Heliyon 10 (2024) e24926

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Research article

Exploring demographical, clinical, and dietary determinants of vitamin D deficiency among adults in Douala, Cameroon during the COVID-19 era

Arlette Flore Moguem Soubgui [a], Wilfried Steve Ndeme Mboussi [a,b], Loick Pradel Kojom Foko [b,c,*], Elisée Libert Embolo Enyegue [d], Martin Luther Koanga Mogtomo [a,b,**]

[a] *Department of Biochemistry, Faculty of Sciences, The University of Douala, Cameroon*
[b] *Centre de Recherche et d'Expertise en Biologie, Douala, Cameroon*
[c] *Department of Animal Organisms, Faculty of Science, The University of Douala, Cameroon*
[d] *Center for Research on Health and Priority Diseases, Ministry of Scientific Research and Innovation, Cameroon*

ARTICLE INFO

Keywords:
Vitamin D deficiency
Epidemiology
COVID-19
Cameroon

ABSTRACT

Background and aim: Vitamin D deficiency (VDD) is a global public health problem in African populations. This study aimed at determining the prevalence, characteristics, and determinants of VDD in the era of SARS-CoV-2/COVID-19. This study was conducted from January to September 2022 in seven health facilities in Douala, Cameroon.
Methods: A structured, pre-tested questionnaire was administered to each participant to collect participants' information. Molecular detection of the SARS-CoV-2 genome was done. A serum level of 25-hydroxyvitamin D < 20 ng/mL was used to diagnose VDD.
Results: A total of 420 participants were included in the study. A Serum levels of 25(OH) vitamin D were reduced in SARS-CoV-2 (+) patients as compared to SARS-CoV-2 (-) patients (21.69 ± 5.64 ng/mL *vs* 42.09 ± 20.03 ng/mL, $p < 0.0001$). The overall prevalence of VDD was 10.2 %. SARS-CoV-2 (+) individuals had nearly two times more risk of being VDD compared to SARS-CoV-2 (-) individuals (aRR = 1.81, $p < 0.0001$). The risk of VDD was reduced by 46 % and 71 % in those consuming cocoa bean or powder regularly (aRR = 0.54, $p = 0.03$) and rarely (aRR = 0.29, $p = 0.02$) as compared to those never consuming it. Likewise, the risk of VDD was reduced by 59 % and 78 % in those consuming sardine fish regularly (aRR = 0.47, $p = 0.002$) and rarely (aRR = 0.22, $p = 0.03$). Overall, the association between VDD and SARS-CoV-2 infection was consistent, i.e., reduced risk of VDD in SARS-CoV-2 (-) individuals, after stratification for confounding variables.
Conclusion: This study outlined a high burden of VDD, a strong link between VDD and SARS–CoV–2, and suggests the possible utility of vitamin D supplementation for COVID-19 patients in Cameroon.

---

[*] Corresponding author. Department of Biochemistry, Faculty of Science, The University of Douala, Cameroon.
[**] Corresponding author. Department of Biochemistry, Faculty of Sciences, The University of Douala, Cameroon.
E-mail addresses: kojomloick@gmail.com (L.P. Kojom Foko), koanga.martin@gmail.com, koanga@yahoo.com (M.L. Koanga Mogtomo).

https://doi.org/10.1016/j.heliyon.2024.e24926
Received 25 July 2023; Received in revised form 28 December 2023; Accepted 17 January 2024

1. Introduction

The coronavirus disease 2019 (COVID-19) has caused enormous losses of human lives in almost all regions of the globe. According to the latest data from the Johns Hopkins Coronavirus Resource Center as of March 10, 2023, this viral pandemic was responsible for ∼677 million cases and ∼6.9 million deaths (https://coronavirus.jhu.edu/map.html). COVID-19 is caused by severe acute respiratory syndrome Coronavirus 2 (SARS–CoV–2), a positive single-strand ribonucleic acid virus belonging to the Coronaviridae family [1].

Vitamin D is a fat-soluble vitamin and steroid hormone produced on the skin upon exposure to sunlight, with the effect of ultraviolet radiation, and also be obtained from exogenous food sources or dietary supplements (e.g., fish oil, egg yolks, mushrooms) [2,3]. Vitamin D is vital for optimal bone mineralization via its action on calcium and phosphorus homeostasis via an increase in the efficiency of the intestinal absorption of dietary calcium, a reduction in calcium losses in urine, and the mobilization of calcium stored in the skeleton [4]. It also has several roles in immunity, neuroprotection, and prevention against diseases such as cancer, type 2 diabetes, and cardiovascular diseases [4–6]. Vitamin D deficiency (VDD), also known as hypovitaminosis D, is a global public health problem, especially in children and pregnant women, who are the most vulnerable groups at risk of deleterious health effects and deaths [7,8]. Vitamin D plays a central role in immune function and defense against infections through upregulation of both innate and adaptive immune response effectors [9], and thus, some yet contradicting works have anticipated a possible association between vitamin D and the natural history of SARS–CoV–2 infection [10–16]. Indeed, these works investigated the clinical value of VDD in the prognostic, predictive, and diagnostic evaluation of SARS–CoV–2 infection outcomes such as infection, complications, hospitalization, and death. Again, there are still differing opinions and ongoing discussions in the scientific community regarding the benefits of vitamin D supplementation in COVID-19 [17–19].

Despite the growing number of studies on the association between vitamin D and SARS–CoV–2, there is still a need for more investigations, especially in African settings such as Cameroon, where COVID-19 has also had enormous health and economic consequences. Since the report of the first case, COVID-19 has been responsible for ∼125,000 cases and ∼2000 deaths in Cameroon as of November 2, 2023 (https://covid19.who.int/region/afro/country/cm). It is crucial to replicate more studies to clearly understand the link between vitamin D and SARS–CoV–2. Here we determined the prevalence, patterns, and determinants of VDD in the era of COVID-19 and analyzed the association between vitamin D and SARS–CoV–2 in Cameroonian individuals visiting health facilities. The impact of demographical, biological, behavioral, and clinical characteristics of patients on the association between vitamin D and SARS–CoV–2 was also evaluated.

2. Materials and methods

2.1. Study design

In this hospital-based cross-sectional study, we determined the extent, characteristics, and determinants of VDD and its relation to SARS–CoV–2 in the context of the confounding role of the demographical, biological, behavioral, and clinical characteristics of patients.

The details of study sites, eligibility criteria, and procedures have been published elsewhere [20–22]. Briefly, 420 patients were recruited at seven health facilities in the town of Douala from January to September 2022. After signing an informed consent form, individual interviews lasting approximately 25 min each were performed using a structured questionnaire to collect demographical, biological, anthropometric, behavioral, and clinical characteristics. Nasopharyngeal samples were collected for molecular detection of SARS–CoV–2 based on retrotranscriptase quantitative polymerase chain reaction (RT-qPCR) analysis of the RdRp, E, et N genes using a DaAnGene® kit (DaAn Gene Co., Ltd, Guangzhou, Guangdong, China) as published earlier [20,21]. Briefly, the RT-qPCR was performed on an on a QuantStudio™ 7 real time thermocycler (Applied Biosystems, Massachusetts, USA). The cycling conditions used at each amplification run were as follows: reverse transcription (45 °C/15 s), followed by initial denaturation (95 °C/2 min), and 45 cycles of [denaturation (95 °C/15 s), annealing (60 °C/30 s), and extension (72 °C/60 s)]. The cycle threshold (Ct) value of RT-qPCR was used to determine viremia and classify patients (negative or positive) as per the manufacturer's instructions. Internal control was included in each amplification for control quality. SARS–CoV–2 was detected in 34 individuals. Blood samples were collected to determine vitamin D.

2.2. Sample size

Patients were recruited consecutively through a random sampling method to limit selection and information biases. The sample size was determined using Lorentz's formula $n = [Z^2 \times p \times (1 - p)]/d^2$, where n = the required sample size, Z = statistics for the desired confidence interval (Z = 1.96 for 95 % confidence level), d = accepted margin of error (d = 5 %), and p = prevalence of VDD in Cameroon. In the absence of recent prevalence studies on VDD in Cameroon, we used the pooled estimate of the VDD prevalence in Africa (17.31 %) [23]. Thus, the minimal sample size required for this study was $n = 219.9 \approx 220$ participants. In this study, a total of 420 patients were included in the study.

