Scientific Research Publishing

Journal of Diabetes Mellitus, 2024, 14, 81-94
https://www.scirp.org/journal/jdm
ISSN Online: 2160-5858
ISSN Print: 2160-5831

Vitamin D, Parathyroid Hormone, Insulin Sensitivity and Islet β-Cell Secretory Function in Diabetic Patients from South Kivu in the Democratic Republic of Congo: Cross-Sectional Study

Dieudonne Masemo Bihehe[1], Ahadi Birindwa Bwihangane[1,2], Jean-Paulin Mukonkole Mbo[3], Michel Hermans[4], Philippe Bianga Katchunga[5*]

[1]Faculté de Médecine, Hôpital Général de Référence de Panzi, Université Evangélique en Afrique, Bukavu, DR Congo
[2]Département de Biologie, Faculté des Sciences, Université Officielle de Bukavu, Bukavu, DR Congo
[3]Département de Médecine Interne, Université de Kisangani, Kisangani, DR Congo
[4]Service d'endocrinologie et de Diabétologie, Cliniques Universitaires Saint-Luc, Université Catholique de Louvain, Bruxelles, Belgique
[5]Département de Médecine Interne, Cliniques Universitaires de Bukavu, Université Officielle de Bukavu, Bukavu, DR Congo
Email: *philkatch@yahoo.fr

How to cite this paper: Bihehe, D.M., Bwihangane, A.B., Mbo, J.-P.M., Hermans, M. and Katchunga, P.B. (2024) Vitamin D, Parathyroid Hormone, Insulin Sensitivity and Islet β-Cell Secretory Function in Diabetic Patients from South Kivu in the Democratic Republic of Congo: Cross-Sectional Study. *Journal of Diabetes Mellitus*, **14**, 81-94.
https://doi.org/10.4236/jdm.2024.142008

Received: January 26, 2024
Accepted: March 24, 2024
Published: March 27, 2024

Abstract

Background: The role of vitamin D and parathyroid hormone in the metabolic profile of type 2 diabetes mellitus in sub-Saharan Africa has not been adequately assessed. The aim of this study was to determine the prevalence of low vitamin D level and secondary hyperparathyroidism and their association with insulin sensitivity and β-cell secretory function among Congolese type 2 diabetics. **Methodology:** Fasting glycaemia, fasting insulin, 25OH D3 and human parathyroid hormone (hPTH) were measured in one hundred and eighty-four type 2 diabetic patients followed as outpatients in South Kivu. Levels of 25OH D3 < 30 ng/ml and hPTH > 65 pg/ml defined low vitamin D and elevated parathyroid hormone levels, respectively. The HOMA model was used to measure insulin sensitivity and β-cell secretory function. **Results:** Medians (IQR) were 25.3 (20.4 - 32.4) ng/ml for 25OH D3 and 53.7 (38.4 - 115.7) pg/ml for hPTH. 58.7% of diabetics had insulin resistance, 126 (68.5%) had low vitamin D and 80 (43.5%) had hyperparathyroidism. In multivariate analysis, hPTH (partial r = −0.28; p = 0.0002) and 25OH D3 (partial r = 0.16; p = 0.03) showed an independent association with insulin sensitivity after adjustment for body mass index and waist circumference. Finally, hPTH (partial r = 0.27; p = 0.0002) was the sole determinant of β-cell secre-

tory function. **Conclusions:** This study confirms the high prevalence of low vitamin D level and secondary hyperparathyroidism and their association with insulin resistance and impaired islet β-cell secretory function among Congolese with type 2 diabetes mellitus. Vitamin D and calcium supplementation should be envisaged for cases of deficiency in this region.

Keywords

Vitamin D, Parathyroid Hormone, Diabetes Mellitus, Insulin Resistance, South Kivu

1. Introduction

Type 2 diabetes mellitus (T2DM) and vitamin D deficiency (VDD) are two major global public health problems. On the one hand, T2DM prevalence, whose major determinants are ageing and obesity, is growing very rapidly, with 537 million diabetics at present. It is estimated that there will be 643 million diabetics by 2030 and 783 million by 2045 [1].

In addition, almost half of the world's population has VDD [2]. Low vitamin D level varies according to ethnicity, geographical location, exposure to sunlight, age, obesity and certain cultural and dietary habits [3].

These two major global public health problems appear to be associated. In fact, several studies show that low vitamin D level contributes to the pathogenesis of T2DM [4] [5]. In fact, there is a positive correlation between prohormone cholecalciferol (25-hydroxyvitamin D or 25OH D3) concentration and insulin sensitivity, as well as impaired β-cell secretory function associated with low vitamin D level [6]. Secondary hyperparathyroidism is a physiological response to low vitamin D and/or hypocalcaemia in phosphocalcic homeostasis. Thus, a high prevalence of low vitamin D level drives an equally high prevalence of secondary hyperparathyroidism. Hyperparathyroidism also contributes to insulin resistance, promoting incident T2DM by pathophysiological mechanisms complementary to those of low vitamin D level [7] [8].

Sub-Saharan Africa, despite its tropical location and high level of sunshine, shows a prevalence of VDD almost the same as Europe [9]. Also in this region, the common form obesity-related insulin-resistant T2DM is increasing rapidly and gradually replacing the lean atypical form of the disease, marked by hyperinsulinaemia followed by early insulinopenia with or without insulin resistance [10]. This epidemiological shift is driven by adoption of unhealthy lifestyles by the general population, particularly in urban areas [11]. Yet, very few studies have investigated the possible contribution of VDD to the phenotypic shift of T2DM in this region. Karau P.B. *et al.* showed a high prevalence VDD among 60.3% of African diabetic patients in Kenya [12]. Also in Kenya, Said J *et al.* did not find associations between insulin sensitivity, β-cell secretion and vitamin D in diabetic patients [13]. He X *et al.*, in China, showed that low vitamin D levels were signifi-

cantly associated with episodes of ketoacidosis in patients with atypical DM [14].

In the Democratic Republic of Congo (DRC), the prevalence of VDD and secondary hyperparathyroidism among diabetic patients and their association with T2DM phenotype have not yet been studied to our knowledge.

