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Prevalence and Factors Associated with Vitamin D Deficiency in Patients with COVID-19 in Parakou in 2021

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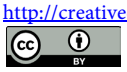

Abstract

Introduction: Coronavirus 19 disease (COVID-19) often presents several serious complications in patients. 25-hydroxyvitamin D [25(OH)D] deficiency is considered a risk factor for severe forms of the disease. **Objective:** The objective of this work was to determine the prevalence and factors associated with vitamin D deficiency in patients with COVID-19 in Parakou in 2021. **Methods:** The method used was a descriptive and analytical cross-sectional study with prospective data collection that covered the period of August 1, 2021, to December 30, 2021. It concerned patients with COVID-19, symptomatic or not, in the commune of Parakou, selected by non-probability sampling. The 25(OH)D assay was performed by an enzyme immunoassay using the heterogeneous phase competition technique. Logistic regression was used to determine the factors associated with 25(OH)D deficiency at the 5% threshold. **Results:** A total of 197 patients with COVID-19 were included in the study with a mean age of 35.4 ± 15.2 years; with a female predominance (52.3%). The overall prevalence of 25(OH)D deficiency was 31.5% (95% CI [25.1 - 38.5]); it was 32.0% in females and 30.8% in males. 25(OH)D deficiency was more observed in patients ≥ 60 years than in patients < 60 years with no significant difference ($p = 0.121$), and in females (32.0%) than in males (30.8%) with no significant difference either ($p = 0.857$). Diabetes ($p = 0.036$), overweight or obesity ($p = 0.032$), severe disease forms ($p = 0.003$) and rhinitis ($p = 0.009$) were significantly associated with 25(OH)D deficiency. Conclusion: One-third of patients with COVID-19 in Parakou in 2021 were 25(OH)D deficient. 25(OH)D deficiency is associated with the severe form of

the disease and with comorbidities justifying supplementation of this vitamin to patients with COVID-19.

Keywords

COVID-19, 25-OH-Vitamin D, Parakou

1. Introduction

The *Severe Acute Respiratory Syndrome Coronavirus* 2 (SARS-CoV-2) emerged in China in December 2019. It was first classified by the World Health Organisation (WHO) as a Public Health Emergency of International Concern (PHEIC), and then as a global health emergency or pandemic [1]. This epidemic has affected the whole world in different ways. As of April 6, 2023, the cumulative number of cases worldwide was 657,977,756 for 6,880,000 deaths. During the same period, Benin recorded 27,999 cases and 163 deaths [2]. The clinical features of COVID-19 can vary from no signs or even mild upper respiratory tract symptoms to severe acute lung injury with subsequent systemic inflammation, a multi-visceral failure and a fatal outcome [3]. Complications of the disease are often seen in people with low immunity and comorbidities. Several factors such as overweight or obesity, uncontrolled diabetes, stress, some kinds of chemotherapy and immunosuppressive drugs, advanced age, and vitamin D deficiency can decrease immunity [4] [5].

Vitamin D deficiency affects more than one billion people at all stages of life worldwide [6]. It occurs most in the elderly, smokers, obese individuals and patients with chronic diseases such as diabetes mellitus, hypertension, and various gastrointestinal diseases [7]. In the last decade, several studies have shown a potential link between vitamin D deficiency and various diseases, especially systemic infections [8]. In clinical studies, low serum vitamin D levels have been associated with acute respiratory tract infections, including COVID-19 [9]. Some recent reviews have assumed that vitamin D insufficiency may compromise respiratory immune function, increasing the risk of severity and mortality of COVID-19 [5] [10]. Radujkovic *et al.* [3] in Germany in a cohort study de- monstrated an association between 25-hydroxyvitamin D [25(OH)D] deficiency and the severity of COVID-19. Patients with 25(OH)D deficiency had a higher rate of hospitalisation; 22% of patients had 25(OH)D levels < 12 ng/mL and 64% had levels <20 ng/mL. 25(OH)D deficiency was associated with a 6-fold higher risk of severe disease progression and an approximately 15-fold higher risk of death.