2.3. Questionnaire

A structured, pre-tested questionnaire was used to collect participants' personal information through 25-min individual interviews (Supplementary file 1). The first part of the questionnaire captured sociodemographic information (age, gender, marital status,

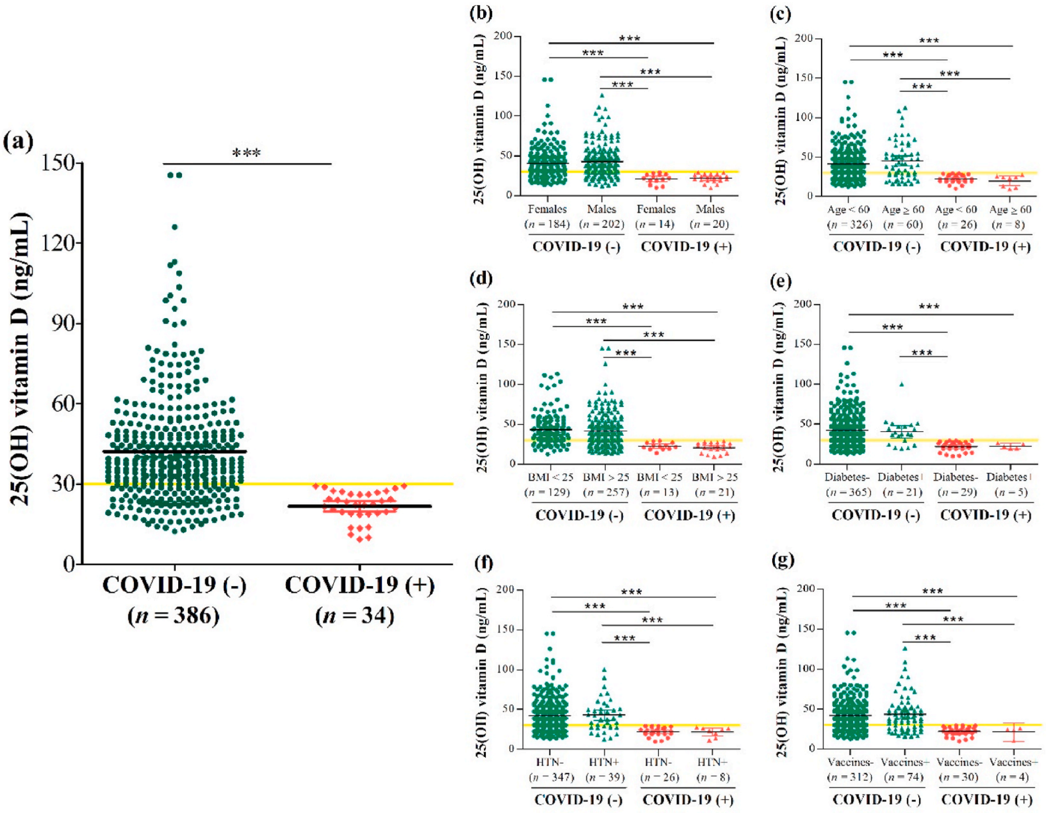

Fig. 1. Variation of vitamin D with regard to SARS-CoV-2 infection (a) and impact of gender (b), age (c), body mass index (d), diabetes (e), hypertension (f) and COVID-19 vaccination uptake (g). BMI: Body mass index, COVID-19: Coronavirus disease 2019, HTN: Hypertension The solid yellow line refers to the cut-off of vitamin D deficiency (<30 ng/mL) One-way analysis of variance (ANOVA) and Duncan's post hoc tests were used to perform pairwise comparisons between groups Statistically significant at $^{*}p < 0.05$, $^{**}p < 0.01$ and $^{***}p < 0.0001$.

educational level, occupation) and anthropometric parameters (weight, height). The second part was designed to document clinical information, including comorbidities (e.g., diabetes, hypertension) and healthcare-seeking behavior. The last part of the questionnaire was focused on participants' habits or practices related to appearance and dietary choices in relation to vitamin D. For instance, participants were asked about their mean sunlight exposure time, usage of brightening creams, and consumption of vitamin D-rich foods (e.g., fatty fish, chocolate, and mushroom) (Supplementary file 1).

2.4. Vitamin D determination

Blood samples were collected by venipuncture and centrifuged for 10 min at 2500 rpm. The resulting serum was used to determine levels of 25-hydroxyvitamin D by competitive ELISA using the colorimetric immunoassay Calbiotech 25(OH) Vitamin D kit (Calbiotech, El Cajon, USA). Analyses were performed on an URIT-660 ELISA microplate reader (PIOWAY, China). A level of 25-hydroxyvitamin D < 20 ng/mL was used to define VDD. Vitamin D was also categorized as insufficient (20–30 ng/mL), normal (30–70 ng/mL), excessive (70–100 ng/mL) and toxic (>100 ng/mL).

2.5. Ethical considerations

Ethical and administrative clearances were issued by the institutional review boards of the University of Douala (N° 2945 CEI-UDo/12/2021/T), Douala Laquintinie Hospital (N° 08179/AR/MINSANTE/DHL), and the Littoral Health Regional Delegation (N° 0038/AAR/MINSANTE/DRSPL/BCASS) (Supplementary file 2). All participants have received a full explanation of the study's objectives and signed an informed consent form before being included in the study.

2.6. Statistical analysis

Data were keyed, coded, and verified for consistency in an Excel spreadsheet (Microsoft Office, USA), and then exported to the statistical package for social sciences – SPSS v16 (SPSS IBM, Inc., Chicago, IL, USA), StatView v5.0 (SAS Institute, Chicago, Inc., IL,

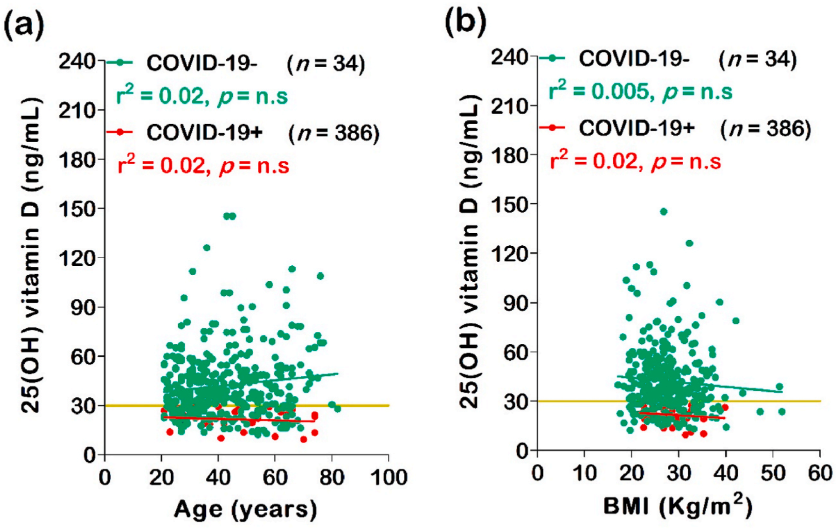

Fig. 2. Correlational analysis between vitamin D with age (a) and body mass index (b). BMI: Body mass index, COVID-19: Coronavirus disease 2019, ns: Not significant The solid yellow line refers to the cut-off of vitamin D deficiency (<30 ng/mL) Pearson correlation test was used r^2 is Pearson determination coefficient The level of statistical significance was set at $p < 0.05$.

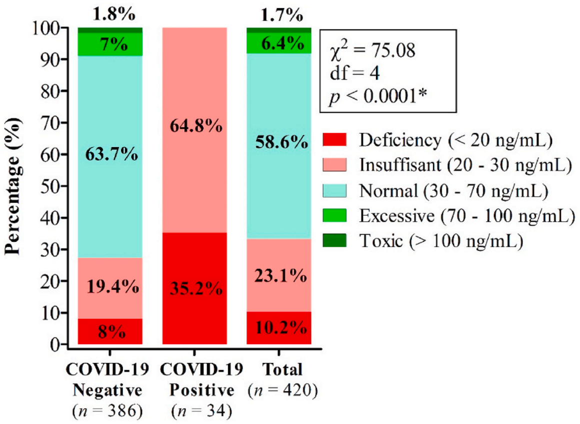

Fig. 3. Prevalence of vitamin D deficiency by SARS-CoV-2 infection. Pearson chi-square test was used to compare proportions χ^2: Decision variable to the chi-square test, COVID-19: Coronavirus disease 2019, df: Degree of freedom *Statistically significant at $p < 0.05$.

USA), and GraphPad v5.03 (GraphPad PRISM, San Diego, Inc., CA, USA) software for statistical analyses. The Kolmogorov-Smirnov test was used to evaluate the Gaussian distribution of quantitative variables. Continuous variables were presented as mean ± standard deviation (SD), while categorical variables were summarized as percentages with 95 % confidence intervals (95 %CI). Percentages were compared using Pearson's independence chi square and Fisher's exact tests. Analysis of variance (ANOVA), unpaired sample Student t, Kruskal-Wallis, and Mann-Whitney tests were used to compare mean values. Duncan's post hoc test was used to perform pairwise comparisons of mean values. Pearson correlation was used to analyze the link between vitamin D, age, and BMI. Univariate and multivariate logistic regression analysis were used to quantify the association between VDD and SARS–CoV–2 by computing the crude and adjusted values of the odds ratio (cOR and aOR), their 95 %CIs, and the level of statistical significance. The resulting cOR and aOR values were then converted into crude and adjusted risk ratios (RR) as proposed earlier [24]. A *p*-value <0.05 was considered statistically significant.

