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Specific scores of glycated hemoglobin in the current diagnosis of cardiometabolic risk dysglycemia in Brazzaville, Republic of Congo

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Abstract

Background and aim: The increase in the incidence of diabetes mellitus is one of the constellations of cardiometabolic risk in the world. As the specific diagnostic thresholds for dysglycemia are absent among African Bantou de Brazzaville, Republic of Congo justified this study. The aim of the study was to determine the performance of glycated hemoglobin in the diagnosis of dysglycemia. **Methods:** The cross-sectional survey involved 500 apparently healthy adult participants. The glycated hemoglobin was modelled using a National Glycohemoglobin Standardization Program certified method and correlated with the Diabetes Control and Complication Trial. Diagnostic performance was defined using analysis of the receptor's operating characteristics. **Results:** The study included 225 men and 275 women, the mean age was 47.4-13.7 years, the levels of hemoglobin glycosylated on an everan erate equal to 5.5-5.9% and 6.0% (Se-100% and Sp-100%) ($p = 0.001$) were characterized by perfect diagnostic performance and prevalence respectively for intermediate/prediabetes-sweetened hyperglycemia (13.8%) and diabetes mellitus (24.4%) with an area under curve equal to one. There was a positive and significant bivariate correlation between older age, fasting blood glucose, and increasing hemoglobin glycosylated to right Y (glycosylated hemoglobin) - 2.683; -0.077 - Age (years) - 0.789 - Glycemia (mmol/L). **Conclusion:** The epidemic of cardiometabolic risk was estimated to be 2/3 of prehypertension/high blood pressure, 4/10 of overweight/obesity and 1/4 of diabetes mellitus in 2018 and significantly higher than reported in 2004. This study showed that the recommended thresholds for diagnosing dysglycemia are not the same for Bantu populations.

Keywords: Glycated Hemoglobin, Performance, Prevalence, Diabetes Mellitus, Brazzaville.

INTRODUCTION

Dysglycemia included diabetes mellitus and intermediate/prediabetes mellitus hyperglycemia [1]. The burden of chronic noncommunicable diseases (NCDs) is growing rapidly worldwide [1]. Diabetes mellitus (DM) is one of four priority NCDs targeted by world leaders [1]. The increase in the incidence of diabetes mellitus in association with overweight/obesity dyslipidemia and high blood pressure (HBP) is one of the constellations of cardiometabolic risk under the impact of the health transition (epidemiological/decrease of infectious diseases, population/life expectancy, nutritional/diet high in fats, salt and sugar against low fruit/vegetable consumption) worldwide and sub-Saharan Africa [1]. Contrary to an old and still widely held view of DM as a disease of rich countries and men, this condition is a major public health problem in developing countries including Brazzaville, Republic of Congo [2-5].

Normality (health/well-being) is defined by culture, gender, ethnicity, quality of life/mental state and the dynamics of epidemiological and biostatistical studies according to the usual diagnostic and therapeutic baseline [6]. With epidemiological data, the fasting blood glucose threshold - 140 mg/dL for the diagnosis of DM 20 years ago [7], lowered to fasting blood glucose levels of 126 mg/dL and post prandial or casual blood glucose levels, 200 mg/dL respectively, before the precocity of diabetic retinopathy according to the World Health Organization (WHO) and the American Diabetes Association (ADA) [1-8]. The same is true for glycosylated hemoglobin (HbA1c) which has also been introduced as a biomarker for the diagnosis of dysglycemia (intermediate hyperglycemia/prediabetes mellitus equal to 5.7-6.4% and DM - 6.5%) [1,8].

However, there are pitfalls, limitations, certain factors (oxidative stress, inflammation, pregnancy,

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glycation, the presence of hemoglobinopathies, kidney failure) and several pathologies that recommend HbA1c instead as diagnostic means of DM or as a glycemic alteration test [9-13]. For the problem of screening and diagnosis of DM, the tests of both the case or the post prandial blood glucose are traditional sets of the Reference Diagnosis of DM [1.6, 14-23]. On the other hand, and with personalized medicine, some biomarkers such as the HbA1c test play predictive, early diagnostic roles (with precision, scientific evidence, early therapeutic initiation, follow-up treatment, patients and health professionals towards the prevention of DS and its complications [1.8].

The International Diabetes Federation (IDF) has estimated that globally, 451 million adults aged 18-99 are living with DM in 2017 [24]. In 2012, DM caused 1.5 million deaths and higher-than-normal blood sugar, which increases the risk of cardiovascular disease and other pathologies was the cause of 2.2 million additional deaths, for a total of 3.7 million deaths involved people under 70 years of age [1]. Percentage of deaths due to hyperglycemia or DS (43%) that occur before the age of 70 is higher in low- and middle-income countries than in high-income countries [1]. In the Republic of Congo, data from the 2004 STEP/WHO study conducted by Kimbally-Kaki *et al* found prevalence rates of DM at 7%, overweight at 18%, obesity at 8.6% and high blood pressure (HTA) at 32.5% [25].

Clinically impressionable, the prevalences of DM and intermediate hyperglycemia are underestimated on fasting blood glucose testing in BZ/RC hospitals in light of socio-economic and political disturbances (ethnic and military conflicts), changes in eating habits, environmental conditions and obesity caused by urbanization and migration of Congolese populations.

With the health transition, rural-urban migration, globalization (globalization/westernization), wars, physical inactivity, exacerbation of poverty, chronic hyperglycemia complex (intermediate hyperglycemia/preglycemia and Diabetes), HTA, overweight/obesity (OW/OB), smoking by cigarette, and excess alcohol in an anxiety-depressive/psychological stress picture health centres in the Republic of Congo [5, 25-28]. The error in the management of cardiometabolic risk does not consider the specific thresholds for ethnicity or gender, capable of early definition of dysglycemia in the cosmopolitan city of BZ/RC.

Indeed, metabolic syndrome (Smet) is differently defined in the United States [29], in Europe for Caucasians [11, 30, 31] and in Asia [32]. Specific thresholds for dysglycemia are absent in African Bantou of Brazzaville, Republic of Congo which justified the initiation of this study. The main objective was to determine the performance of glycated hemoglobin in the diagnosis of dysglycemia. The second objective was to determine the association between advancing age, increasing blood sugar and changes in glycated hemoglobin. The third objective was to assess the secular (evolutionary over time) trend in cardiometabolic risk between 2004 and 2018.

