ECRONICON OPEN ACCESS

EC PAEDIATRICS
Research Article

Estimation and Comparison of Vitamin D Levels and its Interactions in Children with and without Cerebral Palsy

Akshay Jadhav[1]*, Sajitha Nair[2], Sasidharan Ponthenkandath[3] and R Sundaram[4]

[1]Consultant Pediatrician and Pediatric Emergency, Belenus Champion Hospital, Bengaluru, KA, IN [Formerly Fellow Paediatric Critical Care Medicine, (Fellow Paediatric Emergency Care, ECMS), Rainbow Children's Hospital, Marathahalli, Bangalore, India]

[2]Professor, Department of Paediatrics, AIMS, Kochi, India

[3]Chair, Paediatrics and Neonatalogy, and Head, Neonatalogy, Dept of Paediatrics, AIMS, Kochi, India (during this Study), [presently Professor of Pediatrics and Founding Chair, SOM Pediatrics, UC Riverside, CA, US].

[4]Professor and Chair, Department of Biostatistics, AIMS, Kochi, India

***Corresponding Author:** Akshay Jadhav, Consultant Pediatrician and Pediatric Emergency, Belenus Champion Hospital, Bengaluru, KA, IN [Formerly Fellow Paediatric Critical Care Medicine, (Fellow Paediatric Emergency Care, ECMS), Rainbow Children's Hospital, Marathahalli, Bangalore, India].

Received: July 23, 2019; **Published:** July 29, 2022

Abstract

Background: Cerebral palsy (CP) is a diagnostic term used to describe a group of permanent disorders of movement and posture causing activity limitation that are attributed to non-progressive disturbances in the developing foetal or infant brain. This study was done to assess the levels of vitamin D in children with CP and compare with normal healthy children. We also aimed to describe the risk factors for vitamin D deficiency among children with CP.

Methods: This prospective cross sectional observational study included 50 children with CP in the age group of 2 to 15 years subjecting them for assessment of 25 OH vitamin D levels by CLEA method.

Results: Of total of 50 children with CP, 40 children (80%) had vitamin D levels < 20 ng/ml (deficiency). 10 (20%) children with CP had vitamin D levels between 21-29ng/ml (insufficiency) and none of them had vitamin D levels ≥ 30 ng/ml (sufficiency). A significant co relation was found between monotherapy and polytherapy, presence of dental caries and in children with moderate to severe CP. The levels of vitamin D decreased as the duration of antiepileptic drug (AEDs) usage increased. Severe Vitamin D deficiency was also significantly more in CP children (p-0.042).

Conclusion: A majority (80%) of the children with CP were vitamin D deficient. The use of more than one antiepileptic drugs for seizure control, moderate to severe CP (based on GMFCS), presence of dental caries were found to be significant risk factors for low Vitamin D levels. Vitamin D deficiency was significantly higher in children with CP when compared to that of age matched healthy children.

Keywords: *Vitamin D Deficiency; Cerebral Palsy; Epilepsy; Anti-Epileptic Drugs; Hypovitaminosis D; Dental Caries*

Introduction

Cerebral palsy (CP) is a diagnostic term used to describe a group of permanent disorders of movement and posture causing activity limitations that are attributed to non-progressive disturbances in the developing fetal or infant brain. It is one of the most common chronic disabling conditions of childhood. The worldwide incidence is 2 to 2.5/1000 live births [1] and in India the incidence in population based settings is 2 - 2.8/1000 live births [2]. Vitamin D deficiency is considered to be the most common nutritional deficiency in the world and an estimated 1 billion people worldwide are vitamin D deficient. The prevalence of vitamin D deficiency is 50 - 90% in the Indian subcontinent [3]. Vitamin D status of some children and adolescents with CP is possibly sub optimal. The association between vitamin D, antiepileptic drugs (AEDs) and bone health in individuals with epilepsy has been recognized for more than 30 years. Limited weight bearing during ambulation and temporary immobilization following any orthopaedic procedure can also affect bone health [4]. In support of this hypothesis, 25-hydroxy vitamin D levels were assessed in children with CP in view of the paucity of studies from the Indian subcontinent. The primary objective was to study vitamin D levels in children with cerebral palsy (CP) in the age group of 2 - 15 years by assessing serum 25-hydroxyvitamin D levels. Other objectives were: a) to find the association between vitamin D and cerebral palsy by correlating like use of variables antiepileptics, duration of use of antiepileptics, feeding difficulty, clinical profile, growth parameters and gross motor functional classification, b) to assess the serum levels of calcium, phosphorus, and serum alkaline phosphatase in children with cerebral palsy and c) to compare the serum levels of 25-hydroxyvitamin D in children with cerebral palsy with that of normal children.