The aim of this study was to determine the prevalence of low vitamin D level among adult Congolese patients with T2DM and to assess the association between vitamin D and parathyroid hormone levels, on the one hand, and insulin sensitivity and β-cell secretory function, on the other hand.

2. Methods

2.1. Patients

The methodology of this study was partly described in a previous manuscript [15]. This cross-sectional, multicentre study took place in the city of Bukavu (urban area) at the Panzi general referral hospital, the University Clinics of Bukavu and the Saint Luc Clinic of Bukavu, as well as in the rural area of Kaziba, 45 km south of Bukavu, at Kaziba general referral hospital. Between 1 July 2023 and 30 September 2023, T2DM patients, all of Bantu origin, were recruited as they attended one of the above hospitals for an outpatient medical visit. Given a prevalence of DM in the region of 5% [16] and a precision of 4%, a minimum sample size was estimated at 114.

Informed verbal consent to participate in the study was obtained from each patient. The data were collected anonymously and confidentially. Patient privacy and confidentiality and human material were ensured as per the Helsinki Declaration.

Non-diabetic patients, diabetic patients on insulin therapy and/or with stage > 3 chronic kidney disease (CKD) and/or those with insulin sensitivity between 50 and 99%) were excluded from the study, as were patients with primary hyperparathyroidism or non-vitamin D-related secondary hyperparathyroidism (**Figure 1**).

The study protocol was approved by the Ethics Committee of the Official University of Bukavu (UOB/CEM/013/2023).

2.2. Data Collection

Each patient was seen in consultation by a doctor from the investigation team. During the consultation, demographic parameters (age, sex), physical parameters (blood pressure, weight, height, waist circumference (WC) at the umbilicus at the end of expiration using a tape measure) and the medical history of DM (duration, treatment) were obtained. These physical parameters were measured in accordance with the recommendations of scientific societies. Body mass index (BMI) was calculated as the ratio of weight (in kilograms) to the square of height (in meter).

Each patient was subsequently sent to the laboratory for a morning fasting blood sample, with the following tests carried out: fasting glycaemia, serum creatinemia, albuminemia, total cholesterol, high-density lipoprotein cholesterol

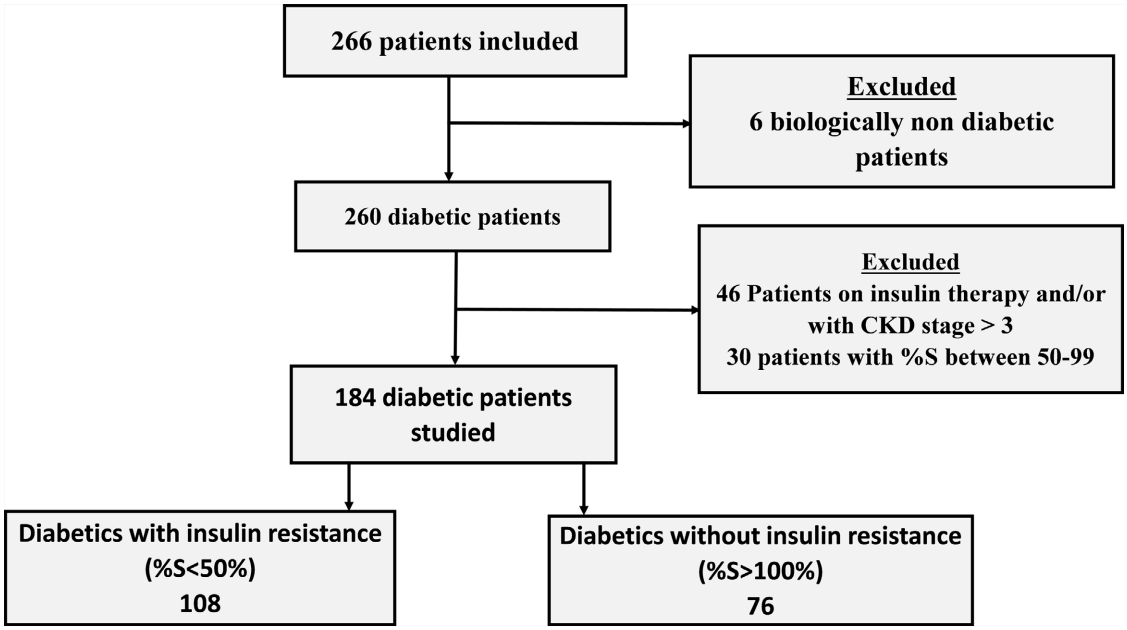


Figure 1. Eligible participants.

(HDL-C) and triglycerides were measured using UV visible spectrophotometry. Low-density lipoprotein cholesterol (LDL-C) was calculated using Friedewald's formula. To do this, we used the Bio Systems BTS-350® spectrophotometer.

Glycated haemoglobin (HbA1c) and serum ionogram were measured on specific automated instruments Genrui PA54® and Genrui GE300® respectively.

With the Product Elisa Plate Analyser®, fasting insulin levels (Ins), 25OH D3 and human parathyroid hormone (hPTH) were measured using an immunochemical method.

The HOMA model, presented as a software program based on fasting glucose/insulin regulatory loop, was used to measure insulin sensitivity (HOMA S, expressed as % of normal (100%)) and β-cell secretory function (HOMA β, also expressed as % of normal (100%)).

2.3. Operational Definitions

DM was defined as fasting glycaemia > 126 mg/dl on several occasions and/or HbA1c > 6.5% and/or chronic use of a glucose-lowering drug [17].

A BMI ≥ 30 kg/m^2 defined obesity [18]. A waist circumference ≥ 80 cm in women and ≥94 cm in men defined central obesity [19].

Low vitamin D was considered to be present when 25OH D3 was <30 ng/ml [20].

Hyperparathyroidism was considered when the hPHT value was >65 pg/ml (laboratory reference).

Hypocalcaemia was defined as less than 2.2 mmol/L (laboratory reference).

In the present study, insulin resistance was considered when Homa-S < 50%. Diabetes with normal insulin sensitivity was defined as Homa-S values ≥ 100% [21].

