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RESEARCH ARTICLE

Vitamin D Status and Associated Factors among Children and Adolescents with Epilepsy in the Watsa Health Zone, Democratic Republic of the Congo

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Abstract

Background: Vitamin D deficiency has been increasingly recognised among children and adolescents with epilepsy, particularly in low-resource settings, where disease-related factors, antiepileptic treatments, and nutritional deficiencies may contribute to reduced serum levels. This study aimed to assess vitamin D status and identify associated factors in children and adolescents with epilepsy in Watsa health zone, Democratic Republic of the Congo. **Methods:** A cross-sectional study was conducted among 43 children and adolescents with epilepsy. Sociodemographic, clinical, nutritional, and treatment-related data were collected. Serum 25-hydroxyvitamin D [25(OH)D] and calcium levels were measured. Associations were explored using bivariate analyses, correlation tests, and multivariable linear regression models. **Results:** The mean age was 11.2 $\pm$ 6.3 years, and 55.8% were male. Most participants (60.5%) had uncontrolled seizures. Vitamin D insufficiency was highly prevalent (69.8%), while 25.6% had deficiency; only 4.7% had normal levels. Mean serum 25(OH)D was 23.5 $\pm$ 4.3 ng/mL. In bivariate analysis, fish (p = 0.002), milk ($p < 0.001$), and egg consumption (p = 0.013) were associated with higher vitamin D levels. No associations were found with age, sex, epilepsy characteristics, treatment, or calcium levels. In multivariable analysis, fish (β = 6.51; $p < 0.001$), milk (β = 4.32; p = 0.001), and eggs (β = 3.62; p = 0.004) remained independent predictors of higher serum 25(OH)D. **Conclusion:** Vitamin D insufficiency is highly prevalent among children and adolescents with epilepsy in Watsa health zone. Dietary intake of fish, milk, and eggs appears to be the main modifiable determinant of serum 25(OH)D levels, highlighting the importance of targeted nutritional interventions in this population.

Keywords: epilepsy, vitamin D deficiency, adolescents, antiepileptic drugs, nutritional factors, sub-Saharan Africa, DRC

1 Introduction

Epilepsy is a chronic non-communicable neurological disorder affecting individuals of all ages and an estimated 50 million people worldwide. Nearly 80% of those affected live in low- and middle-income countries, where access to diagnosis and specialised care remains limited. Nevertheless, up to 70% of people with epilepsy could achieve seizure freedom with timely diagnosis and appropriate treatment [1].

In children and adolescents, epilepsy is a major cause of morbidity, with substantial neurological, psychosocial and metabolic consequences. Beyond seizure control, contemporary epilepsy management increasingly addresses comorbidities and treatment-related complications associated with antiseizure medications [2–4]. In the Democratic Republic of the Congo (DRC), epilepsy constitutes a significant neurological health burden, characterised by a predominance

of generalised seizures, a high proportion of infectious and perinatal aetiologies, and delayed access to specialised neurological care [5].

Vitamin D, initially recognised for its role in calcium and phosphate homeostasis, is now regarded as a neuroactive hormone involved in the regulation of neuronal excitability, neuroinflammation and neuroprotection. Recent experimental evidence suggests that vitamin D modulates key molecular pathways implicated in epileptogenesis, including the regulation of autophagy and PTEN signalling, with potential anticonvulsant effects demonstrated in animal models [6].

Children and adolescents with epilepsy are particularly vulnerable to vitamin D deficiency. This increased risk is multifactorial, reflecting the combined influence of environmental, nutritional and treatment-related factors. Enzyme-inducing antiseizure medications, particularly phenobarbital, carbamazepine and phenytoin, are major contributors to reduced vitamin D status. Through induction of hepatic cytochrome P450 pathways, these medications increase vitamin D metabolic clearance and turnover, leading to lower circulating concentrations of 25-hydroxyvitamin D [25(OH)D] and potential disturbances in calcium–phosphate homeostasis [7, 8]. Even non-enzyme-inducing antiseizure medications have been associated with hypovitaminosis D [9, 10], suggesting the involvement of additional mechanisms that remain poorly understood.

