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Original Research Article

Hypovitaminosis D among type 2 diabetes patients and non-diabetics at Libreville

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ABSTRACT

Background: Type 2 diabetes is resulting from insulin resistance and/or progressively reduced insulin secretion. Vitamin D nuclear receptor present on the β cells of the pancreas promotes the growth, synthesis and secretion of insulin. Furthermore, vitamin D deficiency has been associated with numerous disorders, such as type 2 diabetes, cardiovascular diseases, arterial hypertension, cancer, multiple sclerosis, depression, psychiatric diseases.
Aim: Determine the frequency of hypovitaminosis D among type 2 diabetes patients and those without diabetes in Libreville.
Materials and Methods: The study population was composed of 92 type 2 diabetes patients (cases) and 100 non-diabetics (controls). The vitamin D and glycated hemoglobin were performed using 25 OH Vitamin D total kit and FIA8000 kit respectively. The blood glucose, calcemia and phosphorus were performed using standard spectrophotometric assay.
Results: Insufficient vitamin D (<30ng/mL) was found among 55.2% of the study population that was 57.0% of insufficient vitamin D in cases and 53.3% in controls. In the general population vitamin D was not correlated to blood glucose (r= -0.0270). Thus, with glycated hemoglobin, no correlation was found with vitamin D among cases. However, a weak negative correlation of vitamin D with blood glucose has been found in control group (r= -0.2798).
Conclusion: High hypovitaminosis D was found among cases and controls. Therefore and in regards of studies based on vitamin D supplementation, with an appropriate concentration of vitamin D or calcitriol, glucose homeostasis may be maintained. Moreover, implementation of preventive measures should be done to avoid disastrous consequences of vitamin D insufficiency.

1. Introduction

Type 2 diabetes (T2DM) is a multifactorial disease characterized by a disturbance in carbohydrate, lipid and protein metabolism. This disturbance may be associated with serious complications such as myocardial infarction, stroke and renal failure.[1]

According to the International Diabetes Federation, in 2021, 537 million adults worldwide were living with diabetes mellitus. An estimated 6.7 million people aged 20 to 79 died of diabetes-related causes in 2021. In Africa, the number of people with diabetes was 23.6 million, with a prevalence of 4.5% in 2021. This could rise to 54.9 million by 2045, with a prevalence of 5.2%.[2] In Gabon, a Central African country with a population of 2.3 million in 2022, prevalence was estimated at 5-6%.[3] Type 2 diabetes

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is resulting from insulin resistance and/or progressively reduced insulin secretion.[4] Insulin resistance leads to chronic hyperglycemia, with increased oxidative stress and pro-inflammatory cytokine production, impairing insulin signalling pathways, lipid metabolism, protein synthesis and cell differentiation. It can also alter body concentrations of micronutrients.[5,6]

In view of this, maintaining glycemic control in patients with T2DM requires strategies that combine appropriate dietary hygiene measures with drug therapy. A balanced diet with adequate vitamin and trace element content could reduce glycated hemoglobin levels in T2DM patients by 0.3-2%.[7] Vitamin D has a nuclear receptor which is present on the β cells of the pancreas. This receptor promotes the growth, synthesis and secretion of insulin through its important role in the regulation of several genes, notably those involved in insulin production.[8] Some studies have shown that vitamin D deficiency defined as a serum concentration of 25-hydroxyvitamin D (25(OH)D) below 20 ng/mL is a factor that promotes glycemic imbalance.[9–11] Furthermore, vitamin D deficiency has been associated with numerous disorders, such as cardiovascular diseases, arterial hypertension, cancer, multiple sclerosis, depression, psychiatric diseases, and others.[12,13] However, vitamin D deficiency has been reported to be prevalent in the general population. Data showed 15.7%, >20%, 13%, 7.4% and 5.9% of vitamin D deficiency respectively in worldwide, India, Europe, Canada and United States of America.[14,15]

Setting of strategies to deal with this deficiency was important to improve the health status of the population. What is the current state of this deficiency among type 2 diabetes patients and non-diabetic's patients at Libreville? The aim of this study was to determine the frequency of hypovitaminosis D among patients suffering from type 2 diabetes and those without diabetes in Libreville.

2. Materials and Methods

2.1. Site and type of study

The study took place in Libreville, the administrative and political capital of Gabon. Patients were recruited from the endocrinology and metabolic diseases department of the Centre Hospitalier Universitaire de Libreville (CHUL). The study was a cross-sectional, analytical case-control study conducted from January to September 2022.

