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Socio-anthropometric features and lifestyle in ketosis-prone diabetes vs controls

Kwadjo Anicet Luc Dere^{1,2,*}, Agnon Prisca Djoupo¹, Coulibaly Djenebou², Fofana Seguenan², Gnomblsson Georges Tiahou^{1,2}¹Laboratory of Clinical Biochemistry – Unit of Training and Research of Medical Sciences (Alassane Ouattara University), Côte d'Ivoire²Laboratory of Clinical Biochemistry – Teaching Hospital of Bouaké (RCI), Côte d'Ivoire

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ABSTRACT

Introduction: In West Africa, the various types of diabetes according to WHO or the American Diabetes Association (ADA) are endemic; however, a particular type referred to as atypical ketosis-prone diabetes mellitus requires specific attention.

Methodology: We implemented a case-control study including 101 cases versus 89 controls. Controls are people living in apparent good health and patients are diabetics newly diagnosed and attended hospitals for the first time. We included socio-demographic and anthropometric informations, some questions about dietary habits of participants. We tested fasting plasma glucose and HbA_{1c} according to manufacturer's instructions.

Results: Dietary diversification was lower in patients with less of 10% having a good dietary diversity. Correlation tests showed a significant statistical link in relation with waist circumference and body mass index in accordance with glycaemia in patients newly diagnosed diabetics. Noted a decreasing of mean value of glycaemia in overweight or obese patients, otherwise, the fat gaining was marked as glycaemia lowering. This trend has been related in correlation with HbA_{1c} in patients without significant statistical correlation. We also notified a significant link between amount of diet usually ingested by controls and the variation of HbA_{1c}.

Conclusion: It clearly appears that lifestyle has certainly an impact in the occurrence of metabolic diseases in overall and on diabetes in particular. There is a close link between these diseases with genetic or family predisposition. It seems urgent to act upstream to prevent such diseases living as a burden for our deprived population.

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1. Introduction

Sub-Saharan Africa has been significantly affected by the epidemiological and nutritional transition, without however having controlled the health problems linked to infectious diseases with severe acute episodes. It is in this context that they have to face the increasing prevalence of metabolic and cardiovascular diseases^{1,2} This double burden plunges these

populations into a state of vulnerability on the one hand and could explain the susceptibility and the particularity of certain pathologies on the other hand. Among the various metabolic diseases, diabetes mellitus confers the most significant disease burden, both in large cities and in remote regions. According to data from the World Health Organization (WHO), the incidence and prevalence of type 2 diabetes is greatest in low-income countries. The WHO predicts that by 2030, diabetes will be the 7th leading cause of death worldwide.³

* Corresponding author.

E-mail address: dere.kwadjoanicetluc@gmail.com (K. A. L. Dere).

In West Africa in particular, the various types of this disease according to the classification of the WHO or the American Diabetes Association (ADA) are endemic; however, a particular type referred to as atypical ketosis-prone diabetes mellitus, classified as type 1, requires specific attention. Its main characteristics are the onset of a type 1-like insulin-requiring with severe hyperglycemia and ketosis, with eventual features more typical of type 2.^{4,5} After initiation of insulin therapy, prolonged remission is often possible with the discontinuation of insulin and the maintenance of adequate glycemic control. More remains to know about the molecular mechanisms behind the transient alteration of insulin secretion but it may involve mechanisms of glucotoxicity and lipotoxicity.^{6,7} It is rare in populations with ancestry other than sub-Saharan African.

Recently a team of researchers has highlighted the role played by the mutation of the PAX-4 gene in this type of diabetes.⁸ This study on patients of West African origin also found variants of this mutation which in its homozygous form considerably increases the risk of ketosis at the time of diagnosis due to severe deficiency of insulin secretion. PAX-4 is a morphogenic factor that is expressed very early from the embryonic pancreas. On the other hand, the chronic increase in blood glucose due to unrecognized or poorly controlled diabetes mellitus impairs the stimulation of insulin secretion by pancreatic beta cells and increases the risk of cellular damage caused by reactive oxygen species leading to oxidative stress. This in turn aggravates organic disorders in the beta cells and exacerbates the clinical manifestations of the disease. To better understand this phenomenon, several research teams have carried out work in order to explain the role of beta cell stress in the pathogenesis of diabetes mellitus as well as in the occurrence of complications of this disease.^{8,9}

Although the prevalence of so-called "African" diabetes remains unknown in our population, it seems relevant to spend time to explore it in order to study some socio-anthropometric factors and lifestyle may be prone to this subgroup. We initiated a case-control study within a population living in a same city and having the habits.