Methods

This study was a hospital based cross-sectional study. The study population consisted of children with cerebral palsy in the age group of 2 - 15 years attending the outpatient department or admitted to the pediatric wards of AIMS, Kochi from October 2014 to September 2016. The study was approved by the Institutional Ethics Committee. Informed written consent was obtained from parents/guardian before to the enrollment of subjects.

Children with CP were selected as per the definition proposed by the "International Workshop on Definition and Classification of Cerebral Palsy, April 2006" [5].

All children on vitamin D supplementation, those aged less than 2 years and more than 15 years, and those with neurodegenerative disorders were excluded. Serum levels of 25-hydroxyvitamin D [25(OH)-Vit-D] [7,8] of 50 children with cerebral palsy were estimated and the results were compared to that of age-matched healthy children. Demographic and clinical data were recorded at admission to paediatric ward or at encounter in the outpatient department. Diagnostic evaluation of the child was done with the aid of a detailed history, physical examination and laboratory investigations.

Statistical analysis

Data collected on proforma sheets were compiled with Microsoft Excel. Statistical Analysis was done using IBM Statistics 20 Windows (SPSS Inc. Chicago, USA): a) Numerical variables were expressed as mean and SD. Prevalence of Vitamin D levels and other categorical variables were expressed as frequency and percentages; b) Fisher's Exact test was used to analyze the association of clinical and historical variables with Vitamin D [25-(OH)-Vit-D] levels; c) To compare the mean differences of numerical variables (Laboratory Parameters- Serum Calcium; Serum Phosphorus; Serum Alkaline phosphatase- ALP) between deficiency and insufficiency group, Mann Whitney U tests were applied; d) To obtain the correlation between laboratory parameters and Vitamin D [25-(OH)-Vit-D] levels, Pearson's correlation co-efficient tests were applied; e) Multivariate regression analysis was done to take into consideration the inter-correlation among the different factors and for arriving at a valid conclusion on the comparison of study variables between the two groups.

Results

Mean age of the children with CP was 6.7 years with a SD of 3.423 years. Male to Female (M:F) ratio was 1.94:1. 80% of the children studied had vitamin D deficiency [25(OH)-Vit-D < 20 ng/mL] and the remaining 20% had vitamin D insufficiency [25(OH)-Vit-D 20-29 ng/mL]. Severe vitamin D deficiency [25(OH)-Vit-D < 5 ng/mL] was seen in 18% of the children studied. Vitamin D deficiency showed significant correlation with the following variables like use of multiple antiepileptic drugs ($p = 0.029$), dental caries ($p = 0.045$) and higher

GMFCS levels (p = 0.032). Severe vitamin D deficiency was significantly associated with hypophosphatemia (p = 0.002) and raised Alkaline phosphatase levels (p < 0.001). In the present study vitamin D deficiency was significantly higher in children with CP when compared to that of age matched normal healthy children (p value < 0.001). On multivariate logistic regression, use of more than one antiepileptic (polytherapy with p = 0.041) showed significant correlation with vitamin D deficiency and hypophosphatemia (p = 0.046). Raised serum alkaline phosphatase levels (p = 0.007) showed significant correlation with severe Vitamin D deficiency in children with CP.

Discussion

The vitamin D status of some children and adolescents with cerebral palsy is possibly suboptimal. Although many children with CP are institutionalized or are on antiepileptic drugs, the findings from various studies conducted in the West regarding its effects on bone metabolism in CP cannot be reliably extrapolated, possibly due to various ethnic, geographic and environmental diffenences. There is a paucity of data in this regard from the Indian subcontinent, more apparent in South India.

Demographics

The mean age of the children with CP in the present study was 6.72 ± 3.42 years. 62% of the children studied were in the age group of 6 - 15 years. In a study done by Henderson., *et al*. in 2002 [4], the mean age of children with moderate to severe CP was 9.7 ± 0.6 years (2 - 19 years). Henderson., *et al*. [4] in 1997 studied 125 non-institutionalised children with CP in North Carolina. The mean age of the children studied was 8.7 ± 1.2 years. In the present study male to female ratio is 1.94:1.