2.2. Ethics

This work was carried out in accordance with the recommendations of the Declaration of Helsinki on the use of living beings.[16] Authorization was obtained from the head of the CHUL. Moreover, informed consent was obtained from all participants. They were assured of the confidentiality of data collected during the survey.

2.3. Inclusion and non-inclusion criteria

The population was divided into cases representing patients with diabetes hospitalized or consulting the CHUL Endocrinology and Metabolic Diseases Department, and controls from the general population. Cases were all with type 2 diabetes and controls over 25 years of age who agreed to take part in the study and signed an informed consent form beforeh and.

Excluded from the study were breastfeeding or pregnant women with or without gestational diabetes, immune-compromised patients, sickle-cell patients, dialyzed patients and those with systemic diseases, parathyroid diseases.

2.4. Patient and sample selection

Participants were recruited on a voluntary basis. Following consent and verification of non-inclusion criteria, the clinical examination allowed socio-demographic data collection. This was followed by a general examination and anthropometric measurements.

Venous blood samples were then taken to measure blood glucose, glycated hemoglobin, calcium, phosphorus and vitamin D.

2.5. Dosage of vitamin D, blood glucose, calcemia, phosphorus and HbA1c

Biological assays were performed at the Biochemistry Laboratory of the University of Health Sciences.

The vitamin D assay was performed using the Biomerieux VIDAS 25 OH Vitamin D total kit. This is a quantitative test for the determination of 25-hydroxyvitamin D total in human serum and plasma. The blood glucose, calcemia and phosphorus assay was performed using a Biolabo kit in accordance with the manufacturer's recommendations. Glycated hemoglobin was determined using FIA8000 kit.

2.6. Statistical analysis

Statistical analysis was carried out using Epi info 7.2.5.0. Proportions, means with standard deviations and correlation were calculated. In addition, Mann-Witney/wilcoxon and ANOVA tests were used to compare quantitative and qualitative variables. For a P-value < 0.05, the tests were significant.

3. Results

Socio-demographic data of the study population showed that mean age was 52.3±13.5 years, and women accounted for 55.7% (Table 1).

Mass index and abdominal circumference were 27.1±5.5 kg/m^2 and 89.4±12.9 cm respectively in the general population (Table 1).

Moreover, arterial hypertension was more found in cases (n=56.0%) compared to controls (n=12.0%) P=0.000. Physical activities were practiced by 18.2% of the general population with 6.2% for type 2 diabetes patients and 12.0% for control patients.

Alcohol consumption accounted for 75.0% with control and 37.0% with cases (P=0.000) (Table 1).

Mean average of vitamin D among control and cases was comparable (P=0.467). Mean blood glucose was higher among patients with diabetes (8.8±4.1mmol/L) compared to control (4.8±0.6mmol/L) (Table 2).

Furthermore, insufficient vitamin D was found among 55.2% of the study population that was 57.0% of insufficient vitamin D in cases and 53.3% in controls (Table 2). All controls group subjects had normoglycemia (n=100%). But only 32.0% of diabetic's population was on normoglycemia (Table 2). Normal calcemia was found in most majority of the population. On the other hand, near 50% of subject has abnormal phosphorus concentration (Table 2).

In the general population vitamin D was not correlated to blood glucose (r= -0.0270). However, a weak negative correlation of vitamin D with blood glucose has been found in control group (r= -0.2798). Thus, with glycated hemoglobin, no correlation was found with vitamin D among type 2 diabetes patients (Table 3).

4. Discussion

The aim of our study was to investigate the distribution of vitamin D among type 2 diabetes patients and non-diabetics with a view of improving the management of people healthy. In the total population, hypovitaminosis D of 55.2% was found, with P=0.052. This value is not significant but indicates a high proportion of hypovitaminosis D in the population representing more than half. Hypovitaminosis is common in the general population. In a meta-analysis study carried out in South Asia in 2021 by Siddiqee et al. on the prevalence of vitamin D in adults, they reported that 68% of this population had hypovitaminosis D and more specifically 73% of people with hypovitaminosis were from Pakistan, 67% from Bangladesh and India, 57% from Nepal and 48% from Sri Lanka, a proportion close to our study.[17] Furthermore, in the study conducted by Forrest KY and colleagues in 2011 on the prevalence of diabetes in adults in the USA, the frequency of hypovitaminosis D was 41.6% with 82.1 in blacks and 69.2% in Hispanics.[18] In Africa, a meta-analysis by Mogire and colleagues found 58.54% hypovitaminosis for vitamin D levels below 75mmol/L (<30ng/L).[19] These studies corroborate our findings and suggest that hypovitaminosis D is common in the general population. However, the different variations observed from one country to another are due, among other things, to several factors such as genetics, skin color, seasons, latitude, environment, diet and disease.[20,21]