Several clinical studies have reported a high prevalence of vitamin D deficiency among children with epilepsy, particularly in those receiving long-term antiseizure medication or specific drug classes [9, 11–13]. This finding is clinically relevant, as several studies have suggested that lower serum vitamin D concentrations are associated with greater seizure severity [14, 15]. However, the available evidence remains heterogeneous and does not currently support a causal relationship [16]. From a therapeutic perspective, recent clinical trials suggest that vitamin D supplementation may improve seizure control and modulate biomarkers associated with epileptogenesis, including inflammatory cytokines and neurotrophic factors, although findings remain inconsistent [17, 18]. Taken together, these findings suggest that vitamin D may play a multidimensional role in epilepsy management that extends beyond the correction of a biological deficiency [19]. Furthermore, vitamin D deficiency appears to affect the quality of life of people with epilepsy adversely. A prospective study from India reported significantly lower quality-of-life scores across several domains among patients with vitamin D deficiency, with subsequent improvement following vitamin D supplementation [20].

A recent systematic review and meta-analysis confirmed that vitamin D deficiency is highly prevalent among people with epilepsy, often affecting more than 50% of patients, and that serum vitamin D concentrations are consistently lower than those observed in the general population, irrespective of the type of antiseizure medication used [21]. However, the factors underlying this variability remain inadequately characterised, particularly in resource-limited settings. This evidence gap is especially pronounced in sub-Saharan Africa, where available data remain scarce despite environmental and contextual factors that may substantially influence vitamin D status, including dietary practices, sun exposure, food security and access to healthcare.

To date, no study has systematically evaluated vitamin D status among children and adolescents with epilepsy in the DRC, particularly in rural settings such as the Watsa Health Zone. Against this background, the present study aimed to assess vitamin D status among children and adolescents with epilepsy in the Watsa Health Zone, DRC, and to identify the sociodemographic, clinical, nutritional and treatment-related factors associated with serum vitamin D concentrations.

2 Materials and Methods

2.1 Study design, setting and study period

An analytical cross-sectional study was conducted between 15 January and 31 March 2026 in the Watsa Health Zone, Haut-Uélé Province, DRC. The study was carried out in healthcare facilities within the health zone, primarily at the Watsa General Referral Hospital and selected peripheral health facilities involved in the care of children and adolescents with epilepsy.

2.2 Study population and case definition

The study population comprised children and adolescents aged 1–19 years who had been residing in the Watsa Health Zone for at least three months. Consecutive exhaustive sampling was employed, whereby all eligible patients with epilepsy who provided informed consent (or

whose parents or legal guardians provided consent, as appropriate) were consecutively enrolled during the study period (January–March 2026).

All eligible cases identified and followed in healthcare facilities across the health zone during the study period were systematically recruited, resulting in a final sample of 43 participants. The sample size was therefore pragmatically determined by the total number of eligible cases available in the study area at the time of data collection.

Eligible participants were children and adolescents with active epilepsy diagnosed by trained physicians based on a comprehensive clinical assessment and review of the available medical records. Epilepsy was defined according to the practical clinical definition of the International League Against Epilepsy (ILAE) as the occurrence of at least two unprovoked seizures separated by a minimum interval of 24 hours or one unprovoked seizure fulfilling ILAE criteria for epilepsy. Seizure classification followed the operational recommendations of the ILAE.

2.3 Participant selection and data collection procedures

Sociodemographic, clinical, treatment-related and nutritional data were collected by trained nurses through face-to-face interviews with parents or legal guardians for participants younger than 18 years, and directly from adolescents aged 18–19 years. The variables assessed included sociodemographic characteristics (age, sex and place of residence), clinical characteristics (duration of epilepsy, epilepsy type and seizure control), treatment-related factors (current antiseizure medication use, type of medication and treatment duration), and nutritional factors (regular consumption of oily fish, eggs, milk or dairy products). Nutritional status was assessed using the Body Mass Index-for-Age Z-score (BAZ), categorised as normal weight or underweight.

