Scientific Research Publishing

Open Journal of Pediatrics, 2022, 12, 297-308
https://www.scirp.org/journal/ojped
ISSN Online: 2160-8776
ISSN Print: 2160-8741

Serum Vitamin D Levels of Children with Vernal Keratoconjunctivitis and Normal in Kinshasa

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How to cite this paper: Nkashama, L.M., Lubeji, D.K., Nganga, M.S. and Tshipukane, D.D.N. (2022) Serum Vitamin D Levels of Children with Vernal Keratoconjunctivitis and Normal in Kinshasa. *Open Journal of Pediatrics*, **12**, 297-308.
https://doi.org/10.4236/ojped.2022.122033

Received: March 19, 2022
Accepted: April 24, 2022
Published: April 27, 2022

Abstract

Background: Data on the serum vitamin D3 levels of vernal keratoconjunctivitis (VKC) children are not known well in Central Africa. Children with vernal keratoconjunctivitis are less exposed to sunlight. There is no study that shows the breadth of the serum vitamin D3 levels of vernal keratoconjunctivitis children and normal in our setting. **Purpose:** This study aimed to compare the serum 25-hydroxy vitamin D [25(OH)D3] levels of children with and without VKC. **Methods:** An observational, case-control study was performed from September 2019 to February 2020 in the Ophthalmology Department and the Clinical Biology Department of the University Hospital of Kinshasa. The case group was recruited consecutively in the consultation while the control group was enrolled in the nearest Rehoboth school complex using a systematic sample method (k = 4) on the presence register. Both cases and controls underwent the routine ophthalmological examination of the anterior segment and serum vitamin D3 levels were measured in both cases and controls using Mindray Chimic-Luminescence (CL)-1200i. Data were entered in Microsoft Sheets and analyzed using SPSS version 20.0. The Mann-Whitney-U test (M-U), and the t-Student test were used respectively to compare the mean serum vitamin D3 levels in both cases and controls. The correlation of Spearman (rho) was used to determine the association between Body Mass Index and serum vitamin D3 levels in the case group. **Results:** A total of 75 children with VKC (mean age 7.8 ± 4.4 years) and 75 children without VKC non-atopic control group (mean age 7.9 ± 4.3 years) were enrolled in this study. The vitamin D3 deficiency was more frequent among the case group than in the control group (40% vs 8%, p = 0.0001). Vitamin D3 insufficiency was more frequent in the case group than in the control group (33.3% vs 18.6%, p = 0.04). The mean serum vitamin 25(OH)D3 levels were statistically lower in children with VKC compared to those without (25.5 ± 8.7 ng/ml and

44.3 ± 18.5 ng/ml, p = 0.0001). Time spent outdoors during daylight by children with VKC was statistically lower than children without VKC (1.59 ± 0.71 hours and 2.28 ± 1.08 hours, respectively) (p = 0.0001). Body Mass Index and serum vitamin D3 levels in VKC children showed a negative correlation statistically significant (Spearman, rho = −0.452, p = 0.0001). **Conclusion:** This study showed statistically values of serum vitamin D3 levels in VKC children lower than in children without VKC.

Keywords

Serum 25(OH)D3, Time Spent Outdoors, Vernal Keratoconjunctivitis, Body Mass Index

1. Introduction

Allergic diseases are increasing and well documented in European countries. Red eyes accounted for 15% of ophthalmological consultations and allergic conjunctivitis was the most common diagnosis, with 35% in Eastern Europe and the Middle East countries [1].

Vernal keratoconjunctivitis (VKC) is a chronic, recurrent, bilateral inflammation of the conjunctiva and cornea. Males are affected twice as often as females and it is a global health problem among children that affects the quality of school life and work productivity [2] [3] [4] [5].

In a lot of African schoolchildren studies, VKC prevalence varies from 4% to 6.7% [6] [7].

The main complaints of VKC children are brownish discoloration conjunctiva, itchy eyes, photophobia, tearing, red eyes, eyelids rubbing, and mucoid discharge. In the slit lamp, corneal involvement such as punctate epithelial keratitis, epithelial erosion, shield ulcer, and corneal plaque is observed [8].

Vitamin D is a fat-soluble vitamin that is taken with diet or supplements and it is synthesized in the skin following exposure to sunlight [9].

The rule of vitamin D is to regulate functions in the immune system after the discovery of vitamin D receptor (VDR) on T cells, B cells, neutrophils, macrophages, and dendritic cells (DC), regulation of the Angiotensine-renine system, and the growth of the genes in cells and bone mineralization [10] [11] [12].