In the present study, vitamin D levels were determined in patients with type 2 diabetes and healthy individuals (controls). The proportion of hypovitaminosis D in people with type 2 diabetes and healthy people was 57.0% and 53.3% respectively. Several authors have reported high rates of hypovitaminosis D in people living with type 2 diabetes. Indeed, in Nigeria, Anyanwu et al., in 2020, found a frequency of hypovitaminosis D varying from 63.2% in type 2 diabetics.[22] Similarly, Lei Zhang et al., reported 48.8% vitamin D deficiency in type 2 diabetics in China.[23]

However, in the present study, vitamin D levels in people with type 2 diabetes compared with controls were not significant. These results have been reported by other authors.[22] This may suggest that vitamin D is not a predictive factor in the occurrence of type 2 diabetes. Indeed, several studies of vitamin D supplementation in people living with type 2 diabetes have been conducted to see the impact of vitamin D in the occurrence of type 2 diabetes. In a multicentric randomized trial conducted by Pittas AG et al., people with pre-diabetes were given a dose of 4000 IU/day of vitamin D_3 corresponding at 100ug. The recommended daily dose is 15ug/day for people aged between 1 and 70, and the harmful dose is over 50.000 IU/day[24] for a total of 1211 people. Another group of people (1212) were given a placebo for 2.5 years. At the end of this period, as many people in the placebo group as in the vitamin D group developed diabetes.[25] Furthermore, in our study, vitamin D_3 levels were not correlated with HbA1c. The mean glycated hemoglobin level in our population of people living with diabetes was 7.4±2.1%, indicating that our population had unbalanced diabetes. This could indicate that the pathology was not being monitored optimally. In our study, vitamin D supplementation was not carried out; only oral anti-diabetic treatment, diet and sports activities were prescribed. This had no impact on glycemic control as we found 47% patients with >7% HbA1c.

A randomized controlled trial conducted in Montenegro by Milena Cojic et al. in 2021 on 130 patients with type 2 diabetes on anti-diabetic treatment including metformin, high-dose vitamin D supplementation was carried. In the vitamin D supplementation group, those with hypovitaminosis D (25-hydroxyvitamin D <20ng/ml) received 50000 IU/week for the first 3 months and 14000 IU/week for the following 03 months, and those with vitamin D >20 ng/ml received 14000 IU/week for the 06 months of the study. At the end of this study, the recommended doses of vitamin D significantly reduced HbA1c levels after 6 months of vitamin D supplementation in supplemented patients compared with not supplemented patients.[26] However, vitamin D_3 is only active in the body once it has been converted to calcitriol by vitamin D 25-hydroxylase. Thus, if this enzyme is not synthesized, supplementation with vitamin D_3 will not be effective. For this reason, a study conducted by Xu J et al., in 2015 on

Table 1: Characteristics of the study population

Parameters	Toal N=192	Case N=100	Controls N=92	P value
Age (years)	52.3±13.5	58.2±11.8	46± 12.3	0.000
Gender N (%)				0.411
Female	107 (55.7)	57 (57.0)	50 (54.3)	
Male	85 (44.3)	43 (43.0)	42 (45.7)	
Weight (kg)	73.5±14.7	74.3±14.5	72.6±15.0	0.446
Size (m)	1.6±0.1	1.6±0.1	1.6±0.1	0.182
Abdominal Perimeter (cm)	89.4±12.9	91.6±12.4	86.9±12.9	0.010
Body Mass Index (kg/m^2)	27.1±5.5	27.7±5.4	26.5±5.6	0.137
Physical activities				
Yes	35 (18.2)	12 (12.0)	23 (25.0)	0.015
No	157 (81.8)	88 (88.0)	69 (75)	
AH (%)				0.000
Yes	67 (34.9)	56 (56.0)	11 (12.0)	
No	125 (65.1)	44 (44.0)	81 (88.0)	
SBP (mmHg)	139.4±21.2	146.6±20.7	131.6±19.1	0,000
DBP (mmHg)	88.3±12.2	88.9±12.7	87.8±11.5	0.529
Alcohol N (%)				0.000
Yes	106 (55.2)	37 (37.0)	69 (75.0)	
No	86 (44.8)	63 (63.0)	23 (25.0)	
Tobacco N (%)				0.176
Yes	18 (9.4)	7 (7.0)	11 (12.0)	
No	174 (90.6)	93 (93.0)	81 (88.0)	
Duration of diabetes (years ±SD)		8.8±9.6		