2. Methodology

2.1. Study design

We have implemented a case-control study. Controls are people living in apparent good health and patients are diabetics newly diagnosed and attended one of different hospitals chosen for the first time.

2.2. Study sites

Patients and controls have been recruited in three different hospitals located in Bouaké, precisely in the teaching hospital of Bouaké, in the NGO for caring diabetics and in the service of diabetology of maternal and children hospital

of Bouaké. Different teams have been set up and trained to comply with the protocols for carrying out tests and samples as well as the preservation of blood samples.

2.3. Patients and controls

The patients recruited in this study are youths aged more than 18 years or adults with new-onset diabetes mellitus. Inclusion criteria are ketosis at the time of diabetes diagnosis. Controls were recruited among health providers in good health without any family history of diabetes. Indeed, it's a first degree of family history. Exclusion criteria were represented by the presence of aggravating factors such as infectious diseases, metabolic complications or micro and macro-angiopathies.

2.4. Recruitment

Patients were approached by a member of the clinical staff and their consent was required before their inclusion into the cohort. The diabetic and control populations were comparable with regard to their West African countries of origin and socio-demographic features.

2.5. Sample size calculation

As the prevalence of atypical diabetes mellitus with ketosis tendency is not known, we calculated and estimated the sample size on the basis of diabetes mellitus in Côte d'Ivoire and on the basis of budgetary constraints. We intended to carry out the recruitment and after the time due, we reached to include 190 participants in total (cases and controls). Nobody left the study and definitely we succeeded to include 101 patients versus 89 controls. We made a pre-survey in the different services chosen in order to enquire the data and the availability of personal to approve this study. We conducted this study from November 2020 to April 2021.

2.6. Data collection

We registered demographic information (date of birth, urban/rural dwelling, socioeconomic status) through our study questionnaire. Anthropometrics (weight, height, body mass index (BMI) and its standard deviation (SD), waist circumference and their percentiles were also notified. BMI and WC were categorized, using the current range according to World Health Organization (WHO) definitions; BMI of <18.5 kg/m², 18.5–24.9 kg/m², 25–29.9 kg/m², and 30 kg/m² were used to define underweight, normal, overweight, and obese cases, respectively. WC was defined for both males and females with WC < 94, 94–101.9, and ≥ 102 cm defined as normal, overweight, and obese, respectively for males and <80, 80–87.9, and ≥ 88 cm defined as normal, overweight, and obese, respectively, for females.^{10,11}

In a same time we included in the questionnaire some questions about dietary habits of participants. Blood samples were taken in different tubes for each intended analysis. We used a grey; and pink tube and we stored these samples at -80°C for future analysis. We tested fasting plasma glucose and HbA_{1c} according to manufacturer's instructions.

2.7. Ethical considerations

Approval for the study was obtained from the agreement of the scientific and medical director of the different hospitals in which the survey took place. Written informed consent was obtained from all participants (patients and controls). For patients with sub-literacy, the consent form was read aloud and signed in the presence of a witness. Study personnel was available for questions during the consent process.

2.8. Data analysis

We computed data as part of excel and the others statistical software such as SPSS or Graph Pad Prism5. Partial data were compared between cases and controls. The comparison of means was obtained by the T-test. Results were expressed in means \pm standard deviation. The level of significance of the tests used was set at $\alpha = 5\%$, difference was considered significant for P value < 0.05 .

3. Results

In our cohort, we strove to recruit controls having as similar socio-demographic and anthropometric features as diabetes patients newly diagnosed. However, the mean range age of patients was higher than controls namely 51.56 ± 12.92 against 43.79 ± 13.27 years old. It was similar to waist circumference 90.73 ± 14.73 against 88.89 ± 9.44 for controls (Table 1).