In the Republic of Benin, in accordance with the therapeutic protocol in force, patients with COVID-19 systematically receive vitamin D supplementation regardless of the severity of the disease, without knowing their vitamin D status. The present study was initiated to explore serum vitamin D concentrations in patients with COVID-19, all clinical forms combined, in order to verify the con-

tribution of vitamin D deficiency to the occurrence of severe forms.

The objective of this study was to determine the prevalence, and factors associated with vitamin D deficiency in patients with COVID-19 in Parakou in 2021.

2. Materials and Methods

Study Framework

This study was conducted in the four health facilities in the Parakou-N'Dali zone that host the COVID-19 screening and management sites. These are the Army Training Hospital—University Hospital (HIA-CHU) of Parakou, the Departmental University Hospital of Borgou and Alibori (CHUD-B/A), the Zone Hospital of BOKO (HZB), and the Communal Health Centre (CS COM) of Parakou. The HIA-CHU of Parakou, housing the center for the management of patients with COVID-19, was used as a setting for the collection of data from hospitalized cases. The total 25(OH)D assay was performed at the biochemistry laboratory of CHUD-B/A.

Type and Period of Study

This was a cross-sectional, descriptive and analytical study with prospective data collection from August 1, 2021, to December 30, 2021.

Study Population

The study population consisted of symptomatic and non-symptomatic patients diagnosed as positive for COVID-19 by *reverse transcription polymerase chain reaction* (RT-PCR). Patients of all ages, regardless of sex, with RT-PCR confirmed COVID-19, in self-isolation or hospitalized at HIA-CHU Parakou, were included in the study and gave their free and informed written consent.

Sampling

A systematic census of all subjects with COVID-19 who met the inclusion criteria was made.

Variables

The dependent variable was the serum total 25(OH)D concentration in patients with COVID-19. This was a dichotomous variable scored as "deficiency" when the serum total 25(OH)D level was below 20 ng/mL; and "no deficiency" when the serum total 25(OH)D level was greater than or equal to 20 ng/mL. For reasons of interpretation, serum levels averaging between 20 ng/mL and 30 ng/mL were classified under the category "no deficiency".

The independent variables were socio-demographic data (sex, age, religion, ethnicity, nationality, marital status, occupation), anthropometric measures (weight, height, body mass index, waist circumference), lifestyle (smoking, alcohol consumption), co-morbidity variables (hypertension, diabetes, cancer, heart failure, renal failure, liver cirrhosis, sickle cell disease), clinical variables (clinical signs of COVID-19), and outcome variables (cure or death).

Data collection

Data were collected using a pre-established questionnaire over a period of five (5) months and targeted subjects tested positive for COVID-19 RT-PCR. The

questionnaire was based on clinical and paraclinical data observed on patients COVID-19 over the previous twelve months, as well as a review of the relevant literature. The interviewers who collected the data were fully vaccinated against COVID-19. To ensure the reliability of the results, the investigators were selected from among the specialists who were part of the teams involved in the management of COVID-19 patients. All these staff dedicated to the care of patients were quarantined in accommodations the government requisitioned. At the outset, the respondents were contacted to explain the aims of the study. The questionnaire was then completed by an individual interview, followed by anthropometric measurements and blood sampling. For patients whose condition prevented them from giving their consent, their parent's authorization was requested. It was the parents who helped to fill in certain parts of the questionnaire. Patients whose parents were unable to give consent were simply excluded from the study.

The equipment used to measure the parameters consisted of a height gauge, a bathroom scale, a flexible tape measure of 150 cm, a laser thermometer and a blood pressure device. The records of the hospitalised patients were used. Data were collected by direct interview to each included patient or to his/her legal representative when s/he was unable to answer the questions. Then the measurement of the parameters and a venous blood sample were taken for the determination of a total of 25(OH)D.