3. Results

3.1. *Variation of vitamin D level*

Mean serum levels of 25(OH) vitamin D (ng/mL) were significantly lower in SARS-CoV-2 (+) patients ($n = 34$) when compared to their SARS-CoV-2 (-) counterparts ($n = 386$) (21.69 ± 5.64 ng/mL *vs* 42.09 ± 20.03 ng/mL, $p < 0.0001$) (Fig. 1a). This pattern has

Table 1
Univariate logistic analysis of sociodemographic, clinical, esthetic and food behavior determinants of vitamin D deficiency among participants.

Variables	Categories	cOR (95 %CI)	cRR (95 %CI)	*p*-value
Sociodemographic characteristics				
Health facility	Bangue	1	1	
	Boko	3.02 (0.38–23.71)	3.31 (0.41–5.96)	0.29
	Bonassama	1.54 (0.59–4.00)	1.94 (0.62–2.87)	0.37
	Cité des Palmiers	1.11 (0.47–2.66)	1.43 (0.51–2.18)	0.8
	Deido	1.31 (0.36–4.71)	1.67 (0.39–3.17)	0.67
	New-Bell	2.95 (0.66–13.12)	3.26 (0.69–5.07)	0.15
	Nylon	2.49 (0.56–11.17)	2.89 (0.59–4.79)	0.23
Age (years)	<30	1	1	
	[30–40]	2.78 (0.93–8.31)	3.14 (0.94–4.57)	0.06
	[40–50]	1.28 (0.47–3.48)	1.58 (0.50–2.72)	0.62
	[50–60]	0.84 (0.32–2.22)	1.05 (0.35–1.95)	0.72
	[60–70]	0.52 (0.20–1.32)	0.66 (0.22–1.27)	0.16
	70+	0.95 (0.19–4.71)	1.19 (0.21–3.33)	0.94
Gender	Females	1	1	
	Males	1.64 (0.86–3.10)	2.03 (0.88–2.45)	0.13
Marital status	Single	1	1	
	Married	0.63 (0.32–1.25)	0.74 (0.34–1.23)	0.18
	Widow	0.33 (0.08–1.32)	0.39 (0.09–1.29)	0.11
Educational level	None	1	1	
	Secondary	0.93 (0.25–3.43)	1.18 (0.27–2.66)	0.91
	University	1.44 (0.40–5.19)	1.79 (0.43–3.45)	0.57
Occupation	Student	1	1	
	Formal sector	1.20 (0.43–3.31)	1.46 (0.46–2.69)	0.72
	Informal sector	0.58 (0.20–1.72)	0.71 (0.22–1.60)	0.32
Clinical characteristics				
Comorbidity	No	1	1	
	Yes	0.76 (0.40–1.44)	0.99 (0.43–1.36)	0.41
Obesity	No	1	1	
	Yes	0.84 (0.42–1.60)	1.02 (0.45–1.51)	0.63
Diabetes	No	1	1	
	Yes	0.63 (0.21–1.93)	0.77 (0.23–1.77)	0.42
Hypertension	No	1	1	
	Yes	0.51 (0.22–1.17)		0.11
Regularly seeking health care	No	1	1	
	Yes	0.41 (0.20–0.83)	0.47 (0.21–0.84)	**0.01**[a]
COVID-19	Negative	1	1	
	Positive	3.16 (1.07–5.35)	3.19 (1.08–5.07)	**<0.0001**[a]
Esthetic and food behavior characteristics				
Sunlight exposure time	<1 h	1	1	
	1–3 h	1.51 (0.76–3.02)	1.89 (0.78–2.40)	0.24
	>3 h	1.48 (0.60–3.70)	1.86 (0.63–2.75)	0.39
Usage of brightening creams	No	1	1	
	Yes	0.87 (0.25–3.02)	1.07 (0.27–2.50)	0.82
Dietary supplements	No	1	1	
	Yes	0.78 (0.37–1.65)	0.95 (0.39–1.55)	0.52
Egg yolk uptake	Never	1	1	
	Frequently	0.48 (0.11–2.15)	0.55 (0.12–2.00)	0.34
	Rarely	0.67 (0.15–3.04)	0.76 (0.16–2.69)	0.61
Calf liver uptake	No	1	1	
	Yes	0.57 (0.29–1.11)	0.68 (0.31–1.10)	0.09
Avocado uptake	Never	1	1	
	Frequently	1.89 (0.60–5.99)	2.41 (0.65–3.07)	0.27
	Rarely	3.11 (0.86–11.22)	3.09 (0.88–3.81)	0.08
Butter uptake	Never	1	1	
	Frequently	1.52 (0.72–3.21)	1.90 (0.75–2.50)	0.27
	Rarely	1.42 (0.65–3.10)	1.79 (0.68–2.44)	0.38
Fortified milk uptake	Never	1	1	
	Frequently	1.05 (0.49–2.25)	1.30 (0.52–1.98)	0.91
	Rarely	1.10 (0.45–2.72)	1.36 (0.48–2.30)	0.83
Dark chocolate uptake	Never	1	1	
	Frequently	1.11 (0.45–2.75)	1.32 (0.47–2.3)	0.81
	Rarely	0.68 (0.33–1.44)	0.82 (0.35–1.39)	0.32
Cocoa beans/powder uptake	Never	1	1	
	Frequently	0.65 (0.21–1.99)	0.78 (0.23–1.83)	0.45
	Rarely	0.58 (0.26–1.29)	0.70 (0.28–1.26)	0.18
Watermelon uptake	Never	1	1	
	Frequently	0.63 (0.25–1.59)	0.78 (0.27–1.50)	0.33

(*continued on next page*)

Table 1 (*continued*)

Variables	Categories	cOR (95 %CI)	cRR (95 %CI)	*p*-value
	Rarely	1.16 (0.58–2.32)	1.41 (0.61–2.04)	0.68
Mushroom uptake	Never	1	1	
	Frequently	2.58 (0.33–19.92)	2.96 (0.36–6.50)	0.36
	Rarely	1.12 (0.57–2.21)	1.38 (0.60–1.95)	0.74
Mackerel uptake	Never	1	1	
	Frequently	0.87 (0.19–3.92)	1.04 (0.20–3.13)	0.86
	Rarely	0.74 (0.16–3.51)	0.88 (0.17–2.88)	0.71
Sardine uptake	Never	1	1	
	Frequently	0.70 (0.27–1.82)	0.80 (0.28–1.73)	0.46
	Rarely	0.48 (0.20–1.17)	0.55 (0.21–1.16)	0.11
Tuna fish uptake	Never	1	1	
	Frequently	1.01 (0.33–3.06)	1.24 (0.35–2.52)	0.98
	Rarely	1.05 (0.50–2.19)	1.29 (0.53–1.95)	0.89
Tilapia uptake	Never	1	1	
	Frequently	0.78 (0.17–3.59)	0.97 (0.19–2.81)	0.75
	Rarely	1.65 (0.56–4.80)	1.99 (0.59–3.41)	0.36
Herring fish uptake	Never	1	1	
	Frequently	0.60 (0.17–2.16)	0.74 (0.19–1.93)	0.43
	Rarely	1.69 (0.22–13.15)	2.02 (0.24–5.90)	0.62
Salmon uptake	No	1	1	
	Yes	0.84 (0.28–2.52)	1.03 (0.30–2.18)	0.76
Sole uptake	Never	1	1	
	Frequently	1.54 (0.44–5.34)	1.88 (0.47–3.60)	0.49
	Rarely	1.19 (0.59–2.40)	1.39 (0.62–2.08)	0.62

Univariate logistic regression analysis was used to identify determinants of vitamin D deficiency among participants.
95 %CI: Confidence interval at 95 %, cOR: Crude odds ratio, cRR: Crude risk ratio, COVID-19: Coronavirus disease 2019.
[a] Statistically significant at $p < 0.05$.

remained constant even after subgrouping for the different modalities of variables such as gender, age, comorbidities, and COVID-19 vaccination uptake (Fig. 1b–g). For instance, mean value of 25(OH) vitamin D was significantly reduced in SARS-CoV-2 (+) males compared to SARS-CoV-2 (-) males (Fig. 1b). To be noted, levels of 25(OH) vitamin D were more reduced in SARS-CoV-2 (+) individuals presenting comorbidities when compared to SARS-CoV-2 (+) individuals without comorbidities (Fig. 1d–f). No significant correlation was found between vitamin D, participant's age, and BMI (Fig. 2a and b).

3.2. *Prevalence of vitamin D deficiency*

The overall prevalence of VDD was 10.2 % in the study. Additional vitamin D-related disorders have been found among participants, and these included insufficiency (23.1 %), excess (6.4 %), and toxicity (1.7 %) (Fig. 3). In addition, statistically significant variation was found in the prevalence of these disorders with regard to SARS-CoV-2 infection, with higher rates of VDD seen in SARS-CoV-2 (+) individuals (35.2 % *vs.* 8 %, $p < 0.0001$).

No significant association was found between VDD and sociodemographic information. In contrast, VDD was more frequently seen in patients regularly seeking healthcare (14.4 % *vs.* 6.4 %, $p = 0.01$) (Supplementary file 3). Likewise, no significant association was found between VDD and dietary or esthetic information, with the exception of calf liver uptake. Indeed, the prevalence of VDD was statistically higher in patients consuming calf liver rarely as compared to those consuming it frequently (0 %) (17.6 % *vs.* 0 %, Chi-square test, $p = 0.01$) (Supplementary file 4).