MATERIALS AND METHODS

Study Setting and Design

A joint study comprising an analytical cross-sectional survey (2018) and a retrospective literature study (2004) was conducted with bioclinical and STEP/WHO approaches recognized as standardized tools [33], replicable, flexible depending on the context of the BZ/RC population. Cross-sectional study period: this study took place from February 08 to 22, 2018. Study Framework: the documentary study [5, 25] was conducted at the Brazzaville Hospital and University Centre (CHUB). However, this cross-sectional study was conducted at the Administrative Centre of the City of BZ/RC. The city of Brazzaville has a multi-ethnic population estimated at 1,838,348 at present [34]. It is divided into 9 boroughs (Makélékélé, Bacongo, Poto-poto, Moungali, Ouenze, Talangai, Mfilou, Ndjiri and Madibou).

Population of study

The population of study was a probabilistic sample from the general and eligible population of the city of Brazzaville according to the logogram (Figure 1). Participants were recruited from three Catholic churches in the north, centre and south of the city of Brazzaville. The selection criteria required for inclusion (any person aged at least 18 years of age who have lived in Brazzaville for at least one year, with informed consent) and for exclusion (all participants under the age of 20, DM on treatment, pregnancy, HIV/AIDS, kidney failure, stroke, ischemic heart disease, heart failure and hemoglobinopathy).

Sample size of the cross-sectional study

Random sample size was calculated using the following formula: $n_1 = \frac{Z^2 * p * (1-p)}{d^2}$; Z-parameter related to statistical risk of admitted error-1.96 for an error risk of 0.05%, q- assumed proportion of the target population not having the problem (q= p-1), p- expected prevalence for diabetes mellitus from a recent known, d- prevalence of absolute accuracy-0.05

Given that the prevalence of DM by glycated hemoglobin in the city of Brazzaville has never been studied, it is considered that p = 0.50 and q= 0.50. $n_1 = \frac{1.96^2 * (0.5) * (0.5)}{0.05^2} = 384 = 400$. We add 25% possible loss which makes a total of 500 participants included. Thus 50 participants randomly drawn from lists from the 9 boroughs and the administrative center of the city of Brazzaville.

Variable Methods of Interest

Sociodemographic characteristics (sex, age, socioeconomic level by family income, diet (adequate diet rich in fibre, less salty fruits and vegetables less sweet and less fat, against Westernized diet and education) were collected according to the STEP/WHO questionnaire [33]. Measurements of participants in light clothing and bare feet standing by size (cm), weight (in kg) were obtained according to step/WHO criteria.

Thus, the size was measured using a vertical toise (type SECA 220) to the nearest half centimeter. Weight was measured using an electronic scale (type SECA 762), with an accuracy of 0.1 kg. Body mass index (BMI) is the most common method of assessing overweight and obesity in both men and women [7, 35].

Participants were divided according to BMI into underweight, normal weight, overweight and obese [7, 35]. This index corresponds to the ratio of an individual's weight to the square of his height (kg/m²). It identifies people whose weight status is associated with a health risk:

- BMI - 18.50 indicates underweight;
- BMI between 18.50 and 24.99, is considered normal weight;
- BMI between 25 and 29.99 indicates overweight (overweight);
- BMI 30 is considered obesity (general obesity).

Blood pressure values were obtained using an electronic type blood pressure monitor (OMRON M3 Comfort) after participants rested for at least 15 minutes in a sitting position. Systolic and diastolic pressure values have been replicated three times in a row to have precise blood pressure values.

Blood samples were taken by venous puncture at the bend of the elbow on heparinated tubes and at EDTA in the morning between eight and ten o'clock on subjects on an empty ingel for at least eight hours. Samples taken from heparinated tube were centrifuged to 4°C for 10 minutes at 4000 laps. The blood glucose was measured using the Trinder method using a KENZA MAX BioChemis Try spectrophotometer from BIOLABO, France (the coefficients of variation and reproducibility

were 1 and 1% to 2000 mAbs respectively). HbA1c dosages were performed on an A1CNow(R) drive in BAYER, Germany. This reader can be used to control HbA1c and total hemoglobin using two analytical techniques (immunochemistry and chemistry). When the diluted blood sample is applied, blue microparticles and HbA1c antibodies attach to the reagent. The amount of blue microparticles attached to the strip determines the amount of A1C present in the blood sample.

The percentage of total hemoglobin (Hb) is based on the transformation of hemoglobin into methemoglobin by the sample diluant. Indeed, the color intensity of methemoglobin measured on the reagent is proportional to the concentration of hemoglobin in the blood sample. The test results correspond to the percentage of A1C (A1C - total Hb x 100). The performance of the A1CNow drive was defined by analyzing blood samples taken from 118 normally non-diabetic individuals (fasting blood glucose - 127 mg/dL or 7 mmol/L) from three different sites in the United States. The average percentage of A1C was 5.2% - 0.71% (1 standard deviation). Confidence limits of 95% ranged from 3.9% to 6.5%. The 99% accuracy was verified on two total blood samples, one with low A1C levels (about 6%) and the other with a high A1C rate (about 9%) were analysed 4 times a day for 20 days. The coefficients of variation were 3% for the low rate and 4.02% for the high rate. The quality control procedures recommended by manufacturers for all biochemical tests were followed throughout the study.

Operational definitions

Potential risk factors for DM were defined as gender (men vs. women), advancing age (age 55), socio-economic level was categorized into two categories: those with a level low socio-economic (unemployed, out-of-school or low-income participants), and those with a high average socio-economic level.

The health transition (epidemiological, demographic and nutritional) was defined by the proportion of participants aged around 50, the ratio of OW-OB to underweight (UW) 2 and the proportion of participants with inadequate diet (poor food). The history of cardiovascular risk was defined by the coexistence of high blood pressure (HBP) (systolic blood pressure/diastolic blood pressure 130/85mmHg), stroke and ischemia.

Cardiometabolic heredity (history of obesity, HBP, stroke, ischemic heart disease, heart failure and DM) was related to family history. Cardiometabolic risk was defined by the coexistence (comorbidity) of OW/OB, HBP, and DM. The age-old trend was to compare the evolution of cardiometabolic risk in 2004 [25], 2007 [5] and 2018 (this study).

