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Vitamin D status in children with Cerebral palsy: a Tertiary care center study

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***Abstract*---**Background: Cerebral palsy(CP) is presently defined as a group of permanent disorders of the development of movement and posture, causing activity limitation, that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain. Low vitamin D levels in children with CP are also associated with decreased muscle strength, balance, muscle pain, paresthesias, and poor muscular coordination. Materials & Method: It is the Prospective observational cross-sectional study. The patients in the study group were of both sexes and aged 6 months to 12 years. All children apart from general tests underwent investigations for serum calcium total {By an automated analyzer}, serum phosphorus {By an automated analyzer}, serum alkaline phosphatase (SAP) levels {By an automated analyzer} and 25 OH vitamin D level {By CLIA (chemi luminescence immunoassay) method}. Results: Total 141 Children who satisfied inclusion and exclusion. Male children were 96 (68%) whereas female were 45(32%).The distribution by the CP type was Quadriplegia 44.0%, Diplegia 34.8%, Hemiplegia 7.1%, Monoplegia 1.4%, Hypotonic 2.1%, Dyskinetic 0.7%, Mixed 0.7%, Evolving CP

9.2%. Ambulatory CP children were 60 (42.5%) and non ambulatory were 81 (57.5%). Quadriplegic CP children had most Vit D insufficiency of 23.4%, diplegics CP children had most vit D deficiency (2.1%) whereas 1.4% Quadriplegic CP children had vit D hypervitaminosis. Conclusion: Vit D status in CP children is essential to estimate because they are prone for its deficiency due to poor dietary supplementation, non-ambulation and various antiepileptic drug interaction.

Keywords---Vit. D, antiepileptic drug, Cerebral palsy.

Introduction

Cerebral palsy (CP) is known as a static, non-progressive disorder which is caused by a brain insult or injury in the prenatal, perinatal, and postnatal time period, resulting as a major developmental disability affecting function in children. Basically, it is a non progressive, static encephalopathy with a delayed developmental presentation. Although it may appear to worsen, changes are actually the result of the deficits becoming more obvious as the child grows and matures over time. Its characteristic is inability to normally control motor functions, and it has the potential to have an effect on the overall development of a child by affecting the child's ability to explore, speak, learn, and become independent.[i]

CP is a clinical diagnosis based on signs, symptoms, and medical history rather than laboratory investigations or diagnostically supportive neuroimaging.[ii]
The motor disorders in it are often accompanied by disturbances of sensation, perception, cognition, communication, and behavior, by epilepsy, and by other secondary musculoskeletal problems.[iii]CP as "an umbrella term covering a group of non-progressive, but often changing, motor impairment syndromes secondary to lesions or anomalies of the brain arising in the early stages of its development.[iv]
There are many known and unknown genetic and environmental risk factors and causal pathways leading to CP.[v]

Palisano et al. in 1971 developed Gross Motor Function Classification System (GMFCS) that provides an alternative approach to the classification of cerebral palsy (CP). Based upon the concepts of disability and functional limitation as laid out by the World Health Organization, it classifies children by the level of their motor ability.[vi]

It is a standard observational tool for assessing children with cerebral palsy that evaluated the ability to perform movements such as walking, climbing stairs, running and sitting. According to this scale, children are placed into five grades from I to V in order to their gross motor skills and lower levels represent better gross motor skills, with I as the lightest and V as the most severe level.[vii,viii]

As we know, for normal skeletal system development and mineralization adequate vitamin D level is essential. Vitamin D deficiency if left untreated can cause osteopenia and fractures.[ix]

Children with CP are having limitations in their daily activities. Eg- feeding, dressing, bathing, and mobility due to abnormal muscle tone, involuntary movement, unsteady gait, problems with balance and poor social functioning. These patients usually have poor overall nutrition and insufficient calcium and 25-hydroxy vitamin D intake.[x]