3.3. *Determinants of vitamin D deficiency*

Two determinants of VDD were identified based on univariate logistic analysis: SARS-CoV-2 infection, and frequency of healthcare seeking (Table 1). The risk of VDD was reduced by 53 % in patients regularly seeking healthcare compared to those not regularly seeking healthcare (cRR = 0.47, 95 %CI 0.21–0.84, $p = 0.01$). In contrast, the odds of VDD were more than three times higher in SARS-CoV-2 (+) individuals compared to SARS-CoV-2 (-) individuals (cRR = 3.19, 95 %CI 1.08–5.07, $p < 0.0001$) (Table 1). Furthermore, a one-unit increase in vitamin D was associated with a reduced SARS-CoV-2 (+) infection risk by 15 % (cRR = 0.85, 95 %CI 0.81–0.90, $p < 0.0001$).

Three determinants of VDD (SARS-CoV-2 infection, cocoa bean/powder uptake, and sardine fish uptake) were identified using the multivariate logistic regression analysis (Table 2). SARS-CoV-2 (+) individuals had nearly two times more risk of being VDD compared to SARS-CoV-2 (-) individuals (aRR = 1.81, 95 %CI 1.01–3.29, $p < 0.0001$). The risk of VDD was reduced by 46 % and 71 % in those consuming cocoa bean or powder regularly (aRR = 0.54, 95 %CI 0.09–0.95, $p = 0.03$) and rarely (aRR = 0.29, 95 %CI 0.08–0.85, $p = 0.02$) as compared to those never consuming it (Table 2). Likewise, the risk of VDD was reduced by 59 % and 78 % in those consuming sardine fish regularly (aRR = 0.47, 95 %CI 0.10–0.90, $p = 0.002$) and rarely (aRR = 0.22, 95 %CI 0.05–0.92, $p = 0.03$).

Table 2

Multivariate logistic analysis of sociodemographic, clinical, esthetic and food behavior determinants of vitamin D deficiency among participants.

Variables	Categories	aOR (95 %CI)	aRR (95 %CI)	*p*-value
Sociodemographic characteristics				
Health facility	Bangue	1	1	
	Boko	3.29 (0.27–39.47)	3.51 (0.44–3.61)	0.34
	Bonassama	1.14 (0.33–3.86)	1.47 (0.36–2.81)	0.84
	Cité des Palmiers	1.82 (0.48–6.94)	2.24 (0.52–3.90)	0.38
	Deido	2.80 (0.52–15.22)	3.15 (0.55–5.32)	0.23
	New-Bell	4.96 (0.63–39.28)	4.21 (0.66–6.53)	0.13
	Nylon	3.82 (0.52–28.07)	3.80 (0.55–6.17)	0.19
Age (years)	<30	1	1	
	[30–40[	3.86 (0.81–18.37)	3.44 (0.95–3.26)	0.09
	[40–50[	3.07 (0.60–15.76)	3.39 (0.63–5.94)	0.18
	[50–60[	1.81 (0.29–11.18)	2.18 (0.32–5.22)	0.52
	[60–70[	1.09 (0.16–7.41)	1.36 (0.1–4.31)	0.93
	70+	4.92 (0.22–108.27)	4.50 (0.24–8.32)	0.31
Gender	Females	1	1	
	Males	0.93 (0.33–2.64)	1.20 (0.36–2.19)	0.89
Marital status	Single	1	1	
	Married	0.91 (0.26–3.12)	1.06 (0.28–2.68)	0.88
	Widow	0.83 (0.07–9.65)	0.97 (0.08–5.79)	0.88
Educational level	None	1	1	
	Secondary	0.69 (0.08–5.99)	0.88 (0.09–3.75)	0.74
	University	0.99 (0.11–9.12)	1.26 (0.12–4.62)	0.99
Occupation	Student	1	1	
	Formal sector	0.83 (0.18–3.91)	1.02 (0.20–3.03)	0.81
	Informal sector	0.41 (0.06–2.81)	0.51 (0.07–2.38)	0.36
Clinical characteristics				
Comorbidity	No	1	1	
	Yes	3.46 (0.65–18.48)	3.60 (0.68–5.62)	0.15
Obesity	No	1	1	
	Yes	0.45 (0.09–2.30)	0.55 (0.10–2.04)	0.34
Diabetes	No	1	1	
	Yes	0.89 (0.15–5.33)	1.08 (0.15–3.74)	0.91
Hypertension	No	1	1	
	Yes	0.39 (0.09–1.74)	0.47 (0.10–1.63)	0.22
Regularly seeking health care	No	1	1	
	Yes	0.48 (0.18–1.30)	0.55 (0.19–1.28)	0.15
COVID-19	Negative	1	1	
	Positive	1.87 (1.02–3.27)	1.81 (1.01–3.29)	**0.0001***
Esthetic and food behavior characteristics				
Sunlight exposure time	<1 h	1	1	
	1–3 h	2.01 (0.78–5.14)	2.43 (0.80–3.36)	0.15
	>3 h	1.78 (0.49–6.43)	2.19 (0.52–3.79)	0.38
Usage of brightening creams	No	1	1	
	Yes	0.62 (0.12–3.18)	0.77 (0.13–2.60)	0.56
Dietary supplements	No	1	1	
	Yes	0.95 (0.30–2.97)	1.16 (0.32–2.49)	0.92
Egg yolk uptake	Never	1	1	
	Frequently	0.42 (0.05–3.59)	0.48 (0.05–3.09)	0.42
	Rarely	0.85 (0.10–7.01)	0.96 (0.11–5.08)	0.88
Calf liver uptake	No	1	1	
	Yes	0.53 (0.18–1.56)	0.64 (0.19–1.49)	0.25
Avocado uptake	Never	1	1	
	Frequently	3.33 (0.56–19.81)	3.15 (0.61–4.33)	0.19
	Rarely	4.90 (0.76–31.67)	3.22 (0.80–4.64)	0.09
Butter uptake	Never	1	1	
	Frequently	1.03 (0.31–3.45)	1.32 (0.34–2.63)	0.97
	Rarely	1.10 (0.32–3.81)	1.41 (0.35–2.80)	0.88
Fortified milk uptake	Never	1	1	
	Frequently	1.75 (0.55–5.61)	2.10 (0.58–3.76)	0.35
	Rarely	1.36 (0.37–5.05)	1.66 (0.40–3.52)	0.64
Dark chocolate uptake	Never	1	1	
	Frequently	0.73 (0.17–3.13)	0.91 (0.18–2.63)	0.67
	Rarely	0.70 (0.21–2.30)	0.84 (0.23–2.06)	0.55
Cocoa beans/powder uptake	Never	1	1	
	Frequently	0.45 (0.08–0.95)	0.54 (0.09–0.95)	**0.03***
	Rarely	0.24 (0.07–0.84)	0.29 (0.08–0.85)	**0.02***
Watermelon uptake	Never	1	1	
	Frequently	0.73 (0.14–3.69)	0.90 (0.15–2.90)	0.71

(*continued on next page*)

Table 2 (*continued*)

Variables	Categories	aOR (95 %CI)	aRR (95 %CI)	*p*-value
	Rarely	0.89 (0.31–2.57)	1.09 (0.33–2.22)	0.84
Mushroom uptake	Never	1	1	
	Frequently	2.04 (0.18–23.15)	2.42 (0.20–6.78)	0.57
	Rarely	2.44 (0.79–7.53)	2.82 (0.81–4.40)	0.12
Mackerel uptake	Never	1	1	
	Frequently	2.58 (0.22–30.63)	2.90 (0.23–9.03)	0.45
	Rarely	2.55 (0.22–29.67)	2.87 (0.23–8.95)	0.45
Sardine uptake	Never	1	1	
	Frequently	0.41 (0.09–0.89)	0.47 (0.10–0.90)	**0.002**[a]
	Rarely	0.22 (0.05–0.92)	0.25 (0.05–0.92)	**0.03**[a]
Tuna fish uptake	Never	1	1	
	Frequently	1.51 (0.28–8.13)	1.82 (0.30–4.67)	0.62
	Rarely	1.77 (0.55–5.67)	2.12 (0.58–3.82)	0.34
Tilapia uptake	Never	1	1	
	Frequently	0.36 (0.03–4.45)	0.45 (0.03–3.25)	0.42
	Rarely	2.23 (0.49–10.22)	2.61 (0.52–5.14)	0.31
Herring fish uptake	Never	1	1	
	Frequently	1.13 (0.18–7.25)	1.38 (0.20–4.44)	0.91
	Rarely	1.22 (0.06–27.10)	1.48 (0.07–7.45)	0.89
Salmon uptake	No	1	1	
	Yes	0.49 (0.08–2.91)	0.60 (0.09–2.44)	0.43
Sole uptake	Never	1	1	
	Frequently	3.20 (0.52–19.77)	3.49 (0.55–6.41)	0.21
	Rarely	1.21 (0.40–3.65)	1.50 (0.43–2.82)	0.74

Multivariate logistic regression was used to identify determinants of vitamin D deficiency 95 %CI: Confidence interval at 95 %, aOR: Adjusted odds ratio, aRR: Adjusted risk ratio, COVID-19: Coronavirus disease 2019.