Determination of total 25(OH)D

Principle

The assay was performed using an immuno-enzymatic competitive method with final fluorescence detection. The sample and the pretreatment reagent were brought together to separate the vitamin D from its binding protein. The pretreated sample is taken and transferred to the well containing an alkaline phosphatase-labelled anti-vitamin D antibody (conjugate). The vitamin D antigen bound to the cone competes with the sites of the specific anti-vitamin D conjugate antibody. During the final revelation step, the substrate (4-methyl-umbellifer phosphate) is drawn into the cone and then returned; the enzyme in the conjugate catalyses the hydrolysis reaction of this substrate into a product (4-methyl-umbelliferone), the fluorescence of which is measured at 450 nm. The value of the fluorescence signal is inversely proportional to the concentration of antigen present in the sample. At the end of the test, the results are automatically calculated by the instrument with reference to a stored calibration curve and then printed.

Operating Mode

Using the instrument's external barcode reader, the VIDAS® PTC protocol data was read and stored in the instrument software for update. Calibration was carried out when each new batch of kits was opened and then every 28 days and a quality control check was carried out to ensure the integrity of the reagents. A VITD cartridge and a VITD cone were required for each sample. The total 25(OH)D assay was performed on the decanted sera, and the analysis steps were

managed automatically by the instrument. The results of the assay were obtained in approximately 40 minutes, expressed in ng/mL.

Once the data had been entered, it was checked for consistency and any input errors.

Data Analysis

Data analysis was done using SAS v9.4 (Anthony JAMES, 2020) and Excel (Microsoft, 2019). The explanatory variables retained after univariate analysis were tested for collinearity in order to eliminate those that were correlated. In the event of correlation, only one of these correlated variables was retained for further modelling, choosing the one with the most significant p-value.

Quantitative variables were expressed as mean and standard deviation. Qualitative variables were expressed as the number and percentage of patients. Variables with insufficient numbers for any of the modalities (<5%) were excluded from the analysis, except where a category grouping was possible. Pearson's Chi-square and Fischer's Chi-square tests were performed for each qualitative variable as appropriate. Logistic regression was used to investigate factors associated with vitamin D deficiency. A variable was retained for the construction of the multivariate model by logistic regression when the p-value significance level was less than 0.05. Multivariate analysis using logistic regression was performed to investigate associations between vitamin D deficiency and independent variables in patients with COVID-19. The explanatory variables were presented according to the value of the adjusted odds ratio (adjusted OR) and their 95% confidence interval (CI 95%).

Ethical Aspects

This study was carried out in accordance with the ethical standards in force. The Authorisation N˚884/2021/MS/DDS-B/SA was obtained from the Departmental Health Directorate of Borgou to carry out the survey. Written informed consent was obtained from all patients or their legal representatives. The research protocol for this work was submitted to the Local Ethics Committee for Biomedical Research of the University of Parakou which granted its approval.

3. Results

General Characteristics of the Study Population

A total of 197 patients with COVID-19 were included in the study. Females predominated (52.3%) with a sex ratio (M/F) of 0.91. The mean age was 35.4 ± 15.2 years and the age group [18 to 60] was the most represented (82.7%). The majority of patients were Beninese (94.9%) and the most represented ethnic group was Fon and related (36.5%). Christianity was the most practiced religion (66%) followed by Islam (33%), and more than half of the study population was married (59.4%). Traders and civil servants accounted for 31.5% and 10.7% respectively. Abdominal obesity was observed in 72.6% of the women compared to 27.4% of the men. Table 1 presents the general characteristics of the study population.

Table 1. General characteristics of patients with COVID-19 in Parakou in 2021 (N = 197).

	Workforce	Percentage (%)
Gender		
Male	94	47.7
Woman	103	52.3
Nationality		
Beninese	187	94.9
Foreigners	10	5.1
Marital status		
Single	75	38.1
Divorced	2	1.0
Married	117	59.4
Widow(er)	3	1.5
Ethnicity		
Bariba	46	23.3
Dendi	32	16.2
Fon/Goun/Adja	51	25.9
Otamari/Berba/Waama/Yom	24	12.2
Peulh	21	10.7
Yoruba or Nagot/Idatcha	15	7.6
other**	8	4.1
Religion		
Christianity	130	66.0
Islam	65	33.0
Traditional	2	1.0
Profession		
Artisan	25	12.7
Trader	73	37.1
Student	14	7.1
Civil servant	21	10.7
Housekeeper	19	9.6
Retired	29	14.7
Other***	16	8.1
BMI (kg/m²)		
<18	13	7.3

Continued

[18 - 25[	88	49.7
[25 - 30[	47	26.5
[30 - 35[	18	10.2
≥35	11	6.2
Waist circumference (cm)		
≤70	26	14.7
]70 - 80]	56	31.6
]80 - 90]	54	30.5
>90	41	23.2

*Burkinabe (2.0%), Togolese (3.1%), Tunisian (0.5%); **Lopka (3.5%), Arab (0.5%); ***cultivators (4.0%), cowherd (1.5%), religious (2.5%).