In childhood, 25-hydroxy vitamin D is crucial for bone growth, mineralization, and musculoskeletal health because it promotes the assimilation of nutritional calcium and phosphate. It also regulated numerous cellular functions and would play an important role in the risk of metabolic syndrome, diabetes, autoimmune diseases, and some types of cancer.[xi]

Low vitamin D levels in children with CP are also associated with muscle weakness and with hypovitaminosis D myopathy, characterized by decreased muscle strength and balance, muscle pain, paresthesias, and poor muscular coordination.[xii]

Literature and evidences are very ambiguous about the level of vit. d and its deficiency in CP. The level of vitd also varies from place to place in intra as well intercountries. There are enough evidences supporting since long time back emphasizing the requirement of vitamin D levels for normal mineralization of bone thusskeletal system development of child, its deficiency also leads to many non motor issues like Autistic disorders. So we are investigating the vitamin D status of various sub types cerebral palsy child and also its relation with the various functional level in our part of country.

Materials and Methods

It is the Prospective observational cross-sectional study. Done on patients attending the CP clinic in Physical Medicine and Rehabilitation (PMR) OPD after obtaining the informed consent and institutional ethic permission.(IEC/IGIMS/) The patients in the study group were of both sexes and aged 6 months to 12 years. The study period was for 20 months (from September 2018 to June 2021.) Exclusion criteria were Children already on calcium supplementation, renal or liver disease or malabsorption syndromes or family history of metabolic bone disease.

The diagnosis of cerebral palsy was confirmed based on the history and clinical examination. Informed consent was obtained from either of the parent of the child having CP.

A detailed history was obtained including age, sex, birth history including mode of delivery, gestational age, birth weight, presence of birth asphyxia, neonatal seizures, developmental delay, exposure to sunlight, ambulatory status, seizures, use of antiepileptic drug (AED) (single/multiple drug, duration of treatment, type of antiepileptic drug), history of constipation and feeding difficulties. Complete physical examination of the child including anthropometry was performed with emphasis on evidence of fractures and dental changes. All children apart from general tests underwent investigations for serum calcium total { By an automated analyzer},serum phosphorus { By an automated analyzer},serum alkaline

phosphatase (SAP) levels {By an automated analyzer} and 25 OH vitamin D level {By CLIA (chemi luminescence immunoassay) method}.
Total calcium above 9 mg/dl was considered to be normal. Serum phosphorus in the range of 4-7 mg/dl was considered to be in the normal range. SAP below 400 IU/l was considered normal. Vitamin D insufficiency is defined as serum 25-hydroxyvitamin D levels below 30 ng/ml to 10 ng/ml. Vitamin D deficiency is defined as serum 25-hydroxyvitamin D levels below 10 ng/ml.[xiii] Based on this CP children were further grouped in ambulatory (GMFCS grades- I,II and III) and non ambulatory (GMFCS grades- IV and V).

Statistical Analysis

Information collected and converted into a computer based spreadsheet using free software foundation (FSF), Boston, Massachusetts, USA.

Results

Total 141 Children who satisfied inclusion and exclusion criteria were taken in the study with age group between 6 months to 12 years. Male children were 96 (68%) whereas female were 45(32%).

Table 1
Distribution of children in different age groups

Age	N (Percentage)
< 2 yrs	76 (53.9%)
2-6 yrs	59 (41.8%)
6-12 yrs	6 (4.3%)
Mean age	2.22 yrs
Total	141

The distribution by the CP type was Quadriplegia 44.0%, Diplegia 34.8%, Hemiplegia 7.1%, Monoplegia 1.4%, Hypotonic 2.1%, Dyskinetic 0.7%, Mixed 0.7%, Evolving CP 9.2%. Ambulatory CP children (GMFCS- I,II,III) were 60 (42.5%) and non ambulatory were 81 (57.5%).

