

**Case Report****A Study of Vitamin D Deficiency in Patients of Epilepsy on Anti-Epileptic Drug**<sup>1</sup>Dr. Anuya Chauhan mam, <sup>2</sup>Dr.Gargi Pathak mam, <sup>3</sup>Dr.Devhuti Godhani<sup>1</sup>(Assi. Prof) Dept of paediatrics BJ Medical College Ahmedabad<sup>2</sup>(Prof and HOU) Dept of paediatrics BJ Medical College Ahmedabad<sup>3</sup>(3 year resident) Dept of paediatrics BJ Medical College Ahmedabad**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 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, with comparison between monotherapy and polytherapy.

**Material and Methodology****-STUDY DESIGN :** cross sectional study**-STUDY SETTING :** Pediatric OPD and epilepsy OPD of civil hospital Ahmedabad**-DURATION OF STUDY :** January 2019 – March 2019 (3 months)

-The study was done in pediatric OPD and epilepsy OPD on children &lt;12 years age.

-Cases included those having epilepsy and attending epilepsy OPD, on antiepileptic monotherapy or polytherapy for atleast 6 month.

-Controls included age matched children who were not on any continous medication during the same period of study, selected from patients coming to pediatric OPD.

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

- vitamin D status was defined as severe deficiency, deficiency and sufficiency at 25(OH)D levels &lt;5, &lt;15 and &gt;20 respectively.

**-Inclusion criteria :**

-children with epilepsy aged &lt;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

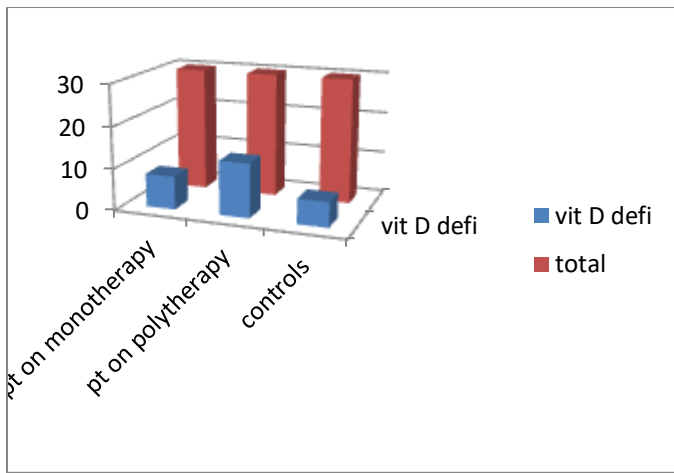
-to study variations in levels of bone markers in children on antiepileptic drug

**Results:**

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

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

	Vit D deficiency
Pt on monotherapy AED (n=30)	8 (26%)
Pt on polytherapy AED(n=30)	13(43%)
Controls(n=30)	6(20%)



The chi-square statistics is 4.127. The p-value is 0.03271. The result is significant at  $p < 0.05$ .

Among patients on monotherapy AED, following was noted

	Vit D deficiency
Patients on valproate (n=18)	5 (27.7%)
Patients on CBZ (n=12)	3(25%)

The chi-square statistics is 0.0165. The p-value is 0.897. The result is not significant at  $p < 0.05$ .

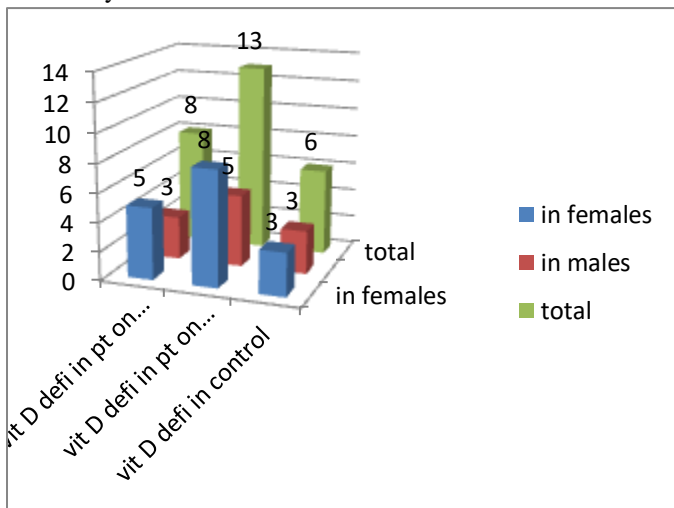
Age range was upto 12 years. There was equal distribution of patients from infancy to 12 years age.

