

Prevalence of vitamin D deficiency and its relationship with epileptic severity in a pediatric department of tertiary care hospital

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Aim

To evaluate the prevalence of vitamin D deficiency in pediatric epileptic patients and to assess if there is any correlation between vitamin D level and disease severity in epileptic patients.

Objective

To estimate vitamin D deficiency and insufficiency as percentage of enrolled patients in pediatric department and to identify if there is any correlation between vitamin D deficiency and factors such as age, sex, BMI, total serum calcium levels, antiepileptic drugs, and types of seizures.

Patients and methods

A prospective interventional clinical study was carried out in a tertiary care hospital between September 2018 and February 2019. We included 30 pediatric epileptic patients of age group 1–14 years from whom the blood samples were withdrawn and were sent to the laboratory for the estimation of vitamin D levels.

Results

The data collected was analyzed using statistical method χ^2 and analysis of variance in Prism 8.0 version. The prevalence of vitamin D deficiency and its correlation with epilepsy was determined. In this study, we found that there was a high prevalence of vitamin D deficiency in pediatric epileptic patients (23 patients out of 30–73%). The other risk factors for vitamin D deficiency found in this study are children of age group 5–10 years (43%), malnourished patients (40%), hypocalcemic patients (40%), and patients who use antiepileptic drugs for more than 2 years (57%).

Conclusion

Based on the aforementioned scientific analysis, it can be concluded that there is a high prevalence of vitamin D deficiency in pediatric patients with epilepsy. So, vitamin D3 supplements should be given for all epileptic children even before the initiation of antiepileptic therapy. Patients' parents were educated on the importance of vitamin D.

Keywords:

antiepileptic drugs, epilepsy, vitamin D deficiency

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Introduction

Epilepsy is characterized by recurrent seizures, which are brief episodes of involuntary movement that may involve a part of the body (partial) or the entire body (generalized) and are sometimes accompanied by loss of consciousness and control of bowel or bladder function. Seizure episodes are a result of excessive electrical discharges in a group of brain cells [1]. Vitamin D is a fat-soluble vitamin that is produced endogenously when ultraviolet rays from sunlight strike the skin and trigger vitamin D synthesis. Hence it is called as sunshine vitamin. Vitamin D can be naturally obtained from dietary supplements [2,3]. Vitamin D test uses the principle of 'chemiluminescent immunoassay.' This test requires 2–3 ml of whole

blood. The sample is taken into a test cartridge to separate the plasma from sample [4]. To that, plasma antibodies reagents will be added and checked for the results [5]. According to many studies conducted clinically, the use of antiepileptic drugs (AED) increases the risk of developing vitamin D deficiency, and correcting vitamin D deficiency prevents seizures in people with epilepsy. Vitamin D has an ability to increase calcium uptake from the intestine, which can alter plasma and brain calcium

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concentrations that may decrease neuronal excitability and prevent seizures [6,7]. There is a consistent association between increasing BMI and lower serum 25-hydroxyvitamin D (25D) concentrations. One hypothesis is that the high content of body fat acts as a reservoir for lipid soluble vitamin D and increases its sequestration, thus determining its low bioavailability. It has also been reported that body fat content is inversely related to serum 25D concentration, and that this associations is stronger than those between 25D and BMI and body weight [8–10]. Low calcium intakes aggravate the consequences of vitamin D deficiency. The active vitamin D metabolite, 1, 25-dihydroxyvitamin D (1, 25(OH) (2) D) binds to the vitamin D receptor in the intestinal cell and stimulates the active calcium transport from the intestine to the circulation. Active calcium absorption decreases when the serum 25-hydroxyvitamin D (25(OH) D) concentration is less than 20 nmol/l. A high calcium intake increases the half-life of 25(OH) D [11]. AED-induced disturbances of bone metabolism are usually accompanied by a decrease in the 25(OH) D level, hypocalcaemia, secondary hyperparathyroidism, and increased bone turnover, with a decrease in bone density. In the pathogenesis of AED-induced bone disease, a central role is played by the pharmacokinetic interaction between the AEDs and vitamin D; the enzyme inducers carbamazepine, phenobarbital, phenytoin, and primidone can activate the pregnane X receptor, which then upregulates expression of the 24-hydroxylases, which can cause vitamin D deficiency [12–16].

