PREVALENCE AND RISK FACTORS OF VITAMIN D DEFICIENCY IN CHILDREN WITH CEREBRAL PALSY- A CASE CONTROL STUDY

Dissertation submitted to

THE TAMILNADU

DR. M.G.R MEDICAL UNIVERSITY, CHENNAI

With Partial fulfillment of the regulations

For the award of the Degree of

MD BRANCH VII
PAEDIATRIC MEDICINE
GOVT. KILPAUK MEDICAL COLLEGE & HOSPITAL
CHENNAI

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI, TAMILNADU

APRIL 2013

CERTIFICATE

Certified that this dissertation entitled "**PREVALENCE AND RISK FACTORS OF VITAMIN D DEFICIENCY IN CHILDREN WITH CEREBRAL PALSY - A CASE CONTROL STUDY"** is a bonafide work done by **Dr.GOMATHY SRIVIDYA. V** post graduate student of Pediatric Medicine, Kilpauk Medical College Hospital, Chennai-10, during the academic year 2011-2013.

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DECLARATION

I declare that this dissertation entitled "**PREVALENCE AND RISK FACTORS OF VITAMIN D DEFICIENCY IN CHILDREN WITH CEREBRAL PALSY - A CASE CONTROL STUDY"** has been conducted by me at Kilpauk Medical College Hospital. It is submitted in part of fulfillment of the award of the degree of M.D (Pediatrics) for the April 2013 examination to be held under **The Tamilnadu DR. M.G.R Medical University, Chennai.** This has not been submitted previously by me for the award of any degree or diploma from any other university.

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ACKNOWLEDGEMENT

I express my sincere thanks to **Prof.P.Ramakrishnan, M.D., D.L.O., Dean**, Kilpauk Medical College, for allowing me to conduct this study using the available facilities at our hospital.

I am greatly indebted to **Prof.Dr.R.Narayana Babu, MD., D.C.H.,** Professor and Head of the Department of Paediatrics, Kilpauk Medical College Hospital, who was my guide for the dissertation. I thank him wholeheartedly for his able guidance and encouragement throughout the study.

I am immensely grateful to **Prof. Dr. M. Kannaki** , **MD., D.C.H.,** former Professor and Head of the Department of Paediatrics, Kilpauk Medical College Hospital, for her support, encouragement and suggestions throughout the initial part of the study. I am greatly indebted to **Prof.Dr.A.Mahali, MD., D.C.H.,** Former Additional Professor of Pediatrics, Kipauk Medical College Hospital, for his support, and suggestions regarding the study. I am indebted to **Dr.P.G.Rajkumar MD., DCH,** former Professor, Department of Pediatrics Kilpauk Medical College Hospital.

I am indebted to **Dr.B.Sathyamurthi, MD., DCH.** Addl Professor and also **Dr.Jeyachandran, MD., DCH,** for their constant support and valuable suggestions. I also thank **Dr.Indhumathy Santhanam MD., DCH,** Professor, Department of Paediatrics, Government Royapettah hospital and Former Professors who have been a great help to me in the past and have helped me in the study.

I would like to express my sincere thanks to **Dr. M. Suganya MD., DCH.,** Assistant Professor, Department of Pediatrics, Kilpauk Medical College Hospital, for her valuable suggestions which have been incorporated in this dissertation.

I would like to thank the Assistant Professors of the Department of Paediatrics at Kilpauk Medical College Hospital, **Dr.Thenmozhi MD., DA., Dr.S.Sridevi MD., DCH., Dr.Adalarasan MD., DCH., Dr.Raja Vijayakrishnan MD, D.C.H., Dr. Partheban MD., Dr.Jeyanthi M.D., D.C.H.**

I also extend my sincere thanks to the departments of Pathology, Biochemistry, Microbiology, KMCH & I specially thank our lab technician for her immense dedication to work and the health care

professionals involved in our hospital for their valuable support throughout my dissertation work.

I thank statistician **Mr. Porchelvan** for having helped with the statistics.

I thank my husband **Dr. R. Prasanna** and my daughter **Ananya** for helping me and also being patient and understanding throughout.

I immensely thank my parents and in laws and am deeply indebted to them for the moral support they have given me in my life.

I thank my colleagues, friends and staff of our hospital for their support.

Finally I thank and dedicate this study to all the children who were a part of this study for their cooperation, without whom, this study would not have been possible.

CONTENTS

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INSTITUTIONAL ETHICAL COMMITTEE
GOVT.KILPAUK MEDICAL COLLEGE,
CHENNAI-10
Ref.No.4098/ME-1/Ethics/2012 Dt:07.06.2012.
CERTIFICATE OF APPROVAL

The Institutional Ethical Committee of Govt. Kilpauk Medical College , Chennai reviewed and discussed the application for approval entitled "A Study on prevalence and risk factors of vitamin D deficiency in children with cerebral palsy – A case control study".submitted by Dr.V.Gomathy Srividya, MD (Paediatrics), PG Student, KMC, Ch-10

The Proposal is APPROVED.

The Institutional Ethical Committee expects to be informed about the progress of the study any Adverse Drug Reaction Occurring in the Course of the study any change in the protocol and patient information /informed consent and asks to be provided a copy of the final report.

GOVT. KILPAUK MEDICAL COLLEGE
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CHAIRMAN, 27/7/12
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INTRODUCTION

Cerebral palsy (CP) is a disorder of aberrant control of movement and posture, appearing early in life secondary to a central nervous system (CNS) lesion or dysfunction that is not the result of recognized progressive or degenerative brain disease. Children with CP face myriad challenges to normal growth.

Vitamin D deficiency, known to occur in children with cerebral palsy is one such challenge and if left untreated can cause osteopenia and fractures. The reasons attributed are multifactorial and include poor sunlight exposure due to their nonambulant nature, nutritional impairment due to feeding difficulties and use of long term anticonvulsants in these children.

Vitamin D deficiency is common even amongst normal children in India despite plenty of sunshine. All Indian studies point to low 25 hydroxy vitamin D levels in the healthy normal pediatric population. The prevalence data of Vitamin D deficiency in healthy children from various studies in India and abroad ranged from 8% to 80% and the reason attributed is low intake of dietary calcium and phosphorus.

Though the occurrence of Vitamin D deficiency in cerebral palsy is well described, the epidemiological data are sparse and hence it was decided to study the prevalence of vitamin D deficiency in children with cerebral palsy and to possibly identify the potential variables associated with increased risk.

Definition of CP

Cerebral Palsy describes a "group of disorders of the development of movement and posture, causing activity limitation that is attributed to non-progressive disturbances that occurred in the developing fetal or infant brain". The motor disorders of cerebral palsy are often accompanied by disturbances of sensation, cognition, and communication, perception, with or without behaviour, and/or by a seizure disorder (1).

Definition of vitamin D deficiency and insufficiency:

Vitamin D insufficiency is defined as serum 25-hydroxyvitamin D levels below 30 ng/mL.

Vitamin D deficiency is defined as serum 25-hydroxyvitamin D levels below 10 ng/mL (2).

CEREBRAL PALSY

The Cerebral palsy is the most common cause of childhood disability. The incidence of CP in developed world is 2-2.5/1000 live births (3). Evaluation of a child with CP requires a multidisciplinary approach with involvement of a dedicated “pediatrician or pediatric neurologist, a physiotherapist, occupational therapist, child psychologist, and a social worker”.

Accurate and early diagnosis of CP is important for addressing co morbidities and also for social reasons. The “at risk” infants should be periodically evaluated after early diagnosis. Probability of CP increases with prematurity, multiple pregnancies, and abnormal perinatal events. Abnormal neurological examination in infants helps in spotting ‘at risk’ children.

In preterm infants, the presence of atypical features like dominant asymmetric tonic neck reflex (ATNR), paucity of movements of any of the limbs, hypotonia/hypertonia predict major motor dysfunction (4). Ultrasound abnormalities of “grade 2-4 leukomalacia” together with early visual and neurocognitive assessment data is a very good predictor for later neurodevelopment (5). All such patients who have risk factors or have abnormal neurological signs should be followed by careful

developmental assessment. A combination of low birth weight with hypertonus at 4 months of age is highly predictive of CP at 7 years as reported by Ellenberg et al (6). The early signs of CP are shown in Table-1.

TABLE - 1

EARLY SIGNS OF CP

a.	Excessive or disorganized movement or paucity of movement
b.	Abnormal stereotyped behavior
c.	Persistent abnormalities of tone, high pitched shrill crying
d.	Feeding problems
e.	Arching of neck and back
f.	Cortical thumb
g.	Delayed social smile
h.	Persistent ATNR

It is usually difficult to diagnose CP during the first half of infancy. This is due to the fact that some normal babies may show abnormal signs that clear up spontaneously.

Cerebral palsy can be classified according to the timing of brain injury such as prenatal, perinatal or postnatal or based on pathology of brain injury e.g. vascular, infective, inflammatory or traumatic. The main divisions in the Edinburgh classification (7) are given in Table 2.

TABLE – 2

CLASSIFICATION OF CP

(a)	Hemiplegia
(b)	Quadriplegia
(c)	Diplegia
(d)	Ataxic CP
(e)	Dyskinesia (including dystonia and athetosis)
(f)	Any other form, including mixed forms

Antenatal origin of Cerebral palsy is indicated by preterm birth, microcephaly , presence of malformation, history of CP in a sibling, intrauterine growth retardation, and presence of pore cephalic cyst or ventriculomegaly (8).

Assessment of General Health:

A CP child should be assessed for general health by assessing the child's nutritional status with anthropometry and signs of vitamin deficiency. Disturbances in growth like limb length discrepancies might be there in hemiplegia or diplegia due to CP itself. Difficulties encountered in feeding are the most important cause of inadequate growth. Lack of sunlight exposure and antiepileptic usage contributes to rickety features. Lower respiratory infections are common due to repeated aspirations. Head circumference should be plotted serially to assess brain growth and microcephaly. Neurocutaneous markers should be searched for. A complete physical and systemic examination should be done to rule out other malformations.

A CP child's nutritional requirements are not the same as for a normal child. The requirement should be based on the anthropometric measures. Length is difficult to measure due to extensive deformities, contractures and dislocations. Alternatively, segmental limb and trunk

measures can be used to compute approximate length. Skin fold thickness using harpenden's calipers can be used as a better measure of nutritional status (9).

Assessment of Feeding and Nutrition:

A CP child is unable to express hunger, unable to ask for food and unable to feed themselves. This associated with their oromotor dysfunction leads to problems in feeding due to thrusting of tongue, tonic bite, and difficulty in chewing, difficulty in co coordinating swallowing (10). Choking due to repeated aspirations due to ineffective cough mechanism and increased Gastro esophageal Reflux due to lax Lower Esophageal Sphincter may cause problems with feeding.

Proper history should be taken regarding the child's usual diet, preferences and what the child chokes on while feeding. A trained therapist should observe the feeding of the baby and try to improve feeding. A contrast study with barium or fluoroscopic analysis can help in assessing the nature of feeding problems and also in recognizing aspiration. Children with CP have numerous feeding difficulties affecting their nutritional uptake and these are further aggravated by lack of awareness among parents (11).

Orthopedic Problems:

A thorough musculoskeletal system examination should be performed in children. Scoliosis, subluxation or dislocation of hip, contractures of tendoachilles and hamstrings, equinus deformity are the usually seen deformities. Reduced bone density as evidenced by bone densitometry and propensity to fractures with trivial injury sue to osteoporosis and extensive bone demineralization is common in children with cerebral palsy (12). Hip subluxation and dislocation may occur due to imbalance of adductors of the hip and flexors whose power is greater than the abductors of the hip and extensors (13). The dislocation causes considerable amount of pain if not treated. The hip which is dislocated causes difficulty in the child's ability to sit and hygiene of the perineum and causes scoliosis. At birth the hip joint is usually normal. Subluxation of hip joint may progress by five and half percent every year, if left untreated. Hip dysplasia can be assessed by examining for asymmetric folds of skin in the thigh and gluteal region. This is also done by Barlow and Ortolani tests in children. Those who are non ambulant, especially those children with spastic- quadriplegia are more prone to dislocate (14). Routine hip ultrasounds are recommended to pick up subluxation. Windswept deformity – "abduction attitude in one joint and adduction

attitude in the other joint due to contracture is seen with severe spastic CP".

Equinus deformity is the usual skeleto- muscular abnormality observed in children with Cerebral Palsy due to contracture of tendoachilles. This causes the typical tip toe gait or toe heel walking in children with Cerebral Palsy.

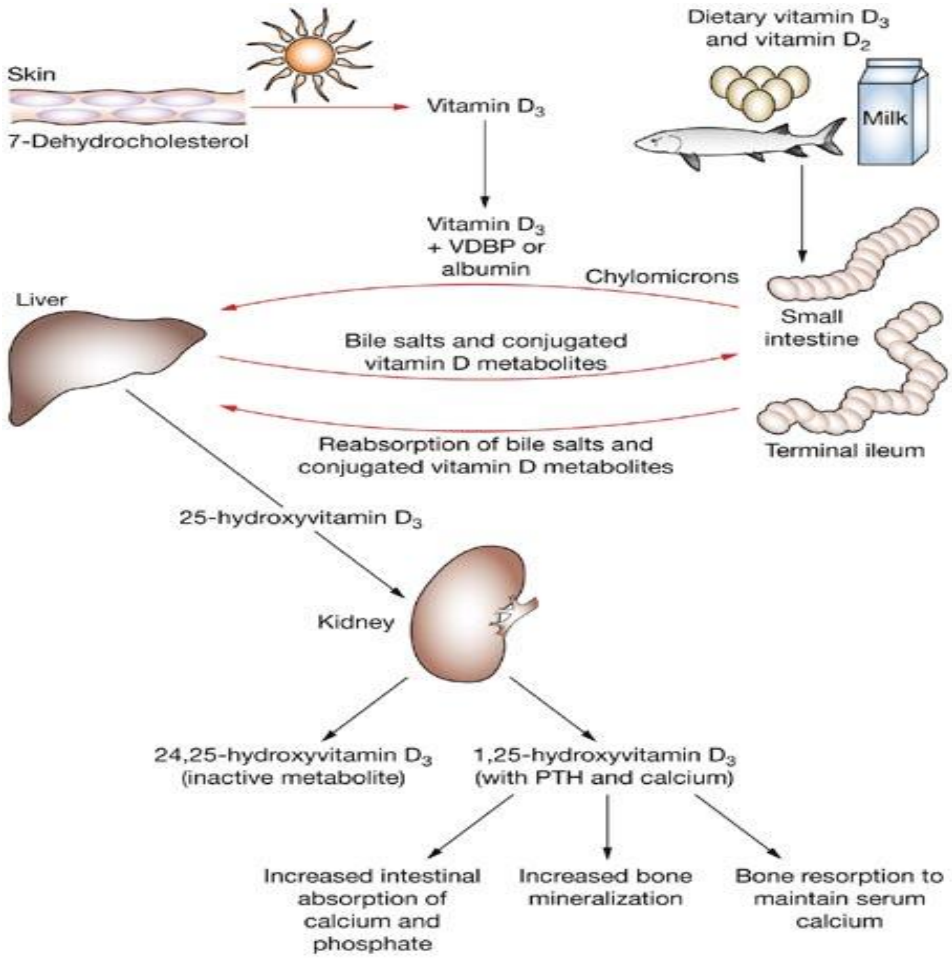
SEIZURE DISORDER:

Seizure disorder is very common in children with CP. 38% of children with Cerebral Palsy had epilepsy in a population based study (15). Numerous types of paroxysmal activity are seen in children with CP and differentiation from actual seizure would be difficult. All types of seizures may be seen in children with CP, though children with hemiplegic CP generally have localization related epilepsy. Seizure disorder in children with Cerebral Palsy is often refractory to treatment (16) and often requires multiple AEDs for seizure control. The etiology also may have bearing on the outcome. CP caused by CNS infections or malformations or grey matter damage have higher prevalence of epilepsy than children with CP of other etiology, and their possibility of becoming free from seizures is rare.

