Original Article

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Effect of Routine Vitamin D Supplementation on the Physical Growth of Exclusively Breastfed Infants at Six Months of Age: An Observational Study

Paediatrics Section

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ABSTRACT

Introduction: Vitamin D is essential for bone mineral metabolism and for the growth and development of the skeleton. The American Academy of Paediatrics and the Indian Academy of Paediatrics recommend the administration of 400 IU per day of oral Vitamin D to all infants in the first year of life. The authors hypothesised that routine supplementation of 400 IU of Vitamin D to exclusively breastfed infants would result in better physical growth.

Aim: To examine the effect of routine vitamin D supplementation (400 IU/day) on the weight, length, and head circumference of term, exclusively breastfed infants at six months of age.

Materials and Methods: An observational study was conducted at Department of Paediatrics, Smt. Kashibai Navale Medical College, Pune, Maharashtra, India, from November 2018 to March 2020, comparing the weight, length, and head circumference at birth and at six months of age for 111 exclusively breastfed term, appropriate for gestational age, healthy infants who were not supplemented with oral Vitamin D (Group-I) with 111 infants who were supplemented with 400 IU of oral Vitamin D daily (Group-II). Infants who presented at the Paediatric Out-Patient Department of SKNMC, Pune at around six months of age were enrolled in the study. Birth data and anthropometry at birth were recorded from available medical records. Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) version 23.0. Quantitative data were presented with the mean and standard deviation. Comparison among the study groups was done using an unpaired t-test as per the results of the normality test. Association among the study groups was assessed with the help of a Student's t-test. A p-value of <0.001 was considered statistically significant.

Results: The mean birth weight, length, and head circumference of infants who were not supplemented with vitamin D (Group-I) were 2907.57±250.18 gm, 53.34±1.47 cm, 35.99±1.067 cm, respectively, and those who were supplemented (Group-II) were 2901.08±231.63 gm, 53.75±1.51 cm, and 35.85±1.09 cm, which were comparable in both groups. At six months, the mean weight, length, and head circumference in Group-I and Group-II were 7211.08±626.39 gm, 70.25±1.58 cm, 43.82±1.19 cm, and 7973.87±532.31 gm, 70.90±1.75 cm, and 45.01±1.34 cm, respectively. There was an increase in anthropometric parameters in both groups. The increase was greater in Group-II than in Group-I and was statistically significant (p<0.001).

Conclusion: Infants supplemented with vitamin D (400 IU/day) demonstrated better physical growth in terms of higher anthropometric values.

Keywords: Growth parameters, Infant growth, Newborn, Sunshine vitamin

INTRODUCTION

Despite India being a tropical country, there are numerous reports suggesting a high prevalence of Vitamin D Deficiency, especially in pregnant women and infants [1-3]. Infants born to Vitamin D-deficient mothers have been shown to have low birth weight and significantly lower growth in the first year of life [4,5]. It is well known that Vitamin D deficiency leads to stunting and growth failure, but whether supplementation of Vitamin D improves physical growth is controversial [6,7].

Vitamin D is critical for bone mineral metabolism and the growth and development of the skeleton [8,9]. Infancy is the most rapid period of skeletal growth and mineral accumulation, so the growth changes can be better appreciated. The American Academy of Paediatrics since 2008 and the Indian Academy of Paediatrics since 2017 have recommended routine administration of 400 IU per day of oral Vitamin D to all breastfed infants from the first few days of life until the end of the first year [10,11]. This recommendation was purely based on the high prevalence of Vitamin D deficiency and the higher incidence of rickets in infants.

Vitamin D affects growth by promoting adequate bone mineralisation and macronutrient metabolism through the regulation of the cell cycle and cell proliferation [12]. Few studies have reported better physical growth with Vitamin D supplementation in children with vitamin D deficiency, but weather routine supplementation has the same effect is not known [13,14].

The present study only included term, appropriate for gestational age, exclusively breastfed infants, thus making it a more homogeneous cohort. Physical growth during infancy depends on intrauterine nutrition and postnatal nutrition. By including only term and appropriate for gestational age infants, the effect of intrauterine nutritional factors affecting growth was minimised.

