

**Research Article**



# Vitamin D deficiency in children on antiepileptic monotherapy and multidrug therapy

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**Abstract:** The medical literature has recently focused on the effects of vitamin D on various aspects of health. In addition to its critical role in calcium homeostasis and bone mineral metabolism, it is now recognized as having a wide range of essential biological functions. The relationship between vitamin D, antiepileptic drugs, and bone health in people with epilepsy has been recognized for more than 30 years. Seizures have an inherent risk of injury, including fractures; comorbidities with poor bone health increase this risk, especially in children with motor performance seizures and children with impaired motor function and coordination. Many AEDs are inducers of hepatic metabolism of cytochrome P450.

## Introduction

Medical literature has recently focused attention on the impact of vitamin D on various aspects of health. Besides its pivotal role in calcium homeostasis and bone mineral metabolism, it is now recognized to serve a wide range of fundamental biological functions. The association between vitamin D, antiepileptic drugs, and bone health in individuals with epilepsy has been recognized for more than 30 years. Seizures themselves pose a risk for injury, including fractures; and the added co-morbidity of poor bone health increase this risk, especially in children with who suffer from seizures with motor manifestations, as well as those with impaired motor function and coordination. Many AEDs are inducers of hepatic cytochrome P450 metabolism. It has been postulated that these AEDs result in increased hepatic metabolism of vitamin D, leading to low vitamin D levels. However, non-enzyme inducing AEDs have also been associated with low vitamin D levels and in turn with poor bone health. Therefore, although the newer AEDs are less-potent enzyme inducers than older AED, they are not necessarily inert in bone metabolism. Studies have reported variable changes in vitamin D levels in children taking AEDs. We aimed to describe the prevalence of and risk factors for

vitamin D deficiency among children with epilepsy on antiepileptic drugs.

## **Material and methodology**

-STUDY DESIGN : case control study

-STUDY SETTING : Pediatric OPD and epilepsy OPD of civil hospital Ahmedabad

-DURATION OF STUDY : January 2019 – March 2019

-A prospective study was done in pediatric OPD and epilepsy OPD on children <12 years age.

-Cases included those having epilepsy and having apparently normal physical and mental development, on antiepileptic monotherapy or polytherapy for atleast 6 month.

-Controls included age matched children who were not on any continuous medication during the same period of study.

-Data including age, weight, height, type of epilepsy, drugs used for treatment of epilepsy, duration of epilepsy, frequency of seizures, duration of antiepileptic therapy were collected.

-Serum calcium, phosphate, alkaline phosphatase (ALP), urea, creatinine, proteins, aspartate amino

transferase(AST) , alanine amino transferase(ALT) , 25 hydroxy vitamin D levels were assessed.

**-Inclusion criteria :**

-children with epilepsy aged <12 years

**-Exclusion criteria :**

- children with metabolic bone disease
- significant renal impairment, hepatic impairment, endocrine disorders
- children on vitamin D supplementation
- children on any other drug likely to affect bone metabolism

**Aims and Objective :**

-to study prevalence and incidence of vitamin D deficiency in children on antiepileptic drug

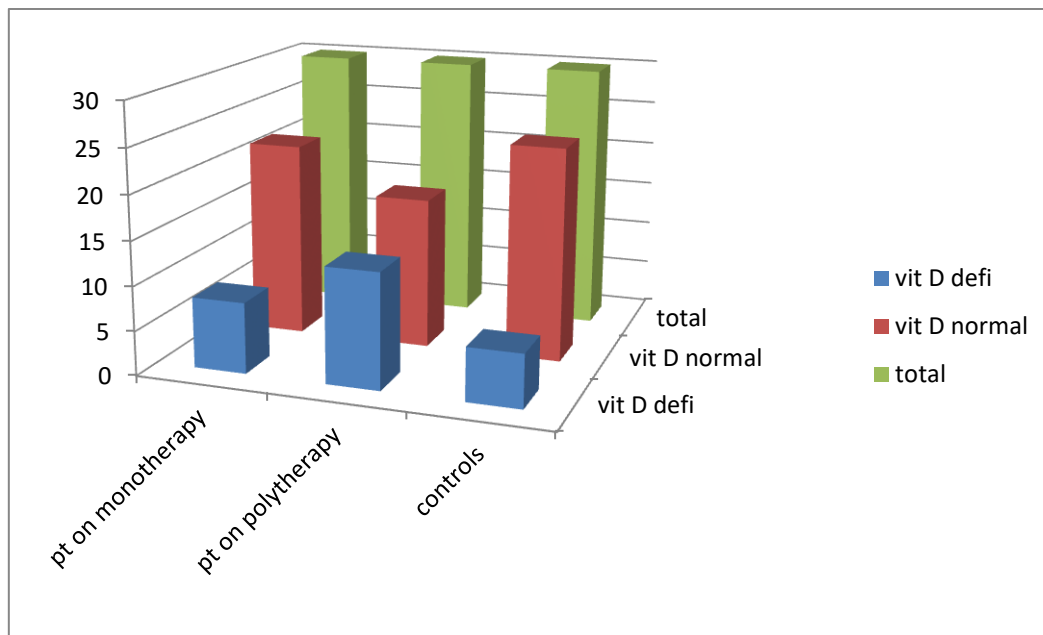
-to study effect of monotherapy and polytherapy of antiepileptic drug on severity of vitamin D deficiency

-to study variations in levels of bone markers in children on antiepileptic drug

**Results :**

Total 30 patients on monotherapy of AED , 30 patients on polytherapy of AED and 30 controls were included in the study.