Vitamin D deficiency may lead to rickets, osteomalacia, and low bone density [13]. Globally, it is estimated that 1.2 billion people have a vitamin D deficiency in all ethnics and age groups. In addition, vitamin D deficiency affects a lot of countries throughout the world in Asia and Sub-Saharan Africa and it has been shown to be associated with allergic disorders [14] [15] [16].

Actually, lower vitamin D levels compared with non-atopic subjects were reported in patients with seasonal allergic conjunctivitis (SAC) [17].

Much research in the world has not found a consensus about the phytopathogenic rule or therapeutic benefits and cutoff of vitamin D deficiency. In the Re-

public Democratic of Congo, the measurement of serum vitamin D3 levels in vernal keratoconjunctivitis children is not well known because of a lack of a screening program in daily practice. Therefore, we aimed to compare the serum vitamin D3 levels of children with and without VKC.

2. Methods of Study Design

2.1. VKC Diagnosis

VKC diagnosis was based on ocular symptoms, including photophobia, brownish discoloration conjunctiva, itchy eyes, eyelids rubbing, tearing, red eyes, tarsal papillary hypertrophy, and perilimbal pigmentation on slit-lamp examination.

2.2. Time Spent Outdoors

The time spent outdoors during daylight was classified in this way:

Inferior to 1 hour = 1, 1 - 5 hours = 2, 6 - 10 hours = 3 and superior to 10 hours = 4.

2.3. Body Mass Index

- Body Mass Index (BMI) was classified according to Obesity Task Force (OTF):
- BMI < Centile OTF-17: thinness
- BMI—Centile OTF-17 - Centile-25: Normal
- BMI—Centile OTF-25 - Centile-30: Excess Weight or overweight
- BMI > Centile OTF-30 = Obesity.

2.4. Measurement of serum vitamin D3 levels

Venous samples were obtained from antecubital in the morning (5CC) and put into Vaccutainers tubes without anticoagulants. After centrifugation at 3000 rotations (turn)/minute for five minutes, we obtained serum samples which were stored at 2˚C to 8˚C for analysis, and 60 microliters (µl) of serum were put in automat Mindray CL-1200i which had Chimic-Luminescence liquid chromatography using an Ultraviolet (UV) detector and reading was performed after forty minutes. In our series, we only measured vitamin 25(OH)D3 levels because it has been shown to provide levels of vitamin D in circulation more effectively than vitamin 25(OH)D2 possibly due to a significantly more stable hormone-receptor complex and the detection limit for vitamin 25(OH)D3 levels was 5 ng/ml. In The World, there is a difficulty to determine the cutoff to define vitamin D deficiency.

2.5. Study Area and Population

The study was conducted in Kinshasa. The Kinshasa area covers an area of 9965 km^2 with a density of 557 inhabitants /km^2 and a population of 12 million.

This town has two season's tropical humid and hot (half September to half May) and dry season (half May to half September). The average temperature varies from

22.5˚C to 25˚C. The growth rate of the Kinshasa population is 5.1% per year.

An observational, case-control study was performed from September 2019 to February 2020 in the Ophthalmology Department and the Clinical Biology Department of University Hospital of Kinshasa.

2.6. Participants' Selection

The participants were divided into two groups:

- Case group: included children with a clinical diagnosis of vernal keratoconjunctivitis from the outpatient Ophthalmology Department. The case group was recruited consecutively in the consultation.
- The inclusion criteria were complaints of vernal keratoconjunctivitis, tarsal papillary hypertrophy, and perilimbal pigmentation on slit-lamp examination.
- Criteria exclusion was the parents, guardians, or children seven years and over who didn't give informed consent before enrollment.
- Control group: included children without VKC from the nearest Rehoboth school complex.
- The inclusion criteria were the parents, guardians, or children seven years and over who gave informed consent before enrollment
- Exclusion criteria included a positive personal or family history of atopy because atopy is a genetic predisposition to develop allergic diseases such as asthma, allergic rhinitis, and atopic dermatitis, which are associated with a low serum vitamin D3 levels.