Patients and methods

A prospective interventional clinical study was carried out to determine the serum levels of vitamin D in 30 epileptic children who were treated with AEDs for more than 6 months [17,18]. All the children of age 2–14 years of both sex, who visited in-patient department of pediatric ward in Gandhi hospital from September 2018 to February 2019 were considered for the study, and the protocol was approved by the Institutional Ethics Committee, with the approval number CMRCP/IEC/2018-19/04.

Exclusion criteria

Patients who were re-admitted with vitamin D deficiency levels, patients with febrile seizures, epileptic patients with other infectious diseases, and patients with neurological diseases such as cerebral palsy or mental retardation were excluded from the study.

Data collection

A special documentation form was designed for the purpose of clinical study, including name, age, sex, inpatient number, date of admission, date of discharge, height, weight, BMI, patient's chief complaints on examination, laboratory findings, past medical, medication history, final diagnosis, drugs on admission, and drugs on discharge. Type of AEDs used if immunotherapy was recorded as single AED, and as polytherapy if more than one AED was used. Informed consent form had been taken from the patient caretakers who are involved in the study for withdrawing blood sample. BMI was calculated from weight (kg) divided by height (m²). We visited inpatient pediatric ward on regular basis for case collection, and the collected cases were reviewed and interpreted. Vitamin D levels were correlated with age, sex, BMI, serum calcium levels, and usage of AEDs [19,20].

Laboratory procedures

Laboratory investigations of vitamin D levels and serum calcium levels were done by using chemiluminescent assay. Severe deficiency is less than 10 ng/ml, deficiency is 10–20 ng/ml, insufficiency is 20–30 ng/ml, sufficiency 25–30 ng/ml, and optimal more than 30 ng/ml.

Statistical analysis

The data were analyzed by using GraphPad prism software version 8.0.1 (GraphPad Software, Inc., San Diego, US). The result is expressed as mean \pm SD. Vitamin D deficiency in epileptic patients based on age, sex, BMI, serum calcium levels, type of seizures, and AEDs usage pattern was estimated by using χ^2 test. The data obtained from 30 participants were analyzed, and the variables were statistically assessed by using two-way analysis of variance. The *P* values obtained after statistical analysis are less than 0.0001, and it considered as statistically significant.