Approximately 5 mL of venous blood was collected from the antecubital vein into Vacutainer® serum tubes containing a gel separator. Samples were centrifuged, protected from light and stored at -20°C within a maximum of four hours after collection. Serum concentrations of 25-hydroxyvitamin D [25(OH)D] were measured using an automated chemiluminescent immunoassay on the ADVIA Centaur XP analyser (Siemens Healthineers, Germany).

Vitamin D status was classified according to the Endocrine Society guidelines [22] as follows: deficiency (< 20 ng/mL), insufficiency (20–29.9 ng/mL), and sufficient vitamin D status (≥ 30 ng/mL). Hypovitaminosis D was defined as a serum 25(OH)D concentration < 30 ng/mL, corresponding to either vitamin D deficiency or insufficiency.

2.4 Statistical analysis

Data were entered and analysed using Stata version 16. Descriptive analyses were performed using frequencies and percentages for categorical variables, and means with standard deviations or medians with interquartile ranges for continuous variables, according to data distribution. Normality of continuous variables was assessed using appropriate methods, including the Shapiro–Wilk test and graphical inspection. Bivariate comparisons between serum vitamin D concentrations and categorical variables were performed using Student's *t*-test or Welch's *t*-test when the assumption of variance homogeneity was not met. Categorical variables with more than two categories were analysed using one-way analysis of variance (ANOVA).

Associations between continuous variables were explored using Pearson's or Spearman's correlation coefficients, depending on the distribution of variables. Simple linear regression analyses were performed to identify factors associated with serum vitamin D concentrations. A multiple linear regression model was subsequently constructed, including clinically relevant variables (age, sex and antiseizure medication use), as well as nutritional factors significantly associated with vitamin D concentrations in univariable analyses (consumption of oily fish, milk and eggs). Results are presented as regression coefficients (β) with their corresponding 95% confidence intervals (95% CIs). Statistical significance was defined as a p-value < 0.05.

2.5 Ethical considerations

The study protocol was approved by the Haut-Uélé Provincial Health Division and the Medical Ethics Committee of the University of Goma (reference: UNIGOM/CEM/017/2024). All required administrative authorisations were obtained from local health authorities before the initiation of data collection.

The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and relevant national guidelines applicable in the DRC. Written informed consent was obtained from all participants. For participants younger than 18 years, consent was obtained

from parents or legal guardians, together with child assent whenever appropriate and feasible. Participants aged 18–19 years provided consent directly.

Participation was voluntary, and participants were informed of their right to withdraw from the study at any time without any impact on their medical care. Confidentiality and anonymity were strictly maintained throughout the study. Data were anonymised, stored on secure password-protected devices, and accessed only by authorised members of the research team. Participants identified as requiring further medical attention were referred to appropriate healthcare facilities.

3 Results

A total of 43 children and adolescents with epilepsy were included in the analysis. The study population was predominantly male (55.8%), with a mean age of 11.2 ± 6.3 years, reflecting a paediatric cohort including both children and adolescents (Table 1). The median duration of epilepsy was 5 years (IQR: 2–8), indicating a population with longstanding epilepsy. More than half of the participants had uncontrolled seizures (60.5%). Focal and generalised epilepsy accounted for 48.8% and 51.2% of cases, respectively.

Table 1 Sociodemographic, clinical, nutritional and biological characteristics of participants (N = 43)

Variable	Value (N = 43)
Age (years), mean ± SD	11.2 ± 6.3
Sex, n (%)	
Male	24 (55.8)
Female	19 (44.2)
Place of residence, n (%)	
Urban	27 (62.8)
Rural	16 (37.2)
Duration of epilepsy (years), median (IQR)	5 (2–8)
Seizure control, n (%)	
Controlled	17 (39.5)
Uncontrolled	26 (60.5)
Epilepsy type, n (%)	
Focal	21 (48.8)
Generalised	22 (51.2)
Current antiseizure medication, n (%)	
None	5 (11.6)
Carbamazepine	10 (23.3)
Valproate (Depakine®)	10 (23.3)
Phenobarbital	18 (41.9)
Duration of antiseizure medication use (months), median (IQR)	36 (12–96)
Regular consumption of oily fish, n (%)	37 (86.1)
Regular consumption of eggs, n (%)	7 (16.3)
Regular consumption of milk or dairy products, n (%)	9 (20.9)
Nutritional status, n (%)	
Normal weight	39 (90.7)
Underweight	4 (9.3)
Vitamin D concentration (ng/mL), mean ± SD	23.5 ± 4.3
Serum calcium concentration (mmol/L), median (IQR)	2.15 (2.10–2.23)