AH: Arterial hypertension, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, SD: Standard deviation

Table 2: Comparison of means and proportions of biological data between cases and controls

Parameters	Total	Cases (N=100)	Controls (N=92)	P value
Vitamin D (ng/mL) (mean±SD)		27.4±9.4	28.6±12.9	0.467
Blood glucose (mmol/L) (mean±SD)		8.8±4.1	4.8±0,6	0.000
Glycated hemoglobin (%)	NA	7.4±2.1	NA	NA
Vitamin D (ng/mL) (%)	106	57 (57.0)	49 (53.3)	0.707
Insufficient	(55.2)	43 (43.0)	43 (46.7)	
Sufficient	86 (44.8)			
Blood glucose (mmol/L) (%)	01 (0.5)	01(1.0)	0 (0.0)	0.000
Hypoglycemia	124	32 (32.0)	92 (100.0)	
Normoglycemia	(64.6)	67(67.0)	0(0.0	
Hyperglycemia	67 (34.9)			
Calcemia (nmol/L)				0.046
Normal	166 (86.5)	82 (82.0)	84 (91.3)	
Abnormal	26 (13.5)	18 (18.0)	8 (8.7)	
Phosphorus (nmol/L)				
Normal	92 (47.9)	46 (46.0)	46 (50.0)	0.341
Abnormal	100 (52.1)	54 (54.0)	46 (50.0)	

N: number of subjects; NA: not applicable, SD: Standard deviation

Table 3: Correlation between vitamin D with glycemia and HbA1c

		Glycemia	HbA1c
Vitamin D	Total	-0.0270	NA
	Cases	0.0573	-0.0221
	Controls	-0.2798	NA

HbA1c: glycated hemoglobin; NA: not applicable

the effect of calcitriol in diabetics noted that the HbA1c percentage improved.[27] Similarly, in the study by Eftekhari et al., who supplemented patients with type 2 diabetes over 12 weeks with low levels of calcitriol, 0.25ug/day, noted that supplementation attenuated the rise in blood glucose and increased insulin production.[28]

Thus, calcitriol would appear to play a role in glucose homeostasis, including beneficial effects on pancreatic β-cell function and insulin action. A vitamin D_3 effect was only observed at very high doses in these studies. In the controls group of the present study, the weak negative correlation observed with vitamin D and blood glucose may explain the fact that with an appropriate concentration of vitamin D or calcitriol, blood glucose could be maintain normal.

5. Conclusion

High hypovitaminosis D was found among type 2 diabetes patients and non-diabetics. Blood glucose and glycated hemoglobin among cases was not correlated to vitamin D. however, a weak negative correlation with vitamin D and blood glucose in controls was found.

Therefore, and in regards of studies based on vitamin D supplementation, with an appropriate concentration of vitamin D or calcitriol, glucose homeostasis may be maintained. Moreover, implementation of preventive measures should be done to avoid disastrous consequences of vitamin D insufficiency.

6. Source of Funding

None.

7. Conflict of Interest

None.

