Original Research Article

Levels of vitamin D in lower respiratory tract infections and asthma in pediatric age group

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Abstract

Background: Vitamin D deficiency is a significant risk factor for severe ALRI and asthma in Indian children <15 years of age. **Objectives:** To determine the serum levels and relationship of vitamin D in lower respiratory infections and asthma in children. **Methods:** Institutional Ethics committee permission was taken before starting the study. This study included 65 (43 boys and 22 girls) hospitalized children of 1 to 15 years of age with clinically diagnosed lower respiratory tract infection (LRTI), Wheeze associated lower respiratory infection (WALRI) and asthma. Written informed consent of the parents was taken. Proper history, General physical and systemic examination with emphasis on respiratory system was performed. Serum vitamin D was estimated using IDS 25-hydroxy vitamin D EIA kit. All data were analyzed by statistical methods in SPSS v.17. **Results:** Out of total 65 patients, 22 (33.8%) patients were females. 80% patients were in the age group of 0-5 years. Majority of the patients (76.9%) were low birth weight. Out of total 65 patients, 35 (53.8%) had normal nutritional status. Out of total 65 patients, 39 (60%) patients had moderate (4-7) respiratory score ,21 (32.3%) had severe respiratory score (8-12) and only 5 patients (7.7%) mild (less 3) respiratory score. 29 (44.6%) patients had deficient (<20 ng/ml) vitamin D level, 22 (33.8%) patients had insufficient (20-30 ng/ml) vitamin D level and only 14 (21.5%) had sufficient vitamin D level. Age groups, gender and vitamin D levels were significantly associated. ($p<0.05$). Serum vitamin D levels and clinical respiratory score, birth weight, nutritional status, history of NICU admission, gestational age and signs of respiratory distress were not significantly associated.($p>0.05$) **Conclusion:** Significantly lower serum 25(OH)D3 levels were noted in asthma, bronchiolitis, LRTI and WALRI in children suggesting that vitamin D deficiency increases the risk of respiratory infection, wheezing illnesses and asthma exacerbations.

Key Words: Vitamin D deficiency, Asthma, lower respiratory tract infections, wheeze associated lower respiratory infections.

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INTRODUCTION

ARI is responsible for about 30 to 50 percent of visits to health facilities and for about 20-40 per cent of admissions to hospital.[1]. The International Study of Asthma and allergies in Childhood [ISAAC] estimated asthma prevalence in India to be 6.2 to 6.8 percent in 6 to 7 years old and 6.5 percent in 13-14 years old with more males affected than females[2]. Vitamin D has received worldwide attention in last of couple decades not only for its importance for bone health in children and adults but also for reducing risk for many chronic diseases including autoimmune diseases, type 2 diabetes, heart disease, many cancers and infectious diseases. Vitamin D deficiency is pandemic due to the fact that most humans have depended on sun for their vitamin D requirement which they now either avoid or wear sun protection for fear of skin cancer3. Vitamin D enhances antimicrobial pathways, which is of relevance to infection-precipitated asthma exacerbations. These mechanisms support a role for vitamin D as secondary prevention to reduce exacerbations and inflammation in asthma.[4] Higher maternal intake of vitamin D during pregnancy is associated with a lower risk of recurrent wheezing in young children [5].Fortification of widely consumed foods, such as edible oil, with vitamin D could contribute to improved vitamin D status in Southeast Asian countries. Vitamin D is of particular interest in asthma due to its immunomodulatory effects. Serum 25- hydroxy vitamin

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D is found to be associated with a wide range of pulmonary diseases, including bacterial and viral respiratory infections, asthma and cancer. Nilofer *et al.* investigated the role of Vitamin D in childhood asthma and allergies. The data showed lower serum 25(OH) D levels in children with asthma, allergic rhinitis and wheezing than healthy children.[6].Vitamin D protect against asthma morbidity probably because of antiviral properties, enhanced steroid responsiveness, down-regulation of atopy .[7] The present study examined the relationship between serum 25(OH)D_3 levels in lower respiratory tract infections and asthma in pediatric age group.