2.4. Statistical Analysis

The distribution of the variables was tested for normality using the Kolmogorov-Smirnov test. Thus, the data are presented, as appropriate, by the median (interquartile range) or the relative frequency in percent. The Chi-square test was used to compare categorical variables.

The non-parametric Kruskal-Wallis test was used to compare several medians.

The association between insulin sensibility and β-cell secretory function respectively according to the alleged risk factors was modelled with multiple linear regressions.

A p-value < 0.05 was considered statistically significant.

MedCalc® version 18.11 software was used for all statistical analyses.

3. Results

3.1. General Characteristics of the Study Population

Table 1 and Figure 1 show the general characteristics of the patients studied. A total of 184 type 2 diabetics were included in the study, 108 (58.7%) of whom were insulin-resistant and 76 (41.3%) without insulin resistance (p = 0.01*). In the whole group, median age was 63.0 (54.2 - 71.0) years, 46.2% of patients were male, and median known T2DM duration was 3.0 (0.0 - 7.0) years.

In both groups, there were no significant (p > 0.05) differences as regards duration of diabetes, age, male sex, systolic blood pressure (SBP), diastolic blood pressure (DBP), routine lipids, estimated glomerular filtration rate (GFR) and metabolic control of DM as reflected by current HbA1c.

Compared with diabetics without insulin resistance, insulin-resistant diabetics had a significantly higher median BMI [27.2 (23.3 - 31.2) Kg/m^2 vs. 22.6 (19.4 - 28.5) Kg/m^2; p = 0.0001*] and WC [94.0 (83.2 - 103.0) cm vs. 83.0 (74.0 - 97.9) cm; p = 0.0002*] and hence a significantly higher incidence of obesity (35.5% vs. 20.3%; p = 0.02*) and central obesity (66.4% vs. 46.7%; p = 0.008*).

3.2. Prevalence of Low Vitamin D Level and Hyperparathyroidism

In the whole group, the median 25OH D3 was 25.3 (20.4 - 32.4) ng/ml, confirming widespread among this sampled population of T2DM patients from South Kivu (Table 1). Median 25OH D3 was significantly lower (about −15%) among insulin-resistant diabetics than in diabetics without insulin resistance [23.8 (19.3 - 31.2) ng/ml vs. 28.1 (22.6 - 39.5) ng/ml; p = 0.002*], whereas the prevalence of low vitamin D level was 68.5%, with no significant difference between the two groups (73.1% vs. 61.8%; p = 0.10) (Table 1).

The prevalence of biological hyperparathyroidism was 43.5%, significantly higher in insulin-resistant diabetics than in diabetics without insulin resistance (60.2% vs. 19.7%; p < 0.0001*) (Table 1).

Figure 2 shows that median 25OH D3 decreased significantly with hPTH tertiles, from 27.6 (22.1 - 39.1) pg/ml to 23.8 (18.0 - 31.2) pg/ml (p = 0.04*). Finally, Hb A1c was similar between patients with VDD and those without VDD: 7.1

Table 1. General characteristics of the patients studied.

	All diabetics	Diabetics with IR	Diabetics without IR	p
Number, n (%)	184 (100.0)	108 (58.7)	76 (41.3)	0.01*
Male sex, n (%)	85 (46.2)	49 (45.4)	36 (47.4)	0.78
Median (IQR)				
DM duration (years)	3.0 (0.0 - 7.0)	2.0 (0.0 - 6.0)	4.0 (0.0 - 8.0)	0.08
Age (years)	63.0 (54.2 - 71.0)	62.0 (54.5 - 70.0)	64.0 (54.2 - 73.0)	0.53
SBP (mmHg)	133.5 (123.0 - 151.0)	134.0 (123.2 - 147.0)	133.0 (120.0 - 159.0)	0.63
DBP (mmHg)	82.0 (74.0 - 92.0)	81.0 (73.2 - 90.0)	84.0 (76.0 - 96.0)	0.10
BMI (Kg/m^2)	25.8 (21.4 - 30.8)	27.2 (23.3 - 31.2)	22.6 (19.4 - 28.5)	0.0001*
WC (cm)	91.2 (78.0 - 101.0)	94.0 (83.2 - 103.0)	83.0 (74.0 - 97.9)	0.0002*
TC (mg/dl)	208.4 (162.1 - 208.4)	196.9 (162.1 - 208.4)	208.4 (162.1 - 208.4)	0.70
HDL-C (mg/dl)	73.3 (50.1 - 81.0)	73.3 (51.2 - 81.0)	73.3 (48.2 - 84.9)	0.87
LDL-C (mg/dl)	110.3 (93.0 - 158.3)	108.1 (96.0 - 158.3)	114.9 (92.6 - 150.5)	0.95
TG (mg/dl)	141.5 (104.3 - 212.3)	141.5 (106.1 - 203.5)	146.0 (97.3 - 212.3)	0.52
Creatinemia (mg/dl)	1.2 (0.9 - 1.4)	1.2 (0.9 - 1.4)	1.1 (0.9 - 1.4)	0.19
FGR ($ml/min/1.73m^2$)	53.0 (43.0 - 72.5)	52.0 (42.5 - 72.0)	53.0 (44.5 - 74.5)	0.51
Glycaemia (mg/dl)	130.0 (114.5 - 202.0)	139.5 (117.5 - 243.0)	124.0 (111.5 - 159.0)	0.01*
Hb A1c (%)	7.2 (5.8 - 9.7)	7.1 (5.7 - 9.8)	7.5 (5.8 - 9.6)	0.95
Ins (µU/ml)	15.9 (5.2 - 27.9)	24.8 (18.6 - 36.0)	5.1 (2.8 - 5.7)	<0.0001*
%B (%)	53.1 (30.3 - 113.7)	97.8 (43.7 - 148.5)	35.1 (17.9 - 47.3)	<0.0001*
%S (%)	36.6 (20.7 - 129.1)	23.3 (13.7 - 32.1)	134.9 (119.7 - 183.5)	<0.0001*
25OH D3 (ng/ml)	25.3 (20.4 - 32.4)	23.8 (19.3 - 31.2)	28.1 (22.6 - 39.5)	0.002*
hPTH (pg/ml)	53.7 (38.4 - 115.7)	75.6 (45.0 - 121.0)	40.1 (33.8 - 61.5)	<0.0001*
Total calcemia (mmol/L)	2.3 (2.2 - 2.4)	2.3 (2.2 - 2.4)	2.3 (2.1 - 2.5)	0.58
Frequency, n (%)				
25OH D3 < 30 ng/ml	126 (68.5)	79 (73.1)	47 (61.8)	0.10
hPTH > 65 pg/ml	80 (43.5)	65 (60.2)	15 (19.7)	<0.0001*
Total calcemia < 2.20 mmol/L	43 (23.4)	22 (20.4)	21 (27.6)	0.25
Obesity	53 (29.3)	38 (35.5)	15 (20.3)	0.02*
Waist obesity	106 (58.2)	71 (66.4)	35 (46.7)	0.008*