The aim of the present study was to determine the effect of routine oral Vitamin D supplementation of 400 IU/day on physical growth, specifically weight, height, and head circumference of exclusively breastfed term infants.

MATERIALS AND METHODS

An observational study was conducted at Department of Paediatrics, Smt. Kashibai Navale Medical College, Pune, Maharashtra, India from November 2018 to March 2020 after obtaining ethical clearance from the Institutional Ethical Clearance Committee (IEC No.-Institutional Ethical committee letter No- SKNMC/Ethics/app/2018/53 dated 5th October 2018) to compare growth parameters (weight, length,

and head circumference) of exclusively breastfed, term, healthy infants who were not supplemented with routine oral Vitamin D (Group-I) with exclusively breastfed, term, healthy infants who were being supplemented with 400 IU of oral Vitamin D daily (Group-II). Informed written consent from parents for their infants to participate in the study was obtained after providing them with detailed information.

Sample size calculation: It was performed using online software (Epitools). For the calculation, the study's power (1-beta) was set at 95%, and the confidence level was taken as 0.95. The assumed baseline of sufficient Vitamin D levels in the control group was 5% (as multiple studies have reported vitamin D deficiency in neonates from 90-96%); and the odds ratio was taken as 5 [15-17]. A total of 222 subjects (111 in each group) were included in the study.

Inclusion criteria: All exclusively breastfed, Infants who were born term and appropriate for gestational age and who did not receive oral supplementation for more than seven days in the last six months were included in Group-I. Term-born infants (born on or after 37 completed weeks) and appropriate for gestational age (Birth weight ≥2.5 kg) at around six months of age (5 months and 20 days to 6 months and 10 days) who were started on oral vitamin D supplementation in the first week of life and continued it (without a break for more than three days at a stretch) were included in the case group of the study (Group-II).

Exclusion criteria: Infants who were on exclusively formula feed or mixed (breastfeed and formula) feed, infants with significant perinatal history, infants with a history of hospitalisation for more than three days, or who had signs of rickets were excluded from the study.

Study Procedure

Infants who reported to the well-baby clinic or the OPD of study Institute of SKNMC, Pune at around six months of age were enrolled in the study. Birth data and anthropometry at birth were recorded from available medical records (Neonatal Discharge card, Immunisation card, or any other available medical record). Weight was measured to the nearest 10 grams using a calibrated electronic weighing machine (TM-5S Digital Baby Weighing Scale from Techocare). Length was measured to the nearest 0.5 cm using an infantometer (Acromedicare), and head circumference was measured to the nearest 0.5 cm by a non expansible measuring tape.

STATISTICAL ANALYSIS

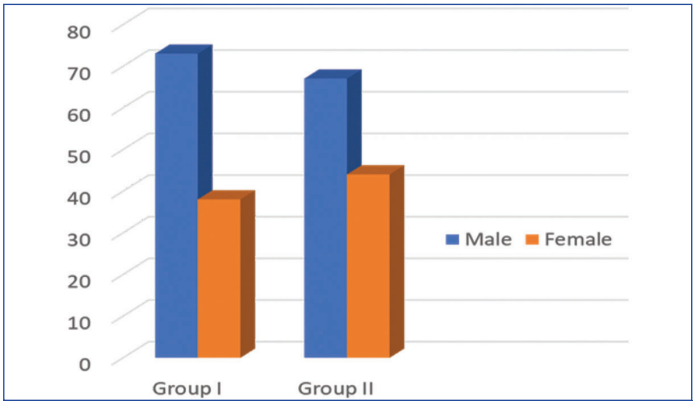
Quantitative data were presented using the mean and Standard Deviation (SD). Comparison among the study groups was performed using an unpaired t-test based on the results of the normality test. Association among the study groups was assessed using a Student's t-test, with a p-value of <0.001 being considered statistically significant.

RESULTS

Both groups were comparable in terms of variables such as maternal age, gestational age, number of pregnancies, and interpregnancy intervals [Table/Fig-1]. There were 73 male infants and 38 female infants in Group-I, compared to 67 male infants and 44 female infants in Group-II [Table/Fig-2].