Measurement of Vitamin D Levels: The currently available assays have antibodies cospecific to both 25(OH)D2 and 25(OH)D3 and hence the terminology 25(OH)D assays are used. The laboratory normally estimates 25(OH)D levels and not 25(OH)D2 or 25(OH)D3][8] . 25(OH)D is the major circulating form of vitamin D with a half-life of 2-3 weeks and its levels are the best available indicators of vitamin D status.

MATERIALS AND METHODS

This was a Hospital based cross – sectional study done at GMERS Medical College, Gotri- Vadodara. This study was conducted after taking approval of IHEC and Scientific committee of GMERS Gotri, Vadodara. Written informed consent of all parents of study children was taken. 65 children between ages of 1 to 15 years old admitted in Pediatric ward of for respiratory tract infection and asthma were included in the study consecutively. The sample size was calculated for estimation of proportion of the enrolled children having their vitamin D levels in 'sufficient' category. Pre-designed, pre-tested and semi-structure questionnaire used for data collections. Children > 15 years of age, patients who received Vitamin D supplementation within last 4 weeks and refusal of consent by parents were excluded from the study. Demographic data, personal and family history, immunization history, nutritional supplementation history was taken as per the protocol. Weight and height were measured using standard techniques and specifications**.** Weight-for-height below -3 SD WHO criterion was used to identify severely acutely malnourished infants and children .We used standard case definitions to identify upper respiratory tract infections and acute lower respiratory tract infections from collected information. Patients who were deficient in vitamin D, treated with standard regimen of vitamin D deficiency.

Determination of serum vitamin D levels

The determination of serum vitamin D in each child was conducted at enrolment using a 5ml blood sample collected into trace element-free tubes. Processing of the collected samples were performed at the biochemistry laboratory. Serum vitamin D (25-Hydroxy vitamin D) was measured by using IDS 25-hydroxy vitamin D EIA kit (Source: IDS Ltd, 10 Didcot Way, Boldon Business Park, Boldon, UK). Currently accepted standards for defining vitamin D status in children and adolescents according to Endocrinal society as follows[9]:

Vitamin D sufficiency: 25(OH) D > or =30 ng/ml
Vitamin D insufficiency: 25(OH) D between 20-30 ng/ml
Vitamin D deficiency: 25(OH) D between < 20 ng/ml.

Statistical analyses

Data was entered in Microsoft Excel and analysis was done using SPSS statistical package. Parameters such as rate, ratio and percentages were calculated. In order to have valid interpretation of rates, 95% confidence intervals (CI) were calculated. To test the significance of the difference among the statistical parameters in different subsets of population, suitable statistical test like chi square was applied. A probability of less than 0.05 was considered for a statistically significant association for all the analyses.

RESULTS AND DISCUSSION

Out of total 65 patients, 29 (44.6%) patients had deficient (<20 ng/ml) vitamin D level, 22 (33.8%) patients had insufficient (20-30 ng/ml) vitamin D level and only 14 (21.5%) had sufficient vitamin D level.

Table 1: Distribution of the patients according to their levels of Vitamin D and gender profile

Levels of Vitamin D	Gender		Total
	Female	Male	
Deficient (<20 ng/ml)	10 (45.4)	19 (44.1)	**29 (44.6)**
	(34.5)	(65.5)	**(100)**
Insufficient (20-30 ng/ml)	11 (50.0)	11 (25.5)	**22 (33.8)**
	(50.0)	(50.0)	**(100)**
Sufficient (>30ng/ml)	1 (4.54)	13 (30.2)	**14 (21.5)**
	(7.1)	(92.9)	**(100)**
Total	**22 (100)**	**43 (100)**	**65 (100)**
	(33.8)	**(65.2)**	**(100)**