Statistical analyses

Category variables were presented in the form of frequency number (n) and proportions (%). Quantitative variables (continuous) were summarized as average, median, interquartile, minimum and maximum. In a univariate analysis, Pearson's Chi square test between two groups and the trend test (biological gradient) between several groups were used to compare percentages between the two groups, while Student's T test and variance analysis (ANOVA) were used respectively to compare averages between two groups and between higher or equal to three groups.

Non-parametric tests were used for abnormal or asymptomatic distribution. The mathematical model of receiver operating characteristics (ROC) calculated the area under the curve (AUC) using the following formula:

$$ASC = \frac{W1 - \frac{n1 - (n1+1)}{2}}{n1 - n0}$$

Blood glucose - 126mg/mL, baseline test, defined certain DM against HbA1c - 6.5% was the new test to be diagnosed if not screened for DM.

The diagnostic performance of HbA1c was defined by sensitivity (Se) and specificity (Sp), and area below the curve (ASC).

The bivariate analysis was used to produce Pearson's single r correlation coefficients between fasting blood glucose and HbA1c blood levels. Multiple linear regression was performed to predict HbA1c variations by independent variables such as age, sex, fasting blood sugar, socioeconomic level. Multivariate logistic regression analysis was used to calculate independent associations between independent variables (sociodemographic, anthropometric and hemodynamic) and dependent variables (DS and all dysglycemias) after adjusting for confusion variables. Probability (P) - 0.05 defined the threshold for significance. All statistical analyses were carried out using statistical Package for Social Sciences (SPSS) version 21.

Ethical Considerations

This study was conducted after receiving approval from the Ethics Committee on Health Sciences Research (ECHSR). The participants all agreed to take a blood test and complete the questionnaire. The results were given individually to the participants. The confidentiality of the information collected was respected.

RESULTS

Descriptive study (participant characteristic, socio-economic level, weight profile and health transition), diagnostic performance of glycated hemoglobin for dysglycemia, determinants of HbA1c, DM and risk cardiometabolic disorder were characterized by their magnitude in the cross-sectional study.

Characteristics of participants

A total of 500 participants, of whom 45% (n=225) men and 55% (n=275) women were recruited: sex ratio of 0.82 close to 1 man:1 woman. The average age of the study population was normally distributed from 47.4-13.7 years, with a median at 47 years, and from the extremes of 18 and 80 years, the interquartile was 37-57 years. The advancing age (age 55 years) represented 30.2% (n=151) of participants compared to 48.4% (n=242) of adult participants (35-54 years) and 21.4% (n=107) of young participants (35 years).

Socioeconomic level

63% (n=317) of participants were of low socioeconomic level compared to 37% (n=185) of medium-high socioeconomic level.

Weight profile of participants

The nutritional status of the population was characterized respectively by 3% (n=15) of underweight, 40.2% (n=201) of normal weight participants, 36.8% (n=184) of overweight participants and 20% (no.100) of obese participants.

Health transition

Among the entire study population, the majority (67%, n=335) were characteristic of the health transition (epidemiological, demographic and nutritional).

HbA1c determinants

There was a positive and significant bivariate correlation between age advancement and increased HbA1c (r -0.784; P-0.0001); the average rate of HbA1c was higher in men and at the low socio-economic level, respectively, than in women and at the high socio-economic level (p=0.0001; results not presented). In multiple linear regression, 63.1% (Adjusted OR=2) vs. 79.5% (unadjusted OR =2) p=0.001 variation in HbA1c concentration was predicted by advancing age and increasing fasting blood glucose levels after adjusting for sex, socioeconomic level and nutritional status (Figure 1) on the right:

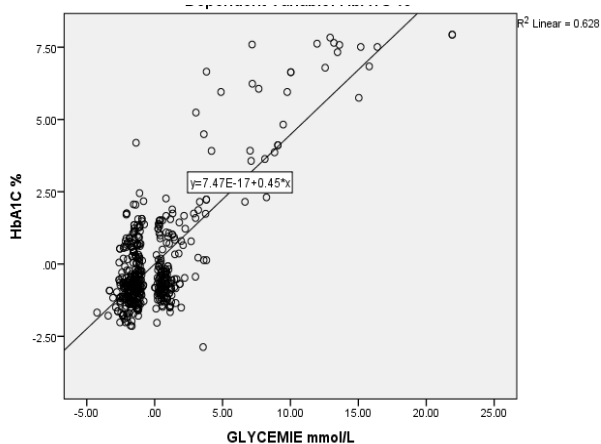


Figure 1: Prediction of glycated hemoglobin relative to age and fasting blood sugar.

$$Y (\text{HbA1c}) - 2.683 - 0.077 - \text{Age (years)} - 0.789 - \text{Glycemia (mmol/L)}$$

Diagnostic performance of HbA1c

Compared to the fasting blood glucose test - 126 mg/dL, the 5.0% on-set HbA1c test was characterized by a perfect diagnostic performance of DM of around 24.4% with AUC=1, Se =100% and Sp=100%; $p=0.0001$. Compared to the fasting blood glucose test of 100 mg/dL, the fasting HbA1c test was characterized by a perfect diagnostic performance of intermediate/prediabetes hyperglycemia (glucose intolerance) of 13.8% (n=69) with AUC=1, Se=100% and Sp=100%; $p=0.0001$. Reliability, validity and repeatability were demonstrated by the coefficient of variation of 4.8% for fasting blood glucose and 4.5% for HbA1c, respectively.

Prevalence of diabetes mellitus

There was a discrepancy in the prevalence rate of DM according to the threshold used: 17.8% (n=89) according to fasting blood glucose - 126 mg/dL versus 24.4% (n=122) according to HbA1c - 6%. The influence of sex was neutral (indifferent $P=0.289$) to 26.7% (n=60/225) in men, comparable to 22.5% (n=62/275) in women. The univariate analysis showed a significant association between socioeconomic level, age advancement and prevalence of DM according to HbA1c - 100%. The low socioeconomic level conferred a 3-times greater risk of DM according to HbA1c (OR-3.2 [IC 95%, 2-5.3]; $P=0.001$). The prevalence rate of DM was estimated at 31.4% (n=99/315) among participants of low socioeconomic level compared to 12.4% (n=23/185) among participants of the medium-high socioeconomic level ($p=0.0001$).