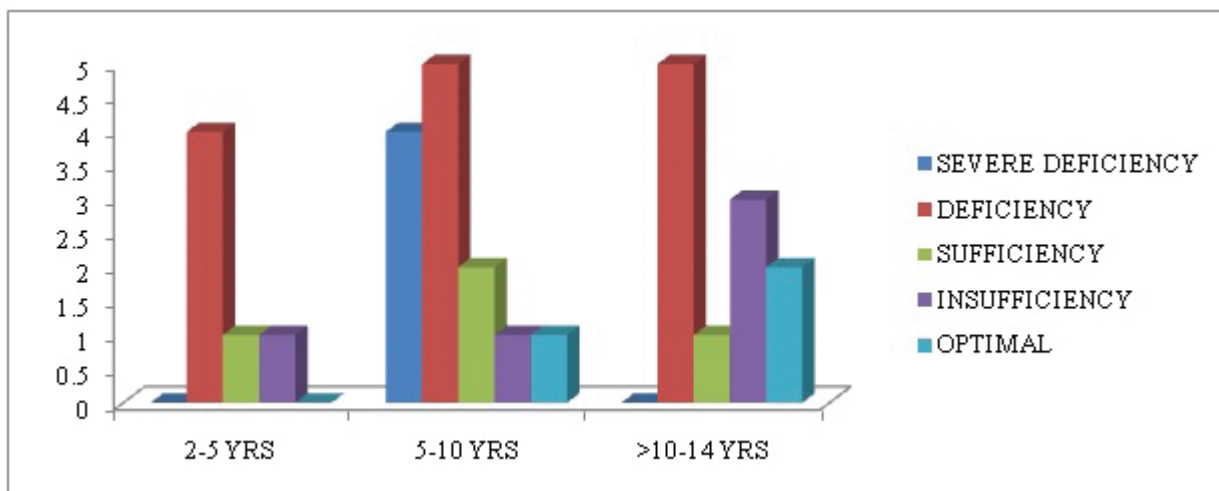
Results

A total of 30 cases were collected, and blood samples were withdrawn from the patient by taking informed consent form from patient caretakers as per inclusion criteria. Of 30 cases, 14 (47%) cases were found to have deficiency of vitamin D, 5 (16.6%) cases were found to have insufficient vitamin D levels, 4 (13.3%) cases were found to have sufficient vitamin D levels, 3 (10%) cases were found to be normal, and 4 (13.3%) cases were found to have severe deficiency of vitamin D.

Correlation of vitamin D with selected variables of epileptic patients

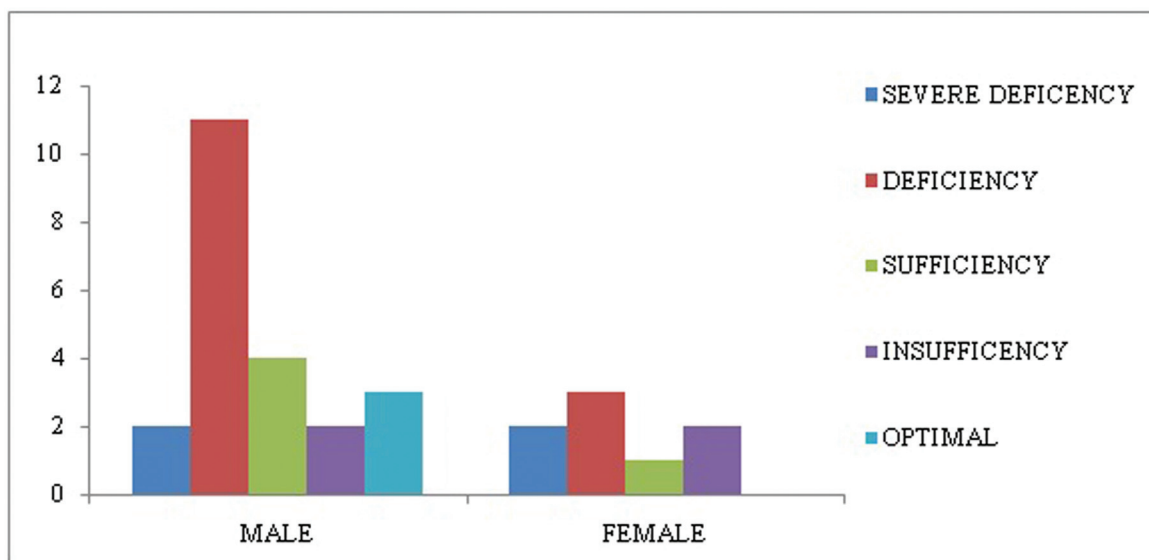
Based on age, 5–10 years (43%) and 10–14 years (37%) of age group children have more prevalence of vitamin D

Figure 1



Graphical representation for vitamin D deficiency in epileptic patients based on age.

Figure 2



Graphical representation for vitamin D deficiency in epileptic patients based on sex.

