (mmol/L)	1.3±0.9
LDL Cholesterol (mmol/L)	2.9±1.2
Triglycerides (mmol/L)	1.8±1.5
Plasma creatinine (µmol/L)	103.1±80.3
Creatinine clearance (mL/min/1.73m²)	109.3±73.3
Micro albuminuria (mg/24h)	77±110

Evaluation of the achievement of therapeutic goals

Systolic blood pressure (SBP) remained high among 43.7% of the patients while the diastolic blood pressure (DBP) was higher among 24.1% of them. Altogether, systolic and/or diastolic pressure was the reference values in 51.9% (316) of patients. Abdominal obesity was more common in female subjects (79.5%) compared to men (56.2%). More than half of study population was overweight or obese (60.9%). LDL cholesterol was high among 38.0% of patients, whereas HDL cholesterol was low among 24.1%, and triglycerides high among 11.5% of patients (table 5).

Table V: Proportion of patients who have not achieved therapeutic goals.

Parameters	Number	Percentage (%)
Blood pressure Systolic Blood pressure (SBP) > 130 mmHg Diastolic blood pressure (DBP) > 80 mmHg	 266 147	 43.7 24.1
Abdominal perimeters Men ≥ 94 cm Women ≥ 80 cm	 147 277	 56.3 79.5
Body mass index ≥ 25 kg/m²	371	60.9
LDL cholesterol ≥ 2.6 mmol/l	231	38.0
HDL cholesterol ≤ 1.03 mmol/l	147	24.1
Hypertriglyceridemia≥ 1.7 mmol/l	70	11.5
Hyperglycemia≥ 7 mmol/l	266	43.7
Glycated hemoglobin ≥ 7%	252	41.4
Creatinine clearance ≤ 60 ml/min/1.73m²	154	22.3
Micro albuminuria≥ 30 mg/24 heures	273	44.8

Modalities of management of cardiometabolic risk factors

Of the 231 patients who had high LDL cholesterol, only 37 (16.0%) had statin therapy In this study, 54.0% of hypertensive patients had antihypertensive therapy, especially by the combination of a diuretic and an angiotensin converting enzyme inhibitor (ACEI) (table 6).

Table VI: Distribution of antihypertensive treatment

Antihypertensive	Frequencies	Percentage (%)
Diuretic and ACEI	126	41.0
Calcium inhibitor, Diuretic and ACEI	42	13.6
Calcium inhibitor alone	35	11.4
Calcium inhibitor and ARA II	21	6.8
Calcium inhibitor and ACEI	21	6.8
ACEI alone	21	6.8
Calcium inhibitor and diuretic	14	4.5
Diuretic alone	7	2.3
Diuretic and ARA II	7	2.3
Total	308	100.0

ACEI: angiotensin converting enzyme inhibitor, ARA II: Angiotensin II Receptor Antagonist

In the study population, 154 patients (25.3%) had impaired renal function, and 50.0% used ACEI. In addition, 273 patients (44.8%) had a high level of microalbuminuria and 105 patients (38.5%) were on ACEI *versus*168.

4. Discussion

The aim of this study was to evaluate diabetes and complications aspects among a population with type 2 diabetes, treated at a tertiary care center, in an African context. To do this, a cross-sectional study was carried out at the endocrinology department of the CHUL. Thiswas a hospital descriptive study with a potential bias given that patients with modification of their treatment in the last year were excluded. Indeed, these excluded patients were potentially those who were likely poorly controlled hence might present with more complications. So, results obtained here could be certainly underestimated.

Despite these limitations, this work showed that the average age of diabetics was relatively young. This result is similar to that found by Peer et al. and in Gabon by Ovono et al.[11,12]Type 2 diabetes affects young adults and the elderly. Despite this age group, majority of study population at low economics level may have been confronted to nonobservance and negligence of the treatment and hygieno-dietary rules. Finally, the effectiveness of the care is questioned. The consequence, of this point of view, is an increase of not only the frequency of diabetes, but also of micro and macrovascular complications. Kengne has detailed this relationship between the prevalence of diabetes and the socio-economic level of African countries.[13] Likewise, Sims and al. showed that the low-income men and women had greater probabilities of suffering from diabetes than the high-income.[14]Similarly, Anjana and al; showed that people in low-income countries has a greater risk of diabetes and mortality rates by cardiovascular diseases.[15]