VITAMIN D

Vitamin D is wrongly termed a vitamin as it can readily be synthesized in the skin. Ultraviolet B radiation (wavelength 290 to 315nm) penetrates the skin and 7-dehydrocholesterol is converted to previtamin D3, which is rapidly converted to vitamin D3 and hydroxylated to active form. Excess previtamin D3 or vitamin D3 is destroyed by sunlight. Therefore excessive exposure to sunlight will not cause vitamin D3 intoxication.

FIG – 1 : VITAMIN D SYNTHESIS



VITAMIN D DEFICIENCY:

Vitamin D insufficiency is defined as serum 25-hydroxyvitamin D levels below 30 ng/mL. Overt vitamin D deficiency is defined as serum 25-hydroxyvitamin D levels below 10 ng/mL (2). The stages and clinical signs of Vitamin D deficiency (17) are shown in table 3.

Months before rickets becomes manifest, latent vitamin D deficiency is seen. Recurrent respiratory tract infections, growth failure, lethargy, irritability are seen associated with vitamin D deficiency. (18–21).

25 OH vitamin D levels are to be measured and not 1,25OH vitamin D as

- It may even be raised due to secondary hyperparathyroidism
- It is an unstable fraction
- Lasts for a shorter t- half
- The amount normally seen in serum is several hundred times less than 25 OH vitamin D
- And also because 25 OH vitamin D is the storage form of vitamin D.

VITAMIN D DEFICIENCY – STAGES AND CLINICAL SIGNS (table 3)

1. Stages of vitamin D deficiency

Stage I

25-OH-D level decreases, resulting in hypocalcemia and euphosphatemia; 1,25-OH_2-D may increase or remain unchanged

Stage II

25-OH-D level continues to decrease; PTH acts to maintain calcium through demineralization of bone; the patient remains eucalcemic and hypophosphatemic and has a slight increase in the skeletal alkaline phosphatase level

Stage III

Severe 25-OH-D deficiency with hypocalcemia, hypophosphatemia, and increased alkaline phosphatase; bones have overt signs of demineralization

2. Clinical signs of vitamin D deficiency

- Dietary calcium absorption from the gut decreases from 30%–40% to 10%–15% when there is vitamin D deficiency
- Low concentrations of 25-OH-D trigger the release of PTH in older infants, children, and adolescents in an inverse relationship not typically seen with young infants; the increase in PTH mediates the mobilization of calcium from bone, resulting in a reduction of bone mass; as bone mass decreases, the risk of fractures increases
  - Rickets

    Enlargement of the skull, joints of long bones, and rib cage; curvature of spine and femurs; generalized muscle weakness
  - Osteomalacia and osteopenia
  - Abnormal immune function with greater susceptibility to acute infections and other long-latency disease states (see below)

3. Potential latent disease processes associated with vitamin D deficiency

- Dysfunction of the innate immune system is noted with vitamin D deficiency
  - Immunomodulatory actions may include
    - Potent stimulator of innate immune system acting through Toll-like receptors on monocytes and macrophages
    - Decrease threshold for long-latency diseases such as cancers (including leukemia and colon, prostate, and breast cancers), psoriasis, diabetes mellitus, and autoimmune diseases (eg, multiple sclerosis, rheumatoid arthritis, systemic lupus erythematosis)

SUNLIGHT EXPOSURE AND VITAMIN D

The main source of vitamin D is synthesis in the skin using cholesterol on exposure to UV-B light. When a light skinned individual is exposed to 10 to 15 minutes of whole body sunlight, within 24 hrs, 10,000 to 20, 000 IU of vitamin D3 is generated; darker individuals need 5 to 10 times more exposure to generate similar amounts of vitamin D3" (22-24). Production of Vitamin D on exposure to UV rays is dependent on lot of factors than just exposure time. These include pigmentation of skin, month of year, BMI, cloud cover, latitude, the amount of pollution of air, the body surface area exposed, and the extent from UV rays, including sunscreens and cloth cover (23,25,26).

Skin pigmentation is most important in synthesis of vitamin D. But the necessary time of exposure for good synthesis in children cannot be determined. Indirect epidemiologic analysis now suggests that the age of onset at which direct sunlight exposure is initiated is even more important than the total sunlight exposure over a lifetime in determining the risk of skin cancer (27, 28).

VITAMIN D & CALCIUM SUPPLEMENTATION:

Vitamin D supplements are necessary to all children from birth. Preterm and low birth weight children should be supplemented vitamin D. Vitamin D supplementation should be given along with calcium supplementation to ensure good bone mineralization (29).Vitamin D deficiency, though biochemical and latent is observed in many normal healthy children and they are in danger of osteomalacia, overt rickets after some time or predisposed to recurrent respiratory tract infections. Diseases that predispose to fat malabsorption and thereby causing fat soluble vitamin deficiency remain deficient despite daily RDA intake of vitamin D and have to be supplemented with higher doses. Children on long term anticonvulsant medications are also found to be deficient in vitamin D in spite of daily RDA due to cytochrome P 450 induction and destruction of vitamin D. In such children, the dose of vitamin D is adjusted according to biochemical tests for 25 OH vitamin D levels and also bone densitometry assessment.

Best marker available to detect vitamin D levels is 25 OH vitamin D. It should be emphasized that serum level of 1, 25(OH) 2D is not a good indicator of vitamin D deficiency because of the reasons already explained.

ANTIEPILEPTIC DRUGS AND BONE STATUS

Bone health is very much affected by anti epileptic drug intake. Vitamin D helps in mineralization of the bone matrix in growing bones (30). Trabecular bone and growth plate is affected. Rickets has been reported in children treated with AEDs (31).

Osteomalacia refers to softening of the bone due to decreased mineralization of the matrix of the bone. Rickets is not seen after completion of bone growth, while osteomalacia can be seen later also. The bone is involved while the growth plate is not. Drug-induced osteomalacia occurs secondary to AEDs and is well known.

Osteoporosis refers to a decrease in the total bone mass predisposing them to frequent fractures. AED are well known to produce drug induced osteoporosis (33). Bone turnover markers may be increased in osteoporosis. Bone formation and resorption determines bone turnover, and both can be affected in osteoporosis. There is net increase in resorption over formation in osteoporosis.

TABLE - 4

MARKERS OF BONE TURNOVER

Bone formation markers:

- Osteocalcin
- ALK (bone-specific)
- Type I collagen - Carboxy-terminal propeptide

Bone resorption markers:

- N-telopeptide of collagen cross-links ,hydroxyproline
- Type I collagen - Cross-linked C-telopeptide

Markers of resorption are due to activity of osteoclasts, the cells that cause bone breakdown. Measurements of bone resorption are done in the serum or urine. Bone formation markers are procollagen markers, osteocalcin (or bone Gla protein) and bone-specific alkaline phosphatase. These markers assess the activity of osteoblasts, bone forming cells. By Valimaki et al, markers of osteoclastic activity are elevated in patients with seizures receiving long-term treatment with Anti epileptic drugs (34)

and after recent initiation of therapy with carbamazepine by verrotti et al (35, 36). Markers of bone formation have also been assessed in patients receiving AEDs. Increase in alkaline phosphatase have been seen in both children and adults receiving AED and the isoenzymes measured showed that the increase in total alkaline phosphatase was due to the bone fraction" (37, 38). According to Richen et al and another study by Sato biochemical abnormalities in adults receiving AEDs include "hypophosphatemia, hypocalcemia, decreased levels of vitamin D metabolites, increased parathyroid hormone (PTH) levels, and increased levels of bone resorption markers and alkaline phosphatase" (34, 38-41).

Pediatric studies reveal findings consistent with both increased and decreased bone turnover. Elevated markers of bone formation and resorption have been reported (35, 36). Compared with children who are not receiving AEDs, children who receive AEDs may have reduced Bone Mineral Density (42-45). The clinical significance of these findings is not clear, as there are no pediatric BMD reference databases.

The abnormalities have been attributed to increased activity of the microsomal P-450 mixed-function oxidase system, resulting in increased conversion of vitamin D to inactive forms, inhibition of intestinal calcium transport directly, and independent of effects on vitamin D, and increased

bone resorption and turnover . Several theories (46) have been proposed to explain the link between AEDs and bone disease **(Table 5)**. No single theory explains all the reported findings, and there may be multiple mechanisms.

TABLE – 5

PROPOSED MECHANISMS OF AED-RELATED BONE DISEASE

- Induction of the microsomal cytochrome P450 enzyme system and conversion of vitamin D to inactive metabolites.
- Decreased calcium absorption
- Altered response to parathormone
- Impaired bone formation
- Hyperparathyroidism
- Altered bone resorption as evidenced by osteoclastic activity
- Deficiency of vitamin K
- Deficiency of calcitonin

AEDs like phenobarbitone, phenytoin and carbamazepine are implicated in causing low vitamin D levels and rickets, osteomalacia and drug indced osteoporosis. (34-36,42,43). Valproate, though not an enzyme inducer has also been studied and shown to cause decreased bone mineral density (40,44). According to Akin R et al, in ambulant children with uncomplicated epilepsy, valproate therapy was associated with a 10 to 14% reduction in BMD (40,43) but this effect was not consistently reproduced (47). Multiple new AEDs have been approved over the past 10 years. Few studies have evaluated the effect of these newer medications on bone mineral metabolism and BMD (44,48,49). Though alteration in bone metabolism is not reported with newer antiepileptics as they are considered to be non enzyme inducers, it cannot be concluded that they do not have any alteration in bone homeostasis as evidenced in the case of valproate. Larger studies with newer antiepileptic drugs are necessary to prove this.

FEEDING DIFFICULTIES IN CP

Decreased food intake when compared to increased nutritional needs, oral - motor dysfunction and altered level of energy expenditure may very much contribute to the decreased nutritional status of the severely neurologically impaired cerebral palsy children. Inappropriate

dietary and energy uptake when compared to nutrient needs usually causes obesity, under nutrition in cerebral palsy children (51, 52).

They are very much unable to express hunger, preferences of food, and satiety, leaving parents responsible for their food intake regulation. (53, 54). The feeding process in these children is very difficult and needs dedication. The amount of food given may not be sufficient to meet the child's energy needs. Problems in Oro - motor function are the most common reason in the pathogenesis of decreased nutrition and it corresponds with the severity of motor impairment (55, 56). Children may present with poor closure of lip, drooling of saliva and frequent thrusting of tongue, resulting in spillage of food particles (57). Swallowing may be slowed down, resulting in collection of food particles in the larynx or pyriform sinuses with propensity for frequent aspiration.

Gastroesophageal reflux, which affects seventy five percent of cerebral palsy children, and prolonged gastric emptying, may account to the loss of vitamins and minerals because of frequent vomiting (58,59).

OSTEOPENIA AND CP

Pathological fractures occur in severely spastic children due to inadequate mineralization of bone (60, 61). In a study by Hahn and another by Hendersen et al, factors responsible for reduced bone mineral density in these children are poor nutritional status, insufficient calcium intake, immobilization and use of anticonvulsants (41,62).

CP children have decreased bone density compared to normal children and this predisposes them to pathological fractures even on trivial injury (63,64).This has been proven by BMD scans done on CP children which showed extensive osteoporosis.

Long bone fracture is a common problem in non-ambulant cerebral palsy (CP) children. This is because their non ambulant status results in increased bone resorption and increases the fragility of the bone. Up to 20% sustain a femoral fracture during their lifetime (65). Other than fractures, deformities, subluxtions and dislocations are common due to altered power between opposing groups of muscles.

Henderson et al found that more severe neurological dysfunction, usage of anticonvulsants and decreased triceps skin fold thickness predisposes to frequent fractures (64).

REVIEW OF LITERATURE

Harinarayanan et al from Tirupathi, Andhra Pradesh studied the prevalence of vitamin D between normal urban and rural subjects. The study was conducted among urban adults and children and results were compared with rural population with gender dispersion. The association with low calcium in the diet was studied and association was analyzed between vitamin D levels and the low dietary calcium. 81.5% urban males and 62.9% urban females were found to be deficient in vitamin D, 14.8% of urban males and 25.7% of urban females were insufficient and 3.7% of males and 11.4% of females in urban setting had normal vitamin D levels. In rural population, among males, deficiency, insufficiency and normal vitamin D values were seen in 76.5%, 14.7% and 8.8% respectively. Among rural females, 72.2% were deficient, 13.9% were insufficient, and 13.9% were found to be normal. The cut off value for vitamin D deficiency in the group was taken as 20 ng/ml(66).

In another study by **Harinarayanan et al** from Andhra Pradesh, low dietary intake of calcium, high phytate intake and high phytate to calcium ratio in diet predisposed to vitamin D deficiency (89).This study was done in tropical country India , in Andhra Pradesh, where sunshine was 8 to 10 hours / day throughout the year. Only adults contributed to be

subjects of the study. Diet recall was done and dietary calcium, phytates and phytate to calcium ratio was studied in urban and rural individuals. The cut off value for vitamin D deficiency was taken as 20 ng/ml. It was found that urban men and women had mean vitamin D values of 18.54 and 15.5 ng/ml respectively while the same in the rural population was 23.7 and 19 ng/ml. This study proved that low dietary calcium intake was statistically significant to produce vitamin D deficiency and insufficiency (67).

Marwaha et al conducted a study in Delhi among 5137 healthy children between ages of 10 and 18 of both sexes. Two socioeconomic strata were compared in this study. Clinical evidence of vitamin D deficiency was found in 10.2% of normal children. The mean vitamin D levels for the entire population were 11.8 ng/ml. The mean value for the low socioeconomic group was 10.4 ng/ml and the same for the upper socioeconomic group was 13.7 ng/ml. In the study, males were found to have higher mean concentrations higher than females. Also, vitamin D deficiency was found to be higher in the lower socioeconomic group than in the upper socioeconomic group, unlike other studies where the upper socioeconomic group showed a higher prevalence of vitamin D deficiency. The cut off values used in the study are severe

hypovitaminosis < 5 ng/ml, moderate hypovitaminosis 5-10 ng/ml and mild hypovitaminosis 10-20 ng/ml (68).