There was a proportional and significant increase (Trend $P=0.034$) in HbA1c prevalence rates with increased age of participants (Figure 2). The effect of nutritional status was indifferent ($P=0.559$) on the prevalence rate of DM according to HbA1c: 23.2% (n=71/306) in general obesity (BMI 25 kg/m²) compared to 26.3% (n=51/194) in the absence of general obesity.

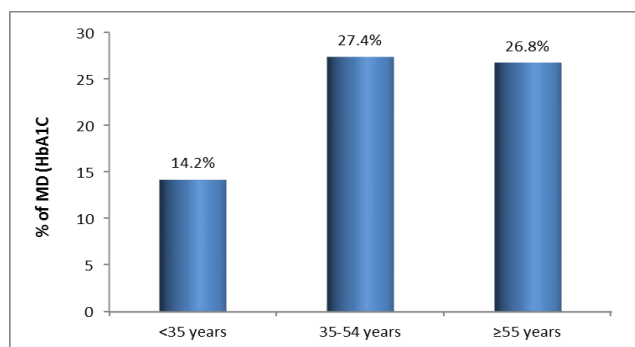


Figure 2: HbA1c prevalence rate by age.

The explanatory variables were male sex, age advancement and low socio-economic level. In multivariate analysis by logistic regression after male adjustment, low socioeconomic level and age - 35 years were identified as independent and significant determinants of the prevalence of Diabetes Sweetened by HbA1c (Table 1). Compared to the female sex, the male sex conferred a 2-fold risk of DM by HbA1c. While compared to the average-high socioeconomic level, the low socioeconomic level conferred a 4-percent greater risk of DM per HbA1c. Similarly, compared to age 35, age 35 conferred a 2-fold risk of DM per HbA1c.

Table 1: DS Determinants by HbA1c

Variables explicatives	Adjusted OR	95% CI	p
Sex Male	1.576	1.020-2.436	0,041
Low socioeconomic level	3.445	2.056-5.773	0,000
Age ≥55 ans	1.929	1.054-3.528	0,033

Cardiovascular Risk

Cardiovascular risk was 2%, 21%, 23% respectively in the age group - 35 years, 35-54 years, 35 years, 35 years. No participants without DM reported cardiovascular risk (0%/n=0), while cardiovascular risk was exclusively in diabetic participants with a biological gradient.

Secular trend of cardiometabolic risk

The evolution of the frequencies of individual components of cardiometabolic risk was summarized in Table 2. There was an exponential and significant trend ($P=0.00001$) respectively in the proportions of overweight/obesity and HBP between 2004 and 2018 against a sudden and significant increase ($P=0.05$) in DM between 2004-2007 and 2018 (incidence of multiplied DM 3) (Figure 3).

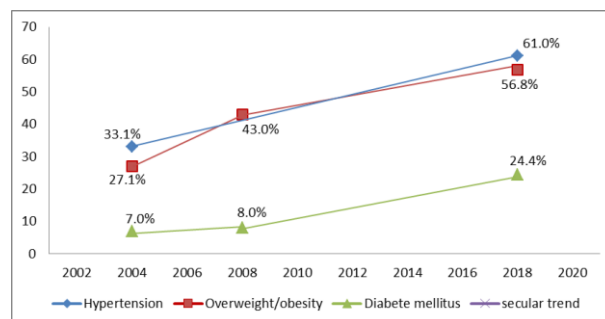


Figure 3: Proportion of cardiometabolic risk components of Kimbally-Kaky *et al* [20], Monabeka *et al* [22] to that of this study as time progresses.

Table 2: Frequency of individual cardiometabolic risk components between 2004 and 2018 in the city of Brazzaville

Risk factors	2004 [20]	2007[22]	2018
	n /N	n /N	n /N
Overweight/Obesity	563/2079	228/530	284/500
Diabetes mellitus	14/199	40/530	89/500
High blood pressure	675/2040		305/500

The epidemic of cardiometabolic risk was epidemic in appearance and estimated at 2/3 prehypertension/HBP, 4/10 of SP/OB and a quarter of DM in the BZ/RC population in 2018 (present study) and significantly higher at the rate of 33.1%, 27.1% and 7% reported in 2004 to BZ/RC ($P=0.0001$). All participants (100%) was not informed about the interaction of heredity and environmental risk factors and risk behaviours (modifiable factors) in the DM.

DISCUSSION

Overall, both hypotheses in this study have been tested and confirmed. Indeed, the present study diagnoses optimal and specific thresholds of intermediate hyperglycemia (prediabetes) and DM. The associated factors and independent determinants of the DM are one of the components of the Smet in the world [29, 31, 36, 37] and in Sub-Saharan Africa [11, 30, 38]. Finally, the trend of epidemic pace of cardiometabolic risk has also been demonstrated.

HbA1c Determinants

The independent determinants of HbA1c (male sex, age advancement and low socio-economic level) were respectively the explanatory variables of the DM epidemic in this study. High-risk male lifestyle (smoking by cigarette, excess alcohol) [11, 14, 27, 39-41], advancing age in the epidemiological/demographic transition [42, 43] and low socioeconomic status were also identified as determinants of HbA1c in this study. Harmful quality of life, depression and anxiety (psychological stress) are well associated with advancing age (hyperinsulinemia) and DM2/Smet in the city of this study, which has suffered from several political-social crises and ethnic conflict in recent decades (1993-1998).

Diagnostic Performance of HbA1c

This study demonstrated an excellent correlation between fasting blood glucose and HbA1c with a simple correlation coefficient close to 1. Contrary to the fasting and HbA1c blood glucose values proposed by ADA and WHO to diagnose intermediate/prediabetes-sweetened hyperglycemia and DS [1,8]. Instead, this study established optimal HbA1c thresholds of 5.5-5.9% and 6% as a new diagnostic test respectively for intermediate/prediabetes mellitus and DM. These reference values varied according to Bantou ethnicity, HIV infection with or without antiretroviral therapy [18, 44] in Brazzaville as is the case for optimal thresholds of hypertriglyceridemia, HDL-c decrease, waist circumference, hip circumference and specific blood glucose for Smet in North America [29], Europe [9] and Asia [36, 45].