Descriptive Statistics	Not supplemented with Vit D (Group-I)				Supplemented with Vit D (Group-II)				p-value
	Min	Max	Mean	SD	Min	Max	Mean	SD	
Maternal age (years)	22	35	29.15	3.34	22	35	29.14	3.40	0.984
Number of pregnancies	1	3	1.73	0.75	1	3	1.74	0.46	0.914
Interpregnancy interval (Weeks)	18	56	32.66	7.37	19	56	32.86	7.46	0.842
Gestational age (Weeks)	37	40	38.68	0.89	37	40	38.61	0.91	0.552

[Table/Fig-1]: Baseline characteristics.
(Test applied: Student's t test. p-value <0.001 is taken as significant)



[Table/Fig-2]: Distribution of gender.

The mean birth weight of infants who were not supplemented with vitamin D (Group-I) was 2907.57±250.18 grams, and those who were subsequently supplemented (Group-II) was 2901.08±231.63 grams, which was comparable in both groups (p=0.841). At six months, the mean weight in Group-I and Group-II was 7211.08±626.39 grams and 7973.87±532.31 grams, respectively, and the difference was statistically significant (p<0.001**).

The mean head circumference of infants who were not supplemented with Vitamin D (Group-I) was 35.99±1.067 cm, and those who were subsequently supplemented (Group-II) was 35.85±1.09 cm, which was comparable in both groups (p=0.325). At six months, the mean head circumference in Group-I and Group-II was 43.82±1.19 cm and 45.01±1.34 cm, respectively, and the difference was statistically significant (p<0.001**).

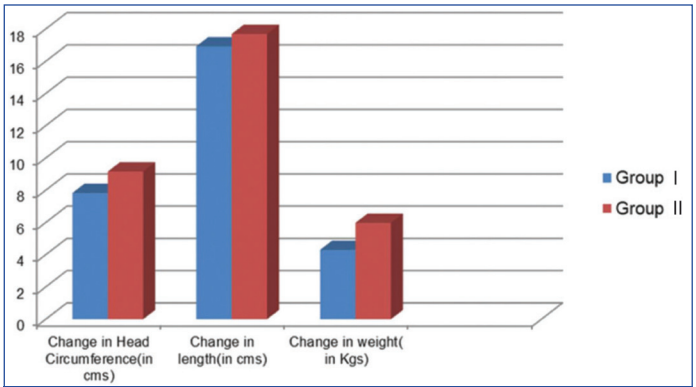
The mean length of infants who were not supplemented with Vitamin D (Group-I) was 53.34±1.47 cm, and those who were subsequently supplemented was 53.75±1.51 cm, which was comparable in both groups (p=0.469). At six months, the mean length in Group-I and Group-II was 70.25±1.58 cm and 70.90±1.75 cm, respectively, and the difference was statistically significant (p=0.004*) [Table/Fig-3].

There was an increase in anthropometric parameters in both groups. The increase was greater in Group-II than in Group-I. The

Parameters	IGroup-I (without supplementation)				Group-II (with supplementation)				p-value
	Min	Max	Mean	SD	Min	Max	Mean	SD	
Weight at birth (in grams)	2510	3570	2907.57	250.18	2510	3640	2901.08	231.63	0.841
Weight at 6 months (in grams)	6100	8820	7211.08	626.39	7010	9150	7973.87	532.31	<0.001**
Length at birth (in cm)	49.5	56.5	53.34	1.47	48.5	57.5	53.75	1.51	0.496
Length at 6 months (in cm)	64.5	73.5	70.25	1.58	65.5	74.5	70.90	1.75	0.004*
Head circumference at birth (in cm)	33.0	38.0	35.99	1.06	32.5	37.5	35.85	1.09	0.325
Head circumference at 6 months (in cm)	40.5	46	43.82	1.19	41.5	48.5	45.01	1.34	<0.001**

[Table/Fig-3]: Anthropometric parameters at birth and at six months of age.
(Test applied: student's t-test. p-value <0.001** is taken as statistically significant)

mean increase in weight was 4303.51±385.51 grams in Group-I compared to 5072.79±393.55 grams in Group-II. The mean increase in length was 16.92±1.14 cm and 17.69±1.49 cm, respectively, in Group-I and Group-II. The mean increase in head circumference from birth was 7.83±0.76 cm in Group-I and 9.16±0.92 cm in Group-II [Table/Fig-4].