This study has also demonstrated that severe vitamin D deficiency (levels < 5ng/ml) was found in 8.6% in comparison to 23.5% in Finnish population studied by **Ala – Houlala et al** (69) and 45.2% in Chinese adolescents studied by **Du X et al** in Beijing (70).

Puri et al conducted a study in Delhi among 3127 school going girls in the age group of 6 -18 yrs. From the study group, 193 girls of lower socio economic status and 211 girls of upper socio economic status was converted into sub group and analyzed. In the subgroup, 29.9% of subjects were found to be vitamin D deficient of which 25.4% were from lower economic status and 34.1% was from higher socioeconomic status. The cut off value for vitamin D deficiency was taken as 10 ng/ml. Also, girls in higher socioeconomic status, though had good nutritional status and higher BMI, were found to be more deficient than their lower socioeconomic counterparts. Also studied was the mean sun exposure between both groups. Mean sunlight exposure which included playing; exercising outdoors, doing other household chores outside the house in sunlight was 45 min/ day in lower socioeconomic group while the same was 25 min/day for the higher socioeconomic group, which was found to

be statistically significant. Also, the mean body surface area exposed to sunlight among the 2 groups was 28 % and 15% in lower and higher economic groups respectively and the BSA exposure were found to be statistically significant (71).

Varying cut off values used to define deficiency, insufficiency and normalcy in vitamin D values by different authors and different classifications makes it difficult in comparing the studies as it alters the number of children in the deficient group . A uniform criteria is necessary between studies to make comparison meaningful. Though the IOM and AAP have defined vitamin D deficiency and insufficiency to be 25 OH D values to be < 10 ng/ml and 10-30 ng/ml respectively and is being used worldwide, there is an increasing trend to use <20 ng/ml as cut off range to define vitamin D deficiency by different authors in face of emerging evidence that parathormone levels starts increasing with vitamin D values of < 20 ng/ml. There is no new consensus guidelines to define vitamin D deficiency to be <20 ng/ml and we have based our study according to the orginal guidelines drawn by IOM and AAP.

In a study by **Balalala et al**, mother's blood , cord blood and blood of the infants at 3 months of age were studied and all uniformly showed

low vitamin D levels in the insufficiency range proving that children of mother's with low vitamin D are prone to be vitamin D deficient(72).

Kumar et al conducted a large study in United States between the years 2001 to 2004 with sample size of 6275 among children 1 to 21 yrs, of which 9% of children were found to be vitamin D deficient. Another 61% were found to be vitamin D insufficient. The cut off values for the study were taken to be <15 ng/ml for deficiency group and 15-30 ng/ml for the insufficiency group. The larger sample size and the time duration of the study ensures that all weather related factors influencing vitamin D deficiency become well distributed throughout the group and the degree of error is very less (73).

Renee et al studied the vitamin D status with risk factors in children with epilepsy. This study was conducted in an urban clinic consisting of patients on antiepileptics, mostly newer generation antiepileptics, although all groups of AED were represented. The cut off value to define vitamin D vitamin D insufficiency was more prevalent in the population than deficiency. Female gender, increased BMI, use of antiepileptics was considered significant risks for developing vitamin D deficiency. Mean level of Vitamin D was found to be 28.37 ng/ml with 5% children alone in the deficiency range. (74).

Hendersen et al did a study on non institutionalized children with cerebral palsy in North Carolina. Calcidiol and calcitriol values were compared with different variables. Prevalence of vitamin D deficiency was 19%. Cut off value for deficiency was taken to be < 10 ng/ml. No statistical significance was found among the different variables analyzed relative to vitamin D levels (75).

AIM OF THE STUDY

- The aim of the study is to find the prevalence of vitamin D status –Vitamin D deficiency and insufficiency in children with Cerebral Palsy and to compare them with normal children.

- To identify the risk factors associated with Vitamin D deficiency in these children.

MATERIALS AND METHODS

STUDY DESIGN

Case control study

PLACE OF STUDY

Pediatric department, Kilpauk Medical College

STUDY PERIOD

June 2012 to December 2012

AGE GROUP

1 to 12 years

INCLUSION CRITERIA:

Children with cerebral palsy attending the pediatric outpatient department and in patient care of our hospital contributed as the subjects of this study. Normal children were randomly selected as controls after informed consent.

EXCLUSION CRITERIA:

The following children with cerebral palsy were excluded from the study:

- Children already on calcium supplementation
- Children with evidence of renal or liver disease
- Children with malabsorption syndromes
- Children with family history of metabolic bone disease

STUDY POPULATION

All children satisfying inclusion criteria

CONTROLS

Age and sex matched controls

MATERIALS AND METHODS

The study was approved by the ethical committee of our hospital. Informed consent was obtained for each subject, both cases and controls from their parent or guardian. There are no conclusive data regarding the prevalence of vitamin D deficiency in children with cerebral palsy. With

existing data, n was computed to be n=32. 32 cases were compared with 32 age and sex matched controls.

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 were subjected to the following investigations: serum calcium-total, serum phosphorus, serum alkaline phosphatase (SAP) levels. These were determined by an automated analyzer. The 25 OH vitamin D levels were estimated by CLIA (chemi luminescence immunoassay) method.

Vitamin D status in children with CP were analyzed with different variables including age, sex, type of CP and functional grade of CP,

sunlight exposure, feeding difficulty, AED use, type of AED, laboratory data and the statistical significance was determined.

Weight less than 3rd percentile for age and head circumference below 3rd percentile according to IAP growth charts were considered to be wasting and microcephaly respectively. 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.

Functional staging of CP in cases was done.

I No limitation of activity

II Moderate limitation of activity

III Moderate to great limitation of activity

IV No useful physical activity.

Vitamin D status in children with CP were analyzed with different variables including age, sex, type of CP, sunlight exposure, feeding difficulty, AED use, type of AED, laboratory data and the statistical significance determined. The association between the type of AED and prevalence of Vitamin D deficiency was also analyzed.

STATISTICAL ANALYSIS OF DATA:

The co relation between variables was analysed by chi square test.

The means of the groups were compared by independent t test.

The data analysis was computed using the SPSS v15 software and p value <0.05 was considered statistically significant.

Based on the data, the possible risk factors for vitamin D deficiency were postulated.

PROFORMA

1. NAME:

2. AGE / SEX:

3. MRD No:

4. ADDRESS:

5. HISTORY:

(i) Normal Delivery / Elective LSCS / Emergency LSCS

(ii) Birth Asphyxia: Yes / No

(iii) Cried immediately after birth: Yes / No

(iv) Birth Wt: <2.5 kg / >2.5 kg

(v) Neonatal seizures: Yes / No If Yes, cause:

(vi) Breast fed: Yes / No

(vii) Developmental delay: Yes / No

(viii) Epileptic: Yes / No If Yes, How long? _____

(ix) On AEDs: Yes / No If Yes, How long? _____

(x) Feeding difficulties: Yes / No If Yes, choking / vomiting / ↑feeding time /others

(xi) Time taken to feed:

(xii) Exposure to sunlight: Yes / No

(xiii) Dental changes: Yes / No

(xiv) Fractures / deformities: Yes / No

6. ANTHROPOMETRY:

Head circumference: _____cm Weight: _____Kg

Microcephaly: Yes / No Wasting: Yes / No

7. LAB VALUES:

(i) Hemoglobin:

(ii) Smear: Microcytosis / Macrocytosis / Dimorphic / others

(iii) Total Calcium: mg/dl

(iv) Serum Phosphorus: mg/dl

(v) Serum Alkaline Phosphatase: IU/l

8. MEDICATION DETAILS:

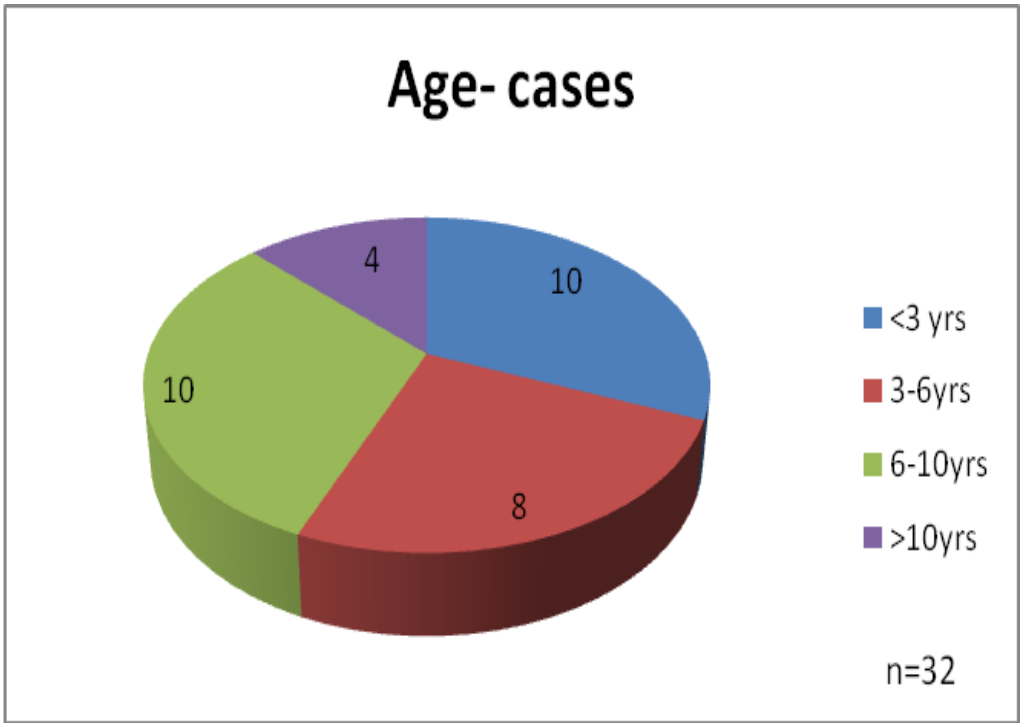
(i) Antiepileptic drug: Phenytoin / Phenobarbitone / Valproate / Carbamazepine / Topiramate / Lamotrigine / others

(ii) No. of antiepileptic drug used:

(iii) Duration of antiepileptic drug: <1yr / 1-3 yrs / >3yrs

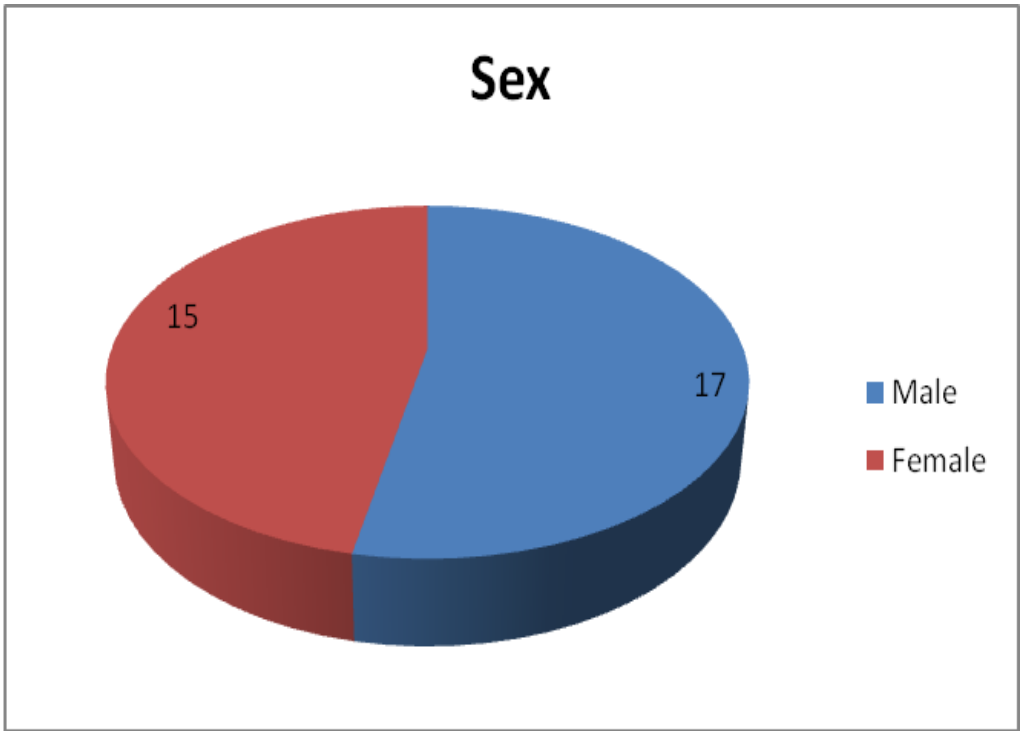
RESULTS AND ANALYSIS

A total of 32 children with cerebral palsy were subjects (cases) of the study. These children were analyzed with another 32 ages and sex matched normal children (controls). The demographic characteristics of the cases are as follows:

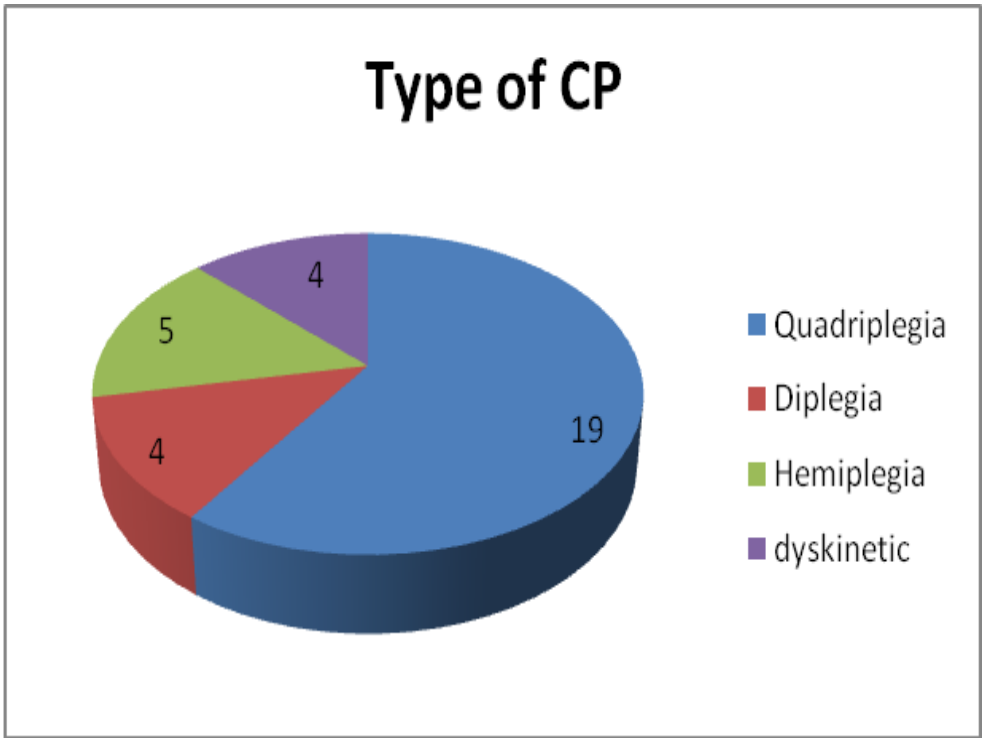


10 (31.2%) children were below 3 years, 8 (25%) between 3-6 years, 10 (31.2%) between 6-10years and 4 (12.5%) were in more than 10 year age group. The mean age of cases was 5.9 years.