Vitamin D deficiency in children with CP

Based on the US Endocrine Society Group classification [7], a serum 25(OH)-Vit-D level of < 20 ng/mL was taken as Vitamin D deficiency and those between 20 - 29 ng/mL were taken as Vitamin D insufficiency. In the present study Vitamin D deficiency was seen in 80% of the children with CP. Whereas 20% had vitamin D insufficiency. Normal Vitamin D levels [serum 25(OH)-Vit-D ≥ 30 ng/mL] were not seen in any child with CP.

In a study by Finbråten AK., *et al*. in 2014 [9], vitamin D deficiency was seen in 72% (n-42) of Norwegian children with cerebral palsy. This finding is consistent with the findings of the present study. Ware., *et al*. in 2013 [10] noted that 34% of Tasmanian children (n-38) with cerebral palsy had vitamin D deficiency. Henderson., *et al*. in 2002 [4] studied serum 25(OH)-Vit D levels in 76 children with moderate to severe CP aged 2 - 19 years from North Carolina who were enrolled as part of a multi-centre cross-sectional observational study under NAGCePP (North American Growth in Cerebral Palsy Project). In this study serum vitamin D deficiency was seen in 53% of children.

Ramya., *et al.* in 2016 [11] conducted a prospective observational study in 86 South Indian children with epilepsy (which also included children with cerebral palsy) to assess Vitamin D levels. 75.5% of children studied had vitamin D deficiency, 17.4% had vitamin D insufficiency and 7.1% had normal vitamin D levels.

Severe vitamin D deficiency in children with CP

According to the US Institute of Medicine (IOM) classification, severe vitamin D deficiency is defined as serum 25(OH)-Vit-D < 5ng/ml. In the present study 18% of the children studied had severe vitamin D deficiency [7,8]. In a similar study done by Henderson., *et al*. in 1997 [4] serum 25(OH)-Vit-D levels were measured in a heterogeneous group of 125 non-institutionalized children and adolescents with cerebral palsy [6]. The study revealed severe vitamin D deficiency in 14% (n-18) children with CP. In 1981 Morijiri., *et al*. [12], carried out an epidemiological study on vitamin D-dependent rickets in 94 severely handicapped institutionalised children with cerebral palsy in three National Hospitals in Ishikawa, Japan, who were on long-term anticonvulsant therapy. They found that severe vitamin D deficiency was seen in 10% (n-9) of the children studied. NJ Shaw., *et al.* in 1994 [13] studied non-ambulant children with cerebral palsy and found that severe vitamin D deficiency was found in 11% (n-9) children.

Association of serum Vitamin D deficiency and historical, clinical and biochemical parameters

Antiepileptic drug usage in children with CP

In the present study 94% of the children studied were on antiepileptic drugs. 78.8% of these children had vitamin D deficiency. Ramya., *et al*. in 2016 [11] studied the status of vitamin D in 86 children with epilepsy who were on antiepileptic drugs. Vitamin D deficiency was seen in 75.6% (n-65) of these children with epilepsy. Ware., *et al*. [10] found that children with CP using anticonvulsants (n-7) had lower mean vitamin D levels than non-anticonvulsant users (n = 31). Shellhaas., *et al*. in their study in 2010 found that Vitamin D deficiency was seen in 25% (n-20) with epilepsy using antiepileptic drugs (n-80) [9].

17% (n-8) of children on antiepileptics (n-47) in the present study were using a single antiepileptic drug (Monotherapy) whereas 83% were using more than one drug for seizure control (polytherapy). 50% of children were on a single antiepileptic drug and 84.11% of children on polytherapy were Vitamin D deficient. This observation was found to have significant statistical correlation (p = 0.029). In a study done by Nettekoven., *et al*. in 2008 [14] serum 25(OH)-Vit-D levels were measured in 38 children using antiepileptic drugs. The study revealed Vitamin D deficiency in 80% (n-20) of children on polytherapy (n-26) and 60% (n-7) using a single antiepileptic drug (n-12). S Ramya., *et al*. in 2016 [11] studied serum 25(OH)-Vit-D levels in 86 children on antiepileptic drugs. This study revealed 79% (n-35) of children on a single antiepileptic drug and 71.4% (n-30) on polytherapy were Vitamin D deficient.