[Table/Fig-4]: Comparison of change in anthropometry.

DISCUSSION

Vitamin D is an essential nutrient that plays a major role in skeletal health and bone mineralisation [18]. In addition to its role in bone health, Vitamin D appears to influence the hepatic secretion of Insulin-like Growth Factor-1 (IGF-1) and Insulin-like Growth Factor-Binding Protein-3 (IGFBP-3) and the expression of IGF-1 receptors in various tissues [19,20]. Thus, an optimal level of vitamin D can promote good health and better physical growth [21].

In a prospective randomised trial, Lin CH et al., found that infants who were supplemented with oral Vitamin D of 400 IU/day had a significantly larger weight and head circumference at four months of age than the placebo group (p=0.014 and 0.020, respectively); however, there was no significant difference in body length at four months of age (p=0.653) [22].

In a randomised control trial by Ganmaa D et al., on Vitamin D supplementation and growth in urban Mongol school children between 12-15 years of age, it was found that those who were supplemented with 800 IU/day of vitamin D had 0.9 (±0.3 SE) cm greater increases in height compared to placebo-treated children. However, there was no significant difference in weight and body mass index [23].

A recent Cochrane systematic review on the effects of oral vitamin D supplementation on linear growth of children under the age of five years concluded that compared to placebo or no intervention, vitamin D supplementation (200 to 2000 IU daily; or up to 300,000 IU bolus at enrollment) may result in little or no difference in linear growth (length/height in cm) among children less than five years of age {Mean Difference (MD) 0.66, 95% Confidence Interval (CI) -0.37 to 1.68} [24].

Mugunthan S et al., in their prospective randomised controlled trial to observe the effect of vitamin D supplementation in vitamin D deficient children between 2 to 5 years of age, found that those supplemented with 400 IU/day of vitamin D and calcium for nine months had a better weight and height standard compared to those who were given only calcium. The mean weight standard deviation in the group supplemented with vitamin D and calcium increased from 0.39±0.02 to 1.54±0.02 kg, compared to 0.42±0.01 to 0.84±0.01 kg in the group that received only calcium. Similarly, the mean height standard deviation in the group supplemented with Vitamin D and calcium increased from 0.37±0.03 to 0.72±0.01 cm, compared to 0.03±0.02 to 0.37±0.07 cm in the group supplemented with only calcium. The increase was statistically significant in the group that received vitamin D and calcium both (p<0.01) [25].

Trilok-Kumar G et al., in their randomised controlled trial on the effects of vitamin D supplementation in infancy on growth, bone parameters, body composition, and gross motor development at age 3-6 years in low birthweight infants, reported an increase in weight, length, and mid-arm circumference at six months in those who were supplemented with Vitamin D. However, these increases in parameters were no longer evident at 3-6 years. The likely explanation given by them is varying beneficial and adverse situations in the intervening years of the children's lives, resulting in a wash-out of differences between the groups. Furthermore, at later ages, a greater sample size is required than at earlier ages for evaluating identical differences in observed anthropometric units because anthropometric changes are less apparent at later ages [26].

Thamke R et al., in their randomised controlled trial on the effect of Vitamin D supplementation on anthropometric measures in exclusively breastfed infants, found better anthropometric parameters in those who were supplemented with routine vitamin D compared to placebo. A significant increase in weight and length was noted at 2.5, 3.5, 6, and 9 months in infants, who were supplemented with routine oral vitamin D [27].

Limitation(s)

The present study did not consider maternal nutritional status, serum Vitamin D levels, and diet during pregnancy and lactation, which can directly affect the physical growth of infants. Additionally, sun exposure in infants was not taken into account in the present study.

CONCLUSION(S)

Infants who were supplemented with vitamin D (400 IU/day) showed better physical growth, as evidenced by higher anthropometric values. Physical growth during infancy depends on intrauterine nutrition and postnatal nutrition. Thus, an optimal level of vitamin D can promote good health and better physical growth.

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