Notes: SD: standard deviation; IQR: interquartile range.

Regarding treatment characteristics, phenobarbital was the most frequently used antiseizure medication (41.9%), followed by carbamazepine and valproate (23.3% each), while 11.6% of participants were not receiving antiseizure medication at the time of assessment (Table 1). Most participants had normal nutritional status, with 90.7% classified as normal weight and 9.3% as underweight. Regular consumption of oily fish was reported by 86.1% of participants, whereas regular consumption of eggs and milk or dairy products was less frequent (16.3% and 20.9%, respectively) (Table 1).

The mean serum vitamin D concentration was 23.5 ± 4.3 ng/mL (Table 1). The distribution of vitamin D status categories demonstrated a high prevalence of hypovitaminosis D among participants (Figure 1). Vitamin D insufficiency was the most common category, affecting 30 participants (69.8%; 95% CI: 54.9–81.4), followed by vitamin D deficiency in 11 participants (25.6%; 95% CI: 14.9–40.2). Only two participants (4.7%; 95% CI: 1.3–15.5) had sufficient vitamin D status (Figure 1).

Bivariate analyses showed that sociodemographic characteristics, including sex and place of

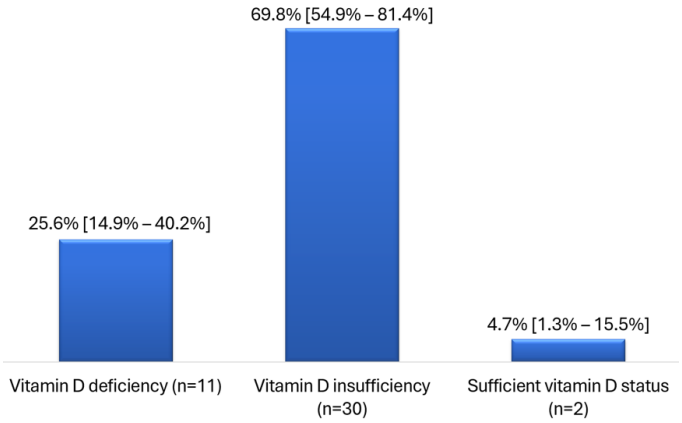

Figure 1 Distribution of participants according to vitamin D status categories (N = 43)

residence, were not significantly associated with serum vitamin D concentrations. Similarly, no significant associations were observed between vitamin D concentrations and clinical characteristics, including epilepsy type, seizure control status or antiseizure medication use (Table 2).

Table 2 Bivariate analysis of serum vitamin D concentrations according to participant characteristics (N = 43)

Variable	N = 43	Vitamin D (ng/mL) mean ± SD	p-value
Sex*			0.714
Male	24	23.30 ± 3.88	
Female	19	23.79 ± 4.89	
Residence*			0.825
Urban	27	23.40 ± 4.24	
Rural	16	23.71 ± 4.55	
Epilepsy type†			0.430
Focal	21	24.05 ± 3.08	
Generalised	22	23.00 ± 5.25	
Seizure control†			0.559
Controlled	17	22.98 ± 5.56	
Uncontrolled	26	23.87 ± 3.32	
Current antiseizure medication‡			0.334
None	5	22.74 ± 3.77	
Carbamazepine	10	24.99 ± 4.63	
Valproate (Depakine®)	10	24.65 ± 4.95	
Phenobarbital	18	22.28 ± 3.79	
Regular consumption of oily fish*			0.002
No	6	18.70 ± 4.35	
Yes	37	24.29 ± 3.81	
Regular consumption of milk or dairy products*			< 0.001
No	34	22.35 ± 3.92	
Yes	9	27.91 ± 2.56	
Regular consumption of eggs*			0.013
No	36	22.81 ± 4.01	
Yes	7	27.14 ± 4.19	
Nutritional status*			0.636
Normal weight	39	23.41 ± 4.20	
Underweight	4	24.50 ± 5.92	

