

Original Research Article

Association of vitamin D levels with simple febrile seizures in under five children: a case control study

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ABSTRACT

Background: There is increasing concern that vitamin D deficiency may play etiological role in Febrile seizures. Few studies have reported vitamin D deficiency in children with recurrent febrile seizures and hypocalcemia seizures. The objective of this study is to explore vitamin D status in children aged 6 months to 5 years with first episode of febrile seizure and to find the association between vitamin D levels and febrile seizure.

Methods: A hospital-based case control study was conducted in sub district hospital, Katra over a period of three years. Cases were children of age group 6 months to 5 years presenting with first episode of simple febrile seizure to the casualty or OPD. For each case, a control was selected with similar age group and same sex who came for short duration fever (<2 days) but without seizures. A 5ml of blood sample for measurement of 25 hydroxy vitamin D was taken from the peripheral vein of each participant by trained laboratory technician. In order to categorise various degrees of vitamin D deficiency, Indian Academy of paediatrics criteria was used. Results were presented in the form of percentages and Odds ratio was calculated as measure of association.

Results: A total of 75 cases and 75 controls were included in the study. Cases and controls were comparable as per baseline characteristics. Strong and significant ($p < 0.01$) association of febrile seizures with vit D levels was observed.

Conclusions: There was a high prevalence of vitamin D insufficiency among cases of simple febrile seizure.

Keywords: Case control study, Febrile seizure, Under-five children, Vitamin D deficiency

INTRODUCTION

Febrile seizures are the commonest cause of seizures in children, occurring in 2-5% of children.¹ The peak incidence is around the age of approximately 18 months. Febrile seizures occurring before 6 months should raise the suspicion of serious infections like bacterial meningitis. Animal studies suggest a possible role of endogenous pyrogens such as interleukin 1 beta that by increasing neuronal excitability, may link fever and seizure activity.² A simple febrile seizure is generalized, tonic clonic in nature, lasts for a few seconds and rarely up to 15 minutes, is followed by a brief period of

postictal drowsiness and occurs once in 24 hours.³ There are many independent risk factors like genetic factors, age, gender, type and duration of seizure, family and developmental history, multiple seizures, perinatal exposure to antiretroviral drugs, history of maternal smoking and alcohol consumption during pregnancy which are potential predictors of recurrent febrile seizures.⁴ There is increasing concern that vitamin D deficiency may play etiological role in Febrile seizures. Vitamin D Deficiency is a major health problem in children and its worldwide prevalence has been estimated at about 1 billion. It prevails to 50-90% among children in India.⁵

Various studies conducted in different parts of the country have reported a widespread prevalence of VDD in all age groups. Vitamin D deficiency is known to be highly prevalent among epileptic patients.^{6,7}

There are a few studies that have reported vitamin deficiency rickets in children with recurrent febrile seizures and incidence of hypocalcemia seizures due to vitamin D deficiency in children.⁸⁻¹⁰

So, authors aimed to explore vitamin D status in children aged 6 months to 5 years with first episode of febrile seizure and to find the association between vitamin D levels and febrile seizure.

METHODS

This was a hospital-based case control study conducted in sub district hospital, Katra over a period of three years.

Inclusion criteria

- Cases were children of age group 6 months to 5 years presenting with first episode of simple febrile seizure to the casualty or OPD of this hospital.

Diagnostic criteria for simple febrile seizures (based on AAP Clinical Practice Guidelines) included seizure associated with fever and seizure was generalized, short duration (less than 15 minutes), no recurrence of seizures within 24 hours, child is otherwise neurologically healthy and without any neurological abnormality before and after the episode of seizure, with age group between 6 months to 5 years.^{2,10}

Exclusion criteria

- Children presenting with atypical febrile seizures, afebrile seizures, those having any signs of CNS infections, sick children, those with neurodevelopmental delay, those with previous history of febrile seizures, those having clinical features of rickets, those with some liver, renal or endocrinal disorders were excluded from the study.