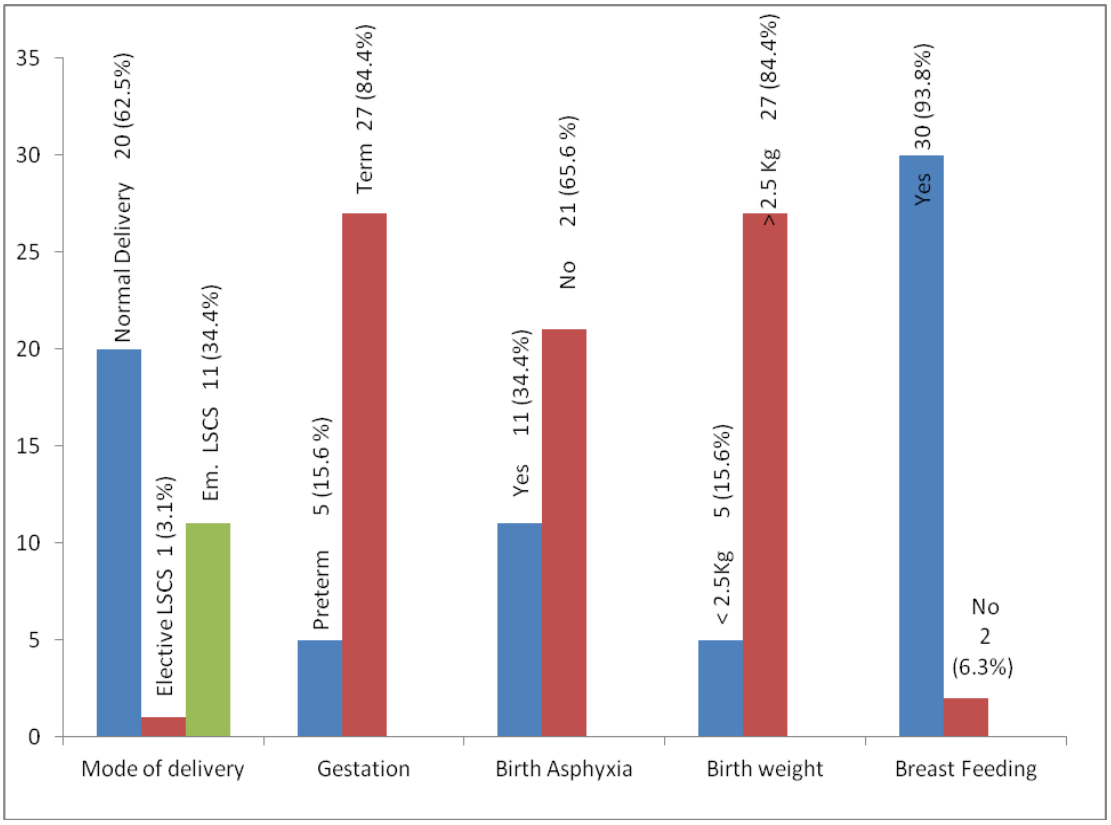
Majority of them (53.1%) were males and the rest 46.9% were females.



59.4% of them were spastic quadriparesis, spastic diplegia was 12.5% and hemiplegia was 15.6%. 4 children belonged to dyskinetic group (12.5%)

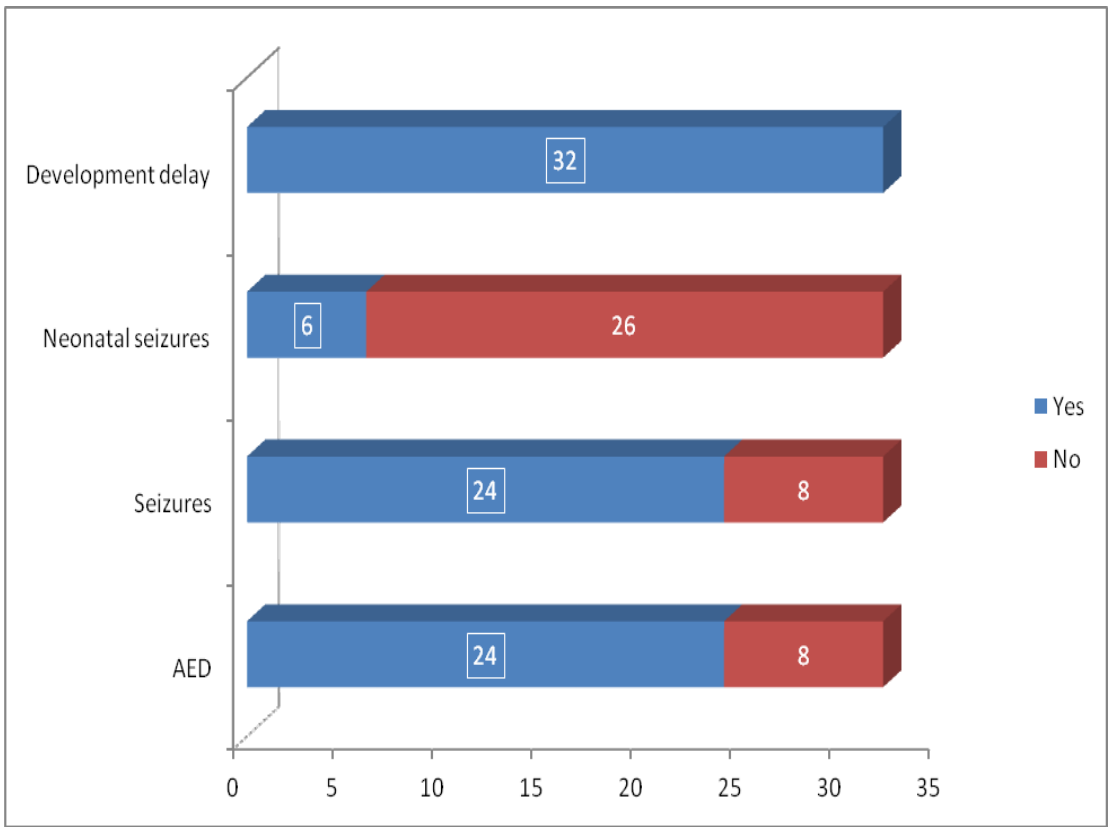


Birth history details of all these children were analyzed with regards to the gestational age, mode of delivery, birth weight and history suggestive of birth asphyxia and the data are depicted on a graph as follows:



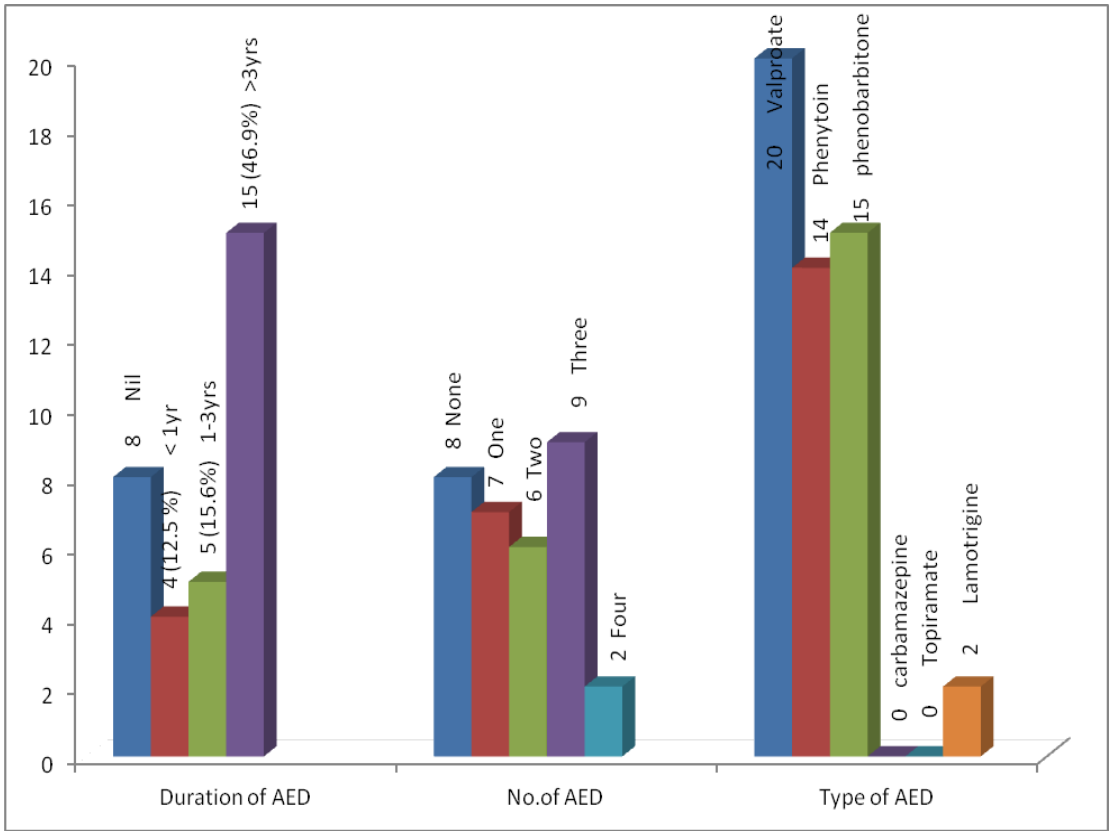
While in controls, 12 (37.5%) were delivered normally, 10 (31.3%) each were emergency and elective LSCS. All 32 controls were term and had no birth asphyxia history. Only 2 controls (6.3%) were less than 2.5 kg at birth while 30 (93.8%) were more than 2.5kg. Similarly 2 control children were not breast fed while a majority of 30 were exclusively fed.

All children in case group had developmental delay, 18.8% had neonatal seizures whereas seizures after neonatal period were found in 75% of them. All 24 (75%) of them were on one or more antiepileptic drugs.



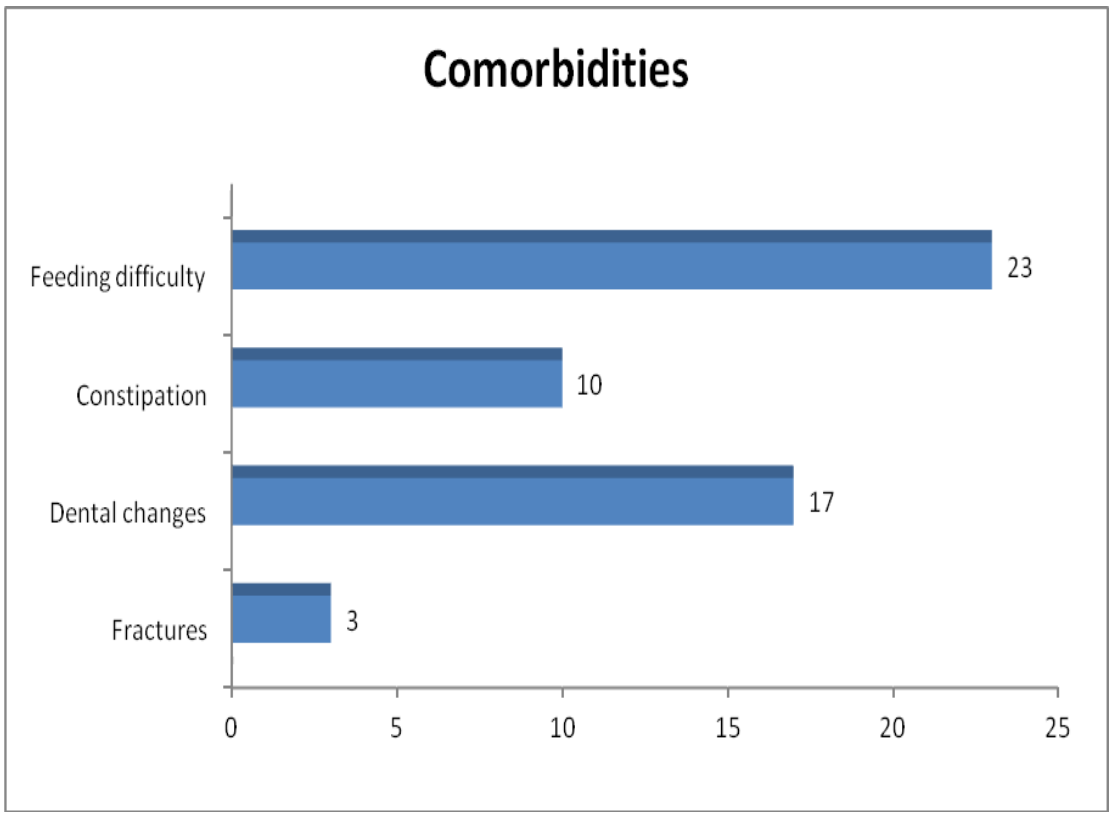
While in the control group none of them had developmental delay or neonatal seizures. Neither they were epileptic nor were they on anti epileptic medications.

As the study is on Vitamin D status in children with cerebral palsy where antiepileptic drugs are implicated to be one of the risk factor of vitamin D deficiency in these children, we gathered information on the number of AEDs used in each child, type of AED and the duration for which it is used to correlate with the vitamin D status in these children.

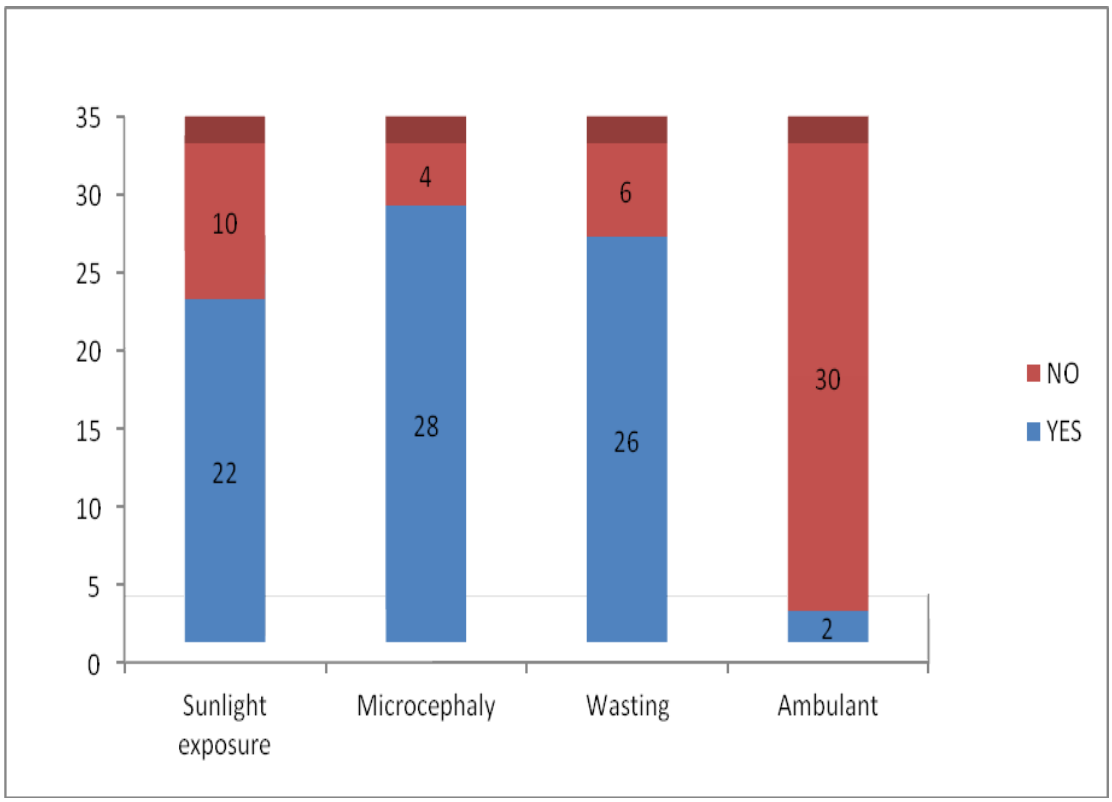


It is clear from the graph that nearly half of the cases were on AED for more than 3 years. While 4 cases (12.5%) were taking drugs for less than one year, 5 cases (15.6%) were taking drugs for one to three years. Only 7 children (21.8%) were on monotherapy whereas majority 17 (53.1%) of them were on more than one drug. 8 children (25%) were not on AED. Sodium valproate was the commonly used drug.