(Figures in the parenthesis are percentages)
Chi square : 7.028 degree of freedom: 2; p<0.05 (p=0.03)

Out of total 65 patients, 22 (33.8%) patients were females and 43 (66.2%) patients were males. Among these 22 female patients, 10 (45.4%) had deficient (<20ng/ml) vitamin D level, 11 (50%) patients had insufficient (20-30ng/ml) vitamin D level and only 1 (4.54%) had sufficient vitamin D level. Out of 43 male patients, 19 (44.1%) had deficient (<20ng/ml) vitamin D level, 11 (25.5%) patients had insufficient (20-30ng/ml) vitamin D level and only 13 (30.2%) had sufficient vitamin D level. Gender and vitamin D levels were significantly associated. (p<0.05). In similar study Harel Z *et al.* showed the prevalence rate of low vitamin D in females, among 68 obese adolescents, 53% females and 47% males with age 15-17 years[10] . Also because of less outdoor activities in females as compared to males and also certain social and cultural taboos that dictate life style patterns such as clothing, they have less exposure to sunlight thus low vitamin D in females as shown in our study.

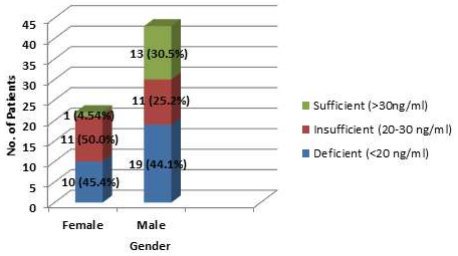

Figure 1: Distribution of the patients according to their levels of Vitamin D and gender profile

Table 2: Distribution of the patients according to their levels of Vitamin D and age groups

Levels of Vitamin D	Age groups			Total
	0-5 years	6-10 years	11-15 years	
Deficient (<20 ng/ml)	18 (34.6) (62.1)	1 10 (83.3) (34.5)	1 (100) (3.4)	**29 (44.6) (100)**
Insufficient (20-30 ng/ml)	21 (40.4) (95.5)	1 (8.3) (4.5)	0	**22 (33.8) (100)**
Sufficient (>30ng/ml)	13 (25) (92.9)	1 (8.3) (7.1)	0	**14 (21.5) (100)**
Total	**52 (100) (80.0)**	**12 (100) (18.5)**	**1 (100) (1.5)**	**65 (100) (100)**

(Figures in the parenthesis are percentages)
Mean age was 3.25 ±3.04 years
Chi square: 10.664 Degree of freedom: 4; p<0.05 (p=0.03)

Out of total 65 patients, 52 (80%) patients were in the age group of 0-5 years, 12 (18.5%) patients were in the age group of 6-10 years and only 1 (1.5%) patients were in the age group of 11-15 years. Among these 52 patients in 0-5 years age group, 18 (34.6%) had deficient (<20ng/ml) vitamin D level, 21 (40.4%) patients had insufficient (20-30ng/ml) vitamin D level and only 13 (25%) had sufficient vitamin D level. Out of 12 patients in 6-10 years age group,10 (83.3%) had deficient (<20ng/ml) vitamin D level, 1 (8.3%) patients had insufficient (20-30ng/ml) vitamin D level and only 1 (8.3%) had sufficient vitamin D level. Only 1 patient was 12 years old who had deficient (<20ng/ml) vitamin D level. Mean age was 3.25 ±3.04 years.

Age groups and vitamin D levels were significantly associated. (p<0.05). Abu Shady *et al.* have suggested that low sun exposure, obesity and low level of maternal education were significant determinants of vitamin D insufficiency in Egyptian school-children 9-11 years [11]. As it has been observed in our study and also some other studies showed same results that school going age group is more deficient in vitamin D levels, may be because of the change in lifestyle of modern society has caused an increase in indoor activities decreasing exposure to sunlight, negligible dietary vitamin D intake because of primarily vegetarian diet and lack of fortification of food with vitamin D in our country.