IR: Insulin resistance, IQR: interquartile range, DM: Diabetes mellitus, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, BMI: Body mass index, WC: Waist circumference, TC: Total cholesterol, HDL-C: High density lipoprotein cholesterol, LDL-C: Low density lipoprotein cholesterol, TG: triglyceride, FGR: Filtration glomerular rate, Hb A1c: Glycated haemoglobin, Ins: Insulin, %β: islet β-cell secretory function, %S: insulin sensitivity, 25OH D3: 25-hydroxyvitamin D3, hPTH: Human parathyroid hormone.

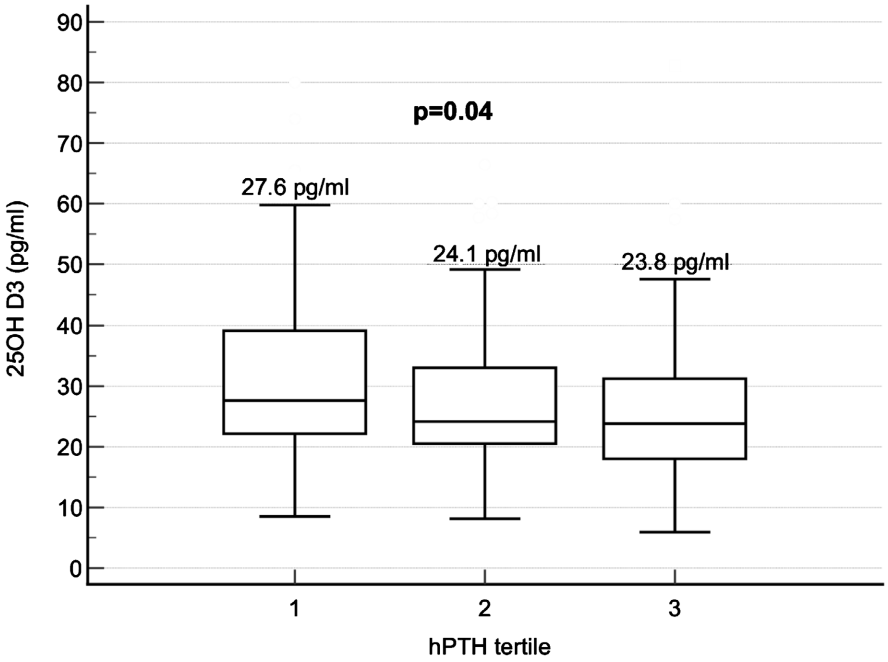


Figure 2. Relationship between 25OH D3 and hPTH.

(5.7 - 9.7) % vs. 7.4 (6.3 - 9.9) % (p = 0.33).

3.3. Vitamin D and Parathyroid Hormone in the Prediction of Insulin Sensitivity

Table 2, Table 3 and Figure 3 show the results of univariate and multivariate linear regressions of insulin sensitivity and β-cell secretory function by respective risk factors.

In univariate analysis (Table 2), the following parameters were significantly associated with insulin sensitivity: hPTH (r = 0.33; p < 0.0001*), BMI (r = 0.26; p = 0.0003*), WC (r = 0.24; p = 0.0004*) and 25OH D3 level (r = 0.17; p = 0.01*).

In multivariate analysis (Table 3), the sole independent predictors of insulin sensitivity were hPTH (partial r = −0.28; p = 0.0002*) and 25OH D3 (partial r = 0.16; p = 0.03*).

3.4. Vitamin D and Parathyroid Hormone in the Prediction of β-Cell Secretory Function

In univariate analysis (Table 2 and Figure 3), the following parameters were associated with β-cell secretory function: hPTH (r = 0.28; p = 0.0001*), BMI (r = 0.14; p = 0.04*) and WC (r = 0.14; p = 0.04*). The association between 25OH D3 and β-cell secretory function was not significant (r = 0.10; p = 0.12).

In multivariate analysis (Table 3), only hPTH (partial r = 0.27; p = 0.0002*) showed an independent effect on β-cell secretory function.

4. Discussion

To our knowledge, the present study is the first to have analysed the association

Table 2. Univariate linear regression analysis of insulin sensibility (%S) and islet β-cell secretory function (%β) respectively according to the alleged risk factors.

	B coefficient	*Standard error*	*r*	*p*
Insulin sensitivity (%S)				
Age (years)	0.57	0.41	0.10	0.16
Male sex	2.02	9.59	0.001	0.82
BMI (Kg/m^2)	−2.78	0.75	0.26	0.0003*
WC (cm)	−1.12	0.31	0.24	0.0004*
25OH D3 (ng/ml)	0.86	0.35	0.17	0.01*
hPTH (pg/ml)	−0.46	0.09	0.33	<0.0001*
Calcemia (mmol/L)	49.2	19.8	0.17	0.01*
Islet β-cell secretory function (%β)				
Age (years)	−0.14	0.36	0.02	0.68
Male sex	1.38	8.49	0.01	0.87
BMI (Kg/m^2)	1.40	0.68	0.14	0.04*
WC (cm)	0.57	0.28	0.14	0.04*
25OH D3 (ng/ml)	−0.48	0.31	0.10	0.12
hPTH (pg/ml)	0.35	0.08	0.28	0.0001*
Total calcemia (mmol/L)	−13.2	17.8		0.45

BMI: Body mass index, WC: Waist circumference, 25OH D3: 25-hydroxyvitamin D3, hPTH: Human parathyroid hormone.