Table 2
Distribution of Vit d in various group of CP children

Diagnosis	Vit D level				Total
	< 9.99 Vit Def.	10-29.9 Vit Insuf.	30-100 Normal	>100.1 Hy. Vit	
Quadriplegia	0 (.0%)	33(23.4%)	27 (19.1%)	2 (1.4%)	62 (44.0%)
Diplegia	3(2.1%)	25(17.7%)	21(14.9%)	0(.0%)	49(34.8%)
Hemiplegia	0(.0%)	5(3.5%)	5(3.5%)	0(.0%)	10(7.1%)
Monoplegia	0(.0%)	1(0.7%)	1(0.7%)	0(.0%)	2(1.4%)
Hypotonic	0(.0%)	3(2.1%)	0(.0%)	0(.0%)	3(2.1%)

Dyskinetic	0(.0%)	1(0.7%)	0(.0%)	0(.0%)	1(0.7%)
Mixed	0(.0%)	1(0.7%)	0(.0%)	0(.0%)	1(0.7%)
Evolving	2 (1.4%)	8(5.7%)	2 (1.4%)	1(0.7%)	13(9.2%)

Mean Vit D level was 31.88 ng/ml.

Table 3
Correlation between the 25(OH)D levels and GMFCS

GMFCS	Vit D level				Total
	< 9.99 Vit Def	10-29.9 Vit Insuf	30-100 Normal	>100.1 Hy. Vit	
I	0(.0%)	2 (1.4%)	3(2.1%)	0(.0%)	5(3.5%)
II	1(0.7%)	15(10.6%)	7(5.0%)	0(.0%)	23 (16.3%)
III	0(.0%)	15(10.6%)	17(12.1%)	0(.0%)	32 (22.7%)
IV	1(0.7%)	14(9.9%)	5(3.5%)	0(.0%)	20(14.2%)
V	3(2.1%)	31(22.0%)	24(17%)	3(2.1%)	61(43.3%)
Ambulatory (I,II,III)	1(0.7%)	32(22.6%)	27(19.2%)	0(.0%)	60(42.5%)
Non ambulatory (IV,V)	4(2.8%)	45(31.9%)	29(20.5%)	3(2.1%)	81(57.3%)

53 CP children were on antiepileptic medication whose relation with vit D is shown in fig.1.

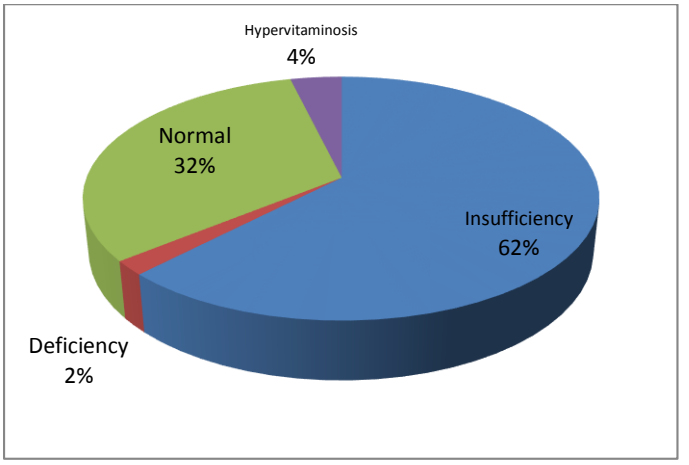

Figure 1: antiepileptic medication status

Discussion

The mean age of CP children in the study was 2.22 years whereas study by Pinar Akpinar mean age of CP children was 7.5 years.[12] Another study by Anju Seth et al had mean age of CP children 4.5 yrs who taken CP children between age group 2 to 10 years.[xiv] The decrease in mean age of CP children is the study was due to increasing awareness and knowledge among parents and clinicians about early features of the disease seeking early interventions.