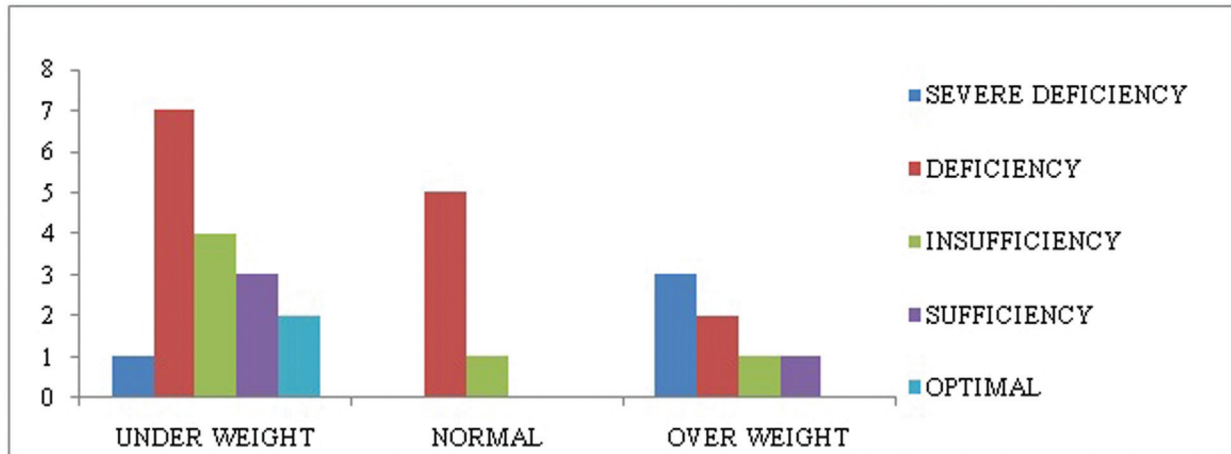
deficiency, with a P -value of less than 0.0001, which indicates that vitamin D level was low in pediatric epileptic patients (Fig. 1). Based on sex, our study results report that boys (36.6%) are more prone to develop vitamin D deficiency than girls, with a P value of 0.0848, indicating nonsignificant difference (Fig. 2). Based on BMI, both underweight and malnourished patients have more vitamin D deficiency (40%), with a P value of less than 0.0001, which indicates a significant difference between vitamin D and low BMI (Fig. 3). Based on serum calcium, it was found that hypocalcemic patients are at more risk to develop vitamin D deficiency than hypercalcemic and normal patients; the obtained P value is less than 0.0001, which indicates significance of vitamin D deficiency with

calcium levels (Fig. 4). Based on the type of seizures, it was found that among different types of seizures, patients with status epilepticus are at more risk to develop vitamin D deficiency, with an obtained P value of less than 0.0001, which indicates significance (Fig. 5). Based on AED duration, patients who took AEDs more than 24 months are in more risk to develop vitamin D deficiency (57%) (Fig. 6 and Tables 1 and 2).

Discussion

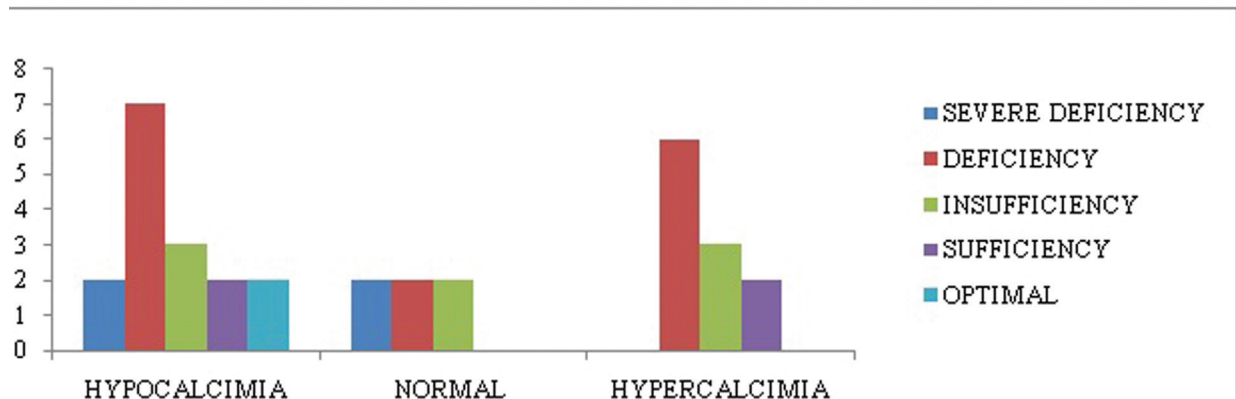
A total of 30 pediatric epileptic patients of mean age 1–14 years were divided into three groups of 2–5, less than 5–10, and less than 10–14 years for evaluating vitamin D levels in the pediatric department of a