Ethnicity-specific thresholds were estimated at 5.85% in Nigeria [18] and 6.27% in Algeria [46] with prevalences close to 24.4% in BZ/RC before the epidemiological, demographic and nutritional transition on the one hand and by the methodology of the 2004 STEP/WHO study.

However, the diagnostic performance of HbA1c -6% for the diagnosis of DM was perfect if not excellent (Se 100% and Sp 100%) in this study and comparable to excellent diagnostic performance and close to Se 100% and Sp 100% of HbA1c - 5.85% (Se-63%, Sp-86%) [18], hbA1c - 6.0% (Se-75.4%, Sp-94.6%) [19] and HbA1c - 6.27% (Se-78%, Sp-88%) [46] for the diagnosis of DM. The use of the ROC curve also demonstrated a perfect diagnostic performance of HbA1c between 5.5% and 5.9% for the diagnosis of intermediate hyperglycemia/prediabetes sweetness (Se 100% and Sp 100%) in this study and comparable to excellent diagnostic performance and close to Se 100% and Sp 100% of HbA1c - 5.75% (Se-54% and Sp-84%) for the diagnosis of intermediate/prediabetes mellitus [18].

Prevalence and Determinants of Diabetes Sweets

The prevalence of DM according to HbA1c - 6% was in the order of 24.4% in this study and 3 times higher than the level of DM according to different method of blood glucose testing [47] (hair blood, venous/plasma) 7% to BZ/RC in 2004 [25] and 7-23% DM in population and clinical studies in Sub-Saharan Africa [15, 35, 48, 49]. Indeed, WHO defines intermediate hyperglycemia by fasting blood glucose - 110 mg/dL but 126 mg/dL [1], while the same WHO defines glucose intolerance by a blood glucose two hours after an oral load of 75 grams of glucose - 140 mg/dL and 200 mg/dL [1]. In addition, a blood glucose level of 200 mg/dL two hours after an oral load of 75 grams of glucose

is often controversial because two fasting blood glucoses - 126 mg/dL are sufficient to make the diagnosis of dysglycemia [14, 15, 18, 39, 50].

However, univariate analysis and multivariate logistic regression-type analysis identified important major associated factors (age advancement, general obesity and low socio-economic level) and independent determinants (male sex, age advancement and low socio-economic level) of the epidemic of the present prevalence of DM to BZ/RC.

Despite its confusing nature, obesity was the tree that hid the forest from the dual epidemic/double nutritional burden-diabésité including type 2 diabetes mellitus (DM2) [42] not specified in this study. The migration of physical inactivity, the abrupt change in lifestyle, globalization/westernization according to the health transition (age advancement, nutritional transition) also explained the exponential trend of SP/OB from 2004 to 2018 to BZ/RC, as reported in other studies [35, 51, 52].

Prevalence of intermediate/prediabetes-sweetened hyperglycemia

The HbA1c rate of 13.8% between 5.5 and 5.9% in the present study was a state of intermediate/prediabetic sweet hyperglycemia between normal glucose homeostasis and future incidence of DM2 and its cardiometabolic complications. HbA1c reflects the lifetime exposure of red blood cells to glucose and reflects the average blood glucose values of the last 3 months [15, 20, 47]. As a result, it is difficult to compare the prevalence of intermediate/pre-diabetes mellitus in this study with other prevalence rates of intermediate/prediabetes mellitus from different countries and different test levels with blood glucose and HbA1c thresholds [53].

Cardiometabolic Risk Factors

The present study found a significant cardiometabolic risk burden close to 50% of participants. Overall, the average cardiometabolic risk burden of 47.4% is double the average burden of Kimbally-Kaki and al estimated at 22.2% in 2004 (p-0.001).

Indeed, pre-hypertension/HBP-OW/OB-dysglycemia comorbidity currently reported in Sub-Saharan Africa [30, 54, 55] and other countries [29, 50, 56] is emerging while the burden of cardiometabolic risk and Smet is decreasing in developed countries [1]. The absence of valid and specific Smet data in Sub-Saharan Africa had imposed specific thresholds on Caucasians [56].

Involvement of Medical biology and perceptive public health and research

Precise data around optimal HbA1c thresholds between 5.5% -5.9% and 6% established by this study will improve primary, primary, preventions, intermediate hyperglycemia and DM with or without micro and macro vascular complications in the Republic of Congo and other Sub-Saharan countries [2, 3, 4]. These Hba1c thresholds in combination with blood glucose levels 100 mg/dL and 126 mg and 126 will be organized for the detection and diagnosis of dysglycemia (intermediate hyperglycemia and DM) will be organized at all secondary and tertiary primary levels in the Republic of Congo and other sub-Saharan countries. Indeed, this study constitutes from the perspective of medicine with 5P (predictive, personalized, precise, participatory with evidence) [57].

So like other blood biomarkers [58, 59], the HbA1c threshold of this study will improve the management of dysglycemia (intermediate hyperglycemia and DM) with an early and scientific diagnosis if not accurate, early prophylactic and pharmacological treatment, and rational therapeutic follow-up for cost-effectiveness in continuing education, public health prospects and research at BZ/RC and sub-Saharan Africa.

The integrated and holistic global approach that brings understanding of pathophysiological mechanisms with psychological, cultural (contextualization) and behavioural (information, education and change around factors) associated with DM) and sustainable development (poverty reduction and gender consideration) will ensure the success of controlling projected cardiometabolic syndrome more than an epidemic in the year 2045 [24].

Inaccessibility to care, physical inactivity [1], increase in smoking per cigarette [1,41], universal absence of health promotion [1], psycho-social stress [1], pollution [1], inappropriate nutrition [1], poverty [1] and ignorance of DS, intermediate hyperglycemia, MS/OB (considered a mark of social well-being) and fear of stigmatization of HIV/AIDS underlie the age-old trend of cardiometabolic risk noted between 2001 and the fear of stigmatization of HIV/AIDS underlie the age-old trend of cardiometabolic risk noted between 200 and 1 BZ/RC, which demonstrated an epidemic allure of DM in nearly 1/5 of the participants living in BZ cosmopolitan and multiethnic city. These optimal HbA1c thresholds will be taught and validated in health centres and universities focused on clinical biology, early treatment and therapeutic follow-up of intermediate/prediabetes mellitus and DM. The HbA1c threshold between 5.5 and 5.9% specific for the Bantou population of BZ/RC avoided inaccuracy, underestimation and overestimation of moderate fasting hyperglycemia (JGH) and glucose intolerance (IAG). Thus, intermediate/prediabetes-sweet endosm and DM according to HbA1c respectively between 5.5 and 5.9% and 6% are proposed for subsequent validation on a much larger sample in both the Republic of Congo and other African countries.