Notes: * Independent-samples Student's *t*-test; † Welch's *t*-test (used when the assumption of variance homogeneity was not met); ‡ one-way analysis of variance (ANOVA).

In contrast, nutritional factors were significantly associated with serum vitamin D concentrations. Participants reporting regular consumption of oily fish had higher mean vitamin D concentrations compared with those without regular oily fish intake (24.29 ± 3.81 ng/mL *vs* 18.70 ± 4.35 ng/mL; $p = 0.002$). Similarly, regular consumption of milk or dairy products and eggs was associated with higher vitamin D concentrations ($p < 0.001$ and $p = 0.013$, respectively) (Table 2).

No significant correlations were observed between serum vitamin D concentrations and continuous variables, including age, duration of epilepsy, duration of antiseizure medication use

and serum calcium levels. Correlation coefficients were weak, suggesting no meaningful linear or monotonic relationship between these variables and vitamin D concentrations (Table 3).

Table 3 Correlation between quantitative variables and serum vitamin D concentrations

Variable	n	Correlation coefficient (r or ρ)	p-value
Age*	43	-0.093	0.553
Duration of epilepsy†	43	-0.103	0.511
Duration of antiseizure medication use†	38	-0.147	0.379
Serum calcium†	43	0.121	0.440

Notes: r: Pearson's correlation coefficient; ρ: Spearman's correlation coefficient. * Pearson correlation; † Spearman correlation.

Results from univariable and multivariable linear regression analyses are presented in Table 4. In univariable analyses, regular consumption of oily fish (β = 5.60; 95% CI: 2.14–9.05; p = 0.002), milk or dairy products (β = 5.56; 95% CI: 2.76–8.36; $p < 0.001$), and eggs (β = 4.34; 95% CI: 0.96–7.71; p = 0.013) was significantly associated with higher serum vitamin D concentrations. No significant associations were observed for age, sex, residence, epilepsy characteristics, seizure control, antiseizure medication use, treatment duration, serum calcium concentration or nutritional status (Table 4).

Table 4 Univariable and multivariable linear regression analysis of factors associated with serum vitamin D concentrations (ng/mL)

Variable	Crude β coefficient	95% CI	p-value	Adjusted β coefficient	95% CI	p-value
Age	-0.064	-0.278 to 0.151	0.553	-0.016	-0.186 to 0.154	0.851
Sex (female *vs* male)	-0.494	-3.193 to 2.206	0.714	-0.338	-2.317 to 1.640	0.730
Residence (rural *vs* urban)	0.306	-2.470 to 3.083	0.825	-	-	-
Duration of epilepsy	-0.026	-0.292 to 0.240	0.847	-	-	-
Seizure control (uncontrolled *vs* controlled)	0.889	-1.844 to 3.621	0.515	-	-	-
Epilepsy type (generalised *vs* focal)	1.043	-1.623 to 3.710	0.434	-	-	-
Duration of antiseizure medication use	-0.004	-0.029 to 0.020	0.713	-	-	-
Regular consumption of oily fish (yes *vs* no)	5.595	2.144 to 9.045	0.002	6.51	3.63 to 9.40	< 0.001
Regular consumption of milk or dairy products (yes *vs* no)	5.561	2.764 to 8.358	< 0.001	4.32	1.96 to 6.67	0.001
Regular consumption of eggs (yes *vs* no)	4.335	0.963 to 7.706	0.013	3.62	1.20 to 6.03	0.004
Serum calcium concentration	1.938	-8.011 to 11.886	0.696	-	-	-
Nutritional status	1.087	-3.524 to 5.698	0.636	-	-	-
Current antiseizure medication						
Carbamazepine *vs* none	2.25	-2.49 to 6.99	0.343	1.03	-2.53 to 4.60	0.559
Valproate *vs* none	1.91	-2.83 to 6.65	0.420	0.91	-3.09 to 4.91	0.647
Phenobarbital *vs* none	-0.46	-4.84 to 3.91	0.832	1.77	-2.14 to 5.67	0.364

Notes: β: regression coefficient; CI: confidence interval.