The present study revealed that 81.4% children on antiepileptics for more than 1 year and 50% children on antiepileptic drugs for less than 1 year were Vitamin D deficient. A downward trend in serum 25(OH)-Vit-D levels was noted with as the duration of antiepileptic drug use increased (Chart 1). Ramya., *et al*. in 2016 [11] noted 70% (n-47) of children on antiepileptic drugs for < 50 months (n-67) and 94.7% (n-18) children on antiepileptic drugs for > 50 months (n-19) were Vitamin D deficient. Fong., *et al*. in 2014 [15] in his study which included 111 children with epilepsy, found that 16.1% (n-9) children on antiepileptic drugs for 2 - 5 years (n-56) and 27.3% (n-15) on antiepileptic drugs for more than 5 years (n-55) were Vitamin D deficient.

Feeding difficulty in children with CP

In the present study 80% (n-40) of children had feeding difficulty. 85% (n-34) of these children were vitamin D deficient. In 2003 aisha K Yousafza., *et al*. [16] studied 141 disabled children in Indian slums aged between 2 to 6 years (including children with cerebral palsy). The study revealed that 35% (n-49) children had vitamin D deficiency.

Dental caries in children with CP

58% of children in the present study had dental caries. 89.7% (n-34) of children with dental caries had vitamin D deficiency. This correlation was statistically significant (p = 0.045). 2008 a study in Brazil [17] by De Camargo., *et al*. showed a prevalence of dental caries in 49.8% of children with cerebral palsy. Literature review did not reveal any data on the association of Vitamin D deficiency and dental caries in children with cerebral palsy.

Clinical features of Rickets in children with CP

The present study revealed that 14% (n-7) of children with CP had clinical features of rickets. All of these children were Vitamin D deficient. Morijiri., *et al.* in 1981 [12] studied serum 25(OH)-Vit-D levels in non-ambulant children with CP and observed that 10% (n-9) of them had clinical features of rickets along with Vitamin D deficiency. S Bhatnagar., *et al.* in 2011 [18] studied 60 children with cerebral palsy of which 15% (n-9) had clinical and radiological evidence of rickets.

BMI in children with CP

In the present study, 36% (n-18) of the children with CP were underweight for age. 46% (n-23) had normal weight for age. 8% (n-4) of them were over-weight and 10% (n-5) were obese. Vitamin D deficiency was seen in 83.3% of underweight children, 78.3% of normal children and 77.8% of children who were overweight and obese. The study conducted by Shellhaas., *et al*. in 2010 [9] showed that the children with elevated BMI (overweight and obese) had a 17% greater risk of being vitamin D deficient.

Clinical features of CP

In the present study, vitamin D deficiency was seen in 88% of children with quadriplegic CP (n-25), 71.4% of children with hemiplegic CP (n-7), 75% of children with Diplegic CP (n-8) and 62.5% of children with hypotonic CP (n-8). Vitamin D deficiency was seen in all children with Mixed CP (n-2).

Severity of CP based on GMFCS

In the present study, 70% of the children with GMFCS level I, 50% of children with GMFCS level II, 66.7% with GMFCS level III, 88.9% with GMFCS level IV and 94.7% with GMFCS level of V had vitamin D deficiency. GMFCS levels were graded based on severity. The two categories were mild CP (CP children with GMFCS level I and II) and moderate to severe CP (CP children with GMFCS III, IV and V). 88.2% of children with moderate to severe CP were found to be Vitamin D deficient and 62.5% of children with mild CP were vitamin D deficient.

In the present study vitamin D deficiency was significantly higher (p-0.032) in children with severe functional limitation having higher GMFCS levels. Henderson., *et al*. [4] found in their study that vitamin D deficiency was seen in 53% of children with moderate to severe CP (GMFCS levels III, IV and V).

Biochemical parameters in children with CP

In the present study, hypocalcaemia was seen in 18% (n-9) and hypophosphatemia in 12% (n-6) of the children studied. Vitamin D deficiency was seen in all children with hypocalcaemia and hypophosphatemia.

22% of the children with CP in the present study had elevated serum alkaline phosphatase levels (serum ALP > 320 IU/L). 81.8% of these children had vitamin D deficiency. In the study by Henderson., *et al*. in 1997 [4], these biochemical abnormalities did not have a statistical correlation with Vitamin D deficiency.