For each case, a control was selected with similar age group and same sex who came for short duration fever (<2 days) but without seizures. Informed consent was obtained from the parents of both the study groups. A 5 ml of blood sample was taken from the peripheral vein of each participant by trained laboratory technician. Blood samples were transferred in cold boxes at 2 to 8°C for measurement of 25 hydroxy vitamin D levels to accredited laboratory. In order to categorise various degrees of vitamin D deficiency, authors used criteria that was mentioned in Indian Academy of Pediatrics 2017 guidelines on vitamin D deficiency.¹¹ Based on these criteria, sufficient are defined as levels >20ng/ml, insufficient as 12-20ng/ml and deficient as levels <12ng/ml.

RESULTS

A total of 75 cases and 75 controls were included in the study. Mean age of cases was 29.6±14.3 months and that of Controls was 29.7±14.2. Maximum cases and controls were in the age group of 6-24 months. Males were more in number 48 (64.9%) as compared to females 26 (35.1%) in both cases and controls with Male to female ratio of 1:0.5 (Table 1).

Table 1: Age distribution of cases and controls.

Age groups (months)	Cases			Controls		
	Male	Female	Total	Male	Female	Total
6-24	24	13	37	24	13	37
25-43	13	06	19	12	06	18
44-60	11	07	18	12	07	19
Total	48	26	74	48	26	74

Table 2: Distribution of cases and controls according to vitamin D status.

Vitamin D status	Cases		Controls	
	N	%	N	%
Deficient	10	13.5	5	6.8
Insufficient	44	59.5	29	39.1
Normal	20	27	40	54.1
Total	74	100	74	100

Among cases, 10 (13.5%) subjects had deficient vitamin D levels. 44 (59.4%) subjects had vitamin D levels in insufficient category and in 20 (27%) subjects' levels were normal. Similarly, in controls, levels of vitamin D were deficient in 5 (6.8%) subjects, insufficient in 29 (39.1%) subjects and normal levels in 40 participants (54.1%) (Table 2).

Strong and significant ($p < 0.01$) association of Febrile seizures with Vit D levels was observed. Persons with

insufficient Vit D levels (<12-20ng/ml) had three times (OR=3.03) more risk of having febrile seizures as compared to persons with normal vitamin D status

(≥20ng/ml) whereas deficient Vitamin D levels (<12ng/ml) were associated with highest risk (OR=4) (Table 3).

Table 3: Association of Vitamin D with febrile seizures.

Vitamin D status	Cases (n=74)	Controls (n=74)	Total (n=148)	Crude (odds ratio)	Adjusted OR
Deficient	10	5	15	4	4
Insufficient	44	29	73	3.03	3.03
Normal	20	40	60	1	1

Chi square for linear trend=9.33 p value<0.01

DISCUSSION

In the present study, maximum cases of febrile seizures were reported in males as compared to females. Similar results were observed by Pour H et al, in 2012 in a study regarding demographic and causative factors of febrile seizures.¹² In study conducted by Pathan HG in 2017, preponderance of males was observed over females among cases of febrile seizures.¹³ In this study authors examined vitamin D status in children with their first episode of febrile seizure, where 59.5% of the cases were having insufficient levels of vitamin D as compared to control group in which only 39.1% of the subjects were having insufficient vitamin D levels. 13.5% of cases had deficient levels of vitamin D as compared to control group in which 6.8% of subjects had deficient levels of vitamin D. Authors reported strong association of febrile seizures with vit D levels.

Persons with insufficient vitamin D levels (<12-20ng/ml) had three times more odds of having febrile seizures as compared to persons with normal vitamin D status (≥20ng/ml) whereas deficient Vitamin D levels (<12ng/ml) were associated with highest risk. Shariatpanahi G et al, conducted a preliminary study to find out any co relation between vitamin D levels and simple febrile seizures in 2015-16 in Children Medical Center in Tehran, Iran.¹⁴ The study concluded that there was a high prevalence of vitamin D insufficiency among patients with simple febrile seizures. The lack of control was limitation of their study. Results of present study are similar to their study i.e., in the present study also there was high prevalence of vitamin D insufficiency among subjects with simple febrile seizure though ours is more promising study design in investigating the relationship. More analytical studies are required to be conducted to generate a strong evidence of Vitamin D deficiency with febrile seizures.

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. Further studies with larger study group are recommended to prove this relationship.

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