Strengths and limitation of the study

Hba1c does not experience variations in the nycthemer, it is much more stable than fasting blood glucose [9, 46]. This study in a valid and factual medicine, established for the first time the optimal thresholds (HbA1c between 5.5 and 6%) in the screening and diagnosis of dysglycemia (intermediate hyperglycemia and DM) in Sub-Saharan Africa.

The second strength of this study was the consideration of traps and limitations [9,10] related to dosage and interpretation (adequate material) of Hba1c prior to the initiation of this study. The 3rd strength of this study is in working with health professionals at each of the participants' respective residences for confirmation of persistent hyperglycemia (3 months) without neglecting the medical records of participants referred for hyperglycemia and DM at the population level BZ/RC. Health professionals are responsible for following the principles of good practice and evidence-based and up-to-date medicine for the management of dysglycemia at BZ/RC and other poor sites in Sub-Saharan Africa.

Nevertheless, its cross-sectional nature has included limitations for not integrating time (only cohort studies or interventions demonstrate causal association between determinants and DM) or lack of control of intra-individual variability fasting blood sugar, which is often dependent on room temperature. Heredity of cardiometabolic risk (family history of obesity and DM) was not reported by all participants (100%) who are ignorant of the place of heredity in the appearance of DM2 related to insulin resistance also predicted by HBP and smoking by cigarette [60] and remains ignorant of the interaction between heredity and environmental and behavioral factors to risk in DM and other cardiovascular risk factors; one last limitation of this study. Indeed, the thresholds of HbA1c between 5.5 and 5.9% and 6% respectively were respectively unable to discriminate against the presence and absence of insulin resistance in black hypertensive patients in West Africa [19].

CONCLUSION

This study determined the essential if not necessary place of specific and specific HbA1c thresholds between 5.5 and 6% in diagnoses of

epidemic rates of intermediate/prediabetes hyperglycemia and DM in BZ/RC and Central Africa. The age-old trend of epidemic gaits of concomitant dysglycemia with other cardiovascular risk factors has been the burden of cardiometabolic risk in a poor BZ/RC environment. This cardiometabolic burden of BZ/RC is comparable to that currently reported in rich and developing countries, including those in Sub-Saharan Africa.

Subsequent validation of HbA1c's specific threshold between 5.5 and 5.9% and 6% will be integrated into a multi-disciplinary and collaborative approach between medical biology, policy makers and health professionals. For public health in the Republic of Congo, priorities will be modifiable and preventable associated factors (while advancing non-modifiable factors in age) of DM initiated and exaggerated by the health transition (OW/OB, intermediate hyperglycemia/prediabetes, HBP), geriatric development, poverty reduction (health insurance), information on cardiometabolic risk reduction.

Conflicts of interest

The authors do not declare any conflict of interest.

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REFERENCES

1. World Health Organization 2016. <http://www.who.int/diabetes/global-report>. WHO/NMH/NVI/16.3
2. Jaffiol C. Le diabète sucré en Afrique: un enjeu de santé publique. Bull. Acad. Natle Méd 2011; 1955(6):1239-1254.
3. Gning SB, Thiam M, Fall F, Ba-Fall K, Mbaye PS, Fourcade L. Le diabète sucré en Afrique Subsaharienne aspects épidémiologiques, difficultés de prise en charge. Med Trop 2007; 67:607-611.
4. OGA ASS, TEBI A, AKA J et Coll. Le diabète sucré diagnostiqué en Côte d'Ivoire: des particularités épidémiologiques. Med Trop 2006; 66:241-6.
5. Monabeka HG, Bouenizabila E, Kibeke P, Nsakala-Kibangou N. L'obésité et le diabète de type 2 en milieu urbain congolais. Annales de l'Université Marien NGOUABI, 2007; 8 (5):38-42.
6. Giroux Elodie. Définir objectivement la santé: une évaluation du concept bio statistique de Boorse à partir de l'épidémiologie moderne. Revue philosophique de la France et de l'étranger 2009; 1 (134):35-58.
7. Drouin P, Blickle JF, Charbonnel B, Eschwege E, Guillausseau PJ, Plouin PF, et al. Diagnostic et classification du diabète sucré les nouveaux critères. Diabetes & Metabolism (Paris) 1999; 25:72-83.
8. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2017; 40(Suppl. 1):S11-S24. DOI: <https://doi.org/10.2337/dc17-S005>
9. Gariani K, Tran C, Philippe J. Hémoglobine glyquée: nouvel outil de dépistage ? Rev Med Suisse 2011; 7:1238-42.
10. Wojtusciszyn A. Les pièges de l'HbA1c. 2014. <http://www.realites-cardiologiques.com>
11. Imoisili OE, and Sumner AE. Preventing Diabetes and Atherosclerosis in Sub-Saharan Africa: Should the Metabolic Syndrome Have a Role ? Curr Cardiovasc Risk Rep 2009; 3(3):161-167. DOI:10.1007/s12170-009-0026-7
12. Marini MA, Fiorentino TV, Andreozzi F, et al. Hemoreological alterations in adults with pre-diabetes identified by hemoglobin a1c levels. Nutr metab cardiovasc dis. 2017; 27:601-608.
13. Chatzianagnostou K, Vigna L, Di Piazza S, Tirelli AS, Napolitano F, Tomaino L, et al. Low concordance between HbA1c and OGTT to diagnose Prediabetes and Diabetes in Overweight or Obesity. Clin Endocrinol 2019; 91 (3):411-416.
14. Rosella LC, Lebenbaum M, Fitzpatrick T, Zuk A, Booth GL. Prevalence of prediabetes and undiagnosed diabetes in Canada (2007-2011) according to fasting plasma glucose and hba1c screening criteria. Diabetes Care 2015; 38:1299-1305. DOI:10.2337/dc14-2474
15. Unwin N, Howitt C, Rose AMC, Samuels TA, Hennis AJM, Hambleton IR. Prevalence and phenotype of diabetes and prediabetes using fasting glucose vs HbA1c in a Caribbean population. Journal of health global 2017; 7(2). <http://www.jogh.org> • doi:10.7189/jogh.07.020407