Figure 3



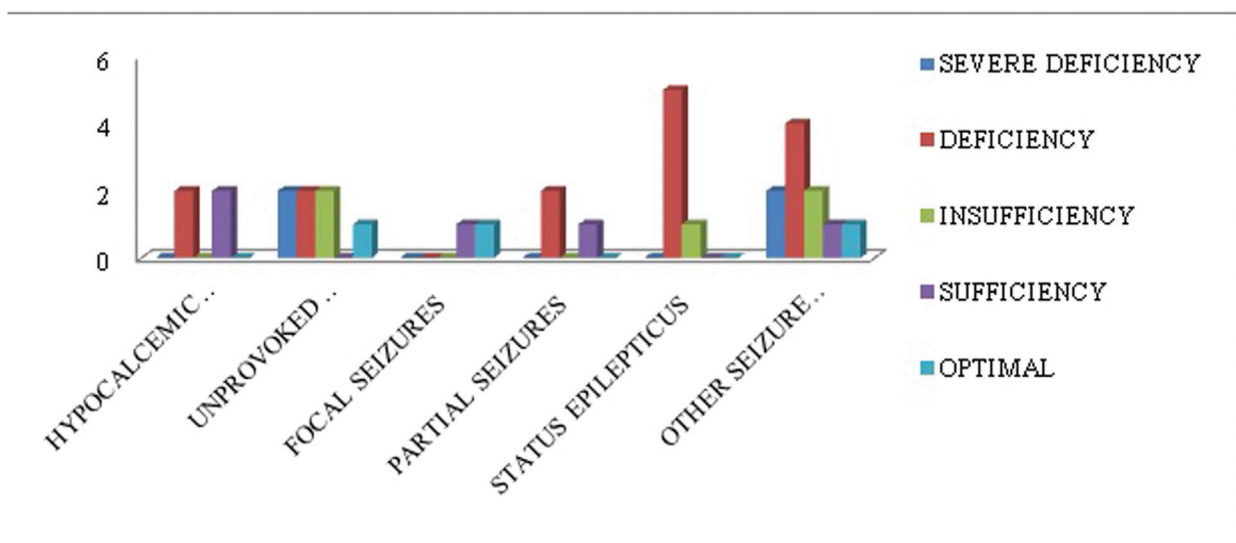
Graphical representation for vitamin D deficiency in epileptic patients based on BMI.

Figure 4



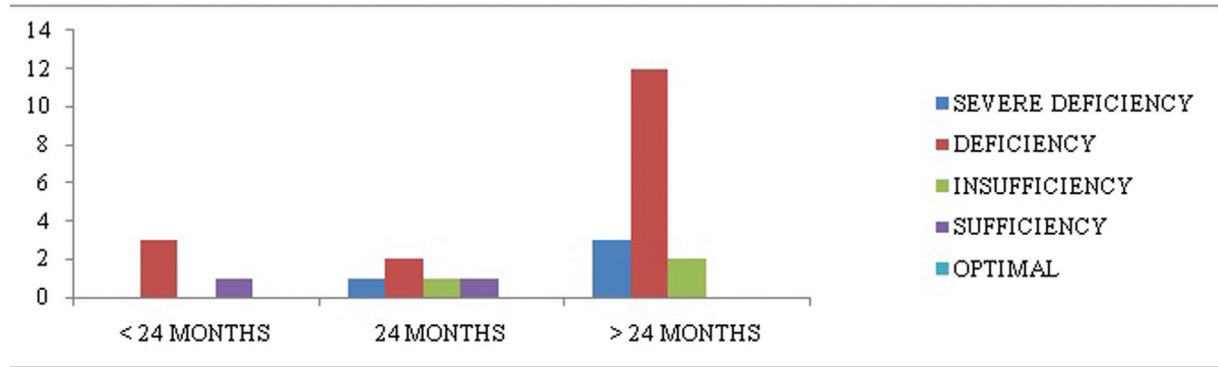
Graphical representations for vitamin D deficiency in epileptic patients based on serum calcium levels.

Figure 5



Graphical representation for vitamin D deficiency in epileptic patients based on type of seizures.

Figure 6



Graphical representation for vitamin D deficiency in epileptic patients based on duration of usage of antiepileptics.