After adjustment for age, sex and antiseizure medication use, regular consumption of oily fish remained independently associated with higher serum vitamin D concentrations (β = 6.51; 95% CI: 3.63–9.40; $p < 0.001$). Similar independent associations were observed for milk or dairy product consumption (β = 4.32; 95% CI: 1.96–6.67; p = 0.001) and egg consumption (β = 3.62; 95% CI: 1.20–6.03; p = 0.004). No independent association was observed for age, sex or antiseizure medication use (Table 4).

4 Discussion

This study demonstrates an extremely high prevalence of hypovitaminosis D among children and adolescents with epilepsy in the Watsa Health Zone. Nearly 96% of participants had serum vitamin D concentrations below 30 ng/mL, including 69.8% with vitamin D insufficiency and 25.6% with vitamin D deficiency. The mean 25-hydroxyvitamin D concentration was 23.5 $\pm$ 4.3 ng/mL. After adjustment, only dietary factors, particularly regular consumption of oily fish, milk and eggs, remained independently associated with higher vitamin D concentrations. In contrast, no significant associations were observed with demographic characteristics, clinical features, antiseizure medication use or seizure control.

The very high prevalence of hypovitaminosis D observed in our study is consistent with findings from the international literature. A recent meta-analysis including 68 studies and more than 7,000 individuals with epilepsy estimated that nearly one in two patients had vitamin D deficiency, with mean vitamin D concentrations significantly lower than those reported in the

general population [21]. However, the prevalence observed in our study was considerably higher. This difference may reflect the combined effects of socioeconomic constraints, dietary patterns, limited access to vitamin D-rich foods, and the absence of routine vitamin D supplementation in our setting. These findings reinforce the importance of hypovitaminosis D as a relevant health concern among children with epilepsy living in resource-limited settings.

This issue is particularly important in sub-Saharan Africa, where access to serum 25-hydroxyvitamin D testing remains limited and where treatment patterns are still largely characterised by the use of older antiseizure medications, particularly phenobarbital and carbamazepine. In this context, Lisimo et al. [23] recently proposed a pragmatic vitamin D supplementation framework based on risk stratification rather than universal biochemical screening, aiming to improve the prevention of bone-related complications among people with epilepsy in resource-constrained settings.

Our findings are consistent with those reported in several paediatric epilepsy cohorts from different geographical settings. In Malaysia, Fong et al. [24] reported that more than 80% of children with epilepsy had hypovitaminosis D. In South Korea, Baek et al. [25] found that 37.1% of children and adolescents receiving antiseizure medications had impaired vitamin D status, including 9.1% with vitamin D deficiency and 28.0% with vitamin D insufficiency. In Thailand, Likasitthananon et al. [13] reported a high prevalence of hypovitaminosis D (71%) among children with epilepsy, comprising vitamin D deficiency in 23.2% and vitamin D insufficiency in 47.8% of participants. Similarly, Abdullah and Mousheer [10] reported an overall prevalence of hypovitaminosis D of 49% among children and adolescents with epilepsy, with significantly lower serum vitamin D concentrations compared with healthy controls ($p = 0.001$). Collectively, these findings suggest that reduced vitamin D status is a frequent feature among children with epilepsy across different geographical regions and healthcare settings.

Although enzyme-inducing antiseizure medications, such as phenobarbital, carbamazepine and phenytoin, are classically associated with induction of hepatic cytochrome P450 enzymes, particularly cytochrome P450 family 3 subfamily A member 4 (CYP3A4), this process accelerates vitamin D catabolism and increases the production of inactive metabolites, ultimately leading to reduced concentrations of 25-hydroxyvitamin D. In contrast, variations in 1,25-dihydroxyvitamin D [1,25$(OH)_2$D] concentrations remain inconsistent due to compensatory hormonal mechanisms. Overall, these processes contribute to increased vitamin D turnover and disruption of calcium–phosphate homeostasis [22, 26].