16. Spinass GA, Lehmann R. Diabète sucré: Diagnostic, classification et pathogénèse. *Forum Med Suisse* 2001; 20:525-29.
17. Braatvedt GD, Cundy T, Crooke M, Florkowski C, Mann JI, Lunt H, *et al.* Understanding the new HbA1c units for the diagnosis of Type 2 diabetes. *New Zealand Medical Journal* 2012; 125 (1362). <https://www.nzma.org.nz/journal/read-the-journal/all-issues/2010-2019/2012/vol-125-no-1362/article-braatvedt>
18. Nguyen KA, Anniza de Villiers NP, Mukasa B, Matsha TE, Mills EJ, Kengne AP. Glycated haemoglobin threshold for dysglycaemia screening, and application to metabolic syndrome diagnosis in HIV-infected Africans. *PLoS ONE* 2019; 14 (1). <https://doi.org/10.1371/journal.pone.0211483>
19. Lorenzo C, Haffner SM. Performance Characteristics of the New Definition of Diabetes. *Diabetes Care* 2010; 33:335-337.
20. Inzucchi SE. Diagnosis of Diabetes. *N Engl J Med* 2012; 367:542-50. DOI:10.1056/NEJMc1103643
21. Sacks DB. Correlation between Hemoglobin A1c (HbA1c) and Average Blood Glucose: Can HbA1c Be Reported as Estimated Blood Glucose Concentration? *Journal of Diabetes Science and Technology* 2007; 1(6).
22. Lisi DM. Applying Recent A1C Recommendations in Clinical Practice. *US Pharmacist*. 2018; 43(10):15-23. https://www.medscape.com/viewarticle/905033_print
23. Cohen RM, Haggerty S, Herman WH. HbA1c for the Diagnosis of Diabetes and Prediabetes: Is It Time for a Mid-Course Correction? *J Clin Endocrinol Metab* 2010; 95(12):5203-5206. <http://jcem.endojournals.org>
24. IDF-ATLAS, 8th Edition 2017. <http://www.diabetesatlas.org/key-messages.html>
25. Kimbally-Kaky GS *et al.* Hypertension Artérielle et autres facteurs de risque cardiovasculaires à Brazzaville au Congo 2004; 19.
26. Mabilia BJR, Mahoungou GKC, Massamba A, Senga P. Consommation de l'alcool chez l'adolescent à Brazzaville (Congo). *Cahiers Santé* 2005; 15(3).
27. Kimbally Kaky GS, Voumbo Y, Gombet T, Ikama MS, Bolanda JD, Gokaba CH, *et al.* Etude de la prévalence de la consommation de l'alcool et du tabac à Brazzaville. *Cardiologie Tropicale* 2008; 33(129).
28. Ellenga MBF, Okoko AR, Mabilia BJR, Ekouya OG, Gombet TR, Kimbally-Kaky SG, *et al.* Prehypertension and Hypertension among Schoolchildren in Brazzaville, Congo. *Hindawi Publishing Corporation International Journal of Hypertension* 2014. <http://dx.doi.org/10.1155/2014/803690>
29. Gaillard T. Consequences of Abdominal Adiposity within the Metabolic Syndrome Paradigm in Black People of African Ancestry. *J. Clin. Med.* 2014; 3:897-912. DOI:10.3390/jcm3030897
30. Gradidge PJJ, Crowther NJ. Review: Metabolic Syndrome in Black South African Women. *Ethnicity & Disease*, Volume 27, Number 2, Spring 2017.
31. Capeau J, Bastard JP, Vigouroux C. Syndrome métabolique et insulino-résistance: physiopathologie. *mt cardio* 2006; 2 (2):155-64.
32. Zhang XH, Zhang M, He J, Yan YZ, Ma JL, Wang K, *et al.* Comparison of Anthropometric and Atherogenic Indices as Screening Tools of Metabolic Syndrome in the Kazakh Adult Population in Xinjiang. *Int. J. Environ. Res. Public Health* 2016; 13:428. <http://www.mdpi.com/journal/ijerph> doi:10.3390/ijerph13040428
33. Approche STEPwise de l'OMS pour la surveillance des facteurs de risque des maladies chroniques. 2003. Rev 1. <http://www.who.int/chps/steps>
34. Atlas des populations. *Creative Commons* 2002 à 2018 - ISSN 1708-5713. <https://www.populationdata.net/pays/Congo>
35. Oguoma VM, Nwose EU, Ulasi II, Akintunde AA, Chukwukelu EE, Bwititi PT, *et al.* Cardiovascular disease risk factors in a Nigerian population with impaired fasting blood glucose level and diabetes mellitus. *BMC Public Health* 2017; 17:36. DOI:10.1186/s12889-016-3910-3
36. Guo H, Liu J, Zhang J, Ma R, Ding Y, Zhang M, *et al.* The Prevalence of Metabolic Syndrome Using Three Different Diagnostic Criteria among Low Earning Nomadic Kazakhs in the Far Northwest of China: New Cut-Off Points of Waist Circumference to Diagnose MetS and Its Implications. *PLoS ONE* 2016; 11(2). DOI:10.1371/journal.pone.0148976
37. Punthakee Z, Goldenberg R, Katz P. Definition, Classification and Diagnosis of Diabetes, Prediabetes and Metabolic Syndrome. *Can J Diabetes* 2018; 42:S10-S15.
38. Mbanya V, Hussain A, Kengne AP. Application and applicability of non-invasive risk models for predicting undiagnosed prevalent diabetes in Africa: A systematic literature search. *Prim care diabetes* 2015; 9(5):317-29.
39. Hilawe EH, Yatsuya H, Kawaguchia H, Aoyama A. Differences by sex in the prevalence of diabetes mellitus, impaired fasting glycaemia and impaired glucose tolerance in sub-Saharan Africa: a systematic review and meta-analysis. *Bull World Health Organ* 2013; 91:671-682. DOI:<http://dx.doi.org/10.2471/BLT.12.113415>
40. Résolution 66/2. Déclaration politique de la Réunion de haut niveau de l'Assemblée générale sur la prévention et la maîtrise des maladies non transmissibles. Soixante-sixième session de l'Assemblée générale des Nations Unies. New York, Organisation des Nations Unies, 2011.