Table 1 Percentage of vitamin D deficiency in selected variables of epileptic patients

Variables	Subvariables	Severe deficiency	Deficiency (10–20)	Insufficiency (20–25)	Sufficiency (25–30)	Optimal (>30 ng/ml)
Age	2–5 years	0	80	20	20	0
	>5–10years	80	100	20	40	20
	>10–14 years	0	80	60	20	40
Sex	Boys	6	36	13	6	10
	Girls	6	10	3	2	0
BMI	Under weight	3	23	10	13	7
	Normal	0	16	0	3	0
	Over weight	10	7	3	3	0
Serum calcium	Hypocalcemic	7	23	7	0	7
	Normal	7	7	0	7	0
	Hypercalcemic	0	20	7	10	0
Type of seizures	Hypocalcemic	0	7	7	0	0
	Unprovoked	7	7	0	7	3
	Focal	0	0	3	0	3
	Partial	0	7	3	0	0
	Status epilepticus	0	17	0	3	0
	AED duration	< 24 months	0	20	7	13
	24 months	3	3	3	0	7
	>24 months	10	23	0	3	0

AED, antiepileptic drug.

tertiary care hospital. Vitamin D has an ability to increase calcium uptake from the intestine, which alters brain concentrations that may decrease neuronal excitability and prevent seizures. Among the total epileptic patients, 73% were found to have vitamin D deficiency. This indicates that epileptic patients are highly susceptible to vitamin D deficiency, which coincides with the study conducted by Pooja *et al.* [11].

Based on age, children of age between 5 and 10 years (43%) and 10 and 14 years (36%) had more prevalence of vitamin D deficiency. According to sex, 22 of the 30 patients enrolled were boys, of whom, 17 boys were found to have vitamin D deficiency. Among the eight girls enrolled, five of them had vitamin D deficiency,

indicating that vitamin D deficiency is seen with both sexes. This study is similar to the study conducted by Smotkin-Tangorra *et al.* [16]. Correlations of vitamin D deficiency with girls and increased BMI are considered as major risk factors to develop vitamin D insufficiency, but our study contradicts the aforementioned study, as most of the patients were underweight owing to malnourishment. Vitamin D insufficiency is a common problem in pediatrics, especially with those who have chronic illness and who are malnourished. There is a significant correlation between serum calcium and vitamin D; active calcium absorption decreases when serum vitamin D concentration decreases. Patients with hypocalcemia had higher prevalence of developing vitamin D deficiency compared with those with

Table 2 Mean vitamin D level in relation to selected variables of epileptic patients

Variables	Subvariables	Mean±SD	P value
Age	2–5 years	24.00±32.863	<0.0001
	>5–10 years	52.00±36.332	
	>10–14 years	40.00±31.623	
Sex	Boys	14.20±12.538	0.0848
	Girls	4.20±3.899	
BMI	Under weight	11.20±7.563	<0.0001
	Normal	3.80±6.943	
	Over weight	4.60±3.912	
Serum calcium	Hypocalcemic	8.800±8.497	<0.0001
	Normal	3.200±2.490	
	Hypercalcemic	7.800±9.257	
Type of seizures	Hypocalcemic	2.800±3.834	<0.0001
	Unprovoked	4.800±3.194	
	Focal	2.00±3.082	
	Partial	1.200±1.643	
AED duration	Status epilepticus	4.000±7.382	0.0015
	<24 months	8.60±8.019	
	24 months	3.20±2.490	
	>24 months	7.80±9.257	

AED, antiepileptic drug.

normal and high calcium levels [13]. According to international clinical study conducted on 30 patients based on types of seizures, patients with status epilepticus are more prone to develop vitamin D deficiency compared with other types, such as focal, partial, or unprovoked seizures. The usage pattern of AEDs alters the calcium, ionized calcium, and vitamin D3 levels of epileptic patients, which eventually results in bone loss, abnormal mineralization, and fractures. The results of this study indicate that the patients who are using AEDs for more than 24 months have more risk to develop vitamin D deficiency.

Conclusion

This study reported the levels of vitamin D in epileptic patients of age group between 1 and 14 years based on six different parameters. We concluded that pediatric epileptic patients have high prevalence of vitamin D deficiency, that is, 23 of 30 (73%) patients. Vitamin D supplements should be given to all epileptic children even before initiation of anti-epileptic therapy, and children with epilepsy should follow a well-balanced diet and good nutritional habits to optimize seizure control.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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