

**A comparative study of vitamin d3 levels in febrile children from 6 months to 5 years of age with and without seizures**

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**Citation this Article:** Dr. Kusum Devpura, Dr. Vishnu Agarwal, Dr. Tikam Chand Kumawat, Dr. Swati Mehta, Dr. Mukesh Solanki, “A comparative study of vitamin d3 levels in febrile children from 6 months to 5 years of age with and without seizures”, IJMSIR- April - 2021, Vol – 6, Issue - 2, P. No. 68 – 72.

**Type of Publication:** Original Research Article

**Conflicts of Interest:** Nil

**Abstract**

**Background:** Febrile seizures are the commonest cause of seizures in children. There is a increasing concern that vitamin D deficiency may play etiological role in febrile seizures. The objective of this study is to assess the serum vitamin D3 level in children from 6 month to 5 years of age with first episode of febrile seizure and to determine the association between vitamin D3 levels and febrile seizure.

**Methods:** A Hospital based comparative observational study was conducted in Department of Pediatrics, S.M.S. Medical College Jaipur from June 2019 to June 2020. 60 cases presenting with first episode of simple febrile seizure of age group 6 months to 5 years of age

were enrolled and 60 control was selected with similar age group and gender who present with fever (duration -atleast 2 day) without seizure. 2ml of the blood sample was taken from the peripheral veins in a uncoated plain glass tube. Sample was sent to laboratory for serum vitamin D3 level and was measured by ADVIA CENTAUR VitaminD3 total assay.

**Result:** Out of 60 cases included in the study ,vitamin D3 level was deficient in 9 cases(15%), Insufficiency in 34 cases(56.67%) and normal in 17 (28.3%).Out of 60 controls, vitamin D3 level was deficient in 1 case(1.67%),insufficiency in 19 cases(31.67%) and normal in 40 cases (66.67%).Strong and significant (p

value < 0.001) association of febrile seizure with vitamin D3 level was observed in our study.

**Conclusion:** There was high prevalence of vitamin D3 insufficiency among cases of simple febrile seizure.

### **Introduction**

Febrile seizures are the most common seizure disorder in children with a worldwide prevalence of 2 to 5% and the peak incidence is around the age of approximately 18 months.<sup>1,2</sup> American academy of Pediatrics (AAP) 2008 defined febrile seizure as a seizure occurring in febrile children between the ages of 6 and 60 months who do not have an intracranial infection, metabolic disturbance, or history of afebrile seizure.<sup>3</sup>

25-Hydroxy vitamin D3 is associated with a variety of medical disorders, for example, diabetes, autoimmune disorders, and cardiovascular problems.<sup>4,5</sup> Its role is also well-defined in epileptic patients.<sup>6</sup> However, its role in febrile seizures is under research and few studies are available, which justify its correlation with febrile seizures and their recurrence. The exact mechanism by which vitamin D3 exerts its beneficial effect in epilepsy is still to be explored. Vitamin D3 receptors as well as the 1-alpha-hydroxylase, the enzyme that produces 1,25(OH)D (the active form of vitamin D3), are distributed widely in the brain.<sup>7</sup> It is suggested that the effect of vitamin D3 in the central nervous system is mediated by both calcemic and non-calcemic actions.<sup>16</sup> The latter includes changes in gene expression in response to the binding of 1,25(OH)D to the nuclear vitamin D3 receptor.<sup>8</sup>

In the last decade, a variety of factors such as hypozincemia,<sup>9</sup> low sodium level, and low vitamin B6<sup>19</sup> were added to the list of risk factors, which increase the incidence and recurrence of simple febrile seizures. Extensive research is currently going on to discover more and more risk factors of febrile seizures, so that

they can be modified to decrease their incidence and recurrence. Keeping in view the above discussion, we aimed to explore vitamin D3 status in children aged 6 months to 5 years with first episode of febrile seizure and to find the association between vitamin D3 levels and febrile seizure.

### **Material and methods**

#### **Place of study**

Department of Pediatrics, S.P.M.C.H.I and attached group of hospitals, S.M.S. Medical College Jaipur, (Rajasthan).

#### **Type of Study**

Hospital based comparative observational study

#### **Study period**

June 2019 to July 2020 or till completion of sample size after approval from ethical committee.

#### **Sample Size**

Sample size is calculated at 95% confidence with alpha error 0.05. Assuming 72.9% and 45.9% of subjects having deficiency of vitamin D3 or insufficiency of vitamin D3 levels among the two groups respectively. Study power of 80%, required sample size will be 60 cases in each group, cases with simple febrile seizure and fever without seizures.

#### **Inclusion Criteria**

##### **Case**

- Children of age group 6 months to 5 years presenting with first episode of simple febrile seizure.

##### **Control**

- Case selected with similar age groups and same sex presented with short duration of fever of at least 2 days but without seizure.

