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Original Article

Factors Influencing Initiation and Discontinuation of Vitamin D Supplementation Among Infants

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Abstract: Background: To determine vitamin D supplementation frequency among infants, factors that influence adherence, and reasons for discontinuation of initiated vitamin D.

Methods: This cross-sectional study was conducted using a questionnaire administered to the mothers via face to face interview on 560 infants aged from 1 to 24 months admitted to outpatient clinics from June to December 2017.

Results: A total of 351 infants were administered vitamin D, and the rate of supplementation in the first year of life was 83%, while it was only 28% between 13 and 24 months. The rate of vitamin D supplementation was higher among infants who were exclusively formula-fed ($p<.05$). When the data were analyzed using logistic regression analysis, only visit family physicians seems to be a statistically significant independent variable in increasing supplementation ($p<.05$).

Compared with family refusal, the rate of discontinuation of vitamin D by the healthcare providers was higher after the first year of life ($p<.05$). The rates of vitamin D discontinuation by healthcare providers, especially by nurses who considered the duration of supplementation adequate, was statistically significantly higher when compared with the fontanel closure and other reasons ($p<0.05$).

Conclusions: The rate of vitamin D supplementation was higher among families who visited family physicians, which suggests the importance of well-baby visits. Since vitamin D supplementation was less common among exclusively breastfed infants, mothers should be educated. Healthcare professionals need further education about the importance of vitamin D supplementation and indications for discontinuation.

Keywords: adherence; healthcare providers; infant, vitamin D, supplementation

1. Introduction

Over the last decade, interest in vitamin D deficiency has grown, as it exerts effects not only on bone mineralization but also on diabetes, cancers, autoimmune diseases, infectious diseases, and others [1-5] . Nutritional vitamin D deficiency is the most common cause of rickets, a condition that affects infants and young children, which causes symptoms including delayed closing of fontanels, morphological anomalies of the lower limbs, short stature, and retardation of growth and development 6] . Vitamin D insufficiency or deficiency may also be detected in children who do not

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show clinical manifestations of rickets. Vitamin D deficiency is more prevalent than rickets and it is a serious health problem both in developing and developed countries [7] .

Daily vitamin D supplementation was recognized as the best intervention to prevent vitamin D deficiency and rickets. In 2016, international experts in pediatric societies released the *Global Consensus Recommendations on Prevention and Management of Nutritional Rickets*. It has been declared that 400 IU/d is adequate to prevent rickets and is recommended for all infants from birth to 12 months of age, independent of their mode of feeding and beyond 12 months of age, all children and adults need to meet their nutritional requirement for vitamin D through diet and/or supplementation, which is at least 600 IU/d [8] . Turkey, Belgium, the United Kingdom, and many countries across Europe and Canada have national programs for vitamin D supplementation [9-10] .

In Turkey, national studies have reported a prevalence of rickets that varied from 1.67 to 19%, and these studies were conducted before the implementation of vitamin D supplementation as a health policy priority [11] . Turkish Ministry of Health started distributing free-of-charge vitamin D bottles to family health centers in 2005 at a dose of 400 IU/day for infants up to 1 year of age as part of the "Project for Prevention of Vitamin D Insufficiency and Protection of Bone Health". Vitamin D supplementation is recommended to be maintained for the first three years of life because the risk for rickets continues, there are no fortified foods with vitamin D in Turkey [12] . After this campaign, even if the prevalence of rickets decreased, vitamin D insufficiency and deficiency are still a problem among infants and children in Turkey [11,13-16] . Thus, evaluation of vitamin D supplementation practices and adherence to recommendations by families and healthcare providers is needed. The objective of this study was to determine vitamin D supplementation frequency among infants, the factors that influence adherence, and the reasons for discontinuation of initiated vitamin D supplementation through a questionnaire administered to the infant's mothers.

2. Materials and Methods

This study was conducted using a questionnaire which is administered face to face to the mothers of 560 infants aged from 1 to 24 months admitted to outpatient clinics at T.R. Health Sciences University Ankara Pediatric Hematology-Oncology Research and Training Hospital between June 2017 and December 2017. The study was approved by the T.R. Health Sciences University Ankara Pediatric Hematology-Oncology Research and Training Hospital Ethics Committee (no:85) and informed consent was obtained from participating mothers. The study questionnaire covered the following topics: infants' delivery week (≥ 38 and <38), type of nutrition (exclusively breastfed, exclusively formula-fed, mixed-fed, fed table foods), concomitant illnesses, medications, whether vitamin D supplementation was received; the person initiating the administration of vitamin D, discontinuation of vitamin D and if discontinued, its reasons and who discontinued, number of persons per household (nuclear or crowded family), education and employment status of the parents and household monthly income. The subsistence wage according to national poverty criteria

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was 400 $ equivalent of Turkish Liras at the time of the study. Family incomes below this sum were defined as a low-income family. Monthly income, which was between the subsistence wages and up to two-fold of the subsistence wage, was defined as middle income. The income above this level was defined as high income. Infants were stratified into two groups based on their age; 1 to 12 months and 13 to 24 months. Twenty mothers who refused to complete the study questionnaire were excluded. No financial assistance was provided to participants. Interviews were recorded by one of the authors (SHK).