[a] Statistically significant at $p < 0.05$.

3.4. Impact of patients' profile on association between vitamin D deficiency and COVID-19

The impact of patients' characteristics on the link between VDD and SARS-CoV-2 infection is summarized in Tables 3 and 4. Overall, the association between VDD and SARS-CoV-2 infection was consistent, i.e., reduced risk of VDD in SARS-CoV-2 (-) individuals, upon stratification for modalities of independent variables, with the exception of age, diabetes status, HTN status, occupation, marital status, and COVID-19 vaccination uptake. Indeed, a reduction in risk of VDD was only found in individuals aged <60 years (OR = 0.14, 95 %CI 0.06–0.34, $p < 0.0001$), non-diabetic (OR = 0.16, 95 %CI 0.07–0.39, $p < 0.0001$), not diagnosed with HTN (OR = 0.15, 95 %CI 0.06–0.38, $p < 0.0001$) and COVID-19 unvaccinated (OR = 0.13, 95 %CI 0.06–0.31, $p < 0.0001$) (Tables 3 and 4).

4. Discussion

Vitamin D deficiency is a major global health concern, especially in Africa, where studies on its burden, patterns, and relation to COVID–19 are still lacking. In this context, the present study was designed to determine the prevalence and patterns of VDD and its relation to COVID–19 among Cameroonian patients.

The prevalence of VDD was 10.2 % in this study, and this finding is lower than that reported in Pakistan (89.14 %), Spain (82 %), Nepal (55.9 %), Ghana (43.6 %), the USA (33 %), and more recently in Slovakia (54–82 %) and Lebanon (31.9 %) [25–30]. This is likely due to differences in the demographics and clinical status of the patients. For instance, in our study, patients were asymptomatic and mildly symptomatic, while patients recruited in these studies were hospitalized. In contrast, similar estimates were reported in Israel (13 %) [31].

The results from this study demonstrate an inverse relationship between circulating vitamin D levels and SARS–CoV–2 positivity in an African population. First, we reported significantly lower levels of vitamin D in SARS–CoV–2-infected patients compared to their SARS–CoV–2-uninfected counterparts. Second, the prevalence of vitamin D deficiency was higher in SARS–CoV–2-infected patients compared to that found in SARS–CoV–2-uninfected patients. Finally, the risk of vitamin D deficiency was nearly twice as high in SARS–CoV–2-infected patients. All these three findings taken together are consistent with the findings of the bulk of systematic reviews and meta-analyses of observational studies and randomized clinical trials, which outlined an increased risk of SARS–CoV–2 infection and/or complications in patients with low vitamin D levels [10,13,15,32–36], even though the link between VDD and SARS–CoV–2 associated mortality is still elusive [33,34]. Vitamin D plays a crucial role of immunomodulator through the improvement of components of the host's innate and adaptive immune response and downregulation of the SARS-CoV-2 associated inflammatory cascades [37,38]. Several mechanisms of action through which vitamin D exerts its anti-SARS–CoV–2 effects have been proposed. Indeed, vitamin D may block the production of angiotensin II by reducing the conversion of renin into angiotensin or inhibiting angiotensin-converting enzymes. The lack or absence of angiotensin II reduces the risk of apoptosis, vasoconstriction, and inflammation processes, which are involved in the pathogenesis of severe acute respiratory distress in COVID-19 infection [37,39].

Our findings also support those on the possible positive effect of vitamin D supplementation on poor outcomes of COVID–19 (i.e., infection, severity, mortality) [40,41]. Of note, a few studies reported no or an inconsistent relationship between vitamin D deficiency

Table 3
Impact of sociodemographic and clinical characteristics on association between vitamin D deficiency and SARS-CoV-2 infection.

Variables	cOR (95 %CI)	*p*-value	cOR (95 %CI)	*p*-value	cOR (95 %CI)	*p*-value
Gender	**Females**		**Males**			
RT-qPCR (+)	1		1			
RT-qPCR (-)	0.22 (0.07–0.72)	**<0.0001**[b]	0.11 (0.04–0.32)	**<0.0001**[b]		
Age (years)	**Age <60 years**		**Age ≥60 years**			
RT-qPCR (+)	1		1			
RT-qPCR (-)	0.14 (0.06–0.34)	**<0.0001**[b]	0.29 (0.06–1.45)	0.13		
Educational level[a]	**Primary**		**Secondary**		**University**	
RT-qPCR (+)	1		1		1	
RT-qPCR (-)	–	–	0.22 (0.07–0.68)	**0.008**[b]	0.15 (0.05–0.50)	**0.001**[b]
Marital status[a]	**Single**		**Married**		**Divorced/Widow**	
RT-qPCR (+)	1		1		1	
RT-qPCR (-)	0.18 (0.03–1.05)	0.05	0.18 (0.07–0.46)	**0.0004**[b]	–	–
Occupation	**Student**		**Formal sector**		**Informal sector**	
RT-qPCR (+)	1		1		1	
RT-qPCR (-)	0.29 (0.02–3.42)	0.32	0.16 (0.06–0.44)	**0.0004**[b]	0.11 (0.02–0.55)	**0.007**[b]
Comorbidity	**No**		**Yes**			
RT-qPCR (+)	1		1			
RT-qPCR (-)	0.12 (0.03–0.40)	**0.0007**[b]	0.20 (0.07–0.59)	**0.003**[b]		
Obesity	**No**		**Yes**			
RT-qPCR (+)	1		1			
RT-qPCR (-)	0.22 (0.08–0.57)	**0.002**[b]	0.08 (0.02–0.35)	**0.0007**[b]		
Diabetes	**No**		**Yes**			
RT-qPCR (+)	1		1			
RT-qPCR (-)	0.16 (0.07–0.39)	**<0.0001**[b]	0.15 (0.02–1.50)	0.11		
Hypertension	**No**		**Yes**			
RT-qPCR (+)	1		1			
RT-qPCR (-)	0.15 (0.06–0.38)	**<0.0001**[b]	0.25 (0.04–1.36)	0.11		
Regularly sick	**No**		**Yes**			
RT-qPCR (+)	1		1			
RT-qPCR (-)	0.04 (0.00–0.23)	**0.0006**[b]	0.29 (0.12–0.73)	**0.008**[b]		
COVID-19 vaccination	**No**		**Yes**			
RT-qPCR (+)	1		1			
RT-qPCR (-)	0.13 (0.06–0.31)	**<0.0001**[b]	0.42 (0.04–4.44)	0.47		

Univariate logistic regression analysis was used to evaluate the confounding role of participants' characteristics on relation between vitamin D deficiency and SARS-CoV-2 infection.

RT-qPCR: Retrotranscriptase quantitative polymerase chain reaction, 95 %CI: Confidence interval at 95 %, cOR: Crude odds ratio, cRR: Crude risk ratio.

[a] One modality of the variable was excluded from the analysis due to small sample size.

[b] Statistically significant at $p < 0.05$.

and COVID–19 related infection, intensive care unit admission, length of hospital stay, ventilator support requirement, and mortality [12,13,17,18,42–45]. Moreover, the benefit of vitamin D supplementation is still elusive in social groups such as children [38]. Differences in design, definitions used for vitamin D deficiency, methodological quality, and populations of individual studies included in these systematic reviews and meta-analyses could explain discrepancies in conclusions. Also, it was proposed that certain variations of the vitamin D binding protein, vitamin D receptor, or genes involved in the vitamin D metabolic pathway may modulate the COVID-19 susceptibility and severity outcomes [46]. The evidence on the association between such genetic variations and COVID-19 outcomes is still missing in Africa, especially in Cameroon. Finally, the authors' conflicts of interest may also be a great determinant of conclusions. For instance, Passini and colleagues pointed out a positive association between favorable conclusions about the positive effect of vitamin D supplementation on COVID–19 outcomes and the presence of conflicts of interest [47].

The important role of food habits, demographics, and comorbidities on the relation between vitamin D deficiency and COVID–19 outcomes was not analyzed in most of the above mentioned systematic reviews and meta-analyses. In the present study, we found a decreased risk of vitamin D deficiency in patients consuming cacao products and sardines either rarely or frequently, compared to those never consuming them. Similar findings were recently reported in the UK and Nepal [28,48]. Fishes such as sardines are known to have a high content of vitamin D [2,3].

Interestingly, the association between VDD and SARS–CoV–2 infection has remained strong even after stratification for food habits, demographics, and comorbidities. Indeed, the risk of VDD was decreased in SARS–CoV–2-uninfected patients, regardless of different categories of variables such as consumption of sardines, tuna, mushrooms, milk, and butter. In contrast, we found that the association between VDD and SARS–CoV–2 infection was modulated with regard to advanced age, no occupation, and matrimonial status. All biological functions, including digestive and immune systems, are impaired in elderly persons [49]. Thus, the risk of VDD and SARS–CoV–2 infection is higher in elderly persons, and this could explain the absence of a statistically significant association between VDD and SARS–CoV–2 infection among participants aged above 60 years enrolled in the present study. Similar findings were recently reported in Lebanon patients infected with SARS–CoV–2 [30]. Also, medications taken by elderly patients could explain our findings. Alzahrani and colleagues outlined a significant association between levels of vitamin D and the number of medications taken by Saudi

Table 4
Impact of food habits on association between vitamin D deficiency and SARS-CoV-2 infection.