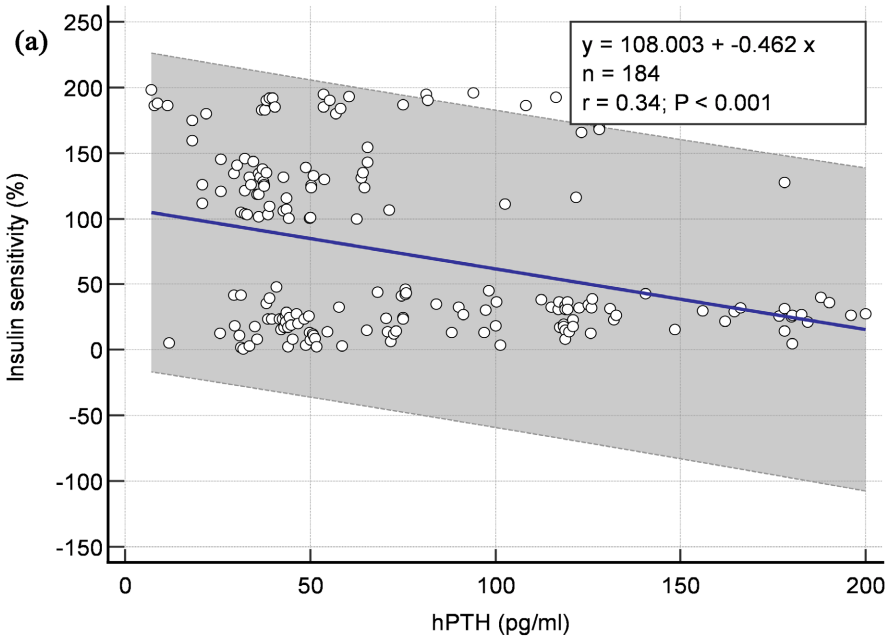
Table 3. Multivariate linear regression analysis of insulin sensibility (%S) and islet β-cell secretory function (%β) respectively according to the alleged risk factors.

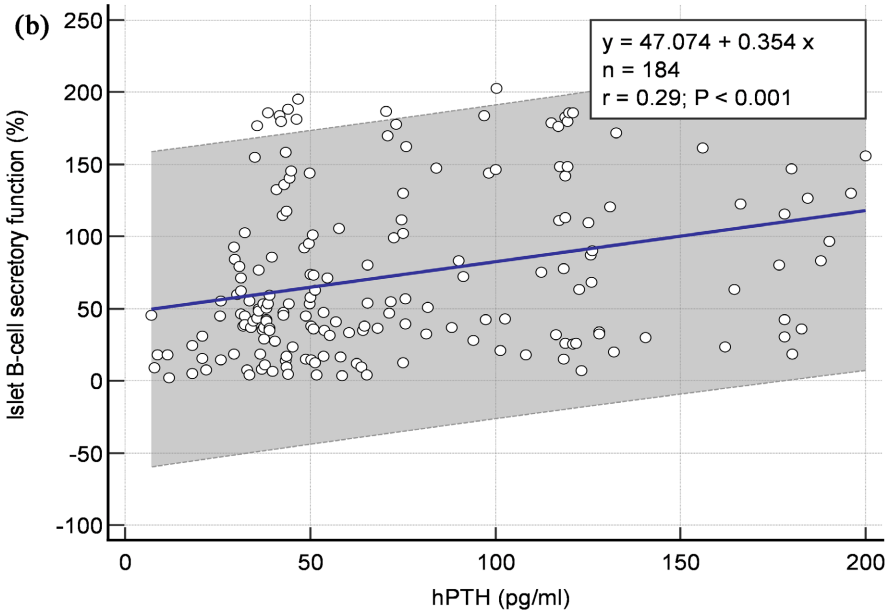
	B coefficient	*Standard error*	*Partial r*	*p*
Insulin sensitivity (%S)				
hPTH	−0.36	0.09	−0.28	0.0002*
250H D3	0.71	0.33	0.16	0.03*
Calcemia	32.7	18.5	0.13	0.07
BMC	−1.70	1.05	−0.12	0.10
WC	−0.34	0.43	−0.05	0.43
Islet β-cell secretory function (%β)				
hPTH (pg/ml)	0.33	0.08	0.27	0.0002*
BMI (Kg/m^2)	0.79	0.98	0.06	0.42
WC (cm)	0.14	0.40	0.02	0.72

BMI: Body mass index, WC: Waist circumference, 25OH D3: 25-hydroxyvitamin D3, hPTH: Human parathyroid hormone.

between vitamin D, parathyroid hormone and the metabolic phenotype of T2DM in the South Kivu Province of the DRC.

Our results highlight three main findings. Firstly, the prevalence of low vitamin D level was high among diabetic patients in South Kivu (68.5%). These results corroborate those of the literature, which reports a high frequency of low vitamin D level across sub-Saharan Africa, despite high levels of sunshine all year round [9]. These results are similar to those of Karau P.B. *et al.* who found a prevalence of low vitamin D level of 60.3% in T2DM patients from Kenya [12]. However, the prevalences of low vitamin D level in South Kivu and Kenya mentioned above are still much lower than those found in Morocco (98.1%) [22], Iraq (89.0%) [23], Korea (85.9%) [24], Italy (75.4%) [25] and the USA (75.0%),