The commonly observed co morbidities in cases with cerebral palsy were feeding difficulties (71.9%), constipation (28.2%), dental changes (56.2%) and fractures (12.5%) in that order.

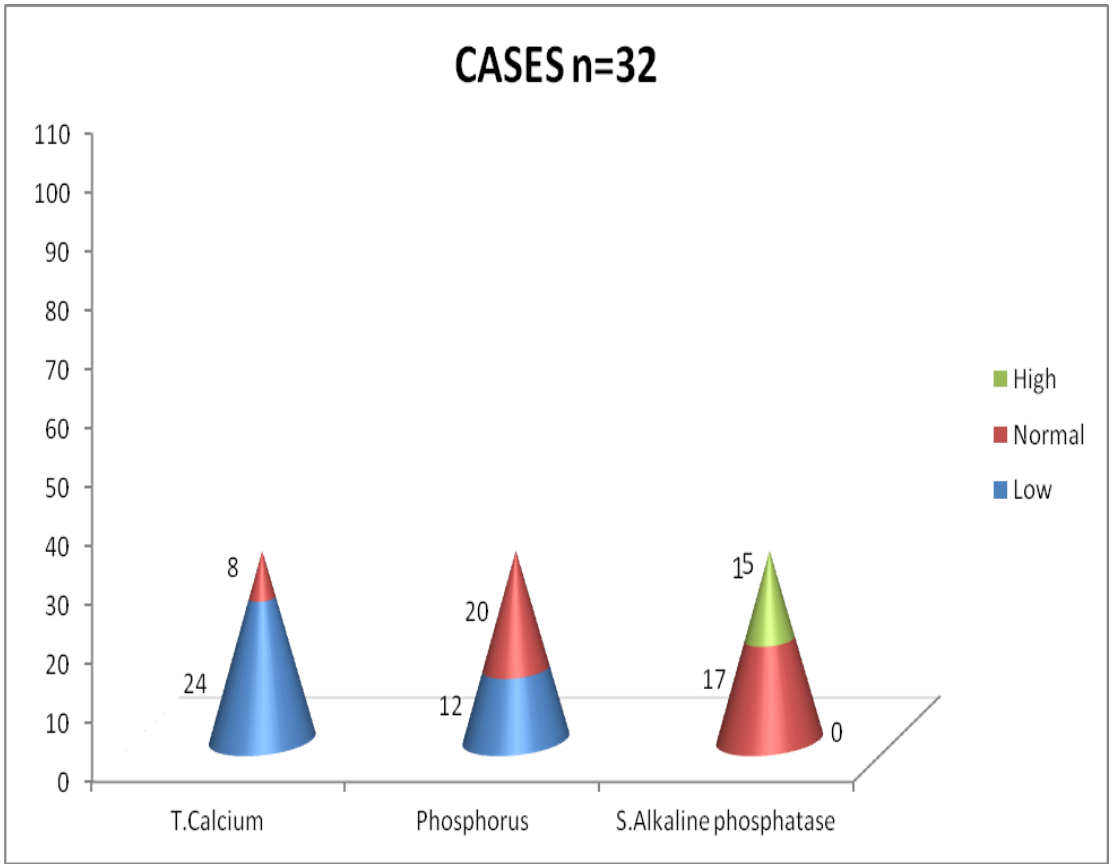


The other parameter implicated in vitamin D deficiency in children with cerebral palsy is the poor sunlight exposure in these children, mainly due to their non ambulant nature. 10(31.25%) of them had poor sunlight exposure.

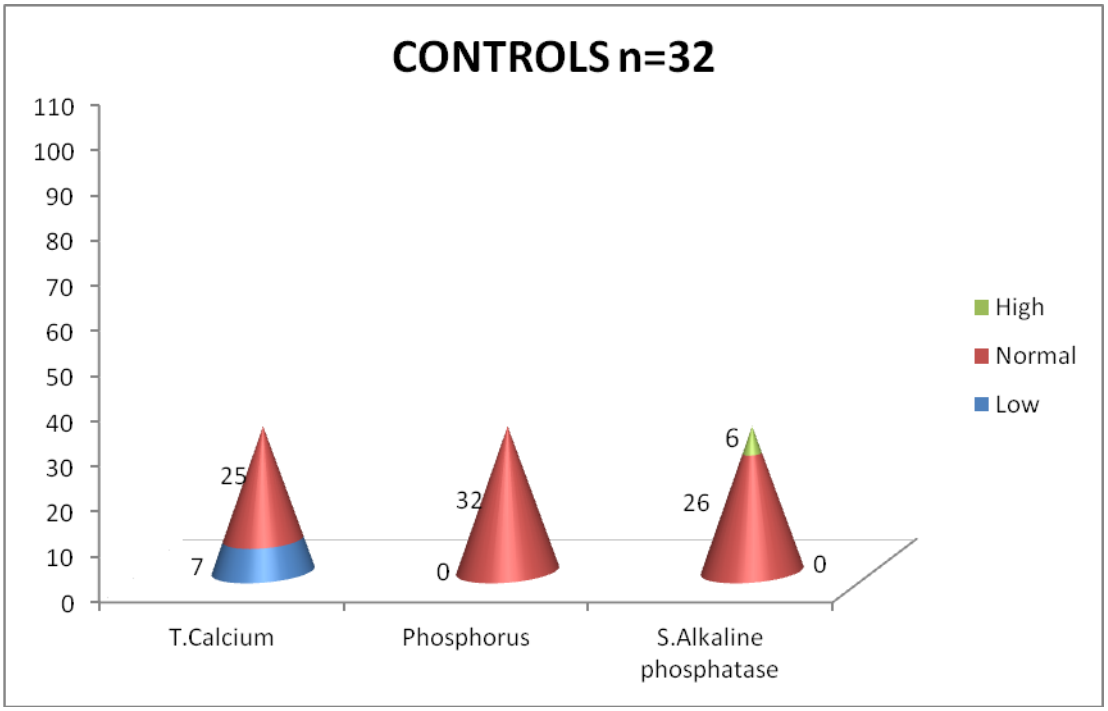


Microcephaly was seen in 28 (87.5%) of the children. 30 children were non ambulant (functional grade 3 and above) while 2 were ambulant (grade 2 and below). In our study, 6.3% belonged to grade II, 34.4% belonged to grade III and 59.4% came under grade IV.

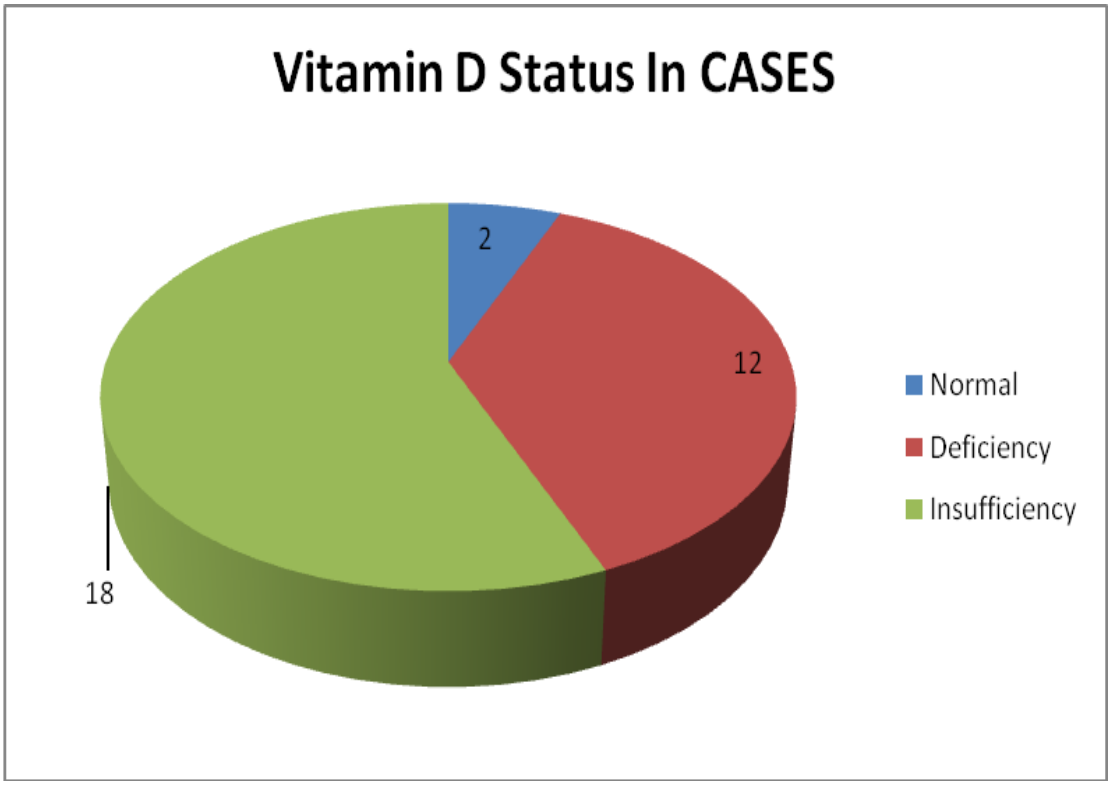
Total calcium, serum phosphorus and serum alkaline phosphatase was done in all children (both cases and controls). In the case group , 24 children (75%) had low total calcium and the rest 8 (25%) had normal total calcium. Low phosphorus was observed in 12 (37.5%) of the children. Serum Alkaline phosphatase (SAP) was normal in 17 (53.1%) whereas it was elevated in 15(46.9%).



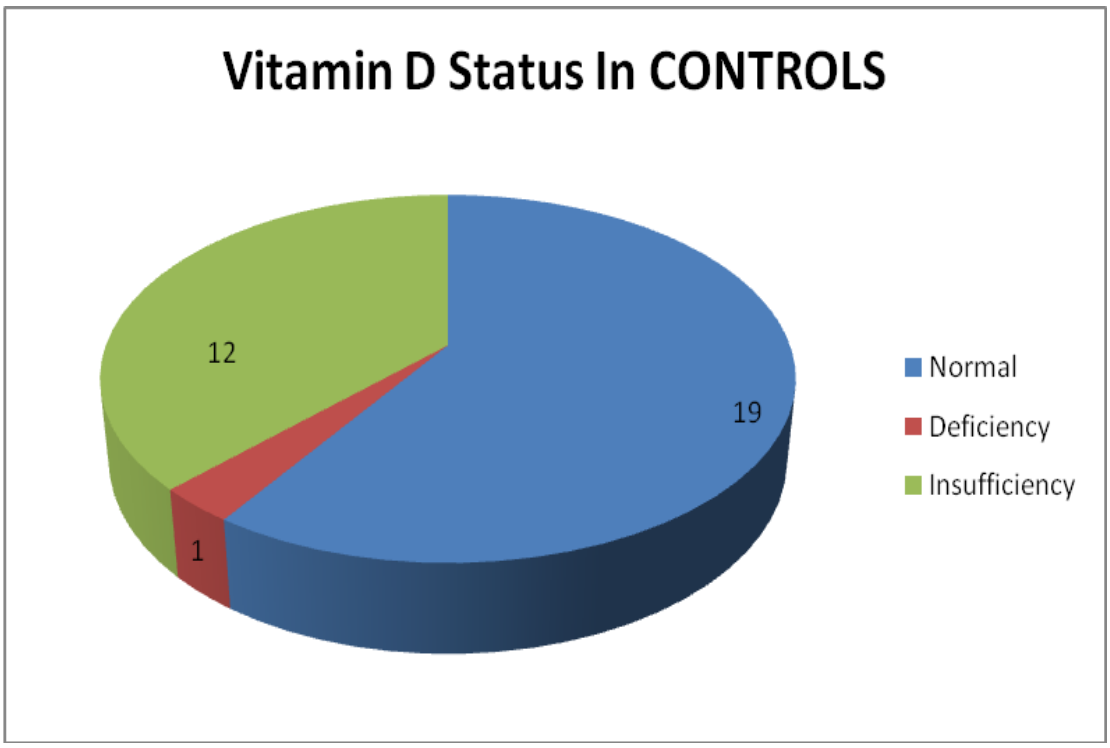
The same was done for all the controls. Serum calcium was low in 7 control children (21.9%) and normal in 25(78.1%). In these children alkaline phosphatase was normal in 26 (81.3%) and elevated in the rest 6 (18.8%). Serum phosphorus was normal in all children.



Vitamin D deficiency was observed in 12 (37.5%) and insufficiency in 18 (56.3%) of children with cerebral palsy.



Similarly vitamin D status was studied in normal control children. It was found that majority of them 19 (59.4%) was normal. While 12 (37.5%) were vitamin D insufficient, one child (3.1%) showed deficient levels



VITAMIN D CASES VS. CONTROLS

Crosstab

			Group		
			Case	Control	Total
vit d	< 10	Count	12	1	13
		% within Group	37.5%	3.1%	20.3%
	10 - 30	Count	18	12	30
		% within Group	56.3%	37.5%	46.9%
	30 - 100	Count	2	19	21
		% within Group	6.3%	59.4%	32.8%
Total		Count	32	32	64
		% within Group	100.0%	100.0%	100.0%

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	24.270[a]	2	.000
Likelihood Ratio	28.083	2	.000
Linear-by-Linear Association	23.386	1	.000
N of Valid Cases	64		

a. 0 cells (.0%) have expected count less than 5. The minimum expected count is 6.50.

37.5% had vitamin D deficiency and 56.3% had insufficiency among CP children. Among, age and sex matched controls, 3.1% were found to be deficient and 37.5% were found to be insufficient. Decreased vitamin D levels were found to be statistically significant in the case group when compared to controls.