Variables	cOR (95 %CI)	*p*-value	cOR (95 %CI)	*p*-value	cOR (95 %CI)	*p*-value
Dietary supplements	**No**		**Yes**			
RT-qPCR (+)	1		1			
RT-qPCR (-)	0.13 (0.05–0.33)	**<0.0001**[b]	0.29 (0.06–1.36)	0.29		
Calf liver uptake	**Never**		**Rarely**		**Frequently**	
RT-qPCR (+)	1		1		1	
RT-qPCR (-)	0.03 (0.00–1.05)	**0.005**[b]	0.16 (0.06–0.48)	**0.0009**[b]	0.12 (0.03–0.51)	**0.004**[b]
Calf liver uptake	**No**		**Yes**			
RT-qPCR (+)	1		1			
RT-qPCR (-)	0.15 (0.06–0.42)	**0.0003**[b]	0.20 (0.06–0.73)	**0.01**[b]		
Butter uptake	**Never**		**Rarely**		**Frequently**	
RT-qPCR (+)	1		1		1	
RT-qPCR (-)	0.24 (0.06–0.91)	**0.03**[b]	0.10 (0.03–0.40)	**0.001**[b]	0.16 (0.04–0.72)	**0.017**[b]
Conserved milk uptake	**Never**		**Rarely**		**Frequently**	
RT-qPCR (+)	1		1		1	
RT-qPCR (-)	0.05 (0.00–0.60)	**0.01**[b]	0.11 (0.02–0.57)	**0.009**[b]	0.21 (0.07–0.58)	**0.002**[b]
Dark chocolate uptake[a]	**Never**		**Rarely**		**Frequently**	
RT-qPCR (+)	1		1		1	
RT-qPCR (-)	0.10 (0.02–0.53)	**0.006**[b]	0.18 (0.07–0.49)	**0.0007**[b]	–	–
Mushroom uptake[a]	**Never**		**Rarely**		**Frequently**	
RT-qPCR (+)	1		1		1	
RT-qPCR (-)	0.17 (0.05–0.55)	**0.003**[b]	0.12 (0.04–0.40)	**0.0005**[b]	–	–
Watermelon uptake	**Never**		**Rarely**		**Frequently**	
RT-qPCR (+)	1		1		1	
RT-qPCR (-)	0.14 (0.05–0.45)	**0.0008**[b]	0.21 (0.06–0.7)	**0.01**[b]	0.07 (0.00–0.86)	**0.03**[b]
Mackerel uptake	**Never**		**Rarely**		**Frequently**	
RT-qPCR (+)	1		1		1	
RT-qPCR (-)	0.05 (0.00–1.53)	0.08	0.12 (0.03–0.52)	**0.004**[b]	0.20 (0.07–0.54)	**0.001**[b]
Sardine uptake	**Never**		**Rarely**		**Frequently**	
RT-qPCR (+)	1		1		1	
RT-qPCR (-)	0.09 (0.02–0.49)	**0.005**[b]	0.13 (0.04–0.39)	**0.0003**[b]	0.37 (0.07–0.64)	**0.024**[b]
Thon uptake[a]	**Never**		**Rarely**		**Frequently**	
RT-qPCR (+)	1		1		1	
RT-qPCR (-)	0.16 (0.06–0.44)	**0.0004**[b]	0.12 (0.03–0.47)	**0.002**[b]	–	–
Tilapia uptake[a]	**Never**		**Rarely**		**Frequently**	
RT-qPCR (+)	1		1		1	
RT-qPCR (-)	0.15 (0.06–0.34)	**0.0001**[b]	0.24 (0.02–2.81)	0.25	–	–
Sole uptake[a]	**Never**		**Rarely**		**Frequently**	
RT-qPCR (+)	1		1		1	
RT-qPCR (-)	0.16 (0.07–0.41)	**0.0001**[b]	0.14 (0.02–0.91)	**0.03**[b]	–	–

Univariate logistic regression analysis was used to evaluate the confounding role of participants' characteristics on relation between vitamin D deficiency and SARS-CoV-2 infection.
RT-qPCR: Retrotranscriptase quantitative polymerase chain reaction, 95 %CI: Confidence interval at 95 %, cOR: Crude odds ratio, cRR: Crude risk ratio.

[a] One modality of the variable was excluded from the analysis due to small sample size.

[b] Statistically significant at $p < 0.05$.

Arabia's elderly patients [50]. Besides, the absence of an association between vitamin D deficiency in students and single people could reflect health inequities, where poorer people, such as students, cannot afford vitamin D-rich and fortified foods [51].

This study should be interpreted in light of its limitations. The cross-sectional design of the study was not appropriate to determine the causal link between VDD and SARS-Cov-2 infection. Second, this study was conducted in Douala, and thus the findings are not generalizable to the whole Cameroonian population. Despite these limitations, this study provides an updated state-of-the-art on the VDD prevalence, its determinants, and its relation to SARS-Cov-2 infection in Cameroon.

5. Conclusion

Here we determined the prevalence, characteristics, and determinants of VDD in the era of COVID-19 in Douala, Cameroon. The overall prevalence of VDD was 10.2 % and was modulated by the sociodemographic, clinical, anthropometric, and behavioral characteristics of the patients. The prevalence of VDD was higher in SARS–CoV–2 infected patients compared to that found in SARS–CoV–2 uninfected patients. Mean serum levels of vitamin D were lower in SARS–CoV–2 infected patients compared to those found in their SARS–CoV–2 uninfected counterparts. Likewise, the proportions of patients with vitamin D insufficiency or deficiency were higher in SARS-CoV-2 (+) individuals. Infection with SARS–CoV–2 was a risk factor for VDD, while consumption of cocoa powder and sardine fish were protective factors against VDD. The association between VDD and SARS–CoV–2 infection remained strong even after stratification for participants' characteristics, with the exception of some parameters such as the patient's age, occupation, marital status, and comorbidities (hypertension and diabetes). This study outlined a high burden of VDD, a strong link between VDD and

SARS–CoV–2, and suggests the possible utility of vitamin D supplementation for COVID-19 patients in Cameroon.

Ethics statement

Ethical and administrative clearances were issued by the institutional review boards of the University of Douala (N° 2945 CEI-UDo/12/2021/T), Douala Laquintinie Hospital (N° 08179/AR/MINSANTE/DHL), and the Littoral Health Regional Delegation (N° 0038/AAR/MINSANTE/DRSPL/BCASS) (Supplementary file 2). All participants have received a full explanation of the study's objectives and signed an informed consent form before being included in the study.

Data availability statement

Any time, the corresponding author provides an additional resource upon reasonable request.

Funding statement

This study has received no external financial support.

CRediT authorship contribution statement

Arlette Flore Moguem Soubgui: Writing – original draft, Visualization, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Wilfried Steve Ndeme Mboussi:** Methodology, Investigation, Data curation. **Loick Pradel Kojom Foko:** Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Methodology, Formal analysis, Data curation. **Elisée Libert Embolo Enyegue:** Visualization, Validation, Investigation, Formal analysis, Data curation. **Martin Luther Koanga Mogtomo:** Writing – review & editing, Visualization, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The authors are grateful to patients having accepted to participate in the study. We also acknowledge support and technical assistance of managing authorities, medical doctors and staff of health facilities.

Abbreviations

95 %CI	Confidence interval at 95 %
ANOVA	Analysis of variance
aOR	Adjusted odds ratio
cOR	Crude odds ratio
aRR	Adjusted risk ratio
BMI	Body mass index
cRR	Crude risk ratio
COVID–19	Coronavirus disease 2019
df	Degree of freedom
HTN	Hypertension
RT-qPCR	Retrotranscriptase quantitative polymerase chain reaction
SARS–CoV–2	Severe acute respiratory syndrome coronavirus 2
SD	Standard deviation
VDD	Vitamin D deficiency

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e24926.

References

[1] S.H. Safiabadi Tali, J.J. LeBlance, J. Sadiq, Tools and techniques for severe acute respiratory syndrome, Clin. Microbiol. Rev. 34 (2021) e00228-20, https://doi.org/10.1128/CMR.00228-20.

[2] Z. Lu, T. Chen, A. Zhang, K. Persons, N. Kkohn, R. BerKowitz, S. Martinello, M. Holick, An evaluation of the vitamin D3 content in fish: is the vitamin D content adequate to satisfy the dietary requirement for vitamin D? J. Steroid Biochem. Mol. Biol. 103 (2007) 642–644, https://doi.org/10.1016/j.jsbmb.2006.12.010.An.