Table 3: Distribution of the patients according to their levels of Vitamin D and gestational age

Levels of Vitamin D	Delivery		Total
	Full term	Preterm	
Deficient (<20 ng/ml)	27 (49.1) (93.1)	2 (20.0) (6.9)	**29 (44.6) (100)**
Insufficient (20-30 ng/ml)	17 (30.9) (77.3)	5 (50.0) (22.7)	**22 (33.8) (100)**
Sufficient (>30ng/ml)	11 (20) (78.6)	3 (30.0) (21.4)	**14 (21.5) (100)**
Total	**55 (100) (84.6)**	**10 (100) (15.4)**	**65 (100) (100)**

(Figures in the parenthesis are percentages) Chi square:2.9; Degree of freedom:2; p=0.23

Out of 65 patients, 55 (84.6%) had full term delivery and only 10 (15.4%) patients had preterm delivery. Among these 55 patients with full term delivery, 27 (49.1%) had deficient (<20ng/ml) vitamin D level, 17 (30.9%) patients had insufficient (20-30ng/ml) vitamin D level and only 11 (20%) had sufficient vitamin D level. Out of 10 patients with preterm delivery, 2 (20.0%) had deficient (<20ng/ml) vitamin D level, 5 (50%) patients had insufficient (20-30ng/ml) vitamin D level and only 3 (30%) had sufficient vitamin D level. Gestational age and levels of vitamin D were not significantly associated. (p=0.23). In consistence with previous study Fallahi *et al.* 2013 found there was no significant difference in vitamin D levels between term and preterm infant mother pair, whereas vitamin D levels in mother and infants are significantly correlated[12]

Out of 65 patients, (Table 5) 8 (12.3%) had history of NICU Admission. 57 (87.7%) had no history of NICU admission. Among these 57 patients with no history NICU admission, 26 (45.6%) had deficient (<20ng/ml) vitamin D level, 18 (31.5%) patients had insufficient (20-30ng/ml) vitamin D level and only 13 (22.9%) had sufficient vitamin D level. Among these 8 patients with history NICU admission, 3 (37.5%) had deficient (<20ng/ml) vitamin D level, 4 (50.0%) patients had insufficient (20-30ng/ml) vitamin D level and only 1 (12.5%) had sufficient vitamin D level. History of NICU admission and levels of vitamin D were not significantly associated. (p=0.56). This is evident from our study that Vitamin D levels were not associated with sick neonates in NICU. However in our study out of 65 patients 29 (44.6) were deficient and 22 (33.8) patients were insufficient thus we recommend Vitamin D supplementation in all neonates irrespective of NICU stay.

Table: 4 Distribution of the patients according to their levels of Vitamin D and history of NICU stay

Levels of Vitamin D	History of NICU stay		Total
	No	Yes	
Deficient (<20 ng/ml)	26 (45.6) (89.7)	3 (37.5) (10.3)	**29 (44.6) (100)**
Insufficient (20-30 ng/ml)	18 (31.5) (81.8)	4 (50) (18.)	**22 (33.8) (100)**
Sufficient (>30ng/ml)	13 (22.9) (92.9)	1 (12.5) (7.1)	**14 (21.5) (100)**
Total	**57 (100) (87.7)**	**8 (100) (12.3)**	**65 (100) (100)**

(Figures in the parenthesis are percentages) p=0.56

Majority of the patients (76.9%) were low birth weight. (<2500 grams) Out of 65 patients, only mothers of 8 (12.3%) had not taken ANC Visit. In our study 55 (84.6%) had full term delivery and only 10 (15.4%) patients had preterm delivery. by Out of 65 patients, 8 (12.3%) had history of NICU admission.