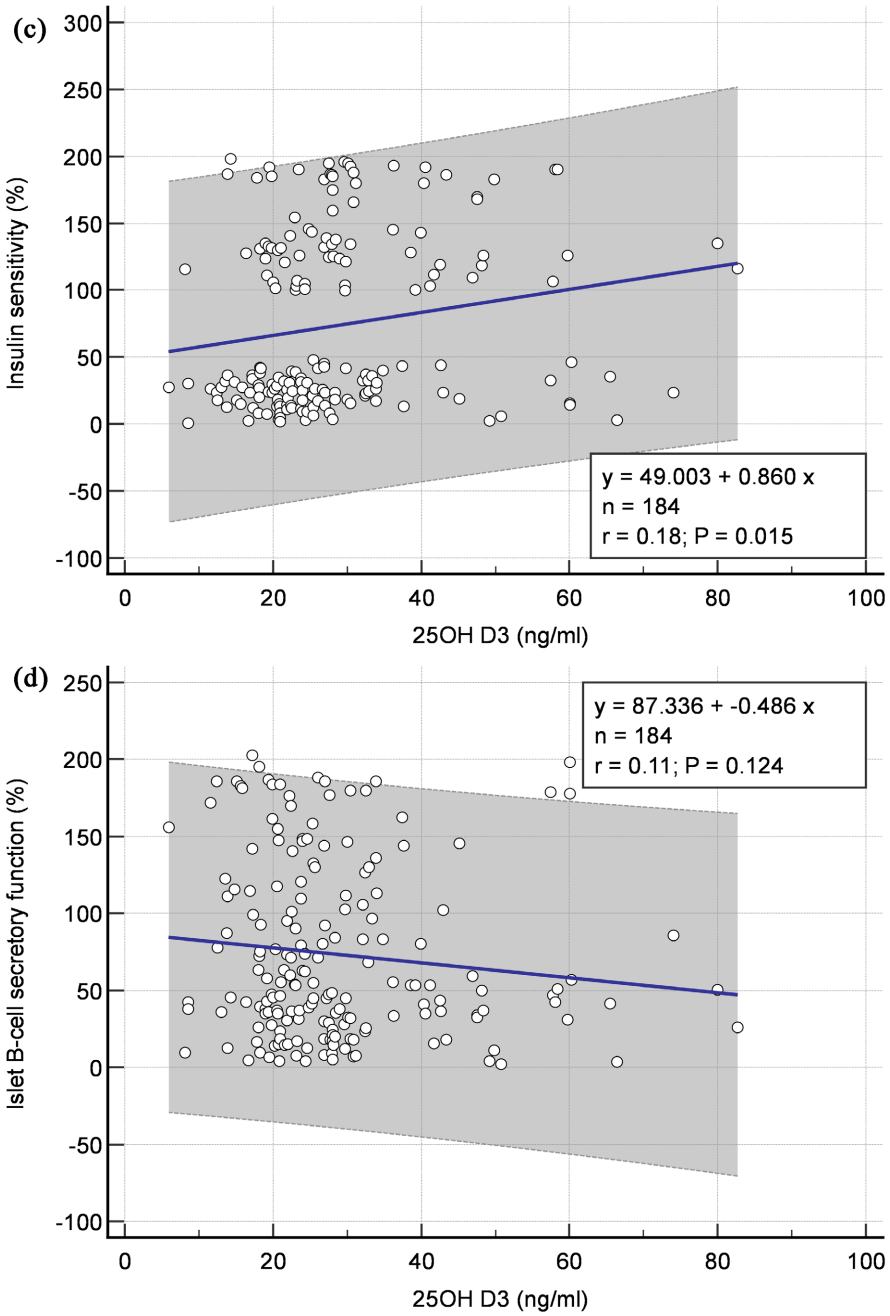


Figure 3. Scatter diagram correlation. (a) Linear regression analysis of insulin sensibility (%S) according to hPTH; (b) Linear regression analysis of islet β-cell secretory function (%β) according to hPTH; (c) Linear regression analysis of insulin sensibility (%S) according to 25OH D3; (d) Linear regression analysis of islet β-cell secretory function (%β) according 25OH D3.

respectively [26].

Secondary hyperparathyroidism is a normal physiological response to low vitamin D level. As expected, a negative correlation was found between vitamin D and parathyroid hormone, and 43.5% of diabetic patients of the present study presented with hyperparathyroidism. Secondary hyperparathyroidism is a nor-

mal physiological response to low vitamin D level.

Bellan M *et al.*, in Italy, found a prevalence of secondary hyperparathyroidism of 50.8% among T2DM, 95.0% of whom had low vitamin D level [27]. These results corroborate our own.

Secondly, this study showed that low vitamin D level and hyperparathyroidism were independent predictors of insulin resistance after adjustment for body mass index and waist circumference. These results corroborate those reported in the literature. Low vitamin D level and primary or secondary hyperparathyroidism independently reduce insulin sensitivity by different pathophysiological mechanisms. Low vitamin D level reduces insulin receptor expression and glucose uptake by glucose transporter type 4 (GLUT-4) [28]. In contrast, reduced expressions of insulin receptor substrate 1 (IRS-1) and GLUT4 may underlie the association between elevated PTH levels and insulin resistance [29].

In the present study, body mass index and waist circumference did not show an independent effect on insulin resistance after adjustment for vitamin D and hPTH. This suggests that a substantial component of obesity-induced insulin resistance may be related to low vitamin D level and secondary hyperparathyroidism. Obesity may also drive low vitamin D level, as a result of accumulation of this fat-soluble hormone in adipose tissue [30]. In addition, low vitamin D level could promote low-grade inflammation [31], which is another driver of insulin resistance in obese subjects.

A third finding of this study was the positive correlation between hPTH level and β-cell secretory function. These results corroborate those of Ljunghall *et al.* who showed elevated insulin secretion thought to be linked to hyperglycaemia in patients with primary hyperparathyroidism prior to parathyroidectomy, This higher secretory capacity decreased significantly post-operatively [8]. The correlation between vitamin D and β-cell secretory function was not significant ($p = 0.10$). However, vitamin D may play a role in islet β-cell function via secondary hyperparathyroidism. But in this study, the clinical relevance of such a link is poor as HbA1c was not different between VDD patients and those without VDD.

Finally, these results suggest systematic screening for VDD in Congolese diabetic patients and supplementation with vitamin D and calcium in cases of deficiency. Indeed, several studies have shown an improvement in insulin sensitivity and secretion in diabetic patients supplemented with vitamin D in cases of deficiency [4] [32].