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

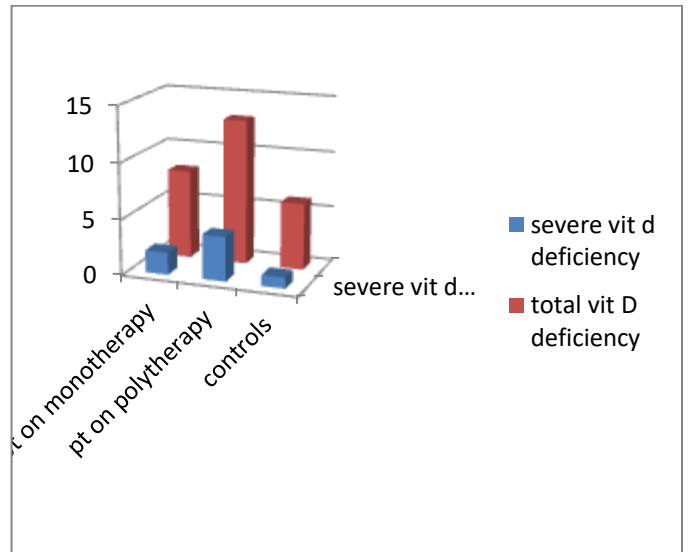
The chi-square statistics is 0.2758. The p-value is 0.0492. The result is significant at  $p < 0.05$ .

Females on AEDs are more susceptible to develop vit D deficiency than males on AEDs.



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.

The levels of serum calcium, phosphate and alkaline phosphate in all 3 groups were noted as follows :

	Low S.calcium	Low S.phosphate	Raised ALP
Pt on AED monotherapy (30)	4 (13.3%)	4 (13.3%)	6 (20%)
Pt on AED polytherapy (30)	8 (26.6%)	8 (26.6%)	11(36.6%)
Controls (30)	5 (16.6%)	5 (16.6%)	2 (6.6%)

Manifestations of vitamin D deficiency either clinically or on X ray were seen as follows :

Vit D deficiency in	Manifestations of vit D defi
Pt on AED monotherapy (8)	3 (37.5%)
Pt on AED polytherapy (13)	8 (61.5%)
Controls (6)	2 (33.3%)

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.

This hospital-based cross-sectional study found a significantly high proportion of children receiving AEDs to have hypovitaminosis D, as compared to controls. The one important limitation of our study is the cross-sectional design; a longitudinal follow up of these children might have been a more accurate reflection of bone health in these children. One study longitudinally followed up children with epilepsy on antiepileptic drugs and found that a high proportion of children had hypovitaminosis D before the start of treatment, and a significant decrease in levels was noted between the initial and the follow up after 6 months

This suggested epilepsy as a risk factor for vitamin D deficiency, which will be augmented by antiepileptic drugs. We did not attempt the bone mineral density estimation by DEXA scan, which accurately reflects the bone health, because of financial constraints and the risk of exposure to X-ray irradiation. Other parameters like osteocalcin levels, serum parathormone levels and calcitonin levels were also not assayed. Some studies noted that AEDs did not show any effect on serum vitamin D levels. Hepatic induction of the cytochrome P450 enzyme system leading to increased catabolism of vitamin D is the principal mechanism reported in case of enzyme-inducing drugs like Carbamazepine . Valproate inhibits the 25- hydroxylase activity on vitamin D in liver mitochondria without inhibiting the components of cytochrome P450- linked mono-oxygenase systems . It is proposed that genetic variations like polymorphisms in vitamin D receptor (VDR) gene may predispose one to vitamin D deficiency. This study shows that serum 25 OH vitamin D levels are significantly low in children on AED. 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. Children on antiepileptic drugs should have regular monitoring of Vitamin D levels, and/ or supplementation with calcium and vitamin D even in children with normal growth and development, no limitation of physical activity and adequate exposure to sunshine. The impact of antiepileptic drugs on bone health is to be addressed by all Pediatricians, as early identification of vitamin D deficiency and supplementation of calcium and vitamin D can help majority of children on long term anticonvulsants.

#### 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 suggest 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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