Multivariate analysis of Vitamin D status in children with CP and controls

Variables	Vitamin D status						P value
	CASES n=32			CONTROLS n=32			
	DEFI-CIENCY	INSUFF-ICIENCY	NORMAL	DEFI-CIENCY	INSUFFI-CIENCY	NORMAL	
Sex							
Male	7	9	1	0	8	9	P > 0.05
Female	5	9	1	1	4	10	
Gestation							
Preterm	1	4	0	0	0	0	P > 0.05
Term	11	14	2	1	12	19	
Birth asphyxia							
Yes	5	4	2	0	0	0	P > 0.05
No	7	14	0	1	12	19	
Birth weight>2.5							
Yes	11	14	2	1	12	19	P > 0.05
No	1	4	0	0	0	0	
Neonatal seizures							
Yes	3	1	2	0	0	0	P > 0.05
No	9	17	0	1	12	19	
Breast feeding							
Yes	10	18	2	1	12	19	P > 0.05
No	2	0	0	0	0	0	
Epilepsy							
Yes	12	11	1	0	0	0	**P=0.000**
No	0	7	1	1	12	19	
AED							
Yes	12	11	1	0	0	0	**P=0.000**
No	0	7	1	1	12	19	
Feeding difficulty							
Yes	11	11	1	0	0	0	**P=0.01**
No	1	7	1	1	12	19	
Sunlight							
Yes	7	13	2	1	12	19	**P=0.046**
No	5	5	0	0	0	0	

Dental							
Yes	8	7	2	0	0	0	**P=0.02**
No	4	11	0	1	12	19	
Fracture							
Yes	2	1	0	0	0	0	P > 0.5
No	10	17	2	1	12	19	
Wasting							
Yes	12	13	1	0	0	0	**P=0.000**
No	0	5	1	1	12	19	

USAGE OF ANTIEPILEPTICS VS VITAMIN D

Crosstab

vit d				Group		Total
				Case	Control	
< 10	aed	Yes	Count	12	0	12
			% within Group	100.0%	.0%	92.3%
		No	Count	0	1	1
			% within Group	.0%	100.0%	7.7%
	Total		Count	12	1	13
			% within Group	100.0%	100.0%	100.0%
10 - 30	aed	Yes	Count	11	0	11
			% within Group	61.1%	.0%	36.7%
		No	Count	7	12	19
			% within Group	38.9%	100.0%	63.3%
	Total		Count	18	12	30
			% within Group	100.0%	100.0%	100.0%
30 - 100	aed	Yes	Count	1	0	1
			% within Group	50.0%	.0%	4.8%
		No	Count	1	19	20
			% within Group	50.0%	100.0%	95.2%
	Total		Count	2	19	21
			% within Group	100.0%	100.0%	100.0%

P=0.000

Antiepileptic drug usage was found to be statistically highly significant when compared between cases and controls in both deficient and insufficient group.

DURATION OF AED VS. VITAMIN D

Crosstab

vit d				Group: Case	Group: Control	Total
< 10	duration	< 1	Count	1	0	1
			% within Group	8.3%	.0%	7.7%
		1 - 3	Count	2	0	2
			% within Group	16.7%	.0%	15.4%
		=> 3	Count	9	0	9
			% within Group	75.0%	.0%	69.2%
		Nil	Count	0	1	1
			% within Group	.0%	100.0%	7.7%
	Total		Count	12	1	13
			% within Group	100.0%	100.0%	100.0%
10 - 30	duration	< 1	Count	3	0	3
			% within Group	16.7%	.0%	10.0%
		1 - 3	Count	2	0	2
			% within Group	11.1%	.0%	6.7%
		=> 3	Count	6	0	6
			% within Group	33.3%	.0%	20.0%
		Nil	Count	7	12	19
			% within Group	38.9%	100.0%	63.3%
	Total		Count	18	12	30
			% within Group	100.0%	100.0%	100.0%
30 - 100	duration	1 - 3	Count	1	0	1
			% within Group	50.0%	.0%	4.8%
		Nil	Count	1	19	20
			% within Group	50.0%	100.0%	95.2%
	Total		Count	2	19	21
			% within Group	100.0%	100.0%	100.0%

P= 0.005

The number of years of anti epileptic drugs intake was found to be highly significant when compared between cases and controls in both the deficient and the insufficient group.

SEIZURE DISORDER VS. VITAMIN D

Crosstab

vit d				Group		Total
				Case	Control	
< 10	epilptic	Yes	Count	12	0	12
			% within Group	100.0%	.0%	92.3%
		No	Count	0	1	1
			% within Group	.0%	100.0%	7.7%
	Total		Count	12	1	13
			% within Group	100.0%	100.0%	100.0%
10 - 30	epilptic	Yes	Count	11	0	11
			% within Group	61.1%	.0%	36.7%
		No	Count	7	12	19
			% within Group	38.9%	100.0%	63.3%
	Total		Count	18	12	30
			% within Group	100.0%	100.0%	100.0%
30 - 100	epilptic	Yes	Count	1	0	1
			% within Group	50.0%	.0%	4.8%
		No	Count	1	19	20
			% within Group	50.0%	100.0%	95.2%
	Total		Count	2	19	21
			% within Group	100.0%	100.0%	100.0%

P =0.000

Presence of seizure disorder was found to be statistically highly significant when compared between cases and controls in both deficient and insufficient group. This is due to the fact that all the patients with seizures were on regular anti epileptic therapy.

FEEDING DIFFICULTY VS. VITAMIN D

Crosstab

vit d				Group		Total
				Case	Control	
< 10	fd	Yes	Count	11	0	11
			% within Group	91.7%	.0%	84.6%
		No	Count	1	1	2
			% within Group	8.3%	100.0%	15.4%
	Total		Count	12	1	13
			% within Group	100.0%	100.0%	100.0%
10 - 30	fd	Yes	Count	11	0	11
			% within Group	61.1%	.0%	36.7%
		No	Count	7	12	19
			% within Group	38.9%	100.0%	63.3%
	Total		Count	18	12	30
			% within Group	100.0%	100.0%	100.0%
30 - 100	fd	Yes	Count	1	0	1
			% within Group	50.0%	.0%	4.8%
		No	Count	1	19	20
			% within Group	50.0%	100.0%	95.2%
	Total		Count	2	19	21
			% within Group	100.0%	100.0%	100.0%

P=0.01

Presence of feeding difficulty was found to be statistically significant in the case group when compared to controls in both deficient and insufficient group.

SUNLIGHT EXPOSURE VS VITAMIN D

Crosstab

vit d				Group		Total
				Case	Control	
< 10	sunlight	Yes	Count	7	1	8
			% within Group	58.3%	100.0%	61.5%
		No	Count	5	0	5
			% within Group	41.7%	.0%	38.5%
	Total		Count	12	1	13
			% within Group	100.0%	100.0%	100.0%
10 - 30	sunlight	Yes	Count	13	12	25
			% within Group	72.2%	100.0%	83.3%
		No	Count	5	0	5
			% within Group	27.8%	.0%	16.7%
	Total		Count	18	12	30
			% within Group	100.0%	100.0%	100.0%
30 - 100	sunlight	Yes	Count	2	19	21
			% within Group	100.0%	100.0%	100.0%
	Total		Count	2	19	21
			% within Group	100.0%	100.0%	100.0%

P=0.046

Poor sunlight exposure was found to be statistically significant when compared between cases and controls in both deficient and insufficient group.

DENTAL CHANGES VS. VITAMIN D

Crosstab

vit d				Group		Total
				Case	Control	
< 10	den	Yes	Count	8	0	8
			% within Group	66.7%	.0%	61.5%
		No	Count	4	1	5
			% within Group	33.3%	100.0%	38.5%
	Total		Count	12	1	13
			% within Group	100.0%	100.0%	100.0%
10 - 30	den	Yes	Count	7	0	7
			% within Group	38.9%	.0%	23.3%
		No	Count	11	12	23
			% within Group	61.1%	100.0%	76.7%
	Total		Count	18	12	30
			% within Group	100.0%	100.0%	100.0%
30 - 100	den	Yes	Count	2	0	2
			% within Group	100.0%	.0%	9.5%
		No	Count	0	19	19
			% within Group	.0%	100.0%	90.5%
	Total		Count	2	19	21
			% within Group	100.0%	100.0%	100.0%

P=0.02

Dental changes of Vitamin D deficiency was found to be statistically significant in the case group when compared to controls in both deficient and insufficient group.

NUTRITIONAL STATUS VS. VITAMIN D

Crosstab

vit d				Group		Total
				Case	Control	
< 10	was	Yes	Count	12	0	12
			% within Group	100.0%	.0%	92.3%
		No	Count	0	1	1
			% within Group	.0%	100.0%	7.7%
	Total		Count	12	1	13
			% within Group	100.0%	100.0%	100.0%
10 - 30	was	Yes	Count	13	0	13
			% within Group	72.2%	.0%	43.3%
		No	Count	5	12	17
			% within Group	27.8%	100.0%	56.7%
	Total		Count	18	12	30
			% within Group	100.0%	100.0%	100.0%
30 - 100	was	Yes	Count	1	0	1
			% within Group	50.0%	.0%	4.8%
		No	Count	1	19	20
			% within Group	50.0%	100.0%	95.2%
	Total		Count	2	19	21
			% within Group	100.0%	100.0%	100.0%

P=0.000

Poor nutritional status was found to be statistically significant when compared between cases and controls in both deficient and insufficient group to cause decreased vitamin D levels.

TYPE OF CEREBRAL PALSY VS. VITAMIN D

Crosstab

vit d				Group: Case	Group: Control	Total
< 10	type of cp	Hemi	Count	2	0	2
			% within Group	16.7%	.0%	15.4%
		Quard	Count	10	0	10
			% within Group	83.3%	.0%	76.9%
		Nil	Count	0	1	1
			% within Group	.0%	100.0%	7.7%
	Total		Count	12	1	13
			% within Group	100.0%	100.0%	100.0%
10 - 30	type of cp	Hemi	Count	3	0	3
			% within Group	16.7%	.0%	10.0%
		Quard	Count	8	0	8
			% within Group	44.4%	.0%	26.7%
		Diple	Count	4	0	4
			% within Group	22.2%	.0%	13.3%
		Dysk	Count	3	0	3
			% within Group	16.7%	.0%	10.0%
		Nil	Count	0	12	12
			% within Group	.0%	100.0%	40.0%
	Total		Count	18	12	30
			% within Group	100.0%	100.0%	100.0%
30 - 100	type of cp	Quard	Count	1	0	1
			% within Group	50.0%	.0%	4.8%
		Dysk	Count	1	0	1
			% within Group	50.0%	.0%	4.8%
		Nil	Count	0	19	19
			% within Group	.0%	100.0%	90.5%
	Total		Count	2	19	21
			% within Group	100.0%	100.0%	100.0%

P=0.002

Similarly when type of cerebral palsy was analyzed between cases and controls it was seen to be highly significant in both the deficient and the insufficient group.

FUNCTIONAL GRADE VS. VITAMIN D

Crosstab

vit d				Group		Total
				Case	Control	
< 10	ft grade	0	Count	0	1	1
			% within Group	.0%	100.0%	7.7%
		Grade Ⅲ	Count	2	0	2
			% within Group	16.7%	.0%	15.4%
		Grade Ⅳ	Count	10	0	10
			% within Group	83.3%	.0%	76.9%
	Total		Count	12	1	13
			% within Group	100.0%	100.0%	100.0%
10 - 30	ft grade	0	Count	0	12	12
			% within Group	.0%	100.0%	40.0%
		Grade Ⅱ	Count	1	0	1
			% within Group	5.6%	.0%	3.3%
		Grade Ⅲ	Count	9	0	9
			% within Group	50.0%	.0%	30.0%
		Grade Ⅳ	Count	8	0	8
			% within Group	44.4%	.0%	26.7%
	Total		Count	18	12	30
			% within Group	100.0%	100.0%	100.0%
30 - 100	ft grade	0	Count	0	19	19
			% within Group	.0%	100.0%	90.5%
		Grade Ⅱ	Count	1	0	1
			% within Group	50.0%	.0%	4.8%
		Grade Ⅳ	Count	1	0	1
			% within Group	50.0%	.0%	4.8%
	Total		Count	2	19	21
			% within Group	100.0%	100.0%	100.0%

P=0.002

When functional grades were compared between cases and controls it was found to be highly statistically significant in both deficiency and insufficiency groups to cause decreased vitamin D levels.

ANALYSIS OF LABORATORY DATA

The mean values of various biochemical parameters are

	VITAMIN D	CALCIUM	PHOSPHORUS	ALKALINE PHOSPHATASE
CASE	**17.98**	**8.21**	**3.54**	**431.3**
CONTROLS	**33.13**	**9.32**	**4.14**	**289.44**

Laboratory data were analysed quantitatively. Calcium, phosphorus, alkaline phosphatase and vitamin D values were compared between cases and controls.

The mean calcium and phosphorous levels among cases were 8.2 and 3.5, while controls showed a mean value of 9.3 and 4.1 respectively. Mean alkaline phosphatase levels among cases were 431, and that of controls was 289.

Mean Vitamin D levels among cases was 17.98 ng/ml while that of controls were 33.13ng/ml.

VITAMIN D DEFICIENCY (<10 ng/ml)VS. LABORATORY DATA

Group Statistics

	Group	N	Mean	Std. Deviation	Std. Error Mean
cal	Case	12	7.542	.6127	.1769
	Control	1	8.800	.	.
phos	Case	12	3.167	.2570	.0742
	Control	1	3.800	.	.
alp	Case	12	533.58	101.522	29.307
	Control	1	680.00	.	.

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
cal	Equal variances assumed	.	.	-1.973	11	.074	-1.2583	.6377	-2.6619	.1452
	Equal variances not assumed			.	.	.	-1.2583	.	.	.
phos	Equal variances assumed	.	.	-2.367	11	.037	-.6333	.2675	-1.2221	-.0445
	Equal variances not assumed			.	.	.	-.6333	.	.	.
alp	Equal variances assumed	.	.	-1.386	11	.193	-146.417	105.668	-378.990	86.157
	Equal variances not assumed			.	.	.	-146.417	.	.	.

Significant p value was found for phosphorous (p = 0.037) when the quantitative lab data was analyzed by T test co relating vitamin D deficiency with laboratory data in cases and controls.

VITAMIN D INSUFFICIENCY (10 – 30 ng/ml) VS. LABORATORY DATA

Group Statistics

	Group	N	Mean	Std. Deviation	Std. Error Mean
cal	Case	18	8.606	.6830	.1610
	Control	12	9.067	.4619	.1333
phos	Case	18	3.739	.5326	.1255
	Control	12	3.850	.2111	.0609
alp	Case	18	373.28	135.022	31.825
	Control	12	409.50	83.632	24.142

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
cal	Equal variances assumed	1.875	.182	-2.042	28	.051	-.4611	.2258	-.9236	.0014
	Equal variances not assumed			-2.206	27.977	.036	-.4611	.2090	-.8893	-.0329
phos	Equal variances assumed	9.458	.005	-.684	28	.499	-.1111	.1623	-.4436	.2214
	Equal variances not assumed			-.796	23.902	.434	-.1111	.1395	-.3992	.1770
alp	Equal variances assumed	.995	.327	-.827	28	.415	-36.222	43.806	-125.955	53.510
	Equal variances not assumed			-.907	27.911	.372	-36.222	39.946	-118.060	45.615

Significant p value was found for calcium (p = 0.036) when the quantitative data was analyzed by T test co relating vitamin D insufficiency (10 – 30 ng/ml) with quantitative laboratory data in cases and controls.