Association of severe vitamin D deficiency and historical, clinical and biochemical variables

12.8% (n-6) of children with CP on antiepileptic drugs (n-47) were found to be severely vitamin D deficient. In children on multiple antiepileptic drugs (n-39), 15.4% (n-6) had severe vitamin D deficiency. Severe vitamin D deficiency was not seen in any child with CP on a single antiepileptic drug (n-8). 12.8% (n-6) children with CP using antiepileptic drugs for more than 1 year, had severe vitamin D deficiency. Severe Vitamin D deficiency was also seen in 12.5% (n-5) of children with feeding difficulty and 17.2% (n-5) of children with dental caries. In children with CP having clinical features of rickets, 14.3% (n-1) had severe Vitamin D deficiency. In children who had moderate to severe CP (GMFCS III, IV, V), 14.7% (n-5) had severe Vitamin D deficiency and 12.5% (n-2) of children with mild CP (GMFCS I and II) had severe vitamin D deficiency. Among hypocalcaemic children, 33.33% (n-3) had severe vitamin D deficiency. Severe vitamin D deficiency had significant statistical correlation with hypophosphatemia (p-0.002) and elevated serum alkaline phosphatase levels ($p < 0.001$).

Vitamin D levels in children with CP and normal healthy children

To compare serum 25(OH)-Vit-D levels in children with CP and those of normal healthy children, 106 healthy children who attended the outpatient department for routine check-up or vaccines were enrolled in the study. These healthy children matched the children with CP in age and sex. In the present study vitamin D deficiency was significantly higher in children with CP ($p < 0.001$). Severe vitamin D deficiency was also significantly more in children were in CP (p-0.042).

Morijiri., *et al*. in 1981 [12] studied serum 25(OH)-Vit-D levels in 94 severely handicapped institutionalised children with cerebral palsy and compared with those of 38 healthy age-matched controls. They found that the serum 25(OH)-Vit-D levels were significantly lower in children with CP when compared to healthy controls.

Association of vitamin D deficiency and various clinical and biochemical variables in children with cerebral palsy (Multivariate Logistic Regression)

On multivariate logistic regression, use of more than one antiepileptic drugs (polytherapy) ($p = 0.041$) showed significant correlation with vitamin D deficiency in children with CP. Hypophosphatemia and elevated serum alkaline phosphatase levels significantly correlated with severe vitamin D deficiency.

Fong., *et al*. in 2014 [15] evaluated prevalence and risk factors for vitamin D deficiency among 111 children on long-term antiepileptic drugs treated in a tertiary neurology clinic in South Queensland, Australia. Multivariate logistic regression analysis identified that children on ≥ 2 antiepileptic drugs were more likely to have vitamin D deficiency.

Demographic Variables	Present study 2016	Ramya S., *et al*. 2016 [12]	Nettekoven., *et al*. 2008 [15]	RC Henderson., *et al*. 2002 [6]
	Vitamin D levels in children with CP	A study of vitamin - D status in epileptic children in age group of 2-15 years	Effects of antiepileptic drug therapy on vitamin D status and biochemical markers of bone turnover in children with epilepsy	Bone density and metabolism in moderate to severe CP
	South India (n-50)	South India (n-86)	Hannover, Germany, (n-38)	North Carolina, USA (n = 76)
Mean Age	6.72 ± 3.42	NA (Age group- 2 to 15 years)	8.4 ± 1.7	9.7 ± 0.6
M:F Ratio	1.94:1	2.44:1	1.92:1	1.77:1

Table 1

Parameter	Details of the studies					
	Present study 2016	Ramya S., *et al*. 2016 [12]	Ware., *et al*. 2013 [11]	RC Henderson., *et al*. 2002 [6]	RC Henderson., *et al*. 1997 [7]	Finbråten AK., *et al*. 2014 [10]
Vitamin D [25(OH)-Vit-D levels as per US Endocrine Society classification] in ng/ml [8,9]	Vitamin D levels in children with CP	A study of vitamin - D status in epileptic children in age group of 2-15 years	Vitamin D status in Tasmanian children with CP	Bone density and metabolism in moderate to severe CP	Vitamin D levels in non-institutionalized children with CP	BMD and vitamin D status in ambulatory and non-ambulatory children with CP
	South India (n-50)	South India (n-86)	Tasmania, South Australia (n-38)	North Carolina, USA (n=76)	North Carolina, USA (n=125)	Norway (n-43)
≤ 20 ng/mL (Vitamin D deficiency)	80% (n-40)	75.5% (n-65)	34% (n-13)	53% (n-40)	22% (n-24)	72% (n-31)
21-29 ng/mL	20% (n-10)	17.4% (n-15)	66% (n-25)	47% (n-36)	41% (n-45)	28% (n-12)
≥ 30 ng/mL < 150 ng/mL	0% (n-0)	7.1% (n-6)	0% (n-0)	25% (n-19)	37% (n-42)	0% (n-0)
> 150 ng/mL	0% (n-0)	0% (n-0)	0% (n-0)	0% (n-0)	0% (n-0)	0% (n-0)
Mean serum 25(OH)-Vit-D levels	12.9734 ± 7.0343 (ng/mL)	---	23 ± 8.7169 (ng/mL)	20.3 ± 0.8 (ng/mL)	23.4 ± 1.4 (ng/mL)	18.0 ± 7.2 (ng/mL)