#### **Exclusion Criteria**

- Children presenting with
- atypical febrile seizures

- afebrile seizures,
- any signs of CNS infections,
- sick children, those with neurodevelopmental delay,
- previous history of febrile seizures
- liver, renal or endocrinal disorders .
- refusal for consent

**Statistical analysis**

- The Fischer's exact test (two-tailed), Chi-square test and Z score were performed to analyse differences in proportions of categorical variables between two groups.
- The level  $p < 0.05$  was considered as the cut-off value for significance.
- All analyses were performed using IBM SPSS statistics. Version 20, for Windows.

**Observation**

Table 1: Distribution of cases according to age

	Cases		Controls	
	No.	%	No.	%
6-24 month	51	85.00	39	65.00
25-43 month	9	15.00	10	16.67
44-60 month	0	0.00	11	18.33
Total	60	100.00	60	100.00

The above table depicts that maximum number of patients in case group (85.00%) and controls group (65.00%) lies in the age group of 6-24 months.

Table 2: Distribution of cases and controls according to gender

	Cases		Controls	
	No.	%	No.	%
Male	43	71.67	40	66.67
Female	17	28.33	20	33.33
Total	60	100.00	60	100.00

Above table depicts that males were more in number 43(71.67%) as compared to females 17 (28.33%) in cases group and males were more in number 40(66.67%) as compared to females 20 (33.33%) in controls group.

Table 3: Distribution of cases and controls according to Vitamin D3 status

	Cases(n=60)		Controls(n=60)	
	No.	%	No.	%
Deficient (<12 ng/ml)	9	15.00	1	1.67
Insufficient (12-20 ng/ml)	34	56.67	19	31.67
Normal ( $\geq 20$ ng/ml)	17	28.33	40	66.67
Total	60	100.00	60	100.00
P value	p<0.001 (S)			

The above table depicts that among cases group 9 (15.00%) patients had deficient vitamin D3 levels. 34 (56.67%) patients had vitamin D3 levels in insufficient category and in 17 (28.33%) patients levels were normal. Similarly, in controls group, levels of vitamin D3 were deficient in 1(1.67%) patients, insufficient in 19 (31.67%) patients and normal levels in 40 patients (66.67%). The difference between both group was found statistically significant.

**Discussion**

The study was conducted in the Department of pediatrics, S.P.M.C.H.I and attached group of hospitals, SMS Medical College, Jaipur, from June 2019 to July 2020.

The study was undertaken to assess the vitamin D3 levels in febrile children from 6 months to 5 years of age with and without seizures.

In this study we enrolled 60 children as cases with febrile seizures and 60 children as control with fever of atleast 2 days without seizures.

In our study, among cases, 9 (15.00%) subjects had deficient vitamin D3 levels, 34 (56.67%) subjects had vitamin D3 levels in insufficient category and 17 (28.33%) subjects had normal levels. Similarly, among controls, the levels of vitamin D3 were deficient in 1(1.67%) subject, insufficient in 19(31.67%) subjects and normal levels in 40(66.67%) subjects. The difference between both the groups was found statistically significant ( $p < 0.0010$ ).

Singh V et al<sup>10</sup> examined vitamin D3 status in children with their first episode of febrile seizure, where 59.5% of the cases were having insufficient levels of vitamin D3 as compared to control group in which only 39.1% of the patients were having insufficient vitamin D3 levels. 13.5% of cases had deficient levels of vitamin D3 as compared to control group in which 6.8% of patients had deficient levels of vitamin D3. Singh V et al<sup>10</sup> reported strong association of febrile seizures with vitamin D3 levels. Children with insufficient vitamin D3 levels ( $< 12-20\text{ng/ml}$ ) had three times more risk of having febrile seizures as compared to children with normal vitamin D3 levels ( $\geq 20\text{ng/ml}$ ), whereas deficient Vitamin D3 levels ( $< 12\text{ng/ml}$ ) were associated with highest risk which is similar to our study.

Shariatpanahi G et al<sup>11</sup> conducted a preliminary study to find out any co relation between vitamin D3 levels and simple febrile seizures in 2015-16 in Children Medical Center in Tehran, Iran. The study concluded that there was a high prevalence of vitamin D3 insufficiency among patients with simple febrile seizures which is also seen in our study.

KaheniS et al<sup>12</sup> found that mean vitamin D3 level was  $24.41 \pm 11.21\text{ng/ml}$  which was in insufficient range. In 3(7.5%) patients, 25 (OH) vitamin D3 level was deficient, 29 (72.5%) patients had insufficient levels and 8 (20%) had sufficient levels.

Rabbani et al<sup>13</sup> reported the prevalence of insufficient vitamin D3 level is 46.6%, and the vitamin D3 deficiency was 7.9% in children younger than two years old in Tehran.

In a study by Motlaghzadeh et al.,<sup>14</sup> the proportion of hypovitaminosis D3 was 66.7% in 2 to 14-year-old, non-obese children which is similar to our study.

### Conclusion

There was a high prevalence of vitamin D insufficiency among cases of simple febrile seizure. Thus, from present study it can be hypothesized that there is a relation between vitamin D deficiency and simple febrile seizures and vitamin D deficiency can be a risk factor for simple febrile seizures.

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