For more than half of the study patients, diabetes had evolved for less than 5 years. This result is similar to that

found by other authors. Indeed, Sobngwi et al. found similar results in Central Africa, as part of the DiabCare Africa project, which did not include Gabon.[16]Similarly, Webb et al in South Africa, found that 47.3% of their patients had diabetes known for less than 5 years.[17]These results are similar to those of other authors.[18]The low proportion of complications could justified this duration, or the fact that patients newly diagnosed with type 2 diabetes consult the most; in fact, a key question arises here and concern the mortality of patients with type 2 diabetes. This mortality could be high because of cardiac or cerebrovascular complications. Early diagnosis cannot be discussed, because Africa has the largest proportion of undiagnosed diabetes.[1]On the other side, mortality due to vascular disease, renal disease, infection or even decompensation of diabetes increases significantly with the duration of diabetes, as shown by Herrington et al.[19] Similarly, Aune et al. showed that subject with type 2 diabetes was at risk of atrial fibrillation.[20]All these parameters increase the risk of early death in subjects with type 2 diabetes, whose blood glucose is not controlled. This result reinforce the relationship between diabetes and heart diseases, as stated by other studies.[21.22]

Among the patients, more than half had a body mass index greater than normal. Weight loss is an important part of the management of type 2 diabetes and should be done according to a structured program.[23]However, in the absence of such program in our context with also only one nutritionist management of weight loss is difficult. The other reason seems to be due to the dietary habits that differ from one region to another. Indeed, the most urbanized countries produce increasingly processed foods likewise the energy values are higher and the nutrient content is very low. This is likely to increase in the future with increasing urbanization, changing lifestyles towards a reduced exercise levels, increased stress and consumption of unhealthy foods. In addition, obesity is an independent risk factor for dyslipidemia and blood pressure, thereby increasing the risk of morbidity and cardiovascular mortality in patients with type 2 diabetes. The dietary management in combination with metformin is therefore an essential part of the initial treatment of patients with type 2 diabetes. Furthermore weight loss is an important goal for these patients overweight or obese.[23]

In this survey, there was a high prevalence of hypertension associated with type 2 diabetes. This is also found in other studies in sub-Saharan Africa,[24] or in China.[25.26]

Indeed, Sobngwi found a prevalence of 79% and Webb et al. found 78.7%.[16.17]This association of hypertension and diabetes increased risk of cardiovascular complications and could be an element of early mortality, as mentioned above.

Regarding to the sample, family history of diabetes was detected in approximately 54.0% of diabetics. This would suggest that diabetes is transmissible. Indeed, outside of susceptibility genes, transmission would be through lifestyle and food hygiene, copied from those of the parents, who have s diabetes themselves. This result suggests that strengthening the education of people with diabetes may be an important tool in the fight to reduce the incidence of type 2 diabetes. Because, those patients could serve as a relay for health professionals who are not in sufficient number to relay messages about to the surveillance and prevention of diabetes by modifying habits and lifestyles.

In terms of oral antidiabetic drugs (OAD) treatment, metformin was used for treated more than half of our patients. Sobngwi et al. found similar proportions, with one OAD in 23.1% of subjects, two OAD in 39.1%.[16] The main difference between their study and ours comes from the fact that they found 5.4% treated with the combination of three or more OAD and 9.8% of patients with a combination of OAD and insulin. Apparently, in this context, practitioners use more often the association OAD and insulin, instead of increasing the number of ADOs in combination. This could be explained by the difficulties to stabilize glycaemia with only oral antidiabetics. This result demonstrates insulin-demand of ours patients and need to develop strategies for improving management quality of type 2 diabetes. This is confirmed by the fact that 41.4% did not reach the therapeutic target of 7.0% of glycated hemoglobin. This result is similar to that of Ali et al. in the United States[27] and Sobngwi et al. in Central Africa,[16]where the percentage of patients who did not reach the target values of glycated hemoglobin was 47.8%. Although glycemic control is still insufficient overall, it increased compared to the result of Ovono in 2011 where the therapeutic target of HbA1c and fasting glucose was not achieved respectively in 88.0% and 76.0% of patients.[11] These results confirm the existence of a chronic imbalance within our study population, by poor glycemic control and not optimal management of diabetes. Causes of this situation could result from poor adherence to treatment regimes, unhealthy diet due to high cost of food. Likewise, it could arise from patients' weariness in respect of hygieno-dietary measures or failure to adequately optimize insulin therapy since it was a population regularly followed claiming to respect the treatment. It has been shown that people with a poor diabetes control was also at higher risk of cardiovascular diseases.[28]In addition, almost half of hypertensive subjects were not treated, while it is an important recommendation to treat these patients by ACEI or ARA II, including a thiazide diuretic in multiple therapy for type 2 diabetes patients with hypertension.[6]