Table 2: *Vitamin D deficiency in various studies.*

Parameter	Details of the studies				
	Present study	**Ware., *et al.* 2013 [11]**	**RC Henderson., *et al.* 1997 [7]**	**Finbråten AK., *et al.* 2014 [10]**	**Morijiri., *et al.* 1981 [13]**
Vitamin D [25(OH)-Vit-D levels as per US Institute Of Medicine (IOM) Classification] in ng/ml [8,9]	Vitamin D levels in children with CP	Vitamin D status in Tasmanian children with CP	Vitamin D levels in non-institutionalized children with CP	BMD and vitamin D status in ambulatory and non-ambulatory children with CP.	Factors causing rickets in institutionalized handicapped children on anticonvulsant therapy
	South India (n-50)	Tasmania, South Australia (n-38)	North Carolina, USA (n = 125)	Norway (n-43)	Japan (n-94)
< 5 ng/mL	18%	0%	14%	0%	10%

Table 3: *Severe Vitamin D deficiency in various studies.*

Antiepileptic drug Use	No (n-3)	3	100	0	0	1.000	Not Significant
	Yes (n-47)	37	78.7	10	21.3		
Monotherapy Vs Polytherapy	Monotherapy (n-8)	4	50.0	4	50.0	0.029	significant
	Polytherapy (n-39)	33	84.6	6	15.4		
Duration of use of antiepileptic drugs	< 1 Year(n-4)	2	50	2	50	0.057	Not Significant
	≥1 Year (n-43)	35	81.4	8	18.6		
Feeding Difficulty	No (n-10)	6	60	4	40	0.182	Not Significant
	Yes (n-40)	34	85	6	15		
Dental Caries	Absent (n-21)	14	66.7	7	33.3	0.045	significant
	Present (n-29)	26	89.7	3	10.3		
C/F of rickets	Absent (n-43)	33	76.7	10	23.3	0.319	Not Significant
	Present (n-7)	7	100	0	0		
WHO BMI Z scores	Underweight (n-18)	15	83.3	3	16.7	0.907	Not Significant
	Normal (n-23)	18	78.3	5	21.7		
	Overweight and Obese (n-9)	7	77.8	2	22.2		
Clinical features of CP	Quadriplegic CP (n-25)	22	88	3	12	NA	NA
	Hemiplegic CP (n-7)	5	71.4	2	28.6		
	Diplegic CP (n-8)	6	75	2	25		
	Hypotonic CP (n-8)	5	62.5	3	37.5		
	Mixed CP (n-2)	2	100	0	0		
Variables		Serum 25-OH Vitamin D levels (ng/mL)				p Value	
	<20		≥20			Interpretation	
	n	%	n	%	0.032	significant	
GMFCS Severity	Mild CP (GMFCS I & II) (n-16)	10	62.5	6	37.5		
	Moderate + Severe CP (GMFCS III, IV & V) (n-34)	30	88.2	4	11.8		
	Hypocalcemia (< 8.50 mg/dL) (n-9)	9	100	0	0	0.174	Not Significant
Hypocalcemia	Normal calcium (8.50-10.5 mg/dL) (n-41)	31	75.6	10	24.4		

Hypophosphatemia	S.Phosphorus ≤ 3.3 mg/dL (n-6)	6	100.0	0	0.0	0.327	Not Significant
	Normal S. Phosphorus (3.3 – 5.8 mg/dL) (n-44)	34	77.3	10	22.7		
Raised serum Alkaline Phosphatase	Normal S. ALP (100 -320 IU/L) (n-39)	31	79.5	8	20.5	1.000	Not Significant
	Elevated S. ALP (> 320 IU/L) (n-11)	9	81.8	2	18.2		