Sample size

The sample size was calculated using Kelsey's formula:

$$N_1 = \left(Z\alpha + Z_1 - \beta\right)^2 \overline{PQ}\left(R+1\right) \Big/ R\left(P_1 - P_2\right)^2$$

$N_2 = RN_1$, N_1 = Number of cases, N_2 = Number of controls, $Z\alpha$ = standard normal deviate for two-tailed test based on alpha level (relates to the confidence interval level), $1 - \alpha$ = 95%, Z_1 = standard normal deviate for one-tailed test based on beta level (relates to the power level), Power level (β) = 80%, R = ratio of controls to cases, R = 1, P_1 = proportion of cases with exposure, P_1 = 20%, P_2 = proportion of controls with exposure, P_2 = 5%, $Q_1 = 1 - P_1$, $Q_2 = 1 - P_2$, Odds Ratio (OR) = 4.75.

N_1 = 77, N_2 = 77, $N_1 + N_2$ = 154. We reduced it to 150.

2.7. Sampling Techniques

The case group was enrolled using the simple random sampling, technical, and the control group used the systematic sampling method (k = 4) on the presence register. The nearest Rehoboth school complex had 12 classrooms with a mean of 25 students. Participants were matched by sex and age.

2.8. Data Collection

Both cases and controls underwent the routine ophthalmological examination of

the anterior segment and serum vitamin D3 levels were measured in both cases and controls using Mindray Chimic-Luminescence (CL)-1200i which takes the serum without anticoagulant in the Clinical Biology Department. A questionnaire was administered about sex, age, parent's profession, and food habits.

2.9. Statistical Analysis

The qualitative variables included sex, age groups, parent's profession, and food habits (milk enriched with vitamin D, fish, eggs, pork butcher products, margarine, and butter) and were expressed as percentages. Comparison of proportions was done with a Chi-squared test and Fisher's exact test was used in the chi-square conditions were not fulfilled.

Quantitative variables included serum vitamin D3 levels, time spent outdoors during daylight, and Body Mass Index. The Endocrine Society Clinical Practice Guidelines considered severe deficiency if 25(OH)D3 was below 10 ng/ml while a level of 25(OH)D3 was between 10 ng/ml and 20 ng/ml and it was accepted as Deficiency, Insufficiency: if 25(OH)D3 was between 20 - 30 ng/ml, normality if 25(OH)D3 was between 30 - 100 ng/ml and toxicity levels of 25(OH)D3 was superior to 100 ng/ml. The mean± standard deviation (SD) or median was used to express the quantitative variables. In both groups, the non-parametric Mann-Whitney U-test (M-U) was used to compare the serum 25(OH)D3 levels and the t-Student test to compare the time spent outdoors during daylight. We used the correlation of Spearman (rho) to determine the association between Body Mass Index and serum vitamin D3 levels in the case group.

The Confidence Interval (95% CI) was used and a significance level was set to a value of $p < 0.05$.

2.10. Ethical Approval

The study received approval from the section of the Ministry of Public Health and the head committee n˚ 188/CNES/BN/PMMF/2019.

3. Results

Sociodemographic, clinical and biological data have been systematically recorded in both groups.

A total of 75 children with VKC (mean age 7.8 ± 4.4 years) and 75 children without VKC non-atopic control group (mean age 7.9 ± 4.3 years) were enrolled in this study.

Their ages ranged from 2 to 16 years in both groups. The age group of 2 to 6 years old was predominant in both cases and controls with 46.6%. There were twice as many boys as girls.

54.7% of the parents of VKC children were informal workers and 65.3% of the parents without VKC were informal workers Table 1.

In Table 2 the consumption rate of milk enriched with vitamin D was similar

Table 1. Sociodemographic characteristics of children with and without VKC.

Variables	Case		Control		p-value
	N = 75	%	N = 75	%	
Gender					
M	50	66.6	50	66.6	0.50
F	25	33.3	25	33.3	0.50
Age/years					
2 - 6	35	46.6	35	46.6	0.50
7 - 11	23	30.6	23	30.6	0.50
12 - 16	17	22.6	17	22.6	0.50
Profession of parents					
Formal	34	45 .3	49	65.3	0.006
Informal	41	54.7	26	34.7	0.006

N = Number; % = percentage; p = probability.

Table 2. Food habits of children with and without VKC.