We documented a low rate of individual dietary diversity score within the two different categories of population. Dietary diversification was lower in patients with less of 10% having a good dietary diversity according to FAO recommendations. Cereals, other vegetables and fats were the more consumed nutrients among recruited patients. The consumption rate of these same diet groups was observed for controls with a mean value of individual dietary diversity score lightly higher (Figure 1).

Correlations study between different parameters showed a significant statistical link in relation with waist circumference and body mass index in accordance with glycaemia in patients newly diagnosed diabetics. Data revealed a decreasing of mean value of glycaemia in overweight or obese patients, this trend has been related in correlation with HbA_{1c} in patients without significant statistical correlation (Table 2). We also notified a significant link between amount of diet usually ingested by controls

and the variation of HbA_{1c}. For controls, our data showed that the bigger quantity of meal ingested the higher HbA_{1c} was. The same tendency was found with fasting glycaemia without any statistical link. For patients, the same trend has been observed. In contrary to these parameters that presented an increasing trend regarding to meal ingested a day and individual dietary diversity score, the mean range of normal physical activity score didn't get a beneficial impact on glycaemia lowering and HbA_{1c} in patients and controls as well. Correlation with age revealed an increasing of fasting glycaemia in controls along with an increasing of HbA_{1c}, as opposed to patients, in whom we found a decreasing of fasting glycaemia with aging. For the whole patients ketones had been found in urines and it was also one of different inclusion criteria.

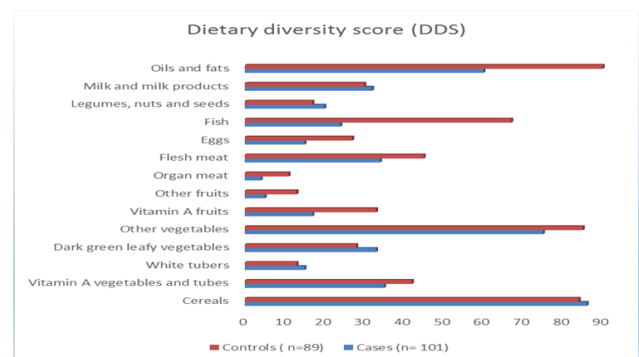


Fig. 1: Individual dietary diversity score between patients and controls

4. Discussion

Diabetes ketoacidosis (DKA) is a usual complication arising during type 1 diabetes. However, it can be encountered during the progression of type 2 diabetes. In type 2 diabetes patients, the proportion of DKA is estimated to be in the range of 0.32 to 2.0 per 1,000 patient-years, while in people with type 1 diabetes, the incidence is higher at 4.6.¹² Notwithstanding, ketosis prone atypical diabetes is a particular entity of diabetes that has been subject of many research studies. Ketosis-prone diabetes (KPD) is a heterogeneous syndrome characterized by patients who present with diabetic ketoacidosis or unprovoked ketosis but do not necessarily have the typical phenotype of autoimmune type 1 diabetes.¹³

In our study, we recruited 101 cases versus 89 controls, a reasonable approximation. Regarding the socio-demographic features of participants, it emerges that there are more women than men with a sex-ratio of 1.96 (approximately 2 women/ 1 men). This trend is in line with the data of Ivorian population. Socio-demographic and anthropometric values were overall higher within cases with respectively a mean value of age estimated to 51.56

Table 1: Socio-demographic and anthropometric features of cases and controls

	Cases (n=101)				Controls (n=89)				
	Mean	SD	Min	Max	Mean	SD	Min	Max	
Ketonuria	++	-	+/-	++++	-	-	-	-	
Glycosuria	+++	-	+	+++++	-	-	-	-	
Age (years)	51.56	12.92	18	87	Age	43.79	13.27	23	88
BMI (Kg.m ⁻²)	25.84	7.18	11.90	48.40	BMI	25.88	4.63	17	42.2
Waist C. (Cm)	90.73	14.73	60	128	Waist C.	88.89	9.44	66	120
Gender	Number (n)		Percentage (%)		Gender	Number (n)		Percentage (%)	
Woman	66		65.34%		Woman	60		67.41%	
Man	35		34.65%		Man	29		32.58%	