Table: 5: Distribution of the patients according to their levels of Vitamin D and birth weight

Levels of Vitamin D	Birth weight		Total
	<2500 grams	≥ 2500 grams	
Deficient (<20 ng/ml)	23 (46.0) (79.3)	6 (40.0) (20.7)	**29 (44.6) (100)**
Insufficient (20-30 ng/ml)	17 (34.0) (77.3)	5 (33.3) (22.7)	**22 (33.8) (100)**
Sufficient (>30ng/ml)	10 (20.0) (71.4)	4 (26.7) (28.6)	**14 (21.5) (100)**
Total	**50 (100) (76.9)**	**15 (100) (23.1)**	**65 (100) (100)**

(Figures in the parenthesis are percentages) p=0.84

Among these 50 patients with low birth weight, 23 (46.0%) had deficient (<20ng/ml) vitamin D level, 17 (34.0%) patients had insufficient (20-30ng/ml) vitamin D level and only 10 (20.0%) had sufficient vitamin D level. Birth weights and vitamin D levels were not significantly associated. (p=0.84). From our study it is evident that birth weight is not associated with low vitamin D levels however out of 29 vitamin D deficient babies 79.3% (23) were of birth weight <2.5 kg and 20.7 %(6) were of birth weight > 2.5 kg, which can be correlated with work done by Wang H *et al.*. that maternal vitamin D deficiency is common during pregnancy and is independently associated with low birth weight and high risk of SGA in term infants [13]. As shown in our study low birth weight neonates had better vitamin D status probably because they have frequent follow ups and supplemented with vitamin D regularly as compared to neonates with normal birth weight. Out of total 65 patients, 35 (53.8%) had normal (weight for height Median to -1SD) nutritional status followed by 14 (21.5%) patients had moderate malnutrition (weight for height >2SD to -3SD), 9 (13.8%) had mild malnutrition (weight for height >1 SD to -2SD)and 7 (10.8%) children had severe acute malnutrition (weight for height<-3SD) with mean weight of 10.9 ± 6.5 kg and mean height of 81.1 ± 24.5 cm. Nutritional status and vitamin D levels were not significantly associated. (p=0.4). However vitamin D deficiency is common in well-nourished children as in severe acute malnutrition requirement of supplements including vitamin D is reduced.

Table 6: Distribution of the patients according to their levels of Vitamin D and clinical respiratory score

Levels of Vitamin D	Clinical respiratory score			Total
	Mild (less than 3)	Moderate (4-7)	Severe (8-12)	
Deficient (<20 ng/ml) or Insufficient (20-30 ng/ml)	4 (80) (7.8)	28 (71.7) (54.9)	19 (90.4) (37.2)	51 (78.5) (100)
Sufficient (>30ng/ml)	1 (20) (7.1)	11 (28.3) (78.6)	2 (9.6) (14.3)	14 (21.5) (100)
Total	**5 (100) (7.7)**	**39 (100) (60.0)**	**21 (100) (32.3)**	**65 (100) (100)**

(Figures in the parenthesis are percentages)p=0.41

Among these 5 patients with mild respiratory score, 4 (80%) had deficient (<20ng/ml) or insufficient (20-30ng/ml) vitamin D level and only 1 (20%) had sufficient vitamin D level. When groups of deficient and insufficient vitamin D level were compared with sufficient Vitamin D level, clinical respiratory scores and vitamin D levels were not significantly associated. (p=0.41). In our study it has been observed that severity of clinical signs is not associated with levels of vitamin D deficiency, however it is evident from review of literature and in our study that lower vitamin D deficiency was found with LRTI and Asthma in pediatric age group. Studies with larger series with long follow up periods should be conducted for definite results. Out of total 65 patients, 35 (53.8%) had LRTI (lower respiratory tract infection), 12 (18.5%) had asthma followed by 11 (16.9%) had bronchiolitis and 7 (10.8%) had WALRI (wheeze associated lower respiratory tract infection.)