VDD varies according to ethnicity, geographical location, exposure to sunlight, age, obesity and certain cultural and dietary habits [3]. However, it was not the aim of this study to identify risk factors for VDD, and data must be interpreted in light of its limitations. Firstly, the methodology and transversal design does not allow a causal link to be established between low vitamin D level, hyperparathyroidism, insulin sensitivity and β-cell secretory function. In addition, the relatively small sample size certainly decreased the statistical power in this study,

which may probably explain the lack of a significant association between obesity/insulin resistance and vitamin D/β-cell secretory function, respectively. Finally, the effects on these same endpoints of vitamin D supplementation in patients with VDD should be the subject of dedicated studies. In addition, prospective studies with a very large sample would provide more valid results.

5. Conclusion

The present study found a high prevalence of low vitamin D level and secondary hyperparathyroidism among type 2 diabetic patients of South Kivu in the Eastern Democratic Republic of Congo. Vitamin D and parathyroid hormone levels were independently linked to insulin resistance, while parathyroid hormone was the sole determinant associated with β-cell secretory function. Vitamin D and calcium supplementation through suitable diet and medication could be envisaged, as elsewhere, for vitamin-deficient patients in this region.

Acknowledgements

This research was partially funded under the Seed Grant for new African Principal Investigator (SG-NAPI Award for 2021: SG-NAPI No. 4500454048) hosted by world Academy of Science (TWAS) and the German Federal Ministry of Education and Research (BMBF).

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Magliano, D.J., Boyko, E.J. and IDF Diabetes Atlas 10th Edition Scientific Committee (2021) IDF Diabetes Atlas [Internet]. 10th Edition, International Diabetes Federation, Brussels.

[2] Amrein, K., Scherkl, M., Hoffmann, M., Neuwersch-Sommeregger, S., Köstenberger, M., Tmava Berisha, A., *et al.* (2020) Vitamin D Deficiency 2.0: An Update on the Current Status Worldwide. *European Journal of Clinical Nutrition*, **74**, 1498-1513. https://doi.org/10.1038/s41430-020-0558-y

[3] Cashman, K.D. (2020) Vitamin D Deficiency: Defining, Prevalence, Causes, and Strategies of Addressing. *Calcified Tissue International*, **106**, 14-29. https://doi.org/10.1007/s00223-019-00559-4

[4] Lips, P., Eekhoff, M., Van Schoor, N., Oosterwerff, M., De Jongh, R., Krul-Poel, Y., *et al.* (2017) Vitamin D and Type 2 Diabetes. *The Journal of Steroid Biochemistry and Molecular Biology*, **173**, 280-285. https://doi.org/10.1016/j.jsbmb.2016.11.021

[5] Sacerdote, A., Dave, P., Lokshin, V. and Bahtiyar, G. (2019) Type 2 Diabetes Mellitus, Insulin Resistance, and Vitamin D. *Current Diabetes Reports*, **19**, Article No. 101. https://doi.org/10.1007/s11892-019-1201-y

[6] Abugoukh, T.M., Al Sharaby, A., Elshaikh, A.O., Joda, M., Madni, A., Ahmed, I., *et al.* (2022) Does Vitamin D Have a Role in Diabetes? *Cureus*, **14**, E30432. https://doi.org/10.7759/cureus.30432

[7] Barnett, M.J. (2023) Association between Primary Hyperparathyroidism and Secondary Diabetes Mellitus: Findings from a Scoping Review. *Cureus*, **15**, E40743. https://doi.org/10.7759/cureus.40743

[8] Ljunghall, S., Palmér, M., Akerström, G. and Wide, L. (1983) Diabetes Mellitus, Glucose Tolerance and Insulin Response to Glucose in Patients with Primary Hyperparathyroidism before and after Parathyroidectomy. *European Journal of Clinical Investigation*, **13**, 373-377. https://doi.org/10.1111/j.1365-2362.1983.tb00116.x

[9] Mogire, R.M., Mutua, A., Kimita, W., Kamau, A., Bejon, P., Pettifor, J.M., *et al.* (2020) Prevalence of Vitamin D Deficiency in Africa: A Systematic Review and Meta-Analysis. *The Lancet Global Health*, **8**, E134-E142. https://doi.org/10.1016/S2214-109X(19)30457-7

[10] Goedecke, J.H. and Mendham, A.E. (2022) Pathophysiology of Type 2 Diabetes in Sub-Saharan Africans. *Diabetologia*, **65**, 1967-1980. https://doi.org/10.1007/s00125-022-05795-2

[11] Santosa, A., Wall, S., Fottrell, E., Högberg, U. and Byass, P. (2014) The Development and Experience of Epidemiological Transition Theory over Four Decades: A Systematic Review. *Global Health Action*, **7**, Article No. 23574. https://doi.org/10.3402/gha.v7.23574

[12] Karau, P.B., Kirna, B., Amayo, E., Joshi, M., Ngare, S. and Muriira, G. (2019) The Prevalence of Vitamin D Deficiency among Patients with Type 2 Diabetes Seen at a Referral Hospital in Kenya. *The Pan African Medical Journal*, **34**, Article No. 38. https://doi.org/10.11604/pamj.2019.34.38.18936

[13] Said, J., Lagat, D., Kimaina, A. and Oduor, C. (2021) Beta Cell Function, Insulin Resistance and Vitamin D Status among Type 2 Diabetes Patients in Western Kenya. *Scientific Reports*, **11**, Article No. 4084. https://doi.org/10.1038/s41598-021-83302-0

[14] He, X., Luo, Y., Hao, J., Wang, C., Gan, K., Zhen, Y., *et al.* (2022) Association between Serum Vitamin D Levels and Ketosis Episodes in Hospitalized Patients with Newly Diagnosed Ketosis-Prone Type 2 Diabetes. *Diabetes, Metabolic Syndrome and Obesity*, **15**, 3821-3829. https://doi.org/10.2147/DMSO.S389609