Table 2: Family and personal records of cases and controls

Category	Variable	Cases (n=101) Frequency (%)	Controls (n=89) Frequency (%)
Family record	Obesity	57 (56.43)	11 (12.35)
	Diabetes	69 (68.31)	22(24.71)
Personal record	Obesity	39 (38.61)	6 (6.74)
	Fasting hyperglycemia	71 (70.29)	5 (5.61)

Table 3: Correlation between socio-anthropometric parameters and lifestyle in comparison to biological parameters

		Cases (n=101)			Controls (n=89)				
		Glucose (Mean±SD)	P value	HbA1C (Mean±SD)	P value	Glucose (Mean±SD)	P value	HbA1C (Mean±SD)	P value
Age	< 30 y	439±167		11.01±2.40		89±15		2.0±0.0	
	30 – 60 y	383±112	0.784	11.79±1.97	0.953	93±16	0.328	2.21±0.75	0.152
	> 60 y	397±114		11.94±2.15		93±12		2.57±0.97	
Gender	F	386±109	0.276	11.79±1.96	0.631	91±18	0.066	2.33±0.89	0.671
	M	396±125		11.78±2.15		97±07		2.06±0.37	
Waist C.	Normal	435±122	0.005*	12.01±2.08	0.701	93±12	0.082	2.19±0.68	0.446
	High	380±102		11.44±2.25		95±12		2.17±0.44	
	Underweight	473±137		11.53±2.15		86±08		2.00±0.00	
BMI	Normal	418±111	0.001*	12.29±1.80	0.262	94±18	0.715	2.19±0.68	0.251
	High	347±96		11.40±2.12		92±14		2.29±0.85	
Dietary diversity	Insufficient (≤ 5)	388±115	0.664	11.74±1.99	0.893	86±12	0.202	2±0	0.861
	Normal (> 5)	391±115		11.84±2.07		94±16		2.30±0.85	
Physical activities	Low (<600 met/min.)	387±112	0.792	11.71±2.03	0.894	92±16	0.635	2.24±0.78	0.577
	Normal (>600 met/min.)	415±154		12.82±1.71		94±13		2.25±0.70	
Meal /day	≤ 3	387±111	0.177	11.79±2.00	0.669	93±16	0.770	2.25±0.78	0.251
	>3	406±142		11.78±2.26		87±05		2±0	
Quantity ingested/meal	Normal	389±112	0.357	11.71±2.12	0.310	92±15	0.565	2.20±0.67	0.000*
	High	392±131		12.17±1.42		97±31		3.33±2.30	

years old by opposition to 43.79 years old for controls; a mean value of waist circumference of 90.73cm for cases versus 88.89 cm for controls and a mean value of body mass index of 25.84 for cases versus 25.88 for controls. The mean values of BMI and WC within the two different subgroups show a trend for weight gaining and particularly overweight or obesity. These results are in line with data reported by several authors.^{10,14-16} Interrelation between obesity and other metabolic disorders is now well documented and including hypertension, diabetes, cardiovascular disease, dyslipidemia, and some cancers.¹⁷ Almost 88% of those with T2DM are viewed as overweight or obese.¹⁸ Moreover, similar findings were observed. The prevalence of overweight and obesity among type 2 diabetes has been documented.^{15,19}

Our population lifestyle has tremendously changed these last decades owing to urbanization of big cities along with the change of dietary habits.²⁰ Indeed, an important range of the people preferred fast food, soft drinks, and mayonnaise and so on. Such eating preferences are responsible in the development of overweight and obesity among population and many actions are promoted to reduce the intake of fat and sugar leads to body weight control and prevents overweight and obesity.^{16,19} The misfeeding has led to nutritional transition that has a huge impact on the prevalence of chronic diseases and adverse effects on their evolution precisely for obesity, diabetes and hypertension, to name a few. More than three meal ingested a day together with no physical activities represent the substratum of this bad quality of life.^{15,19}

Some results emerging from our cohort showed values in opposition to expected trend. Differences between our findings and other study findings may be due to the limited sample size and population, as well as the study setting. Indeed, the mean value of glycaemia and HbA1C seems lower for patients in overweight, obese and having a normal range of physical activities. In contrary to amount and the number of food ingested a day together with individual dietary diversity. This could be due to a bias in the recruitment of patients or the impact of glucotoxicity and/or lipotoxicity at the time of diagnosis.