Prevalence of 25(OH)D Deficiency

The overall prevalence of 25(OH)D deficiency in patients with COVID-19 was 31.5% (CI 95% [25.1 - 38.5]). This prevalence was 32.0% (CI 95% [23.4 - 41.6]) in women and 30.8% (CI 95% [22.4 - 40.8]) in men. By age group, the prevalence of 25(OH)D deficiency was 25% (CI 95% [11.9 - 46.9]) in patients under 18 years of age, 30.7% (CI 95% [24.1 - 38.1]) in patients between 18 and 60 years of age, and 50% (CI 95% [26.8 - 73.2]) in patients 60 years of age and older.

Factors Associated With 25(OH)D Deficiency

In univariate analysis, there was no significant association between lifestyle and 25(OH) deficiency ($p > 0.05$). No socio-demographic characteristics were significantly associated with 25(OH)D deficiency ($p > 0.05$). Table 2 shows the univariate analysis of 25(OH)D deficiency according to socio-demographic and anthropometric characteristics.

Univariate analysis of 25(OH)D deficiency according to comorbidities and clinical manifestations

There was a significant association between diabetes ($p = 0.000$) and 25(OH)D deficiency. Similarly, there was a statistically significant association between fever ($p = 0.000$), cough ($p = 0.007$), rhinitis ($p = 0.002$), asthenia ($p = 0.012$), breathing difficulty ($p = 0.000$) and 25(OH)D deficiency. Table 3 shows the univariate analysis of 25(OH)D deficiency according to comorbidities and clinical manifestations.

Multivariate Analysis of Factors Associated with 25(OH)D Deficiency in Patients with COVID-19

In multivariate analysis, there was a significant association between diabetes, overweight or obesity, rhinitis, the severe form of the disease and 25(OH)D deficiency. Indeed, diabetic patients (adjusted OR = 4.4; $p = 0.036$) were four times more likely to have 25(OH)D deficiency; overweight or obese patients were twice as likely to have 25(OH)D deficiency (adjusted OR = 2.4; $p = 0.032$). Rhinitis ($p = 0.009$) and the severe form of the disease ($p = 0.003$) were significantly asso

Table 2. Univariate analysis of 25(OH)D deficiency according to socio-demographic and anthropometric characteristics. (N = 197).

	Total	25(OH)D Deficiency		PR	CI 95%	p
		n	%			
Gender						0.857
Male	94	29	30.8	1		
Woman	103	33	32.0	0.9	[0.6 - 1.4]	
Age (years)						0.121
<60	183	55	30.1	1		
≥60	14	7	50.0	1.2	[0.1 - 1.3]	
Nationality						0.918
Beninese	187	59	31.5	1.1	[0.3 - 5.3]	
Foreign	10	3	30.0	1		
Marital status						0.320
Married	117	40	34.2	1.2	[0.8 - 1.9]	
Other[1]	80	22	27.5	1		
Profession						0.057
Trader	73	17	23.3	0.6	[0.3 - 1.0]	
Other[2]	124	45	36.3	1		
BMI (kg/m²)						0.008
<25	101	23	20.7	1		
≥25	76	29	38.2	2.3	[1.2 - 4.5]	
Abdominal obesity						0.081
No	115	27	23.5	1		
Yes	62	25	40.3	1.6	[1.3 - 4.6]	

PR: Prevalence Ratio; CI: Confidence Interval; p for Chi-square test; BMI: Body Mass Index. [1]The other variables are presented in the marital status section of the description of socio-demographic characteristics; [2]The other variables are presented in the occupation section of the description of socio-demographic characteristics.

ciated with 25(OH)D deficiency. Indeed, COVID-19 patients with 25(OH)D deficiency were three times more likely to develop rhinitis (adjusted OR = 2.7) and had a higher risk of developing the severe form (adjusted OR = 1.3). Table 4 shows the factors associated with 25(OH)D deficiency in patients with COVID-19 in multivariate analysis.