[15] Bihehe, D.M., Bwihangane, A.B., Mbo, J.-P.M., Muhindo, C.T., Hermans, M. and Katchunga, P.B. (2024) Dynamics in the Prevalence of Insulin Resistance between 2005 and 2023 in Type 2 Diabetics in South Kivu in the East of the Democratic Republic of Congo: Cross-Sectional Studies. *Journal of Diabetes Mellitus*, **14**, 28-40. https://doi.org/10.4236/jdm.2024.141004

[16] Katchunga, P., Masumbuko, B., Belma, M., Kashongwe Munogolo, Z., Hermans, M.P. and M'Buyamba-Kabangu, J.R. (2012) Age and Living in an Urban Environment Are Major Determinants of Diabetes among South Kivu Congolese Adults. *Diabetes & Metabolism*, **38**, 324-331. https://doi.org/10.1016/j.diabet.2012.02.008

[17] American Diabetes Association (2022) Standards of Medical Care in Diabetes-2022. *Diabetes Care*, **45**, S1-S2. https://doi.org/10.2337/dc22-Sint

[18] Alberti, K.G., Zimmet, P., Shaw, J. and IDF Epidemiology Task Force Consensus Group (2005) The Metabolic Syndrome: A New Worldwide Definition. *The Lancet*, **366**, 1059-1062. https://doi.org/10.1016/S0140-6736(05)67402-8

[19] Alberti, G., Eckel, R., Grundy, S., Zimmet, P., Cleeman, J., Donato, K., *et al.* (2009) Harmonizing the Metabolic Syndrome. A Joint Interim Statement of the I.D.F Task Force on Epidemiology and Prevention, NHL and Blood Institute, AHA, WHF, IAS, and IA For the Study of Obesity. *Circulation*, **120**, 1640-1645. https://doi.org/10.1161/CIRCULATIONAHA.109.192644

[20] Holick, M.F., Binkley, N.C., Bischoff-Ferrari, H.A., Gordon, C.M., Hanley, D.A.,

Heaney, R.P., *et al.* (2011) Evaluation, Treatment, and Prevention of Vitamin D Deficiency: An Endocrine Society Clinical Practice Guideline. *The Journal of Clinical Endocrinology & Metabolism*, **96**, 1911-1930. https://doi.org/10.1210/jc.2011-0385

[21] Hermans, M.P. (2007) Diabetic Macro- and Micro Vascular Disease in Type 2 Diabetes. *Diabetes and Vascular Disease Research*, **4**, S7-S11. https://doi.org/10.3132/dvdr.2007.019

[22] Safi, S. and Ouleghzal, H. (2015) Serum Vitamin D Status in Moroccan Patients with Type 2 Diabetes Mellitus. *Medecine des Maladies Metaboliques*, **9**, 67-72. https://doi.org/10.1016/S1957-2557(15)30018-3

[23] Al-Timimi, D.J. and Ali, A.F. (2013) Serum 25(OH) D in Diabetes Mellitus Type 2: Relation to Glycaemic Control. *Journal of Clinical and Diagnostic Research*, **7**, 2686-2688. https://doi.org/10.7860/JCDR/2013/6712.3733

[24] Lee, J.I., Oh, S.J., Ha, W.C., Kwon, H.S., Sohn, T.S., Son, H.S., *et al.* (2012) Serum 25-Hydroxyvitamin D Concentration and Arterial Stiffness among Type 2 Diabetes. *Diabetes Research and Clinical Practice*, **95**, 42-47. https://doi.org/10.1016/j.diabres.2011.09.006

[25] Zoppini, G. and Galletti, A. (2015) Lower Levels of 25-Hydroxyvitamin D3 Are Associated with a Higher Prevalence of Micro Vascular Complications in Patients with Type 2 Diabetes. *BMJ Open Diabetes Research & Care*, **3**, e000058. https://doi.org/10.1136/bmjdrc-2014-000058

[26] Kos, E., Liszek, M.J., Emanuele, M.A., Durazo-Arvizu, R. and Camacho, P. (2012) Effect of Metformin Therapy on Vitamin D and Vitamin B_{12} Levels in Patients with Type 2 Diabetes Mellitus. *Endocrine Practice*, **18**, 179-184. https://doi.org/10.4158/EP11009.OR

[27] Bellan, M., Guzzaloni, G., Rinaldi, M., Merlotti, E., Ferrari, C., Tagliaferri, A., *et al.* (2014) Altered Glucose Metabolism Rather than Naive Type 2 Diabetes Mellitus (T2DM) Is Related to Vitamin D Status in Severe Obesity. *Cardiovascular Diabetology*, **13**, Article No. 57. https://doi.org/10.1186/1475-2840-13-57

[28] Mitri, J. and Pittas, A.G. (2014) Vitamin D and Diabetes. *Endocrinology and Metabolism Clinics of North America*, **43**, 205-232. https://doi.org/10.1016/j.ecl.2013.09.010

[29] Chang, E., Donkin, S.S. and Teegarden, D. (2009) Parathyroid Hormone Suppresses Insulin Signaling in Adipocytes. *Molecular and Cellular Endocrinology*, **307**, 77-82. https://doi.org/10.1016/j.mce.2009.03.024

[30] Karampela, I., Sakelliou, A., Vallianou, N., Christodoulatos, G.S., Magkos, F. and Dalamaga, M. (2021) Vitamin D and Obesity: Current Evidence and Controversies. *Current Obesity Reports*, **10**, 162-180. https://doi.org/10.1007/s13679-021-00433-1

[31] Zhou, A. and Hyppönen, E. (2023) Vitamin D Deficiency and C-Reactive Protein: A Bidirectional Mendelian Randomization Study. *International Journal of Epidemiology*, **52**, 260-271. https://doi.org/10.1093/ije/dyac087

[32] Li, X., Liu, Y., Zheng, Y., Wang, P. and Zhang, Y. (2018) The Effect of Vitamin D Supplementation on Glycemic Control in Type 2 Diabetes Patients: A Systematic Review and Meta-Analysis. *Nutrients*, **10**, Article No. 375. https://doi.org/10.3390/nu10030375