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Prevalence of Vitamin D Deficiency and its Association With Short Stature in Indian Children With Down Syndrome

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ABSTRACT

Objective: *To study the prevalence of Vitamin D deficiency by assessing 25(OH) Vitamin D levels in children with Down syndrome and to assess its effect on height, bone age and other related biochemical markers (calcium, phosphorus and alkaline phosphatase).*

Methods: *This was a prospective study in a tertiary care hospital in South India where consecutive children with Down syndrome between the ages of 5 months - 16 years seen over one year were included. The height, weight (and head circumference of children less than 3 years) were plotted on growth charts for Indian children (Indian Academy of Pediatrics) and for children with Down syndrome as described by Cronk.*

Results: *Fifty six children with Down syndrome were enrolled. Prevalence of 25(OH) vitamin D deficiency using a cut off value of 10 ng/ml was 26.8%. There was no significant effect of 25 (OH) Vitamin D deficiency on height (p = 0.26) and bone age (p = 0.3). The independent samples T test showed no difference in the values of serum calcium, phosphorus and alkaline phosphatase in children with 25 (OH) Vitamin D levels < 10ng/ml and >= 10ng/ml.*

Conclusion: *There was no significant effect of vitamin D deficiency on height, bone age and other associated biochemical markers in these children.*

KEYWORDS : – Down syndrome, Vitamin D, growth

INTRODUCTION

Down syndrome was described by John Langdon Down in 1866. It is the most frequent genetic cause of mild to moderate mental retardation and occurs in about 1 in 800 live births. In 1959 Lejeune, Gautier and Turpins determined that Down syndrome was caused by trisomy 21.[1]

Children with Down syndrome are shorter than their peers. Average height at most ages is around the 2nd centile for the general population. [2] For the majority, the cause of growth retardation is not known. Children with the syndrome are more prone to conditions like congenital heart disease, sleep related upper airway obstruction, celiac disease, thyroid hormone deficiency, deficiency of insulin like growth factor 1 and nutritional inadequacy caused by feeding problems which are associated with poor growth. [2, 3]

Adults with Down syndrome are prone for osteoporosis. [4] Vitamin D deficiency is known to result in both deficient growth and osteoporosis. There is little data on Vitamin D levels in children with Down syndrome and the effect it has on growth. Only one study so far has looked at the Vitamin D status in children with Down syndrome. This was done on a group of 21 children in Spain in 1992 and did not show deficiency of Vitamin D in any of these children.[5] No study so far has looked at the incidence of Vitamin D deficiency in children with Down syndrome in the Indian population and if this was associated with short stature or delayed bone age. This is important as Vitamin D deficiency is relatively easy to treat. Correction of Vitamin D deficiency may prevent osteoporosis in the adult Down syndrome as life expectancy of these individuals has increased.

There is no standard definition for Vitamin D deficiency in the Indian population. Pettifor in an editorial in *Indian Paediatrics* recommended a cutoff of 25(OH) Vitamin D value <10 ng/ml and this was used in our study.[6]

MATERIALS AND METHODS

The study design and protocol were approved by the institutional review board and ethics committee. The study was conducted over one year between October 2007 and September 2008 in the Department of Paediatrics, Christian Medical College, Vellore – a tertiary care medical center in South India. Sixty two consecutive children between the ages of 5 months - 16 years suspected to have Down syndrome were enrolled. Five children's parents were not willing to take part in the study and one child's cytogenetic analysis did not show Down syndrome. Thus a total of 56 children with cytogenetically confirmed Down syndrome participated in the study.

Informed consent was obtained from the parents. Measurements were taken by the primary investigator or trained nurses. Length was measured on the infantometer in those less than 2 years or those who could not stand. In older children the stadiometer was used to measure the height. Weight was checked on a calibrated sensitive electronic weighing scale to the closest 10 grams. The head circumference was measured using non stretchable tapes to the nearest millimeter taking the maximum occipitofrontal diameter.