Food Habits	Case		Control		p-value
	N = 75	%	N = 75	%	
Milk enriched with vitamin D					
Yes	66	88	61	81.3	0.18
No	9	12	14	18.7	0.18
Offal					
Yes	28	37.3	22	29.3	0.19
No	47	62.7	53	70.7	0.19
Fish					
Yes	67	89.3	66	88	0.50
No	8	10.6	9	12	0.50
Eggs					
Yes	61	81.3	54	72	0.09
No	14	18.7	21	28	0.09
Pork butcher products					
Yes	43	57.3	38	50.7	0.25
No	32	42.7	37	49.3	0.25
Margarine					
Yes	51	68	63	84	0.011
No	24	32	12	16	0.011
Butter					
Yes	12	16	25	33.3	0.006
No	63	84	50	66.7	0.006

N = Number; % = percentage; p = probability.

in both groups (88% vs 81.3%, p = 0.18). Eating fish was similar in two groups (89.3% vs 88%, p = 0.50) and eating butter was less frequent in vernal keratoconjunctivitis children than without (16% vs 33.3%, p = 0.006). Other characteristics of food habits are shown in Table 2.

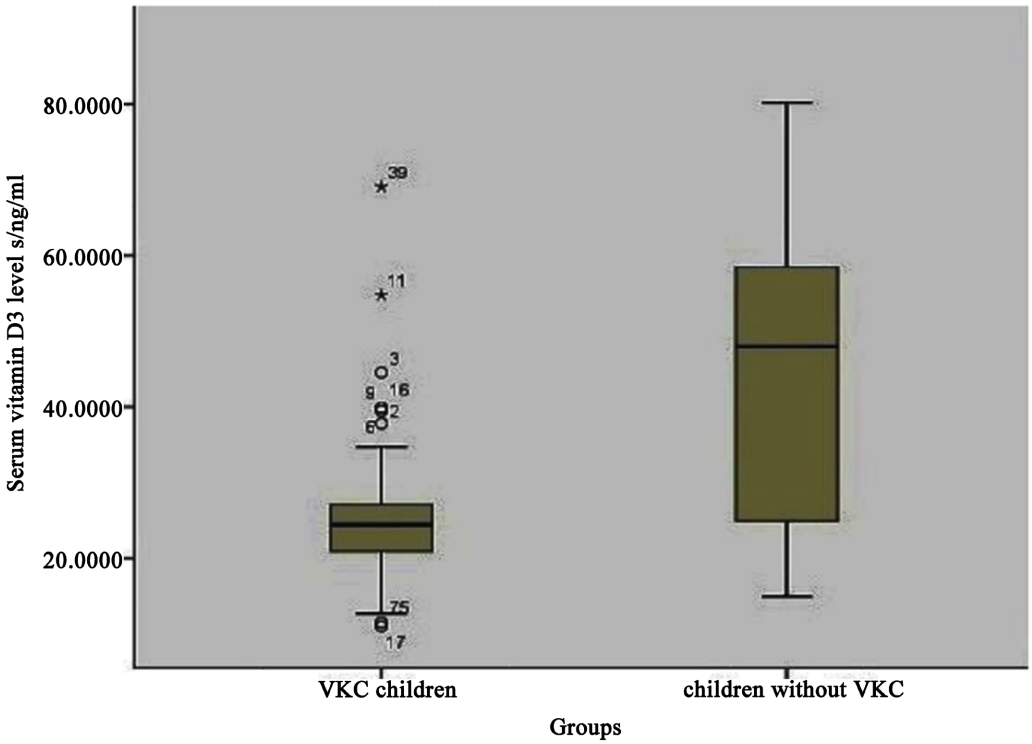
The vitamin D3 deficiency was more frequent among the case group than in the control group (40% vs 8%, p = 0.0001). Vitamin D3 insufficiency was more frequent in the case group than in the control group (33.3% vs 18.6, p = 0.04) Table 3.

The mean serum vitamin D3 levels of the case group were 25.5 ± 8.7 ng/ml, median 24.5 ng/ml ranging from 11.1 ng/ml to 69.2 ng/ml, and 44.3 ± 18.5 ng/ml, median 48.09 ng/ml ranged from 15.07 to 80.2 ng/ml in the control group. The mean serum vitamin D3 levels of the case group were significantly lower than in the control group (p = 0.0001) (Figure 1).

Table 3. Pattern of serum vitamin D3 levels among children with and without VKC according to the Endocrine Society Clinical Practice Guidelines.

Serum vitamin D levels/ng/ml	Case		Control		p-value
	N = 75	%	N = 75	%	
Normality: 30 - 100 ng/ml	20	26.6	55	73.3	0.0001
Insufficiency: 20 - 30 ng/ml	25	33.3	14	18.6	0.04
Deficiency: 10-20 ng/ml	30	40	6	8	0.0001

N = Number; % = percentage; p = probability; ml = milliliter; ng = nanogram.



ml = milliliter; ng = nanogram.

Figure 1. Box plot of mean serum vitamin D3 levels among children with and without VKC.