Table 7: Distribution of the patients according to their levels of Vitamin D and Diagnosis

Levels of Vitamin D	Diagnosis				Total
	Asthma	Bronchiolitis	LRTI	WALRI	
Deficient (<20 ng/ml)	9 (31.0) (75.0)	2 (6.9) (18.2)	17 (58.6) (48.6)	1 (3.4) (14.3)	**29 (100) (44.6)**
Insufficient (20-30 ng/ml)	2 (9.1) (16.7)	5 (22.7) (45.5)	13 (59.1) (37.1)	2 (9.1) (28.6)	**22 (100) (33.8)**
Sufficient (>30ng/ml)	1 (7.1) (8.3)	4 (28.6) (36.4)	5 (35.7) (14.3)	4 (28.6) (57.1)	**14 (100) (21.5)**
Total	**12 (18.5) (100)**	**11 (16.9) (100)**	**35 (53.8) (100)**	**7 (10.8) (100)**	**65 (100) (100)**

(Figures in the parenthesis are percentages) p=0.02 (p<0.05)

Out of 12 patients with asthma, 9 (75.0%) had deficient (<20ng/ml) vitamin D level, 2 (16.7%) patients had insufficient (20-30ng/ml) vitamin D level and only 1 (8.3%) had sufficient vitamin D level. Out of 11 patients with bronchiolitis, 2 (18.2%) had deficient (<20ng/ml) vitamin D level, 5 (45.5%) patients had insufficient (20-30ng/ml) vitamin D level and only 4 (36.4%) had sufficient vitamin D level. Out of 35 patients with LRTI, 17 (48.6%) had deficient (<20ng/ml) vitamin D level, 13 (37.1%) patients had insufficient (20-30ng/ml) vitamin D level and 5 (14.3%) had sufficient vitamin D level. Out of 7 patients with WALRI, 1 (14.3%) had deficient (<20ng/ml) vitamin D level, 2 (28.6%) patients had insufficient (20-30ng/ml) vitamin D level and 4 (57.1%) had sufficient vitamin D level. Diagnosis in these patients and their vitamin D levels were significantly associated (p<0.05). Vitamin D may influence asthma by regulating the expression of disease-susceptibility genes and through modulation of T regulatory cells. Vitamin D has also been shown to increase serum levels of the immune-modulatory cytokines through vitamin D Receptors (VDRs)[14]. Low vitamin D level is associated with impaired lung function in asthmatic children, thus lower serum vitamin D levels are a contributory factor in bronchial asthma[15].

CONCLUSION

In our study, age groups, gender and vitamin D levels were significantly associated. Higher the age group more was vitamin D deficiency. Females were more vitamin D deficient as compared to males. However no significant association was found between serum vitamin D levels and clinical respiratory score, birth weight, nutritional status, history of NICU admission, gestational age and signs of respiratory distress. In the present study, significantly lower serum 25(OH)D3 levels were noted in asthma, bronchiolitis, LRTI and WALRI in children which suggests that vitamin D deficiency increases the risk of respiratory infection, which may contribute to the incidence of wheezing illnesses in children as well as adults and cause asthma exacerbations. Thus, vitamin D may be related to lower respiratory tract infections, asthma and its severity.

LIMITATIONS OF STUDY

Most of the patients with respiratory distress had vitamin D deficiency or insufficiency, though the symptoms of

respiratory distress were not significantly correlated with vitamin D deficiency in our study, probably because of small sample size. Confounding factors like amount of sun exposure, clothing habits and dietary intake of vitamin D could have an influence on the results. Inclusion of other biochemical parameters like calcium, phosphorus, alkaline phosphate, parathyroid hormone, could not be done which would have given a better picture of vitamin D status. More extensive study with larger sample size with apparently healthy individuals as a control group is required to establish a reference range of vitamin D in that region of country as it may vary according to geographical location and ethnicity.