4. Discussion

Prevalence of 25(OH)D Deficiency

The overall prevalence of 25(OH)D deficiency in this study was 31.5% (95%

Table 3. Univariate analysis of 25(OH)D deficiency according to comorbidities and clinical manifestations of patients with COVID-19 in 2021 in Parakou (N = 197).

	Total	25(OH)D Deficiency		PR	CI 95%	p
		n	%			
HBP						0.080
Yes	34	15	44.1	0.7	[0.5 - 1.0]	
No	163	47	28.8	1		
Diabetes						0.000
Yes	18	13	72.2	2.6	[1.8 - 3.8]	
No	179	49	27.4	1		
Heart failure						0.185
Yes	3	2	66.7	0.2	[0.01 - 2.5]	
No	194	60	30.9	1		
Sickle-cell disease						0.677
Yes	5	2	40.0	0.7	[0.1 - 4.2]	
No	192	60	31.3	1		
Fever						0.000
Yes	93	41	44.1	2.1	[1.3 - 3.4]	
No	104	21	20.2	1		
Headaches						0.078
Yes	93	35	37.6	0.6	[0.3 - 1.0]	
No	104	27	25.9	1		
Cough						0.007
Yes	126	48	38.1	1.9	[1.1 - 3.2]	
No	71	14	19.7	1		
Rhinitis						0.002
Yes	75	33	44.0	1.1	[0.4 - 0.7]	
No	122	29	23.7	1		
Asthenia						0.012
Yes	121	46	38.0	1.8	[1.1 - 2.9]	
No	76	16	21.1	1		
Myalgia						0.129
Yes	47	19	40.4	0.5	[0.2 - 1.1]	
No	150	43	28.7	1		
Anosmia						0.336
Yes	60	16	26.7	1.4	[0.7 - 2.7]	

Continued

No	137	46	33.6	1		
Difficulty breathing						0.000
Yes	64	31	48.4	2.1	[1.4 - 3.1]	
No	133	31	23.3	1		
Diarrhoea						0.195
Yes	10	5	50.0	0.4	[0.1 - 1.5]	
No	187	57	30.5	1		

PR: Prevalence Ratio; CI: Confidence Interval; p for Chi-square test, HBP: High Blood Pressure.

Table 4. Multivariate analysis of factors associated with 25(OH)D deficiency in patients with COVID-19 in Parakou in 2021. (N = 197).

	Total	25(OH)D Deficiency		Adjusted OR	CI 95%	p
		Yes	%			
Diabetes						0.036
No	179	60	33.5	1		
Yes	18	13	72.2	4.4	[1.1 - 8.0]	
Rhinitis						0.009
No	122	37	30.3	1		
Yes	75	36	48.00	2.7	[1.2 - 6.0]	
Form of the disease						0.003
Not severe	159	50	31.4	1		
Severe	38	23	60.5	1.3	[1.0 - 3.2]	
BMI (kg/m²)						0.032
<25	101	23	20.7	1		
≥25	76	29	38.2	2.4	[1.2 - 4.7]	
Fever						0.102
No	104	21	20.2	1		
Yes	93	41	44.1	1.2	[1.1 - 2.1]	
Cough						0.121
No	71	14	19.7	1		
Yes	126	48	38.1	1.5	[1.7 - 4.2]	
Difficulty breathing						0.151
No	133	31	23.3	1		
Yes	64	31	48.4	2.4	[1.5 - 3.8]	
Asthenia						0.118
No	76	16	21.1	1		
Yes	121	46	38.0	1.9	[1.5 - 3.1]	

OR: Odds Ratio; CI: Confidence Interval; p for Chi-square test.