Blood was collected for complete blood count, calcium, phosphorus, alkaline phosphatase, 25 (OH) Vitamin D levels (by automated chemiluminescent immunoassay) and karyotyping. X-ray of the left hand and wrist was done for bone age. This was compared to Gruelich and Pyle standards by a radiologist to determine if this was appropriate for age or more than one standard deviation away. Features of rickets were also looked for.

There are no standardized growth charts for Indian children with Down Syndrome. Hence, the height and weight were plotted on 2 growth charts – growth charts for Indian children as recommended by the Expert group of the Indian Academy of Pediatrics (IAP) [7] and growth charts for children with Down syndrome as described by Cronk. [8] Head circumference for children less than 3 years was plot-

ted on the IAP chart as the Cronk chart has no head circumference graphs. The data was analyzed by SPSS software version 15.

RESULTS

42 boys (75%) and 14 girls (25%) were included in the study. The mean age was 4.3 years with median of 2.9 years

Anthropometric measurements

The height and weight were plotted on both growth charts and the data is summarized in table 1. There was poor correlation between the two charts (kappa for height for age was -0.120 and for weight for age was 0.33). Sixty three percent of the children were less than the 3rd centile on the IAP height chart and 7% were less than the 5th centile on the Cronk Chart. Half of the children were less than the 3rd centile on the IAP weight chart and 18% were less than the 5th centile on the Cronk chart. Eighty six percent of the children less than 3 years had head circumference less than the third centile on the IAP chart. There was no statistical difference between the two sexes on comparison of the height and weight of the children either by the IAP or the Cronk chart.

Table 1. 25(OH) Vitamin D levels vs. height and weight as plotted on Indian Academy of Paediatrics and Cronk charts

		Height						Weight					
		<3rd centile		3rd – 50th centile		> 50th centile		<3rd centile		3rd – 50th centile		> 50th centile	
Growth Chart		IAP	Cronk*	IAP	Cronk*	IAP	Cronk*	IAP	Cronk*	IAP	Cronk*	IAP	Cronk*
25(OH) Vitamin D Level	<10 ng/mL (n=15)	9	0	5	10	1	5	7	1	5	9	3	5
	>=10 ng/mL (n= 41)	26	4	14	19	1	18	21	9	13	21	7	11

***Note: The categories in the Cronk charts are <5 centile, 5-50th centile and >50th centile**

25(OH) Vitamin D levels

The mean serum 25(OH) vitamin D level was 16 ng/ml (SD 8.76). Fifteen (26.8%) of the children had 25(OH) vitamin D level <10ng/ml with 73% of these being less than 3 years of age. There was no difference in Vitamin D levels between the two sexes (p=0.6).

There was no difference in the height (p=0.75) and weight (p=0.95) in the children who had Vitamin D levels less than 10 ng/mL and those who had higher when plotted on the IAP growth charts. Similarly there was no difference when plotted on the Cronk chart (p= 0.26 for height and 0.41 for weight) (Table 1).

Bone age and related biochemical markers

Data from 55 children was used as one child did not have the X-ray done. 15% of the children had bone age less than one standard deviation from appropriate bone age. There was no significant reduction in bone age in those with Vitamin D deficiency (p=0.3) (Table 2).

Table 2 also shows the calcium, phosphorus and alkaline phosphatase values for children with Vitamin D levels less than and equal to or more than 10 ng/mL. The independent samples T test was used to compare the values in the 2 groups. There was no statistical difference in the biochemical indices in the 2 groups. The significance (2 tailed) values for calcium was 0.837, phosphorus 0.166 and alkaline phosphatase 0.713. There was no significant difference in different age groups (sig 0.177).