[3] U. Lehmann, H.R. Gjessing, F. Hirche, A. Mueller-Belecke, O.A. Gudbrandsen, P.M. Ueland, G. Mellgren, L. Lauritzen, H. Lindqvist, A.L. Hansen, A.T. Erkkilä, G. K. Pot, G.I. Stangl, J. Dierkes, Efficacy of fish intake on Vitamin D status: a meta-analysis of randomized controlled trials, Am. J. Clin. Nutr. 102 (2015) 837–847, https://doi.org/10.3945/ajcn.114.105395.

[4] J. Janoušek, V. Pilařová, K. Macáková, A. Nomura, J. Veiga-Matos, D.D. da Silva, F. Remião, L. Saso, K. Malá-Ládová, J. Malý, L. Nováková, P. Mladěnka, Vitamin D: sources, physiological role, biokinetics, deficiency, therapeutic use, toxicity, and overview of analytical methods for detection of vitamin D and its metabolites, Crit. Rev. Clin. Lab Sci. 59 (2022) 517–554, https://doi.org/10.1080/10408363.2022.2070595.

[5] E. Rebelos, N. Tentolouris, E. Jude, The role of vitamin D in health and disease: a narrative review on the mechanisms linking vitamin D with disease and the effects of supplementation, Drugs 83 (2023) 665–685, https://doi.org/10.1007/s40265-023-01875-8.

[6] T. Bin Chen, C.M. Chang, C.C. Yang, I.J. Tsai, C.Y. Wei, H.W. Yang, C.P. Yang, Neuroimmunological effect of vitamin D on neuropsychiatric long COVID syndrome: a review, Nutrients 15 (2023) 3802, https://doi.org/10.3390/nu15173802.

[7] De Regil, L. Maria, Palacios, Cristina, K. Lia Lombardo, PenaRosas, J. Pablo, Vitamin D supplementation for women during pregnancy, Cochrane Database Syst. Rev. 15 (2012) CD008873, https://doi.org/10.1002/14651858.CD008873.pub2.Vitamin.

[8] K. Amrein, M. Scherkl, M. Hoffmann, S. Neuwersch-Sommeregger, M. Köstenberger, A. Tmava Berisha, G. Martucci, S. Pilz, O. Malle, Vitamin D deficiency 2.0: an update on the current status worldwide, Eur. J. Clin. Nutr. 74 (2020) 1498–1513, https://doi.org/10.1038/s41430-020-0558-y.

[9] D.D. Bikle, Vitamin D regulation of immune function during covid-19, Rev. Endocr. Metab. Disord. 23 (2022) 279–285, https://doi.org/10.1007/s11154-021-09707-4.

[10] H.A. Dissanayake, N.L. de Silva, M. Sumanatilleke, S.D. de Silva, K.K. Kobawaka Gamage, S. Dematapitiya, P. Katulanda, Prognostic and therapeutic role of vitamin D in COVID-19: systematic review and meta-analysis, FEBS J. 287 (2020) 3693–3702.

[11] A. Bassatne, M. Basbous, M. Chakhtoura, O. El Zein, M. Rahme, G. El-Hajj Fuleihan, The link between COVID-19 and VItamin D (VIVID): a systematic review and meta-analysis, Metab. Clin. Exp. 119 (2021) 154753.

[12] Y. Hu, J.Y. Kung, A. Cave, H.L. Banh, Effects of vitamin D serum level on morbidity and mortality in patients with COVID-19: a systematic review and meta-Analysis, J. Pharm. Pharmaceut. Sci. 25 (2022) 84–92, https://doi.org/10.18433/jpps32590.

[13] M. Pereira, A. Dantas Damascena, L.M. Galvão Azevedo, T. de Almeida Oliveira, J. da Mota Santana, Vitamin D deficiency aggravates COVID-19: systematic review and meta-analysis, Crit. Rev. Food Sci. Nutr. 62 (2022) 1308–1316, https://doi.org/10.1080/10408398.2020.1841090.

[14] J.H. Bae, H.J. Choe, M.F. Holick, S. Lim, Association of vitamin D status with COVID-19 and its severity, Rev. Endocr. Metab. Disord. 23 (2022) 579–599, https://doi.org/10.1007/s11154-021-09705-6.

[15] L. Szarpak, Z. Rafique, A. Gasecka, F. Chirico, W. Gawel, J. Hernik, H. Kaminska, K.J. Filipiak, M.J. Jaguszewski, L. Szarpak, A systematic review and meta-analysis of effect of vitamin D levels on the incidence of COVID-19, Cardiol. J. 28 (2021) 647–654, https://doi.org/10.5603/CJ.a2021.0072.

[16] S.J. Gilani, M.N. Bin-Jumah, M.S. Nadeem, I. Kazmi, Vitamin D attenuates COVID-19 complications via modulation of proinflammatory cytokines, antiviral proteins, and autophagy, Expert Rev. Anti Infect. Ther. 20 (2022) 231–241, https://doi.org/10.1080/14787210.2021.1941871.

[17] A. Beran, M. Mhanna, O. Srour, H. Ayesh, J.M. Stewart, M. Hjouj, W. Khokher, A.S. Mhanna, D. Ghazaleh, Y. Khader, W. Sayeh, R. Assaly, Clinical significance of micronutrient supplements in patients with coronavirus disease 2019: a comprehensive systematic review and meta-analysis, Clin. Nutr. ESPEN. 48 (2022) 167–177, https://doi.org/10.1016/j.clnesp.2021.12.033.

[18] D. Rawat, A. Roy, S. Maitra, V. Shankar, P. Khanna, D.K. Baidya, Vitamin D supplementation and COVID-19 treatment: a systematic review and meta-analysis, Diabetes Metabol. Syndr. 15 (2021) 102189.

[19] F. Hadizadeh, Supplementation with vitamin D in the COVID-19 pandemic? Nutr. Rev. 79 (2021) 200–208, https://doi.org/10.1093/nutrit/nuaa081.

[20] A.F. Moguem Soubgui, E.L. Embolo Enyegue, L.P. Kojom Foko, W.S. Ndeme Mboussi, G. Deutou Hogoue, S.P. Mbougang, S.M. Sanda, I.U. Fotso Chidjou, V. F. Fotso, S.A. Nzogang Tchonet, C. Medi Sike, M.L. Koanga Mogtomo, Epidemiological situation of SARS-CoV-2 infection in Douala, the most populated and highly heterogeneous town of Cameroon: a post-vaccination update, Acta Trop. 241 (2023) 106864, https://doi.org/10.1016/j.actatropica.2023.106864.

[21] O. Loteri, A.F. Moguem Sobgui, L.P. Kojom Foko, W.S. Ndeme Mboussi, C. Medi Sike, E.L. Embolo Enyegue, M.L. Koanga Mogtomo, COVID-19 and comorbidities in Douala , Cameroon, Int. J. Trop. Dis. Heal. 43 (2022) 21–38, https://doi.org/10.9734/IJTDH/2022/v43i1730658.

[22] A.F. Moguem Soubgui, L.P. Kojom Foko, E.L. Embolo Enyegue, W.S. Ndeme Mboussi, J.P. Mbebi Enone, I. Ntatou Lemouchele, M.L. Koanga Mogtomo, Confounding role of comorbidities and COVID–19 vaccination uptake in clinical utility of hematological biomarkers in Cameroonian patients infected with SARS–CoV–2, IJID Reg 8 (2023) 129–136, https://doi.org/10.1016/j.ijregi.2023.08.003.

[23] R.M. Mogire, A. Mutua, W. Kimita, A. Kamau, P. Bejon, J.M. Pettifor, A. Adeyemo, T.N. Williams, S.H. Atkinson, Prevalence of vitamin D deficiency in Africa: a systematic review and meta-analysis, Lancet Global Health 8 (2020) e134–e142, https://doi.org/10.1016/S2214-109X(19)30457-7.

[24] J. Zhang, K.F. Yu, What's the relative risk? A method of correcting the odds ratio in cohort studies of common outcomes, JAMA 280 (1998) 1690–1691.

[25] D.O. Meltzer, T.J. Best, H. Zhang, T. Vokes, V. Arora, J. Solway, Association of vitamin D status and other clinical characteristics with COVID-19 test results, JAMA Netw. Open 3 (2020), https://doi.org/10.1001/jamanetworkopen.2020.19722.

[26] J.L. Hernández, D. Nan, M. Fernandez-Ayala, M. Garciá-Unzueta, M.A. Hernández-Hernández, M. López-Hoyos, P. Muñoz-Cacho, J.M. Olmos, M. Gutiérrez-Cuadra, J.J. Ruiz-Cubillán, J. Crespo, V.M. Martínez-Taboada, Vitamin D status in hospitalized patients with SARS-CoV-2 infection, J. Clin. Endocrinol. Metab. 106 (2021) E1343–E1353, https://doi.org/10.1210/clinem/dgaa733.

[27] S.A. Sakyi, M.H. Antwi, L. Ahenkorah Fondjo, E.F. Laing, R.K.D. Ephraim, A. Kwarteng, B. Amoani, S.C. Appiah, B. Oppong Afranie, S. Opoku, T.A. Buckman, Vitamin D deficiency is common in Ghana despite abundance of sunlight: a multicentre comparative cross-sectional study, J. Nutr. Metab. 2021 (2021) 9987141, https://doi.org/10.1155/2021/9987141.