CI [25.1 - 38.5]). A higher prevalence was found in several studies, including Karonova *et al.* [11] in 2020 in Russia (71.3%), Karahan *et al.* [12] in 2020 in Turkey (69.1%), Pizzini *et al.* [13] in 2020 in Austria (65%), Radujkovic *et al.* [3] in 2020 in Germany (64%), and Ye *et al.* [14] in 2020 in China (42%). However, this prevalence was higher than that found by Merzon *et al.* [15] in 2020 in Israel (13.4%). These inequalities could be justified by differences in the prevalence of 25(OH)D deficiency in the general population around the world. In Russia, the prevalence of 25(OH)D deficiency was 84% [16], and in Germany 57% [17]; contrarily, in North Africa, specifically in Morocco, the prevalence was 28% [6]. Regions at the 35th degrees north latitude corresponding to the entire territory of the Russian Federation, Turkey, Europe, and almost all of North America and China receive insufficient ultraviolet (UV) radiation, especially during the autumn-winter months, rendering the synthesis of vitamin D from sunlight almost impossible in these areas [16].

The prevalence of 25(OH)D deficiency in female patients was 32.0% and in male patients 0.8%. In contrast, Hernandez *et al.* [18] in Spain in 2020 found a higher prevalence of 25(OH)D deficiency in men (49.0%) than in women (25.9%). Alguwaihes *et al.* [19] in Saudi Arabia in 2020 reported in their study a prevalence of 25(OH)D deficiency of 75.8% (male) and 72.5% (female). Several population-based studies [6] [20] have reported a high prevalence of 25(OH)D deficiency in women. Female subjects are at risk of 25(OH)D deficiency due to low bone mass [21], and the wearing of covering clothes due to religious beliefs or community habits.

In the present study, the prevalence of 25(OH)D deficiency was high (50%) in patients aged 60 years and over. It was 30.7% in patients aged [18 - 60] years, and 25% in patients under 18 years. Radujkovic *et al.* [3] in 2020 in Germany also found a higher prevalence of 25(OH)D deficiency in patients aged 60 years and over (14%) than in patients under 60 years (8.1%). In contrast, Meltzer *et al.* [22] in Chicago in their 2020 study reported 6.1% prevalence of 25(OH)D deficiency for patients over 65 years of age and 22.3% for patients under 50 years of age. The high prevalence of 25(OH)D deficiency in the elderly could be explained by a decrease in skin synthesis of vitamin D due to ultraviolet radiation as a result of skin ageing. Additionally, it could be explained by the often sedentary lifestyle due to the loss of mobility which limits sun exposure and thus promotes 25(OH)D deficiency [23]. The results reported by Meltzer *et al.* [22] could be explained by the large proportion (78%) of patients under 65 years of age in their sample.

Factors Associated With 25(OH)D Deficiency

This study has not found any significant association between socio-demographic data and 25(OH)D deficiency. However, some authors have reported an association between age and 25(OH)D deficiency. These include D'Avolio *et al.* [24] in 2020 in Switzerland for patients over 70 years of age ($p = 0.037$), and Meltzer *et al.* [22] in Chicago in 2020 for patients under 50 years of age ($p = 0.02$). De Smet

et al. [25] in Brussels, Belgium 2020 reported an association between male gender and 25(OH)D deficiency (p = 0.046). In the literature review, the socio-demographic factors associated with 25(OH)D deficiency in the general population are advanced age (>65 years), and female gender [20]. Elderly people are most affected by 25(OH)D deficiency due to reduced skin regeneration resulting in a slowdown in 25(OH)D synthesis. In developed countries, the population aging has resulted in an increase in the number of nursing homes, thus limiting the movement of elderly people [23]. This could justify the result found by D'Avolio *et al.* [24].

In the present study, overweight and obesity were associated (adjusted OR = 2.4; p = 0.032) with 25(OH)D deficiency. Overweight and obese patients had a twofold increased risk of 25(OH)D deficiency. In contrast, Hernandez *et al.* in Spain in 2020 did not find a significant association (p = 0.428) between BMI and 25(OH)D deficiency [18]. This result found in the present study could be explained by the volumetric dilution of 25(OH)D which is the most likely mechanism for the inverse relationship between serum 25(OH)D levels and BMI. 25(OH)D levels and BMI in obese individuals [26] [27]. Indeed, 25(OH)D is mainly distributed in serum, muscle, fat tissue and liver, compartments that are increased in obesity. Although obese and lean subjects have similar amounts of 25(OH)D, in overweight and obese individuals, the 25(OH)D is distributed in a larger volume, resulting in lower serum concentrations [26]. Other explanations have been proposed such as altered 25(OH)D metabolism, behavioural factors such as reduced exposure to sunlight, and reduced consumption of vitamin D-fortified foods. In addition, increased body fat may act as a storage site for 25(OH)D, as it is a lipophilic hormone [28].