In our study spastic quadriplegic CP children (44.0%) were most common which is also supported by study by Toopchizadeh et al having most common quadriplegics 43.1 %.[xv] and other past studies. But in last two decades, spasticDiplegic CP is getting more percentage[xvi,xvii,xviii]. Non ambulatory children were more (57.5%) than ambulatory as parents of severely affected CP children seeks more treatment options and getting referrals. This is against the result of study by Pinar Akpinar.[12]

In our study Quadriplegic CP children had most Vit D insufficiency of 23.4%, diplegics CP children had most vit D deficiency (2.1%) whereas 1.4% Quadriplegic CP children had vit D hypervitaminosis. Vitamin D deficiency (<10 ngm/ml) was observed in 3% only and insufficiency in 55% (10-30 ngm/ml) of children with cerebral palsy. Hypervitaminosis (>100 ng /ml) observed in 2% CP children. In a study by Monahar et al[xix]the prevalence of decreased vitamin D in cases was 93%. 32% deficiency and insufficiency was 61%. Whereas in control population this study, prevalence of decreased vitamin D was 49%.This is one study which used the cut off value for deficiency as <10 ng/ while in most other studies have used higher cut off of 12-20 ng/ml to define deficient state. This study reported the mean vitamin D levels among case group were 17.98 and the control group was 33.13 ng/ml. Butnone of the controls have any clinical signs of Vitamin D deficiency.

A study by Pinar Akpinar Vitamin D deficiency (≤12 ngm/ml) was in 33.3%, insufficiency (>12-≤20 ngm/ml) in 26.4% CP children.[16]Another study by Toopchizadeh et al Vitamin D deficiency (≤20 ngm/ml) was in 44.6%, insufficiency (>20-≤30 ngm/ml) in 23.1% CP children.[15] In astudy from south India[xx]the mean vitamin D levels of urban males was 18.54 ng/ml while in females it was 28.35 ng/ml. Among rural population, mean was 29.24 ng/ml for men and 29.21 ng/ml for women.In another study by Marwaha et al[xxi] in healthy school going children in North India, the mean vitamin D levels in low and high socioeconomic group were 10.4 and 13.7 ng/ml.

Thus, Prevalence of vitamin D deficiency/insufficiency in normal population varies between 10%-70% in various studies.[xxii] In our study among ambulatory CP children (GMFCS-I,II,III) Vitamin D deficiency (<10 ngm/ml) was found in 0.7% and insufficiency (10-29.9 ngm/ml) in 22.6% cases. Among Non ambulatory CP children (GMFCS-IV,V) Vitamin D deficiency (<10 ngm/ml) was found in 2.8% and insufficiency (10-29.9 ngm/ml) in 31.9% cases. Among 28.5% Non ambulatory CP children (GMFCS-IV,V) Vitamin D deficiency found in 47 % and insufficiency in 16.7% cases. Study by Pinar Akpinar among Ambulatory CP children (GMFCS-I,II,III) Vitamin D deficiency found in 28.4 % and insufficiency in 30.2% cases and among non Ambulatory CP children (GMFCS-I,II,III) Vitamin D deficiency found in 47 % and insufficiency in 16.7% cases.[12]

Severe 25-hydroxy vitamin D deficiency (VDD) can result in rickets, metabolic bone disease, and hypocalcemia during infant and childhood growth.[xxiii]Cognitive impairment, dementia, psychosis, and autism have been added to the list of neurological manifestations of decreased vitamin D levels.Long-term use of valproic acid (anti-epileptics)[xxiv] in treating children with epilepsy can lead to a reduction in 25-OH-vitd and BMD. Measurements of 25-OH-vitd and BMD should

be performed regularly in children taking the drug to detect early osteopenia caused by the drug.

Ours being a tertiary referral centre, most CP children of this study were prior seen by various level of educated as well as not qualified health care practioners in our part of country. Even after all efforts had been taken to exclude CP child with prior Vit D but some may have been given without any prescription. This may have been one of the reasons of hypervitaminosis in said CP children.

Conclusion

Vit D status in CP children is essential to estimate because they are prone for its deficiency due to poor dietary supplementation, non-ambulation and various antiepileptic drug interactions. But they may also prone of hypervitaminosis due to over supplementation especially non ambulatory CP children as they get more medical referrals and repeated supplementations. Case Control studies may show more insight in future studies.

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