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References

1. Tjeck OP, Souza A, Mickala P, Lepengue AN, Batchi BM. 2017.
2. 2021.
3. *Countrymeters Gabon Population*. 2023;.
4. Nasykhova YA, Tonyan ZN, Mikhailova AA, Danilova MM, Glotov AS. Pharmacogenetics of type 2 diabetes progress and prospects. *Int J Mol Sci*. 2020;21(18):1–26.
5. Veronese N, Watutantrige-Fernando S, Luchini C, Solmi M, Sartore G, Sergi G, et al. Effect of magnesium supplementation on glucose metabolism in people with or at risk of diabetes: a systematic review and meta-analysis of double-blind randomized controlled trials. *Eur J Clin Nutr*. 2016;70(12):27530471–27530471.
6. Shah M, Vasandani C, Adams-Huet B, Garg A. Comparison of nutrient intakes in South Asians with type 2 diabetes mellitus and controls living in the United States. *Diabetes Res Clin Pract*. 2018;138:47–56.
7. Lifestyle Management: Standards of Medical Care in Diabetes-2018. *Diabetes Care*. 2018;4(Supplement_1).
8. Guadarrama-López AL, Valdés-Ramos R, Be MC. Type 2 diabetes, PUFAs, and vitamin D: Their relation to inflammation. *J Immunol Res*. 2014;.
9. Usluogullari CA, Balkan F, Caner S, Ucler R, Kaya C, Ersoy R. The relationship between microvascular complications and vitamin D deficiency in type 2 diabetes mellitus. *BMC Endocr Disord*. 2015;15(1).
10. Neveen RM, Abeer A, Roy RM. The effect of vitamin D deficiency on glycemic control in patients with type 2 diabetes mellitus. . *Healthcare in Low-resourcce Settings*. 2023;4(4):122–8.
11. Wu J, Atkins A, Downes M, Wei Z. Vitamin D in Diabetes: Uncovering the Sunshine Hormone's Role in Glucose Metabolism and Beyond. *Nutrients*. 1997;15.
12. Milic S, Mikolasevic I, Krznaric-Zrnic I, Stanic M, Poropat G, Stimac D. Nonalcoholic steatohepatitis: Emerging targeted therapies to optimize treatment options. *Drug Des Devel Ther*. 2015;9:4835–4845.
13. Vranić L, Mikolašević I, Milić S. PMCID. 2019.
14. Amrein K, Scherkl M, Hoffmann M, Neuwersch-Sommeregger S, Köstenberger M, Berisha T, et al. Vitamin D deficiency 2.0: an update on the current status worldwide. *Eur J Clin Nutr*. 2020;74(11):7091696–7091696.
15. Cui A, Zhang T, Fan XP, Wang Z, Zhuang H, Y. Global and regional prevalence of vitamin D deficiency in population-based studies from 2000 to 2022: A pooled analysis of 7.9 million participants. *Front Nutr*. 2023;10:1070808–1070808.
16. World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects. *World Medical Association*. 2013;310(20):2191–2194.
17. Siddiqee MH, Bhattacharjee B, Siddiqi UR, Meshbahurrahman M. PMCID. 2009.
18. Forrest KY, Stuhldreher WL. Prevalence and correlates of vitamin D deficiency in US adults. *Nutr Res*. 2011;31(1):21310306–21310306.
19. Mogire RM, Mutua A, Kimita W, Kamau A, Bejon P, Pettifor JM. Prevalence of vitamin D deficiency in Africa: a systematic review and meta-analysis. *Lancet Glob Health*. 2019;8(1):7024961–7024961.
20. Janssen CE, Globig AM, Grawitz B, Bettinger A, Hasselblatt D, P. PMCID. 2019.
21. Ammar M, Heni S, Tira MS, Khalij Y, Hamdouni H, Amor D. Variability in response to vitamin D supplementation according to vitamin D metabolism related gene polymorphisms in healthy adults. *Eur J Clin Nutr*. 2022;77(2):9514197–9514197.
22. Anyanwu AC, Olopade OB, Onung SI, Odeniyi IA, Coker H, Fasanmade OA. Serum vitamin D levels in persons with type 2 diabetes mellitus in Lagos, Nigeria. *Int J Diabetes Clin Res*. 2020;7:133–133.
23. Zhang L, Wang J, Yang Y, Dong Y. 178-LB: Prevalence of Vitamin D Deficiency among Patients with Type 2 Diabetes in Qingdao. *China Diabetes*. 2022;71(Supplement_1):178–178.
24. Amstutz V, Favrat B, Cornuz J, Krieg MA. Vitamine D : actualité et recommandations. *Rev Med Suisse*. 2011;(319):2332–2338.
25. Pittas AG, Dawson-Hughes B, Sheehan P, Ware JH, Knowler WC, Aroda VR. Vitamin D Supplementation and Prevention of Type 2 Diabetes. *N Engl J Med*. 2019;381(6):6993875–6993875.
26. Cojic M, Kocic R, Klisic A, Kocic G. 2021.
27. Xu J, Xiong H, Chen P. The effects of calcitriol on albuminuria in patients with type 2 diabetes mellitus. *Int J Diabetes Dev Ctries*. 2015;35(3):418–423.
28. Eftekhari MH, Akbarzadeh M, Dabbaghmanesh MH, Hasanzadeh J. Impact of treatment with oral calcitriol on glucose indices in type 2 diabetes mellitus patients. *Asia Pac J Clin Nutr*. 2011;20(4):22094836–22094836.

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