Table 2. Comparison of serum calcium, phosphorus, alkaline phosphatase levels and bone age in children with Vitamin D levels < 10 ng/mL and >=10 ng/mL

	Vitamin D < 10 ng/mL	Vitamin D >= 10 ng/mL	p value
Calcium mg/dL (mean ±SD)	9.06 ± 0.34	9.03 ± 0.58	0.83
Phosphorus mg/dL (mean ± SD)	5.53 ± 0.67	5.21 ± 0.77	0.166
Alkaline Phosphatase U/L (mean ± SD)	186.87 ± 43.88	193.34 ± 62.31	0.713
Bone age			
< 1 SD	1	7	0.29
Normal	14	30	
> 1SD	0	3	

DISCUSSION

Vitamin D deficiency is associated with rickets and short stature in children. However Kremer has shown that Vitamin D levels have a positive correlation with height even in the absence of rickets in young women. [9] Our study was conducted to see if Vitamin D deficiency was one of the factors contributing to short stature in children with Down syndrome as this aspect has not been looked at before. Fifty- six consecutive children - 42 boys (75%), and 14 girls (25%) were included in the analysis. The sex of the child had no effect on the various parameters looked at in this study.

Anthropometry

Growth monitoring is a screening tool to diagnose nutritional, chronic systemic and endocrine disease at an early age. The height and weight of each child was plotted on the IAP growth charts and growth charts by Cronk for Children with Down syndrome. As expected, the height of 63% of the children and weight of 50% were below the third centile on the IAP growth chart. Indian children with Down syndrome appear to be smaller than their American counterparts with 59% below the 50th centile for height on the Cronk chart and 71% for weight.

25(OH) Vitamin D levels

Studies in India among children have used different levels ranging from <9 mg/ml to 20 mg/ml of Vitamin D to assess hypovitaminosis. [10, 11, 12] Hence the prevalence of Vitamin D deficiency ranged from 2% to 83%. Keeping this in mind, Pettifor recommended a cut off value of 10 ng/ml to define vitamin D deficiency.[6] In our study, 26.8% of children with Down syndrome had 25 (OH) Vitamin D levels below 10 ng/ml. The prevalence of low vitamin D levels was more in children less than 3 years (p0.051). This could be because of low exposure to sunlight in this age group.

Our study did not show significant difference in the height and weight when plotted on the IAP or Cronk chart when vitamin D levels were less than 10 ng / ml or more.

Del Arco et al in 1992 published their findings from 21 children with Down syndrome in Cantabria, Spain. The average values of the three Vitamin D metabolites were comparable to those of an age-matched group both in winter and summer. No child with Down syndrome showed values below the normal range, either in Vitamin D metabolites, or in the other parameters of calcium metabolism.[5] They did not correlate vitamin D levels with the growth of the children. They suggested that these children do not require Vitamin D when appropriate sunlight exposure is provided. Our study differed from theirs in that a quarter of the children had Vitamin D deficiency.

25(OH) Vitamin D levels with relation to bone age and biochemical markers

Bone age is the average age at which bones in children reach a level of maturity. It corresponds to the age of the child in normal children. There was no statistically significant difference in the bone age between the groups with 25(OH) vitamin D levels below and above 10 ng/ml (p= 0.3). There was one X-ray suspicious of rickets (X-ray reported as mild fraying of the distal ulnar and radial metaphyses – which could have been artefactual because of suboptimal positioning). This child's 25(OH) vitamin D level was 21.5 ng/ml, with normal serum calcium, phosphorus and alkaline phosphatase levels.

The limitation of our study was the lack of standardized growth charts for children with Down syndrome in the Indian population. There is lack of consensus on what level of 25(OH) vitamin D should be used as the cut off for vitamin D deficiency and hence we followed the guidelines stated by Pettifor.

CONCLUSION

The present study provides useful information regarding the Vitamin D levels in children with Down syndrome and its correlation with the height of children with Down syndrome. The prevalence of 25(OH) Vitamin D deficiency (level <10ng/ml) in children with Down syndrome was 26.8%. There was no significant association of 25(OH) Vitamin D deficiency in the height, weight, bone age and other related biochemical markers in these children.

Conflicts of interest: None

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