41. HHS Public Access. Heart Disease and Stroke Statistics. *Circulation*. 2017; 135(10):e146-e603. Doi:10.1161/CIR.0000000000000485
42. Ekpebgh CO, Longo-Mbenza B, Okwe AN, Ogbera AO, Tonjeni NT. Advanced age, altered level of consciousness and a new diagnosis of diabetes are independently associated with hypernatremia in hyperglycaemic crisis. *BMC Endocrine Disorders* 2011; 11:8. <http://www.biomedcentral.com/1472-6823/11/8>
43. Longo-Mbenza B, Lasi On'kin JBK, Okwe AN, Kabangu NK, Fuele SM. Metabolic syndrome, aging, physical inactivity, and incidence of type 2 diabetes in general African population. *Diabetes & Vascular Disease Research* 2010; 7(1):28-39. <https://www.sagepub.co.uk/journalsPermission.nav> DOI:10.1177/1479164109346362
44. Yip CYW, Sequeira IR, Plank LD, Poppitt SD. Prevalence of Pre-Diabetes across Ethnicities: A Review of Impaired Fasting Glucose (IFG) and Impaired Glucose Tolerance (IGT) for Classification of Dysglycaemia. *Nutrients* 2017; 9:1273. <http://www.mdpi.com/journal/nutrients> doi:10.3390/nu9111273
45. Jiang Y, Katwyk SRV, Mao Y, Orpana H, Agarwal G, Margaret de Groh, *et al.* Évaluation du risque de dysglycémie dans la région de Kitikmeot (Nunavut) au moyen de l'outil CANRISK. Promotion de la santé et prévention des maladies chroniques au Canada Recherche, politiques et pratiques. 2017; 37 (4). <https://www.researchgate.net/publication/316026008>
46. Belkacema S, Semrouni M. Le seuil optimal d'HbA1c pour prédire le diabète sucré définie par l'HGPO sur une population Algéroise à haut risque. *Annales d'Endocrinologie* 2018; 79:260-280.
47. Sherwani SI, Khan HA, Ekhzaimy A, Masood A, Sakharkar MK. Significance of HbA1c Test in Diagnosis and Prognosis of Diabetic Patients. *Biomarker Insights* 2016; 11:95-104. DOI:10.4137/BMI.S38440
48. Amoussou-Guenou D, Wanvoegbe A, Hermans M, Agbodande A, Boko M, Amoussou-Guenou AF, *et al.* Prevalence and Risk Factors of Diabetes Mellitus in the Adult Population of Porto-Novo (Benin). *Journal of Diabetes Mellitus* 2015; 5:135-140. <http://www.scirp.org/journal/jdm>. <http://dx.doi.org/10.4236/jdm.2015.53016>
49. Lasi On'kin JBK, Longo-Mbenza B, Okwe AN, Kabangu NK, Mpandamadi SD, Wemankoy O, *et al.* Prevalence and risk factors of diabetes mellitus in Kinshasa Hinterland. *Int J Diabetes & Metabolism* 2008; 16:97-106.
50. Nwose EU, Richards RS, Bwititi PT, Igumbor EO, Oshionwu EJ, Okolie K, *et al.* Prediabetes and cardiovascular complications study (PACCS): international collaboration 4 years' summary and future direction. *BMC Res Notes* 2017; 10:730.
51. Lasi On'kin JBK, Longo-Mbenza B, Okwe AN, Kabangu NK. Survey of abdominal obesities in an adult urban population of Kinshasa, Democratic Republic of Congo. *Cardiovascular Journal Of Africa* 2007; 18.
52. Adeniyi OV, Yogeswaran P, Longo-Mbenza B, Goon DT. Uncontrolled Hypertension and Its Determinants in Patients with Concomitant Type 2 Diabetes Mellitus (T2DM) in Rural South Africa. *PLoS ONE* 2016. DOI:10.1371/journal.pone.0150033
53. Jiang F, Hou X, Lu J, Zhou J, Lu F, Kan K, *et al.* Assessment of the Performance of A1CNow+ and Development of an Error Grid Analysis Graph for Comparative Hemoglobin A1c Measurements. *Diabetes Technology & Therapeutics* 2014. DOI:10.1089/dia.2013.0289
54. Motala AA, Esterhuizen T, Pirie FJ, Omar MAK. The Prevalence of Metabolic Syndrome and Determination of the Optimal Waist Circumference Cutoff Points in a Rural South African Community. *Diabetes Care* 2011; 34. <http://care.diabetesjournals.org>
55. Ekoru K, Murphy GAV, Young EH, Delisle H, Jerome CS, Assah F, *et al.* Deriving an optimal threshold of waist circumference for detecting cardiometabolic risk in sub-Saharan Africa. *International Journal of Obesity* 2018; 42:487-494. <http://www.nature.com/ijo>
56. Société Francophone du Diabète. Position des experts ADA-EASD sur la prise en charge de l'hyperglycémie chez les patients diabétiques de type 2: une stratégie centrée sur le patient. *Revue de Formation Médicale Continue* 2012; 6:1957-2557.
57. Bariza B, Warda L. Intégration du Big-Data et la Médecine Personnalisée 2017.
58. Khan HA, Sobki SH, Ekhzaimy A, Khan I, Almusawi IA. Biomarker potential of C-peptide for screening of insulin resistance in diabetic and non-diabetic individuals. *Saudi Journal of Biological Sciences* 2018; 25:1729-1732.
59. Lyonsa TJ and Basub A. Biomarkers in diabetes: hemoglobin a1c, vascular and tissue markers. Published in final edited form as: *Transl Res* 2012; 159(4):303-312.

60. Longo-Mbenza B, Ngoma DV, Nahimana D, Mayuku DM, Fuele SM, Ekwanzala F, *et al.* Screen detection and the WHO stepwise approach to the prevalence and risk factors of arterial hypertension in Kinshasa. *Eur J Cardiovasc Prev Rehabil* 2008; 15(5):503-8.