Table 4: *Association of serum Vitamin D deficiency in children with CP.*

Variables		Serum 25-OH Vitamin D levels (ng/mL)				p Value	
		<5		≥5			Interpretation
		n	%	n	%		
GMFCS Severity	Mild CP (GMFCS I & II) (n-16)	2	12.5	14	87.5	1.000	Not Significant
	Moderate + Severe CP (GMFCS III, IV & V) (n-34)	5	14.7	29	85.3		
	Hypocalcemia (< 8.50 mg/dL) (n-9)	3	33.3	6	66.7	0.100	Not Significant
Hypocalcemia	Normal calcium (8.50-10.5 mg/dL) (n-41)	4	9.8	37	90.2		
Hypophosphatemia	Serum Phosphorus < 3.3 mg/dL (n-6)	4	66.7	2	33.3	0.002	Significant
	Serum Phosphorus 3.3-5.8 mg/dL (n-44)	3	6.8	41	93.2		
Raised serum Alkaline Phosphatase	Normal S. ALP (100 -320 IU/L) (n-39)	1	2.6	38	97.4	<0.001	Significant
	Elevated S. ALP (> 320 IU/L) (n-11)	6	54.5	5	45.5		

Table 5: *Association of severe Vitamin D deficiency in children with CP.*

Total	Serum 25-OH Vitamin D levels (ng/mL)				Mean ± SD	p Value
	<20		≥20			
	n	%	n	%		
CP children (n-50)	40	80.00	10	20.00	12.97 ± 7.03	<0.001
Healthy Children (n-106)	35	38.67	65	61.32	1.25 ± 12.02	
Total	Serum 25-OH Vitamin D levels (ng/mL)					p Value
	<5		≥5			
	n	%	n	%		
CP children (n-50)	7	14	43	86		0.042
Normal healthy children (n-106)	5	4.7	101	95.3		

Table 6: *Vitamin D levels in children with CP and normal healthy children.*

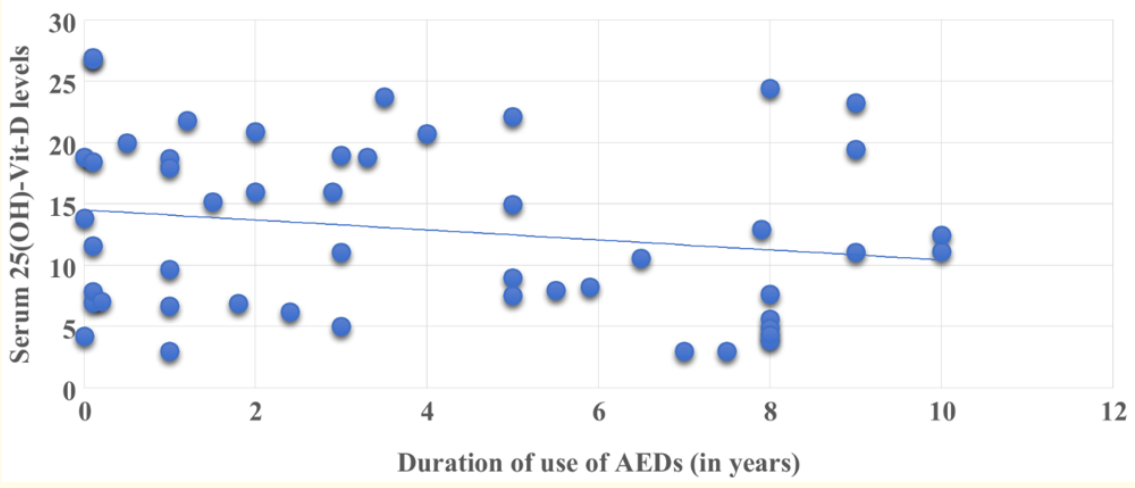

Figure 1: *Variation of serum vitamin D levels and duration of use of antiepileptic drugs in children with CP.*

Conclusions

In the present study, 80% of the children with cerebral palsy were vitamin D deficient. Vitamin D deficiency was significantly higher in children with CP when compared to that of age matched healthy children. As part of the multi-disciplinary approach in the management of children with CP, it is important to monitor serum 25(OH)-Vit-D levels regularly and supplement vitamin D whenever needed.