The mean time spent outdoors during daylight by VKC children was 1.59 ± 0.71 hours, median 1 hour, ranged from 1 hour to 3 hours, 2.28 ± 1.08 hours, median 2 hours, and ranged from 1 hour to 4 hours in the control group. The comparison of the meantime spent outdoors during daylight between the case group and the control group was statistically significant (p = 0.0001) **Figure 2**.

Body Mass Index and serum vitamin D3 levels in VKC children showed a negative correlation statistically significant (rho = -0.452, p = 0.0001) The serum vitamin D3 levels are decreasing and the Body Mass Index is increasing in VKC children (**Figure 3**).

4. Discussion

The purpose of the study was t to compare the serum vitamin D3 levels of children with and without VKC.

There are many studies around the world investigating the association between vitamin D deficiency and allergic diseases [18] [19].

In the current study, the serum vitamin D3 levels were significantly lower in the case group than in the control group (p = 0.0001). This finding agrees with the growing evidence of the role of vitamin D in allergic disease [17].

Many case-control studies showed higher rates of vitamin D deficiency among allergic patients than in controls [20] [21].

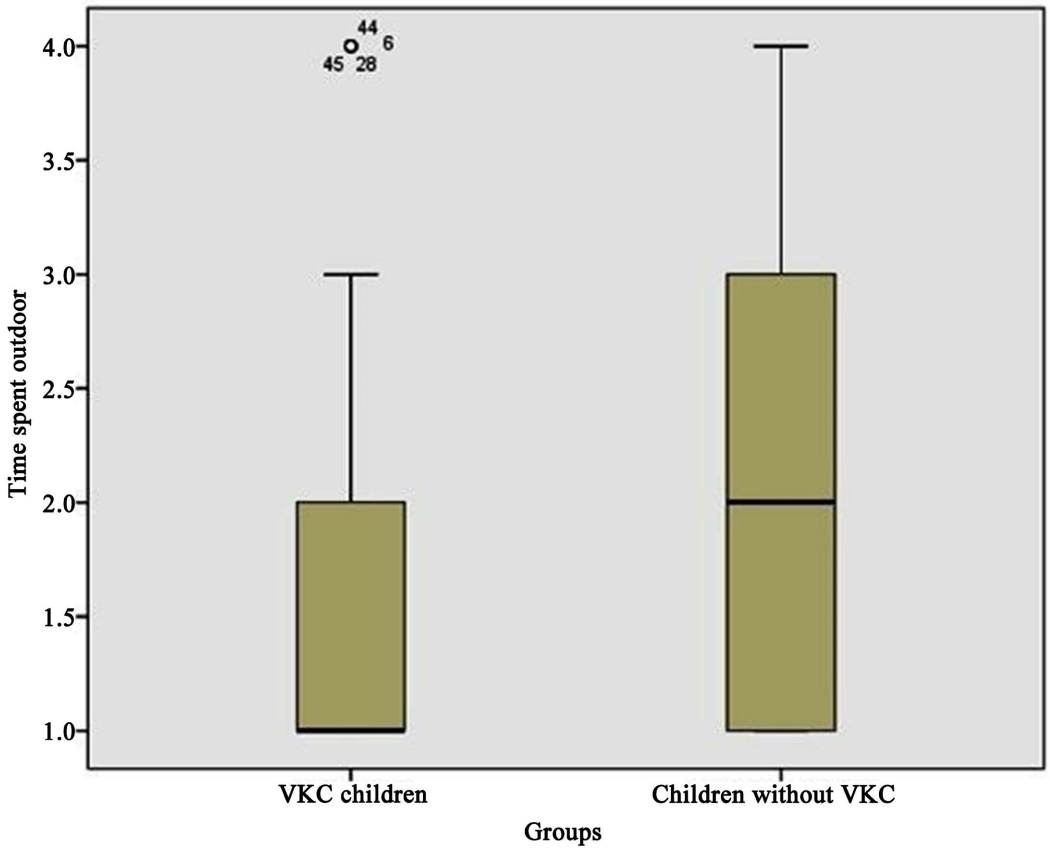
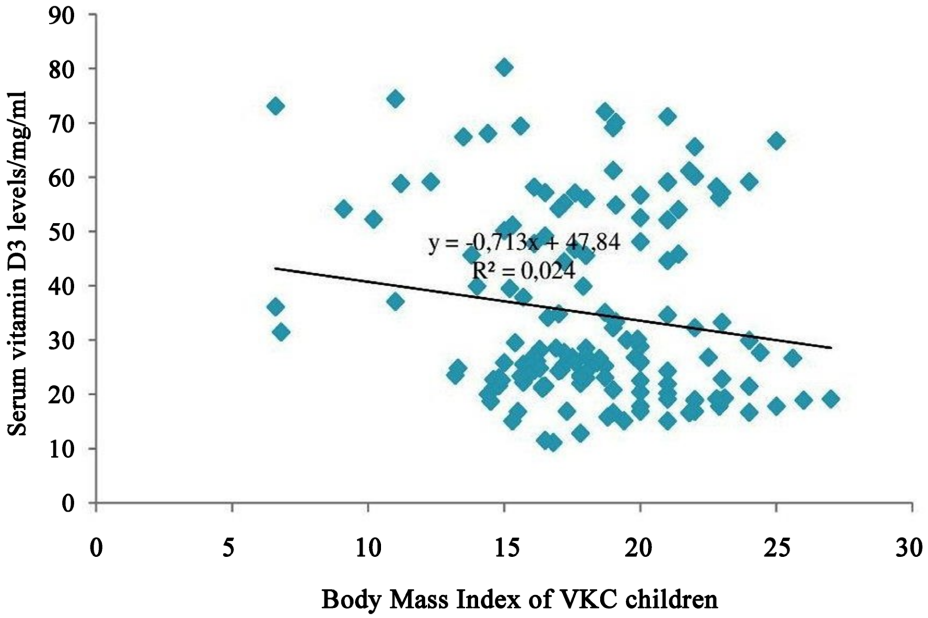