LDL cholesterol concentration was elevated in 38.0% of patients and only 16.2% of them were treated with statins. The LDL cholesterol control levels (62.0%) are close to those of Rao et al. in the United States with control rates ranging from 64.0 to 71.8%,[29]and Sobngwi in Central Africa in 2012.[16] However, our results seem to be better than the control rate of 56.8% of the national diabetic population in the United States and Webb in South Africa.[17.29] The high cost of lipid-lowering treatment, despite of the National Fund allocated for Health and Social Welfare, was a limiting factor to the respect of the medical prescription as our study population was mostly unemployed. In addition, statins prescription is not generalized is this area. All this suggest high cardiovascular risk, because dyslipidemia was not intensively monitored. LDL-cholesterol was suboptimal among this population which is fairly young compared to European population with diabetes and high LDL-cholesterol.[31]

Microalbuminuria was detected among 45.8% of patients and the estimated glomerular clearance was below 60 ml/min/1.73m² among 22.3% of the population. This result is similar to the results found by Rao et al. in the United States (51.5%).[29]Indeed, Koye et al. have shown that kidney failure due to diabetes is becoming more common than that due to infections in low-income countries like ours.[31]The presence of microalbuminuria among diabetic is a general marker of severity of the disease, especially according to the cardiovascular risk. To reduce this risk, the ADA recommends submitting the patient under CEI at the maximum tolerated dose.[6]However, in this study only 38.5% were under CEI. This exposes the study population with acute kidney injury.[32] In this work, 5.7% had diabetic retinopathy (DR). These results are comparable to those previously found by Ovono et al. in 2011,[11] and by Thomas et al. in South Africa in 2015, which was between 5.0% and 10.0%.[32]In contrast, the prevalence of diabetic retinopathy found was lower than that of Jingi et al. (17.4%) in Cameroon and Pirie et al. in Durban (South Africa) .[33.34]As the latter authors have shown, the prevalence of diabetic retinopathy increases with the duration of diabetes. In our population, this average duration was 5 years. Thus, it is traditional to consider that diabetic retinopathy occurs about 15 years after the onset of diabetes. Therefore, intensive glycemic control, especially in the first years of diagnosis, may reduce the risk of diabetic retinopathy development and progression . However, in our study, the average duration of diabetes was 6 years, which could justify the small proportion of diabetic retinopathies observed. This is consistent with a high rate of mortality for these patients. All these complications should be improved by setting-up a major population management as stated by other authors.[36]

5. Conclusion

The study conducted among type 2 diabetic patients followed in a hospital department, has provided valuable data on cardiometabolic aspects. The monitoring was not optimal in view of the number of patients who have not reached the therapeutic targets and the distribution of therapeutic modalities to patients. This high cardiovascular risk should be reduced among these patients by vigorous treatment of diabetes and comorbidities and by setting therapeutic education. The quality of diabetes information is challenged by the low rate of doctors and the existence of a single dietitian. Correcting these problems is a novel challenge in low-income countries.

6. Conflict of interest

Authors state that they have no conflict of interest.

Authors' Contribution

OAF: wrote the protocol and the manuscript.
MBA: verified the protocol, realized the experiments and the first draft
TE: patients recruitment and clinical examination
BAS: patients recruitment
NAGR: Manuscript correction and verification
NR: Manuscript correction and verification
NME: Manuscript correction

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