Diabetes was significantly associated with 25(OH)D deficiency (p = 0.036). Diabetic patients (adjusted OR = 4.4) were four times more likely to have 25(OH)D deficiency. Radujkovic *et al.* [3] in 2020 in Germany reported an association (p = 0.04) between diabetes and 25(OH)D deficiency. In contrast, Hernandez *et al.* in Spain in 2020 found in their study an association between hypertension (p = 0.035) and 25(OH)D deficiency [18]. In the literature review, low 25(OH)D levels are commonly observed in diabetic patients in the general population and are associated with higher fasting blood glucose levels. 25(OH)D therefore has a potential effect on glucose homoeostasis. 25(OH)D deficiency impairs its action on insulin stimulation and secretion by pancreatic β-cells [29].

Rhinitis was significantly associated (p = 0.009) with 25(OH)D deficiency in the present study. Patients with 25(OH)D deficiency (OR = 2.7) were three times more likely to develop rhinitis. However, Hernandez *et al.* [18] in Spain in 2020 did not find a significant association (p = 0.662) between clinical signs and 25(OH)D deficiency. Some authors have reported a relationship between rhinitis and 25(OH)D in patients with acute respiratory infections. Patients with rhinitis would have low serum 25(OH)D levels and vitamin D supplementation would improve symptoms [30] [31].

The severe form of the disease was significantly associated with 25(OH)D deficiency (p = 0.003). Similarly, several authors such as Karonova *et al.* [11] in Russia (p = 0.029) in 2020, Ye *et al.* [14] in 2020 in China (p = 0.034), and Radujkovic *et al.* [3] in 2020 in Germany (p = 0.004) found a significant association between 25(OH)D deficiency and disease severity. Macaya *et al.* [32] in Spain reported an association between 25(OH)D deficiency and severe disease (p = 0.002) in patients under 67 years of age. 25(OH)D modulates the function of the immune system through stimulation of macrophages and dendritic cells. It plays a role in regulating and suppressing the cytokine inflammatory response that causes the acute respiratory distress syndrome that characterises the severe and often lethal forms of COVID-19 [33]. Thus, it can be concluded that 25(OH)D deficiency is therefore a risk factor for severe forms of COVID-19.

The main limitation of this study was the lack of a control group of healthy subjects to allow comparison of their plasma 25(OH)D concentrations with those of the COVID-19 patients.

Future research could examine the relationship between 25(OH)D deficiency and the severity of COVID-19, taking into account potential confounding factors such as age, co-morbidities and socio-economic status.

5. Conclusion

Almost one-third of COVID-19 patients in Parakou in 2021 have 25(OH)D deficiency. The prevalence of 25(OH)D deficiency is higher in patients aged 60 years and over, and in female patients. Diabetes, overweight, rhinitis and severe COVID-19 are associated with vitamin D deficiency in these patients. Vitamin D measurement is therefore important for a better follow-up of patients infected with SARS-CoV-2 in order to avoid severe forms. Vitamin D supplementation of patients with COVID-19 would therefore be justified to prevent the severe form of the disease.

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Authors' Contributions

MAMA CISSÉ I.: supervision of data collection, writing of the article;
ADABA YYVL.: protocol writing, data collection, and analysis;
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GOUNONGBÉ ACF.: writing of the article;
ADJOBIMEY M.: writing the article;

AYÉLO P.: writing the article;
HINSON AV.: writing of the article;
MIKPONHOUÉ R.: writing of the article;
GOMINA M.: design of the study, supervision of data collection, assay of total 25(OH)D and validation of the final version of the manuscript.

Conflicts of Interest

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

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