Figure 2. Box plot of mean time spent outdoors among children with and without VKC.



ml = milliliter; ng = nanogram.

Figure 3. Correlation between serum vitamin D3 levels and Body Mass index in VKC children.

Generally, vitamin D is a fat-soluble vitamin whose main source is synthesized in the skin following exposure to sunlight or secondary with diet supplements [10]. VKC children are photophobic, avoid outdoor activities, and don't receive enough sunshine, which could explain the vitamin D3 deficiency in this group [22].

The dramatic increase in media time such as watching television, using the internet or computers, listening to music, and playing video games may explain the insufficiency and deficiency rate of serum vitamin D3 levels in children without VKC [23].

The authors such as Binkley, Nansera *et al.* have found poor absorption of vitamin D in melanoderm subjects [14] [24].

The population of Kinshasa is mainly melanoderm and this genetic factor could explain the deficiency or insufficiency of serum vitamin D3 levels in two groups. Diet and cooking procedures are different throughout the world; it may also explain the deficiency or insufficiency of serum vitamin D3 levels in the case group and the control group [25].

In the present study, the serum vitamin D3 levels had a negative correlation statistically significant with Body Mass Index in the VKC children (rho = −0.452, p = 0.0001).

The negative correlation may be explained because decreasing the vitamin D could result from the sequestration of hormones by lipid cells hypertrophic in obesity and this finding is in agreement with the study of Korn *et al.* who reported (rho = −0.278, $p < 0.001$) [26] [27].

There are some limitations and constraints associated with the present study.

The first limitation is related to a case-control study that was performed from

September 2019 to February 2020 where it is a very hot climate in Kinshasa.

We could not perform the serum vitamin D3 assays at another period time for organizational and time reasons. Secondarily, the parents of children underestimated the time spent outdoors during daylight, the duration and the rhythm or quantity of eating butter, eggs, offal, fish, margarine, pork butcher product, and drinking milk enriched with vitamin D were not determined. Nevertheless, this is the first study providing new insights among VKC children in Kinshasa about serum vitamin D3 levels.

5. Conclusion

This study showed statistically values of serum vitamin D3 levels in VKC children lower than in children without VKC.

Impact Statement

In daily practice, the Ophthalmologist should change the habits in the management and prescribe vitamin D3 to VKC children having deficiency or insufficiency.

Acknowledgements

The authors would like to thank all parents or guardians who gave their consent to realize this study, the Medical staff of the Ophthalmology Department, the Clinical Biology Department of the University Hospital of Kinshasa, and the Head committee of the nearest Rehoboth school complex for their collaboration.

Authors' Contributions

Design: Léon Muamba Nkashama, David Kayembe Lubeji.
Data Collection: Léon Muamba Nkashama, Mireille Solange Nganga.
Analysis Data: Léon Muamba Nkashama.
Redaction: Léon Muamba Nkashama, Dieu donné Nyembue.

Conflicts of Interest

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

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