[28] O. Sherchand, J.K. Baranwal, B. Gelal, Epidemiology and determinants of vitamin D deficiency in Eastern Nepal: a community-based, cross-sectional study, Internet J. Endocrinol. 2022 (2022), https://doi.org/10.1155/2022/1063163.

[29] J. Smaha, P. Jackuliak, M. Kužma, F. Max, N. Binkley, J. Payer, Vitamin D deficiency prevalence in hospitalized patients with COVID-19 significantly decreased during the pandemic in Slovakia from 2020 to 2022 which was associated with decreasing mortality, Nutrients 15 (2023) 1132, https://doi.org/10.3390/nu15051132.

[30] D. Harkous, N. Ghorayeb, M.H. Gannagé-Yared, Prevalence and predictors of vitamin D deficiency in Lebanon: 2016–2022, before and during the COVID-19 outbreak, Endocrine 25 (2023) 654–663, https://doi.org/10.1007/s12020-023-03483-8.

[31] E. Merzon, D. Tworowski, A. Gorohovski, S. Vinker, A. Golan Cohen, I. Green, M. Frenkel-Morgenstern, Low plasma 25(OH) vitamin D level is associated with increased risk of COVID-19 infection: an Israeli population-based study, FEBS J. 287 (2020) 3693–3702, https://doi.org/10.1111/febs.15495.

[32] M. Ben-Eltriki, R. Hopefl, J.M. Wright, S. Deb, Association between Vitamin D status and risk of developing severe COVID-19 infection: a meta-analysis of bbservational studies, J. Am. Coll. Nutr. 41 (2021) 679–689, https://doi.org/10.1080/07315724.2021.1951891.

[33] R. Ghasemian, A. Shamshirian, K. Heydari, M. Malekan, R. Alizadeh-Navaei, M.A. Ebrahimzadeh, M. Ebrahimi Warkiani, H. Jafarpour, S. Razavi Bazaz, A. Rezaei Shahmirzadi, M. Khodabandeh, B. Seyfari, A. Motamedzadeh, E. Dadgostar, M. Aalinezhad, M. Sedaghat, N. Razzaghi, B. Zarandi, A. Asadi, V. Yaghoubi Naei, R. Beheshti, A. Hessami, S. Azizi, A.R. Mohseni, D. Shamshirian, The role of vitamin D in the age of COVID-19: a systematic review and meta-analysis, Int. J. Clin. Pract. 75 (2021) 1–16, https://doi.org/10.1111/ijcp.14675.

[34] M.O. Kaya, E. Pamukcu, B. Yakar, The role of vitamin D deficiency on COVID-19: a systematic review and meta-Analysis of observational studies, Epidemiol. Health. 43 (2021) 1–15, https://doi.org/10.4178/epih.e2021074.

[35] F. Petrelli, A. Luciani, G. Perego, G. Dognini, P. Luigi, A. Ghidini, Therapeutic and prognostic role of vitamin D for COVID-19 infection : a systematic review and meta-analysis of 43 observational studies, J. Steroid Biochem. Mol. Biol. 211 (2021) 105883.

[36] A. Teshome, A. Adane, B. Girma, Z.A. Mekonnen, The impact of vitamin D level on COVID-19 infection: systematic review and meta-analysis, Front. Public Health 9 (2021) 624559, https://doi.org/10.3389/fpubh.2021.624559.

[37] S. Ashique, K. Gupta, G. Gupta, N. Mishra, S.K. Singh, S. Wadhwa, M. Gulati, H. Dureja, F. Zacconi, B.G. Oliver, K.R. Paudel, P.M. Hansbro, D.K. Chellappan, K. Dua, Vitamin D—a prominent immunomodulator to prevent COVID-19 infection, Int. J. Rheum. Dis. 26 (2023) 13–30, https://doi.org/10.1111/1756-185X.14477.

[38] M. Nicolae, C.M. Mihai, T. Chisnoiu, A.L. Balasa, C.E. Frecus, L. Mihai, V.V. Lupu, I. Ion, A.C. Pantazi, A. Nelson Twakor, A. Andrusca, C.S. Cambrea, I.A. Arghir, A. Lupu, O.C. Arghir, Immunomodulatory effects of vitamin D in respiratory tract infections and COVID-19 in children, Nutrients 15 (2023) 3430, https://doi.org/10.3390/nu15153430.

[39] V. Contreras-Bolívar, B. García-Fontana, C. García-Fontana, M. Muñoz-Torres, Vitamin D and COVID-19: where are we now? Postgrad. Med. 135 (2023) 195–207, https://doi.org/10.1080/00325481.2021.2017647.

[40] O. D`Ecclesiis, C. Gavioli, C. Martinoli, S. Raimondi, S. Chiocca, C. Miccolo, P. Bossi, D. Cortinovis, F. Chiaradonna, R. Palorini, F. Faciotti, F. Bellerba, S. Canova, C. Jemos, E.O. Salé, A. Gaeta, B. Zerbato, P. Gnagnarella, S. Gandini, Vitamin D and SARS-CoV2 infection, severity and mortality: a systematic review and meta-analysis, PLoS One 17 (2022) e0268396, https://doi.org/10.1371/journal.pone.0268396.

[41] S.R. Varikasuvu, B. Thangappazham, A. Vykunta, P. Duggina, M. Manne, H. Raj, S. Aloori, COVID-19 and vitamin D (Co-VIVID study): a systematic review and meta-analysis of randomized controlled trials, Expert Rev. Anti Infect. Ther. 20 (2022) 907–913, https://doi.org/10.1080/14787210.2022.2035217.

[42] A. Kazemi, V. Mohammadi, S.K. Aghababaee, M. Golzarand, C.C.T. Clark, S. Babajafari, Association of vitamin D status with SARS-CoV-2 infection or COVID-19 severity: a systematic review and meta-analysis, Adv. Nutr. 12 (2021) 1636–1658, https://doi.org/10.1093/advances/nmab012.

[43] M. Sayed, Z. Mahmoud, E. Amira, M.A. Mahmoud, A. Yehia, A. Alaa, S. Fassad, R. Elgendy, E. Adnan, A. Baset, H.A. Elsayed, Hospital and laboratory outcomes of patients with COVID - 19 who received vitamin D supplementation : a systematic review and meta - analysis of randomized controlled trials, Naunyn-Schmiedeberg's Arch. Pharmacol. (2023) 607–620, https://doi.org/10.1007/s00210-022-02360-x.

[44] C. Argano, R.M. Bocchio, G. Natoli, S. Scibetta, S. Corrao, Protective effect of vitamin D supplementation on COVID-19-related intensive care hospitalization and mortality : definitive evidence from meta-analysis and trial sequential analysis, Pharmaceuticals 16 (2023) 130.

[45] L. di Filippo, M. Uygur, M. Locatelli, F. Nannipieri, S. Frara, A. Giustina, Low vitamin D levels predict outcomes of COVID-19 in patients with both severe and non-severe disease at hospitalization, Endocrine 80 (2023) 669–683, https://doi.org/10.1007/s12020-023-03331-9.

[46] N. Charoenngam, A. Jaroenlapnopparat, S.K. Mettler, A. Grover, Genetic variations of the vitamin D metabolic pathway and COVID-19 susceptibility and severity: current understanding and existing evidence, Biomedicines 11 (2023), https://doi.org/10.3390/biomedicines11020400.

[47] C.S.M. Passini, M.B. Cavalcanti, S.A. Ribas, C.M.P. de Carvalho, C. Bocca, F. Lamarca, Conflict of interests in the scientific production on vitamin D and COVID-19: a scoping review, Front. Public Health 10 (2022) 821740, https://doi.org/10.3389/fpubh.2022.821740.

[48] J.P. Sutherland, A. Zhou, M.J. Leach, E. Hyppönen, Differences and determinants of vitamin D deficiency among UK biobank participants: a cross-ethnic and socioeconomic study, Clin. Nutr. 40 (2021) 3436–3447, https://doi.org/10.1016/j.clnu.2020.11.019.

[49] Y. Chen, S.L. Klein, B.T. Garibaldi, H. Li, C. Wu, N.M. Osevala, T. Li, J.B. Margolick, G. Pawelec, S.X. Leng, Aging in COVID-19: vulnerability, immunity and intervention, Ageing Res. Rev. 65 (2021) 101205.

[50] A.M. Alzahrani, L.S. Emam, M.S. Alsharif, A.Y. Hakami, S.S. Aga, Clinical identification of hypovitaminosis D among elderly attending primary care centre in Saudi Arabia, Biochem. Res. Int. 2022 (2022) 6341645, https://doi.org/10.1155/2022/6341645.

[51] A. Arabi, N. Chamoun, M.P. Nasrallah, H.M. Tamim, Vitamin D deficiency in Lebanese adults: prevalence and predictors from a cross-sectional community-based study, Internet J. Endocrinol. 2021 (2021) 3170129, https://doi.org/10.1155/2021/3170129.