Acknowledgments

The authors would like to thank all the parents and children by making this study successful by their cooperation and active participation.

Conflict of Interest

None to be declared

Source of Support

None to be declared

Authorship

Dr. Akshay Jadhav, Dr. Sajitha, Dr. Jayakumar, Dr. Sasidharan, Dr. Sundaram Dr. Manu Raj contributed to the conception and design, acquisition, analysis and interpretation of data; Dr Akshay Jadhav and Dr Srikrishnan Rameshbabu contributed to enrollment of study participants; Dr Akshay Jadhav did the interpretation of data, and prepared the initial draft; Dr. Sajitha Nair did the revision of the draft manuscript. Dr. Vijaya Kumar Chattu gave the final critical revisions for the manuscript. All the authors have agreed with the final manuscript. Dr Ravi Sankaran contributed by helping enrollment of study participants, especially with advanced GMFCS levels and follow-ups.

Acknowledgement

Dr Srikrishnan Rameshbabu gave the final critical revisions for the manuscript.

Bibliography

1. Rosen MG and Dickinson JC. "The incidence of cerebral palsy". *American Journal of Obstetrics and Gynecology* 167.2 (1992): 417-423.
2. Gladstone M. "A review of the incidence and prevalence, types and aetiology of childhood cerebral palsy in resource-poor settings". *Annals of Tropical Paediatrics* 30.3 (2010): 181-196.

3. Harinarayanan CV and Joshi SR. "Vitamin D status in India - Its implications and remedial measures". *Journal of the Association of Physicians of India* 57 (2009): 40-48.

4. Henderson RC., *et al*. "Bone density and metabolism in children and adolescents with moderate to severe cerebral palsy". *Pediatrics* 110.1 (2002): e5.

5. "The definition and classification of cerebral palsy". *Developmental Medicine and Child Neurology* 49 (2007): 1-44.

6. Richard C Henderson. "Vitamin D Levels in Non-Institutionalized Children with Cerebral Palsy". *Journal of Child Neurology* 12.7 (1997): 443-447.

7. Ross AC., *et al*. "The 2011 report on dietary reference intakes for calcium and vitamin D from the Institute of Medicine: what clinicians need to know". *The Journal of Clinical Endocrinology and Metabolism* 96.1 (2011): 53-58.

8. Holick MF., *et al*. "Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline". *The Journal of Clinical Endocrinology and Metabolism* 96.7 (2011): 1911-1930.

9. Finbråten AK., *et al*. "Bone mineral density and vitamin D status in ambulatory and non-ambulatory children with cerebral palsy". *Osteoporosis International* 26.1 (2015): 141-150.

10. Ware T., *et al*. "Vitamin d status in tasmanian children with cerebral palsy". *Journal of Paediatrics and Child Health* 49.4 (2013): E349-E350.

11. Ramya S., *et al*. "A study of vitamin-D status in epileptic children in age group of 2-15 years". *International Journal of Advances in Medicine* 3.2 (2016): 319-323.

12. Morijiri YU and Sato TA. "Factors causing rickets in institutionalized handicapped children on anticonvulsant therapy". *Archives of Disease in Childhood* 56.6 (1981): 446-449.

13. Shaw NJ., *et al*. "Osteopenia in cerebral palsy". *Archives of Disease in Childhood* 71.3 (1994): 235-238.

14. Nettekoven S., *et al*. "Effects of antiepileptic drug therapy on vitamin D status and biochemical markers of bone turnover in children with epilepsy". *European Journal of Pediatrics* 167.12 (2008): 1369-1377.

15. Fong CY and Riney CJ. "Vitamin D deficiency among children with epilepsy in South Queensland". *Journal of Child Neurology* 29.3 (2013): 368-373.

16. Yousafzai AK., *et al*. "Feeding difficulties in disabled children leads to malnutrition: experience in an Indian slum". *British Journal of Nutrition* 90.6 (2003): 1097-1106.

17. DE Camargo MA and Antunes JL. "Untreated dental caries in children with cerebral palsy in the Brazilian context". *International Journal of Paediatric Dentistry* 18.2 (2008): 131-138.

18. S Bhatnagar and N Purohit. "Rickets in Cerebral Palsy children". *IJPMR* 22 (2011): 17-20.

Volume 11 Issue 8 August 2022