DISCUSSION

Vitamin D deficiency is a common association in children with Cerebral Palsy due to known reasons like poor sunlight exposure, non-ambulatory nature, anticonvulsant use and feeding difficulties. Though the association is existent and well described in literature, the epidemiological data available regarding the same is less. This made us to do this study to highlight the proportion of children with cerebral palsy who have Vitamin D deficiency and to compare them with normal controls to find statistical significance and also to identify the possible risk factors causing it to enable early identification, periodic monitoring and supplementation with calcium and vitamin D to prevent the development of fractures and deformities.

In this study, we have tried to correlate the vitamin D status in children with cerebral palsy in relation to the nutritional status, anticonvulsant use, feeding difficulty, poor sunlight exposure, and type of CP and functional grade of CP which have been implicated as possible causes for vitamin D deficiency in these children.

VITAMIN D AND CP

It is a popular belief that rickets and vitamin D deficiency are not common in India, a tropical country, because of abundant sunlight exposure. But there is now increasing evidence that this statement is not correct. Vitamin D deficiency has been well documented among all age groups like neonates, toddlers, school children, pregnant women, and adult males and females residing in rural and urban India.

There are studies from both north and south India. (76, 66, 67) These studies clearly state the fact that approximately 75 to 85% of the groups studied have varying degrees of vitamin D deficiency or insufficiency (hypovitaminosis D). One more important data drawn out in these studies is the fact that dietary intake of vitamin D, nutrition and amount of sunlight exposure has a great impact on the vitamin D levels in the population. One of the studies has shown a big impact on dietary calcium supplementation to a group of children (67).

The usage of different cut off points for vitamin D levels for insufficiency and deficiency by various authors has made it difficult to compare the results of published research by different authors and has complicated comparisons between different communities and populations. Also the latitude, solar zenith angle, uv radiation, amount of

cloud cover, time duration of exposure to sunlight, body surface area exposed to sunlight is different among different parts of the world and also different in various areas of our own country and therefore comparisons between the different groups are not possible.

In our study, the prevalence of decreased vitamin D in cases was 93.8 %. Whereas in our control population the prevalence of decreased vitamin D was 40.6%. The prevalence of vitamin D deficiency in study group was 37.5% and insufficiency was 56.3%. In the control group, vitamin D deficiency amounted to 3.1%, while insufficiency amounted to 37.5%. In both populations, insufficiency was found to be commoner than deficiency. There is a significant association between low vitamin D in CP children when compared to normal population.

The prevalence of decreased vitamin D in our cases was 93.8 % which was statistically significant, while in the control group, decreased vitamin D levels amounted to 40.6%. This increased prevalence of decreased vitamin D levels in CP children is statistically significant and this is not an incidental occurrence but due to the multiple reasons like feeding and swallowing issues resulting in poor nutrition, lack of adequate intake of calcium rich food, lack of exposure to sunlight and

added burden due to anti-epileptic medications whose analysis will follow.

None of the controls showed any clinical signs of Vitamin D deficiency but alteration in serum calcium and alkaline phosphatase were noted in some children.

The prevalence of vitamin D deficiency in CP children by Hendersen et al had a prevalence of deficiency of 19% while our study has a deficiency of 37.5%. Though the prevalence of vitamin D deficiency/insufficiency in normal population varied between 10% to 70% in various studies, it was 40.6% in our normal controls (75).

There have been no Indian studies to compare vitamin D levels and risk factor analysis in CP children and therefore mean vitamin D values cannot be compared with Indian population. Harinarayanan et al conducted a study about vitamin D status in general population in Tirupathi (66). As it is nearby our place of study and also enjoys the same amount of sunshine and cloud cover as our study place, the values of vitamin D and result analysis would be meaningful if compared with our population. The mean vitamin D levels of urban males in the above mentioned study 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 our study, we have mean Vitamin D levels of 17.98 ng/ml. In our control population, we get a mean vitamin D value of 33.13 ng/ml.

In a study by Marwaha et al 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. While all studies uniformly report higher prevalence of vitamin D deficiency in higher socio economic, urban and white collared population, this study gives a 42.3% prevalence of 25 (OH)D deficiency in lower socioeconomic group when compared to higher socioeconomic group which had a 27% prevalence (68). In our study, the control population had a 3.1% and 37.5% prevalence of deficiency and insufficiency. This is one study which used the cut off value for deficiency as <10 ng/ml as in our study while other studies have used higher cut off of 20 ng/ml to define deficient state. In our study, the mean vitamin D levels among case group was 17.98 while that of the control group was 33.13 ng/ml.

In a study by Balalala et al, who studied maternal, cord and infant blood sample vitamin D, the mean vitamin D levels was 22.99, 19.36, 18.19 ng/ml respectively (72). The vitamin D levels of blood of infants was 18.19ng/ml. Our study population does not comprise infants.

In the United States, a study done by Kumar et al over four years in a large group of 6000 children reports that 9% of children were deficient and 61% were insufficient (73). Our study has a deficiency prevalence of 3.1% and insufficiency prevalence of 37.5%. This study gives comparable results as the population as it was a large group and uniformly distributed to negate weather factors influencing vitamin D levels.

Usage of either 15 ng/ml or 20 ng/ml in these reference studies as cut off values for vitamin D deficiency increases the number of children in the deficiency group in the above studies. Standard value for cut off for vitamin D levels is 10 ng/ml(77). Though different researchers have indicated the need for raising the cut off to 15 or 20 ng/ml, as the parathormone level starts increasing with these levels of 25 OH vitamin D, and is being used as cut off in US and other countries, there has been no recommendation to change the cut off value in India as of now. So we have conducted our study with cut off value for 25 OH vitamin D deficiency as 10 ng/ml.

USAGE OF ANTIEPILEPTICS & SEIZURES VS VITAMIN D

In a population based study (15), 38% of children with CP had epilepsy but in our study 75 % had seizures. Our hospital being a tertiary

care centre, we had a higher prevalence of seizure disorder in CP in our study due to higher referral rates for refractory seizures.

In our study, majority 24 (75%) of them were on anticonvulsants and the commonly used anticonvulsant was valproate constituting 68.5% of the total. 43.75% children were on phenytoin and 46.85% children were on phenobarbitone.

But alteration of vitamin D status due to individual AEDs could not be analyzed as most patients were on polytherapy and co relation with vitamin D deficiency could not be obtained.

DURATION OF AED VS. VITAMIN D

The duration of AED intake has been found to be statistically significant in altering vitamin D levels. Longer the duration of intake, higher is the alteration. This has also been found to be the same as in earlier studies, which show alteration to low values and also decreased BMD with, chronic anti convulsant usage. (47, 48).

Reports of altered calcium, vitamin D, and bone metabolism associated with anticonvulsant medication use are numerous. Biochemical abnormalities have included decreased serum calcium, 25-hydroxycholecalciferol (calcidiol), and phosphorus, and elevated alkaline

phosphatase (AP) **(**41, 78), although other investigators have found no association between anticonvulsant use and one or more of these variables (79, 80). In our study, Vitamin D deficiency has been significantly associated with low serum phosphorous levels. Probably the stage of vitamin D disease, though deficient, is in a compensated state due to increased parathormone levels or probably performing ionic calcium studies would reflect low calcium levels better.

FEEDING DIFFICULTY VS. VITAMIN D

Children with cerebral palsy consume less dietary energy than unaffected children. A high proportion of children with cerebral palsy (CP) are growth retarded and underweight (81). Under nutrition has been documented in 29% to 46% of children with cerebral palsy (82, 83) while in our study 26 (81.3%) were undernourished. Wasting was statistically significant in our data and it contributed to vitamin D deficiency.

Feeding problems occur frequently in children with cerebral palsy (11, 83). Inability to suck, problems associated with breast-feeding, difficulty in the introduction of solid foods, problems with drinking liquids, inability in biting or chewing solids, and coughing and choking during meals were usual parental complaints in our study.

Feeding difficulties were observed in 81.3% of children in our study and it was statistically significant when compared with vitamin D status. The commonest difficulty encountered is the prolonged feeding time due to difficulty in swallowing, tongue thrusting, and aspirations. Children with cerebral palsy take two to twelve times longer to swallow mashed food and up to fifteen times longer to chew and swallow solids compared with normal children. Longer mealtimes may not compensate for their feeding difficulty (57). In one report, 28% of parents required more than 3 hours daily to feed their child and 3% required more than 6 hours daily (84).

Minerals like Iron, selenium, zinc, essential fatty acids, and vitamins C, D, and E were found to be deficient in 15% to 50% of these populations (64, 85, and 86).

FRACTURES & DENTAL CHANGES VS VITAMIN D

Osteopenia is prevalent in neurologically impaired children (64). Inadequate supply of critical nutrients for bone formation adds to the negative impact of immobility, lack of weight-bearing and use of anti-convulsants on bone health, and may also cause reduced muscle strength. In our study, fractures were seen in only 3 (9.4%) of the children and this was not statistically significant with Vitamin D status.

Quadriplegics are mostly associated with fractures and all the three children who had fractures were quadriplegics. An increased amount of long-bone fractures has been seen in children and adolescents with quadriplegic cerebral palsy in residential setup and conclusion was given that vitamin D deficiency was the major point contributing to the occurrence of fractures in the population studied. (87)

At the same time dental changes were seen in 53.1% which was statistically significant when compared to vitamin D levels.

TYPE OF CEREBRAL PALSY VS. VITAMIN D

In our study, spastic quadriparesis constituted the most common type of CP seen in 59.37%, spastic diplegia in 12.5%, hempiplegia in 15.62% and dyskinetic 12.5% each. There were a significant statistical association between the type of CP and the vitamin D status.

Ünay B et al (88) in their analysis have demonstrated that BMD of the children with CP was very low when compared to the normal children, and that quadriplegic CP type were more prone to have low bone mineralization than hemiplegic patients.

SUNLIGHT EXPOSURE & FUNCTIONAL GRADE VS VITAMIN D

In our study, poor sunlight exposure was seen in 68.75 % of the CP children and there was a significant association between poor sunlight exposure and the presence of Vitamin D deficiency / insufficiency which have been well supported in literature as mentioned earlier.

In our study, 2 (6.3%) belonged to functional grade 2, 11(34.4%) belonged to functional grade 3 and 19 (59.4%) belonged to functional grade 4. There was a significant correlation between non ambulation and osteopenia in children with CP as in other studies (78, 89).

The major reason for the poor sunlight exposure was their non ambulant nature as functional grade IV was observed in 59.3%. Bischof et al in their study have stressed unless sunlight exposure is guaranteed, vitamin D supplementation should be considered in children especially if they are on AED (87).

However, more studies with a larger sample size on the Vitamin D status on various pediatric age groups and comparison studies with high risk population such as cerebral palsy are necessary before any concrete conclusions can be made as most of the studies published have

highlighted the same. All the variables have to be studied prospectively and logistically to get a stronger recommendable conclusion.

ANALYSIS OF LABORATORY DATA

In our study of 32 CP children, 24(75%) of children had low calcium, 12 (37.5%) had low phosphorus and the rest were normal. Serum Alkaline phosphatase (SAP) was normal in 16 (50%) of children while the levels were elevated in 46.8% of CP children. When comparing this with control population, Phosphorus and calcium were statistically significant in deficiency and insufficiency group respectively.

Hals et al. found vitamin D deficiency (25-OH-vitaminD_3 < 25 nmol/L) in three out of 13 disabled patients, despite regular vitamin supplementation (85) which accounts to 23%. The percentage of children with Vitamin D deficiency was found to be 14.4% and Vitamin D insufficiency was 4.8%. The overall abnormalities in Vitamin D status was found in 19.2%.

VITAMIN D SUPPLEMENTATION

Fisher in 1988 have recommended 4000 IU/m2/day of vitamin D for children with CP and Lee recommended 1000 IU/day. Jekovec-Vrhovšek in 2000 (90) have studied the baseline BMD in children with

CP and compared the bone density after 9 months of administering 0.25mcg /day of calcitriol and 500mg/day of calcium and have found significant increase in the BMD after treatment. Though American academy of Pediatrics in their clinical report (17) have recommended higher dose of Vitamin D in those at risk, no clear consensus have been made regarding the exact dosage regimen for children with CP.

LIMITATIONS

Ideally the vitamin D levels should have been compared with parathormone levels to give the study a fulfillment but due to cost constraints the same could not be done. We wish a larger prospective case control study will bring out much more details to form some kind of recommendations

The other limitation was not performing bone mineral density in our study subjects as this would have made the study throw a light on the bone mineral density status in children with cerebral palsy as no literature on the same is available in Indian children. The reasons for not performing bone mineral density was the difficulty to perform the test in these patients technically, non availability of reference standards in Indian children to compare the results, difficulty in getting matched

controls as healthy subjects could not be compared with children with CP and the cost involved in performing the test.

Vitamin D deficiency being a preventable condition, a proactive approach is needed to target these potential risk factors to suspect and thereby treat whenever required. Regular nutritional assessment is necessary to identify malnourished children. Gastrostomy tube placement should be considered early in their nutritional rehabilitation programme. Parental education regarding the need for adequate sunlight exposure should also be stressed. Vitamin D and calcium supplementation should be considered in those at risk. As the prevalence of vitamin D deficiency is reported to be high in otherwise healthy subjects, further studies are required to have clear consensus regarding prophylactic calcium and vitamin D supplements, their dosage and duration of the treatment in high risk groups like cerebral palsy.