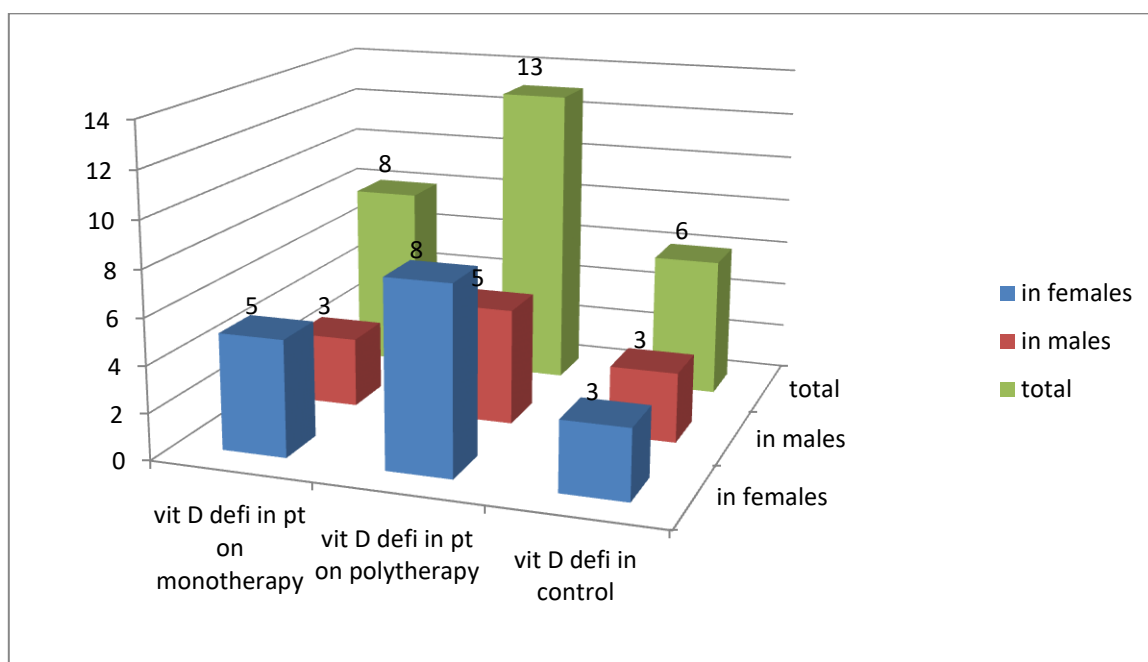
Vit D deficiency was seen in 8 (26%) of patients on monotherapy , 13 (43%) of patients on polytherapy and 6 (20%) of controls.



Age range was upto 12 years. There was equal distribution patients from infancy to adolescence. Sex distribution was as follows in all :

	Vit D deficiency in females	Vit D deficiency in males	Total
Pt on monotherapy AED	5 (62.5%)	3 (37.5%)	8
Pt on polytherapy AED	8 (61.5%)	5 (38.5%)	13
Controls	3 (50%)	3 (50%)	6
Total	16 (59.2%)	11 (40.8%)	27

This suggest preponderance of female (59.2%) as compared to male (40.8%).



The distribution of levels of vit D deficiency was as follows :

	Total Vit D deficiency	Severe Vit D deficiency
Pt on monotherapy AED	8	2 (25%)
Pt on polytherapy AED	13	4 (30.7%)
Controls	6	1 (16.6%)

This shows severe vitamin D deficiency is seen more in patients on polytherapy of AED.

Thus, clinical manifestations of vitamin D deficiency are more frequently seen in patient taking anti epileptic drugs as compared to control group.

**Discussion:**

Vitamin D is an essential nutrient that maintains the homeostasis of calcium and phosphorous in the body. The importance of vitamin D was recently emphasized when it was reported that it has several non-skeletal physiological functions too. Many AEDs are inducers of hepatic cytochrome P450 metabolism. It has been postulated that these AEDs result in increased hepatic metabolism of vitamin D, leading to low vitamin D levels. However, non-enzyme inducing AEDs have also been associated with low vitamin D levels and in turn with poor bone health. Therefore, although the newer AEDs are less-potent enzyme inducers than older AED, they are not necessarily inert in bone metabolism. Research has shown that adult epilepsy patients on AEDs

can exhibit deficiency of vitamin D. In pediatric patients, however, controversies still remain regarding the effect of AEDs on vitamin D levels.

This study showed that the serum levels were significantly lower in patients on anti epileptic drugs .

Vit D deficiency showed preponderance to females as compared to males.

Chances of vit D deficiency increases with increase in duration of AED and number of AED.

One limitation of this study was that vit D levels were not assessed before AED use

One previous study showed that patients who took anticonvulsants for more than 2 years had normal vitamin D levels, although BMD was found to be decreased; these authors mentioned the possibility of high vitamin D intake among the experimental group. However, we ruled out any vitamin supplementation in our study

**Conclusion :**

We found vitamin D deficiency to be highly prevalent among children with epilepsy on AED.

The high prevalence of hypovitaminosis D suggests that, almost all children with epilepsy are at risk. Increased duration of AED therapy was associated with increased risk of vitamin D deficiency. Increased attention on the part of both pediatric neurologists and pediatricians to vitamin D status among children with epilepsy is warranted as vitamin D has a vast impact on health of children other than bone health such as reducing the frequency of seizures, immunity, autoimmune disease and malignancy to mention a few.

Thus, this study suggests that patient on Anti-epileptic drug should be Monitored for Vit-D deficiency at regular interval. Vit-D supplements and Calcium should be given to all patients on Anti-epileptic Drugs.

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