However, hypovitaminosis D cannot be attributed solely to the iatrogenic effects of antiseizure medications. Experimental and observational evidence suggests that vitamin D may also play a modulatory role in epilepsy through neuroprotective and anti-inflammatory mechanisms, as well as through its potential involvement in the regulation of neuronal excitability. Vitamin D deficiency has been associated with increased seizure susceptibility, suggesting a possible biological interaction with epileptic activity, although the underlying mechanisms remain incompletely understood and no definitive causal relationship has been established. Preliminary findings from interventional studies have also suggested improved seizure control following correction of vitamin D deficiency [19]. This complexity is supported by several recent studies. The multicentre study by Dong et al. [14] identified only modest differences in vitamin D status according to antiseizure medication exposure after adjustment for nutritional and environmental factors. Similarly, the meta-analysis by Liu et al. [21] reported that the high prevalence of hypovitaminosis D persisted across different clinical characteristics, including antiseizure medication type. Finally, the narrative review by Guo et al. [16] highlighted that the causal relationship between antiseizure medications and vitamin D deficiency remains uncertain, largely due to the potential influence of multiple confounding factors.

The absence of an association between serum vitamin D concentrations and duration of antiseizure medication exposure observed in our study contrasts with some previous reports describing a progressive decline in vitamin D concentrations during follow-up [24]. This discrepancy may be explained by several factors, including heterogeneity in treatment regimens, the predominance of already low vitamin D concentrations in our population, which may have limited the observable variability, and the relatively small sample size. Furthermore, the effect of cumulative treatment exposure may have been attenuated in a context of pre-existing vitamin D deficiency, where a biological plateau effect could obscure a potential dose–time relationship.

We also found no association between serum vitamin D concentrations and seizure control. This observation is consistent with findings from several cross-sectional studies, including that of Saing et al. [27], which reported no correlation between 25-hydroxyvitamin D concentrations and seizure frequency or severity among children with drug-resistant epilepsy. Similarly, a

randomised controlled trial by Pattnaik et al. [28] did not demonstrate a significant reduction in seizure frequency after six months of vitamin D supplementation compared with placebo, despite increased vitamin D receptor expression and reductions in some biomarkers associated with epileptogenesis.

Conversely, other studies have suggested that achieving vitamin D sufficiency during prolonged supplementation may be associated with improved seizure outcomes. The multicentre study by Chassoux et al. [18] reported that long-term supplementation was associated with a progressive reduction in seizure frequency and improved quality of life, although the primary endpoint was not achieved at the end of the controlled phase. Earlier, Holló et al. [19] reported an approximately 40% median reduction in seizure frequency following correction of vitamin D deficiency among patients with drug-resistant epilepsy.

These apparently inconsistent findings suggest that the potential benefits of vitamin D supplementation may depend on several factors, including baseline vitamin D status, duration of supplementation, achievement of adequate target concentrations, and patient-specific pathophysiological mechanisms. Further studies are needed to clarify which subgroups of individuals with epilepsy are most likely to benefit from vitamin D optimisation.

The biological mechanisms linking vitamin D and epilepsy continue to be actively investigated. Beyond its classical role in calcium–phosphate metabolism, vitamin D contributes to neuroprotection, modulation of neuroinflammation, synaptic plasticity and regulation of multiple genes involved in neuronal excitability. Recent experimental studies have shown that preventive vitamin D supplementation reduced seizure frequency, limited hippocampal injury, and modulated the phosphatase and tensin homolog (PTEN), calcium-sensing receptor (CaSR), and autophagy pathways in murine models of epilepsy [6]. In addition, vitamin D supplementation has been reported to increase vitamin D receptor (VDR) expression and reduce several biomarkers associated with epileptogenesis, including high mobility group box 1 (HMGB1) and neurotrophin-3 (NT-3) [17]. These experimental findings support the hypothesis that vitamin D may exert neuroprotective effects beyond its established role in bone metabolism.