CONCLUSION

The prevalence of vitamin D deficiency in children with CP was found to be 37.5% while insufficiency amounted to 56.3% and a total alteration in vitamin D status in CP children was 93.8%. The prevalence of vitamin D deficiency in age and sex matched controls was found to be 3.13% while insufficiency amounted to 37.5% and a total alteration in vitamin D status was 40.63%. The presence of feeding difficulties, poor sunlight exposure, poor nutritional status, and the use of antiepileptic drugs, type of CP and the functional grade of CP had statistically significant association with Vitamin D deficiency in these children. Periodic monitoring, early identification and appropriate calcium and vitamin D supplements may prevent complications like fractures, etc. Hypovitaminosis D is very common and represents latent stage of vitamin D deficiency. Appropriate treatment with vitamin D supplements and calcium is necessary for treatment of vitamin deficiency and replenishment of stores.

age	sex 1=m 2=f	delivery 1=nor 2=em 3 =el	gest 1= pre 2= term 3= post	ba 1=y 2=n
5	2	1	2	1
1	2	3	2	1
4	1	1	1	1
1	1	1	1	2
4	2	1	1	2
5	1	2	2	1
1	2	2	2	1
10	1	1	2	1
6	2	1	2	2
2	2	1	2	2
3	2	1	2	2
2	1	1	2	2
11	1	1	2	2
7	1	1	2	2
8	1	1	1	2
3	1	1	2	2
12	1	2	2	2
9	2	1	2	2
10	1	2	2	1
6	2	1	2	2
9	1	2	2	1
7	2	2	2	1
3	2	2	2	1
8	2	1	2	2
2	1	2	2	2
12	2	1	2	2
7	1	1	1	2
1	1	2	2	2
11	2	1	2	2
4	1	1	2	2
10	1	2	2	1
5	2	2	2	2

bw1=<2.5 2=>2.5	n.seizures1=y 2=n	bf 1=y 2=n	d delay 1=y 2	epilptic 1=	aed 1=y 2=	aed years
1	1	1	1	2	2	0
2	1	1	1	2	2	0
1	2	2	1	1	1	3
1	2	1	1	2	2	0
1	2	1	1	1	1	3
2	1	1	1	1	1	3
2	2	1	1	1	1	0.1
2	2	1	1	1	1	4
2	2	1	1	1	1	3
2	2	1	1	1	1	2
2	2	1	1	1	1	3
2	2	1	1	1	1	2
2	2	1	1	1	1	10
2	2	1	1	1	1	6
1	2	1	1	1	1	3
2	2	1	1	2	2	0
2	2	1	1	1	1	7
2	2	1	1	1	1	5
2	1	1	1	1	1	10
2	2	1	1	2	2	0
2	2	1	1	1	1	7
2	1	1	1	1	1	6
2	2	1	1	1	1	2
2	2	1	1	1	1	5
2	2	1	1	2	2	0
2	2	1	1	1	1	8
2	2	1	1	2	2	0
2	2	1	1	1	1	0.7
2	2	2	1	1	1	7
2	2	1	1	2	2	0
2	1	1	1	1	1	9
2	2	1	1	1	1	4

fd 1=y 2=n	cons 1=y 2=	sunlight 1=	den 1=y 2=n	frac 1=y 2=n	mic y=1 n=2	was y=1 n=2	calc1=<7 2=7
2	2	1	2	2	1	1	2
2	2	1	1	2	1	2	3
2	1	1	1	2	1	1	2
1	2	1	2	2	2	2	2
2	2	1	1	2	1	2	3
1	1	2	1	1	1	1	2
1	1	2	2	2	1	1	3
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1	2	2	2	2	1	1	2
1	2	2	1	2	1	1	2
1	2	2	1	2	1	1	2
1	1	2	1	2	1	1	1
1	2	1	1	2	1	1	2
1	2	1	1	2	1	1	3
1	2	1	2	2	1	1	3
1	2	1	2	2	1	1	2
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2	2	1	2	2	1	2	2
2	2	1	2	2	2	1	3
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1	2	1	2	2	1	1	2
1	1	1	1	2	1	1	2
1	2	1	2	2	2	1	2
1	1	1	1	2	1	1	2
1	1	2	1	1	1	1	2

phos1=<3.5, 2	alp 1=<150 2=	vit d 1=<10 2=10-30 3=30-100 4=:	calcium	phosphoru
2	2	2	8.2	3.5
2	2	3	9.2	4
1	3	1	8	3.2
2	2	2	9	3.5
2	2	2	9	3.5
1	3	1	7	3.4
2	2	2	9	4.5
2	2	2	9	4.5
1	3	1	7.6	3.2
2	2	2	8.8	4.5
2	3	1	8.6	3.4
1	3	2	7.5	3.2
1	3	1	6.8	2.5
2	3	1	7.4	3.5
2	2	2	9.6	4.5
2	2	2	9.4	4.5
1	3	1	7	3.2
1	3	2	7.4	2.8
1	3	1	7	3
2	2	2	8.6	3.5
2	2	2	9	3.5
1	3	1	8.5	3.2
1	3	1	7.8	3
2	1	2	8.8	3.5
2	2	2	9	3.5
1	3	2	7.2	3.2
2	2	2	9	3.5
2	3	1	7.8	3.2
1	2	1	7	3.2
2	2	2	8.2	3.8
2	3	3	8.4	4
2	2	2	8.2	3.8

alp	vit d	no of aed	eptoin 1=y	pheno 1=y	valp 1=y 2=	car y=1 n=2	top y=1 n=	lamo 1=y 2	nil 1=y 2=n
300	28.82	0	2	2	2	2	2	2	1
300	34.52	0	2	2	2	2	2	2	1
450	9.88	2	1	2	1	2	2	2	2
350	15.4	0	2	2	2	2	2	2	2
400	13.3	1	1	2	2	2	2	2	2
500	9.63	2	2	2	1	2	2	1	2
250	24	2	1	2	1	2	2	2	2
360	29.9	1	2	2	1	2	2	2	2
480	6.21	1	2	1	2	2	2	2	2
250	10.2	2	2	1	1	2	2	2	2
450	7.86	2	2	1	1	2	2	2	2
500	24.1	1	2	1	2	2	2	2	2
800	3.9	3	1	1	1	2	2	2	2
485	7.8	3	1	1	1	2	2	2	2
250	29.3	1	2	2	1	2	2	2	2
280	25.2	0	2	2	2	2	2	2	1
480	9.9	3	1	1	1	2	2	2	2
800	28.6	4	1	1	1	2	2	2	2
600	8	4	2	2	1	2	2	1	2
284	21.44	0	2	2	2	2	2	2	1
340	23.42	1	2	2	1	2	2	2	2
478	8.66	3	1	1	1	2	2	2	2
480	6.62	3	1	1	1	2	2	2	2
380	28.6	1	1	2	2	2	2	2	2
300	28	0	2	2	2	2	2	2	1
560	10	3	1	1	1	2	2	2	2
350	23.4	0	2	2	2	2	2	2	1
600	6.88	3	1	1	1	2	2	2	2
600	6.28	3	1	1	1	2	2	2	2
400	24.2	0	2	2	2	2	2	2	1
380	34.8	3	1	1	1	2	2	2	2
365	26.8	2	2	1	1	2	2	2	1

duration	1	type of cp	l ft grade
	4	2	4
	4	5	2
	3	1	3
	4	3	3
	2	5	3
	3	2	4
	1	2	4
	3	5	3
	2	2	4
	1	2	4
	3	2	4
	2	2	4
	3	2	4
	3	2	4
	3	1	3
	4	2	4
	3	1	3
	3	2	4
	3	2	4
	4	3	2
	3	1	3
	3	2	4
	2	2	4
	3	1	3
	4	3	3
	3	2	4
	4	5	3
	1	2	4
	3	2	4
	4	3	3
	2	2	4
	1	2	4

age	sex 1=m 2=f	delivery 1=nor 2=em 3 =el	gest pre=1 term=2 post=3	ba 1=y 2=n
5	2	1	2	2
1	2	1	2	2
4	1	1	2	2
1	1	2	2	2
4	2	3	2	2
5	1	1	2	2
1	2	2	2	2
10	1	3	2	2
6	2	1	2	2
2	2	2	2	2
3	2	3	2	2
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11	1	2	2	2
7	1	3	2	2
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7	1	1	2	2
1	1	2	2	2
11	2	3	2	2
4	1	1	2	2
10	1	2	2	2
5	2	3	2	2

bw1=<2.5 2=>2.5	n.seizures1=y 2=n	bf 1=y 2=n	d delay 1=y 2	epilptic 1=	aed 1=y 2=	aed years
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2	2	1	2	2	2	0

fd 1=y 2=n	cons 1=y 2=	sunlight 1=	den 1=y 2=n	frac 1=y 2=n	mic y=1 n=2	was y=1 n=2	calc1=<7 2=7
2	2	1	2	2	2	2	3
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2	2	1	2	2	2	2	3
2	2	1	2	2	2	2	2
2	2	1	2	2	2	2	3
2	2	1	2	2	2	2	2

phos1=<3.5, 2	alp 1=<150 2=150-400 3=>400	vit d 1=<10 2=10-30 3=30-100	cal	phos
2	2	3	9.6	4
2	2	3	9.2	3.8
2	2	3	9	4.5
2	2	3	9.4	4.2
2	3	1	8.8	3.8
2	2	2	9.2	4.2
2	2	3	9.2	4.5
2	2	3	9.2	4.8
2	2	2	8.6	3.8
2	2	3	9.4	4.8
2	2	3	9.6	4
2	3	2	8.4	3.8
2	2	2	9.2	3.6
2	3	2	8.8	3.8
2	2	2	9.6	4
2	2	3	10.2	5
2	2	3	10.4	4.8
2	2	3	9.6	4
2	2	2	9	3.6
2	2	3	9.6	4
2	2	3	9	3.6
2	2	3	9.4	4.6
2	2	3	9.2	4.5
2	3	2	8.8	3.6
2	2	3	9.8	4.2
2	2	2	9.8	3.8
2	2	3	9.4	4.2
2	2	3	9.2	4
2	2	3	10.4	5
2	3	2	8.8	3.8
2	2	2	9.8	4.2
2	3	2	8.8	4

alp	vit d	no of aed	phe 1=y 2=r	pheno 1=y 2	valp 1=y 2=r	car1=y 2=n	top 1=y 2=n	lamo 1=y 2=
160	41.66	0	2	2	2	2	2	2
160	54.52	0	2	2	2	2	2	2
168	31.8	0	2	2	2	2	2	2
188	38	0	2	2	2	2	2	2
680	9.37	0	2	2	2	2	2	2
388	19.3	0	2	2	2	2	2	2
182	36.88	0	2	2	2	2	2	2
220	34.6	0	2	2	2	2	2	2
188	21.6	0	2	2	2	2	2	2
150	55.8	0	2	2	2	2	2	2
168	30.6	0	2	2	2	2	2	2
500	25.3	0	2	2	2	2	2	2
392	19.8	0	2	2	2	2	2	2
480	23.4	0	2	2	2	2	2	2
400	26.1	0	2	2	2	2	2	2
150	88.1	0	2	2	2	2	2	2
158	79.4	0	2	2	2	2	2	2
358	48.4	0	2	2	2	2	2	2
400	10.7	0	2	2	2	2	2	2
162	35.8	0	2	2	2	2	2	2
400	11	0	2	2	2	2	2	2
182	33.4	0	2	2	2	2	2	2
168	30.4	0	2	2	2	2	2	2
460	10.9	0	2	2	2	2	2	2
192	34.6	0	2	2	2	2	2	2
388	17.8	0	2	2	2	2	2	2
162	33.4	0	2	2	2	2	2	2
182	32.3	0	2	2	2	2	2	2
158	60.3	0	2	2	2	2	2	2
490	19.1	0	2	2	2	2	2	2
368	24.4	0	2	2	2	2	2	2
460	21.6	0	2	2	2	2	2	2

nil 1=y 2=n	duration	1= type of cp l	ft grade
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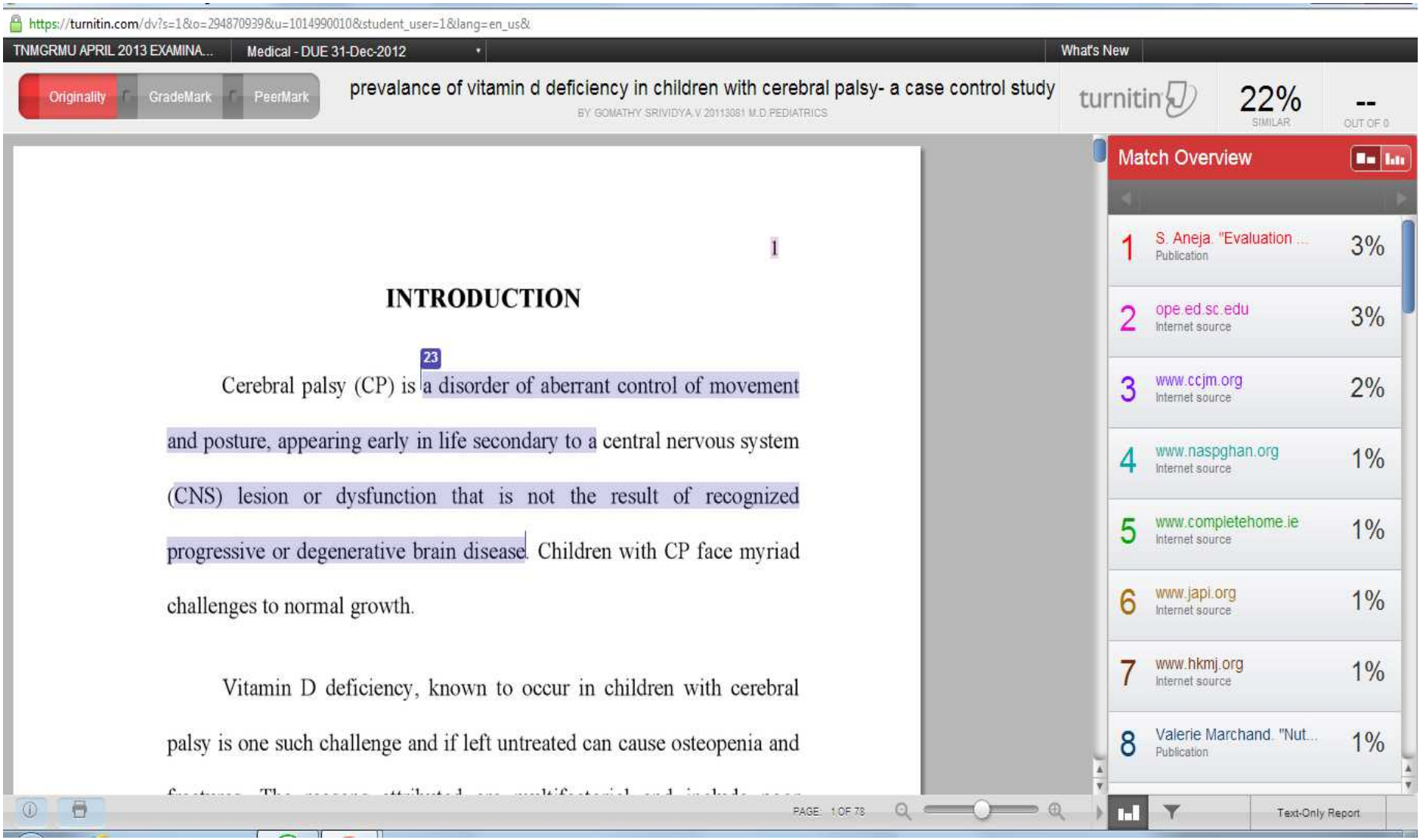
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INTRODUCTION
23
Cerebral palsy (CP) is a disorder of aberrant control of movement and posture, appearing early in life secondary to a central nervous system (CNS) lesion or dysfunction that is not the result of recognized progressive or degenerative brain disease. Children with CP face myriad challenges to normal growth.
Vitamin D deficiency, known to occur in children with cerebral palsy is one such challenge and if left untreated can cause osteopenia and
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