Several studies reported a diagnosis driven lifestyle, behavior change and physical activity. In a study conducted by Schneider et al., it was found that participants who were diagnosed diabetics were more likely to increase their physical activity.²¹ Another study reported the diagnosis as a motivational factor for participants to exercise and follow a healthy diet.²² These findings may be explained that diagnosis is acting as a threat or call to action, and therefore contributing to a change in lifestyle, behavior and habits.²²

Obirikorang et al., in their study aiming to appreciate the prevalence of obesity among newly diagnosed type 2 diabetic patients in Ghana, they reported that participants

knew that poor dietary habit is a major cause for obesity and also hypertension and stroke were the commonly known complications of obesity. Dietary modification and regular physical activity were the common management approaches of obesity known by participants. More than one out of five North Americans born in 2000 will have type 2 diabetes mellitus (T2DM) in their lifetime. In fact, T2DM is likely to constitute a major health problem for all populations who currently adopt Western lifestyle. T2DM results from the interaction of environmental factors and genetic variants that are still little or not known to date.²³

Our data, related to cases, corroborate the trend of family record. We found, about 56.4% and 68.3% of the cases reported a family history of overweight and diabetes respectively. Regarding personal record of cases, 70.29% have previously presented fasting hyperglycemia. These results prove the high inherited link into the transmission of type 1 or type 2 diabetes. The hereditary basis of diabetes mellitus is confounded with multifactorial inheritance decisive and interactions of both genetic and ecological factors. The illness is not inherited itself; rather an enhanced susceptibility to the illness. It is known since primordial times that offspring are fairly similar to their parents and that some characters are transferred from parents to offspring. Genetics is the study of the transmission of these inherited individualizes or characteristics in generations. It has been estimated that the human genome involves approximately 20,000 to 25,000 protein-coding genes and non-protein coding genes, DNA sequence variants associated with chromosomal dynamics and other functional fundamentals.²⁴

It emerges from this investigation that some important differences exist in the mean values for different parameters into two different subgroups. These important values of fasting glycaemia for patients naïve of treatment were manifested by ketosis or an inaugural ketoacidosis state leading to coma, and required an urgent therapy. Such values of fasting glycaemia for patients without any precipitating factors recognized would explain a chronic and persistent state of hyperglycaemia evolving since a long time and related to high level of HbA1C ranging from 6.4% to 15.5%.

For controls, this trend didn't the same. We found that 12.3% of overweight participants and 24.7% of patients have got a family record of these pathologies. As personal record only 6.7% of obesity was found. Also, we found a positive correlation between the quantity of food ingested with the mean value of fasting glycaemia and HbA1C. This tendency was statistically significant for HbA1C. It's the case for age, waist circumference, BMI and dietary diversity. These findings are in accordance with literature.^{10,11} Both obesity and type 2 diabetes are strongly associated with an unhealthy diet and physical inactivity. Physical and environment are important factors on diet and physical activity behavior along with other parameters such

as cultural factors.²⁵ Sedentary behavior is also linked to obesity. In a recent British study, authors found that people with type 2 diabetes recorded greater amounts of sedentary time compared with their non-diabetic counterparts. For this reason, Exercise plus dietary changes have been found to be effective in preventing the onset of type 2 diabetes in high risk individuals for those with impaired glucose tolerance or those with metabolic syndrome as well.

5. Conclusion

At the end of our study, it appears that lifestyle of people have certainly an impact in the occurrence of metabolic diseases in overall and on diabetes in particular. This certainly argues for a close link between these diseases with genetic or family predisposition. Excess food intake, excess weight gaining along with physical inactivity represent a triad that triggering these diseases. It seems urgent to act upstream to prevent such diseases living as a burden for our deprived population.

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7. Conflict of Interest

There are no conflicts of interest.

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Author biography

Kwadjo Anicet Luc Dere, Assistant Professor

Agnon Prisca Djoupo, Assistant Professor

Coulibaly Djenebou, Biologist

Fofana Seguenan, Biologist

Gnomblesson Georges Tiahou, Professor and Head

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