RECOMMENDATIONS

Our study emphasizes the need for serum vitamin D estimation in various respiratory illnesses even in face of protein energy malnutrition so that appropriate and timely therapeutic intervention can be initiated to decrease morbidity and mortality in children <15 years. Given the high frequency of hypovitaminosis D found in this study, there is a need to work more on health promotion activities to this community targeting the importance of physical activities, exposure to sunlight and use of diets rich in vitamin D. We recommend vitamin D supplementation should be given to patients with asthma and lower respiratory tract infections.

REFERENCES

1. Park's, text book of Preventive and Social Medicine.23 Edition. Acute Respiratory Infections 177–178.
2. P.G.Text Book of PAEDIATRICS Piyush Gupta 2nd Edition 2022-2023.
3. Holick MF. Vitamin D deficiency. N Engl J Med 2007;357:266-281 DOI: 10.1056/NEJMra070553
4. Pfeffer, Paul and Hawrylowicz, Catherine. (2017). Translating Basic Research into Clinical Practice: Vitamin D in Asthma – Mechanisms of Action and Considerations for Clinical Trials. Chest. 153. 10.1016/j.chest.2017.09.005.
5. Camargo CA Jr, Rifas-Shiman SL, Litonjua AA, Rich-Edwards JW, Weiss ST, Gold DR, *et al.*. Maternal intake of vitamin D during pregnancy and risk of recurrent wheeze in children at 3 y of age. Am J Clin Nutr. 2007;85:788-95.
6. Ali NS, Nanji K. A Review on the Role of Vitamin D in Asthma. *Cureus*. 2017;9(5):e1288. Published 2017 May 29. doi:10.7759/cureus.1288
7. Abdulbari Bener, Mohammad S. Ehlayel, Hale Z. Bener, Qutayba Hamid, The impact of vitamin D deficiency on asthma allergic rhinitis and wheezing in childrenJ Family Community Med. 2014 Sep-Dec; 21(3): 154–161
8. Grace Paul, Jhon M Brem *et al.*.Vitamin D and Asthma, AM J Respir crit care Med.2012 Jan 15; 185(2): 124-32.
9. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, *et al.*. Evaluation, treatment and prevention of vitamin D deficiency: an Endocrine Society. Practice guideline. J. Clin Endocrinol Metab. 2011;96:1911-30.
10. Harel Z, Flanagan P, Forcier M, Harel D. Low vitamin D status among obese adolescents: prevalence and response to treatment. J Adolesc Health 2011; 48:448.
11. Shady MM, Youssef MM, Shehata MA, El-Din EM, ElMalt HA. Association of Serum 25-Hydroxyvitamin D with Life Style and Dietary Factors in Egyptian Prepubescent Children. *Open Access Maced J Med Sci*. 2015;3(1):80-84. doi:10.3889/oamjms.2015.006
12. Fallahi, M., Afjeh, A., Saneifard, H., Namazi, N., Kazemian, M., Tabatabaee, S. Comparison of Vitamin D Level in Preterm and Term Infant–Mother Pairs: A Brief Study. *Iranian Journal of Neonatology IJN*, 2016; 7(1): 32-36. doi: 10.22038/ijn.2016.6662
13. Wang H, Xiao Y, Zhang L, Gao Q. Maternal early pregnancy vitamin D status in relation to low birth weight and small-for-gestational-age offspring. *J Steroid Biochem Mol Biol*. 2018;175:146-150. doi:10.1016/j.jsbmb.2017.09.010
14. Hyppönen E, Power C. Hypovitaminosis D in British adults at age 45 y: nationwide cohort study of dietary and lifestyle predictors. *Am J Clin Nutr*. 2007;85(3):860-868. doi:10.1093/ajcn/85.3.860
15. Holick MF, Chen TC. Vitamin D deficiency: a worldwide problem with health consequences. *Am J Clin Nutr*. 2008;87(4):1080S-6S. doi:10.1093/ajcn/87.4.1080S

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