A major original contribution of our study is the identification of dietary factors as independent determinants of vitamin D concentrations. Children who regularly consumed oily fish, milk or eggs had significantly higher serum vitamin D concentrations, with adjusted increases ranging from 3.6 to 6.5 ng/mL. These foods represent important natural sources of vitamin D, particularly in populations with limited access to fortified foods. In a setting such as the DRC, where food fortification programmes and routine supplementation strategies remain limited, dietary intake represents a potentially important intervention pathway. This finding is particularly relevant given that nearly 91% of participants had normal anthropometric nutritional status, indicating that the absence of undernutrition does not necessarily protect against specific micronutrient deficiencies.

From a clinical perspective, our findings support the need for increased awareness, monitoring and consideration of vitamin D supplementation among children and adolescents with epilepsy, in line with recent Endocrine Society recommendations suggesting empirical vitamin D supplementation in children and adolescents, particularly those at increased risk of deficiency [28], as well as emerging evidence supporting proactive management of high-risk populations [20, 21]. However, in many African settings, routine vitamin D testing remains constrained by limited availability and cost. In this context, the Consensus Statement on Vitamin D in the Healthy European Paediatric Population highlights the importance of a comprehensive preventive strategy combining a diversified diet rich in vitamin D sources (fish, eggs and dairy products), adequate sunlight exposure and targeted supplementation among high-risk groups [29].

In resource-limited environments, where these preventive strategies may not be fully achievable, a pragmatic approach based on clinical risk stratification and targeted empirical supplementation, as proposed by Lisimo et al. [23], may be particularly relevant. Our findings support this approach, given the very high prevalence of hypovitaminosis D observed (approximately 95% of participants), suggesting that children and adolescents with epilepsy in similar settings may represent a priority group for systematic nutritional intervention rather than isolated individual screening alone.

Beyond skeletal outcomes, correction of vitamin D deficiency has also been associated with improvements in quality of life and certain clinical parameters, particularly fatigue, although its direct effect on seizure control remains uncertain [18, 20].

This study has several limitations that should be acknowledged. First, the cross-sectional

design prevents the establishment of causal relationships between the investigated factors and vitamin D status. Second, the relatively small sample size may have limited statistical power to detect associations, particularly across different antiseizure medication categories. Third, several factors known to influence vitamin D concentrations, including sunlight exposure, skin pigmentation, seasonal variations, and serum measurements of parathyroid hormone or alkaline phosphatase, were not assessed. Finally, the absence of a non-epileptic control group limits comparisons with the general paediatric population.

Despite these limitations, this study represents, to our knowledge, the first investigation documenting vitamin D status among children and adolescents with epilepsy in the DRC. It highlights an alarmingly high prevalence of hypovitaminosis D and emphasises the potential importance of dietary factors in this setting. These findings also provide empirical support for the risk-based vitamin D supplementation framework recently proposed for sub-Saharan Africa [23]. They support the integration of vitamin D status assessment where feasible and, when biochemical testing is not readily available, the consideration of targeted preventive supplementation combined with nutritional education within epilepsy care programmes. Nevertheless, longitudinal studies and intervention trials conducted in African settings are required to determine the clinical effectiveness, feasibility and cost-effectiveness of these strategies.

5 Conclusion

This study identifies hypovitaminosis D as a highly prevalent and potentially modifiable comorbidity among children and adolescents with epilepsy in DRC. Nutritional factors, particularly regular consumption of oily fish, milk and eggs, emerged as the main determinants of serum vitamin D concentrations, whereas no significant association was observed with antiseizure medication use or other clinical characteristics. These findings support the integration of nutritional assessment, dietary counselling and context-adapted vitamin D supplementation strategies into paediatric epilepsy care in resource-limited settings. Prospective studies are warranted to determine whether improving vitamin D status translates into better clinical outcomes, including seizure control, bone health and quality of life.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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