Statistical Analysis

Data obtained from the study was entered into the IBM SPSS Statistics Version 22.0 software. Chi-square test was used for univariate analysis. We further investigated the influence of different factors on the supplementation by multivariate logistic regression. A p-value of less than 0.05 was considered to indicate a significant difference between groups. Data were expressed as numbers and percentages in tabulated form.

3. Results

Of a total of 560 infants participating in the study, 351 (62.6%) received vitamin D. The rate of supplementation during the first year of life was 83%, whereas it was only 28% between 13 to 24 months of life. There was no significant relation between infant's gender, delivery week, concomitant illnesses, medications, and vitamin D supplementation (p>.05, Table 1).

When compared by nutrition type, the rate of supplementation was higher among exclusively formula-fed infants. Vitamin D supplementation was initiated by family physicians in 264 (75.2%) and by pediatricians in 87 (24.8%) of the infants. Supplementation rate was statistically significantly higher among families who regularly visited their family physicians and had their babies vaccinated on time (p<.05, Table 1).

Table 1. Vitamin D Supplementation Practices

	Distribution in study population (n.=560)	Vitamin D supplementation across subgroups		P
		Supplemented n:351	Nonsupplemented n:209	
	n %	n %	n %	
Gender				
Female	252 (45)	151 (59.9)	101 (40.1)	.22
Male	308 (55)	200 (64.9)	108 (35.1)	
Receiving vitamin D by age				
1-12 months	353 (63)	293 (83)	60 (17)	
13-24 months	207 (3)	58 (28)	149 (72)	<.**001**

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Delivery week				
Preterm (<38	190 (33.9)	122 (64.2)	68 (35.8)	
Term (≥38	370 (66.1)	229 (61.8)	141 (38.2)	.76
Feeding status				
exclusively breastfed	279 (49.8)	162 (58)	117 (42)	
exclusively formula-fed	116 (20.7)	94 (81)	22 (19)	**<.001**
mixed-fed	90 (16)	70 (77.7)	20 (22.3)	
fed table foods	75 (33.3)	25 (33.3)	50 (66.7)	
Concomitant ilnesses				
Yes	168 (30)	105 (62.5)	63 (37.5)	.95
No	392 (70)	246 (62.7)	146 (37.3)	
Regular medication intake				
Yes	100 (17.8)	61 (61)	39 (39)	.70
No	460 (82.2)	290 (63)	170 (37)	
Regular visit to family physician				
Yes	536 (95.7)	342 (63.8)	194 (36.2)	**<.001**
No	24 (4.3)	9 (37.5)	15 (62.5)	
Vaccinated on time				
Yes	549 (98)	349 (63.5)	200 (36.5)	**<.001**
No	11 (2)	2 (18.1)	9 (81.9)	

The rate of vitamin D supplementation among infants was higher in nuclear families than in crowded families (p<.05; Table 2). Supplementation rates were not associated with the presence of a sick child in the family, the number of children, household monthly income, paternal education and employment status, maternal age, education, and employment status (p>.05; Table 2).

Table 2. Demographic Characteristics of Families by Vitamin D Supplementation Status

	Distribution in study population (N.=560)	Vitamin D supplementation across subgroups		P
		Supplemented n:351	Nonsupplemented n:209	
	n %	n %	n %	
Number of siblings				
None	160 (28.5)	103 (64.3)	57 (35.7)	.85
1	204 (36.4)	124 (60.8)	80 (39.2)	
2-3	174 (31)	109 (62.6)	65 (37.4)	
≥4	22 (4.1)	15 (68.2)	7 (31.8)	
Sick siblings				

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Yes	52 (9.2)	33 (63.4)	19 (36.6)	
No	508 (90.8)	318 (62.5)	190 (37.5)	.90
Number of people living at home				
Nuclear family	438 (78.2)	284 (64.8)	154 (35.2)	
Extended family	122 (21.8)	67 (54.9)	55 (45.1)	**.04**
Monthly in come				
<1400 tl	49 (8.7)	31 (63.2)	18 (36.8)	
1400 tl-1999 tl	195 (34.8)	115 (58.9)	80 (41.1)	.43
2000 tl-2999 tl	176 (31.4)	110 (62.5)	66 (37.5)	
≥3000 tl	140 (25.1)	95 (67.8)	45 (32.2)	
Paternal Education Level				
Uneducated	10 (1.8)	4 (40)	6 (60)	.23
Primaryschool	95 (16.9)	58 (61)	37 (39)	
Middleschool	186 (33.2)	112 (60.2)	74 (39.8)	
Highschool	185 (33)	118 (63.7)	67 (36.3)	
University	84 (15.1)	59 (70.2)	25 (29.8)	
Workingstatus of father				
Unepmloyed	10 (1.8)	7 (70)	3 (30)	.62
Employed	550 (98.2)	344 (62.5)	206 (37.5)	
Age of mother				
<18 years	5 (0.9)	3 (60)	2 (40)	.69
18-35 years	473 (84.5)	300 (63.4)	173 (36.6)	
> 35 years	82 (14.6)	48 (58.5)	34 (41.5)	
Maternal education level				
Uneducated	23 (4.1)	16 (69.5)	7 (30.5)	.78
Primaryschool	161 (28.7)	100 (62.1)	61 (37.9)	
Middleschool	144 (25.7)	87 (60.4)	57 (39.6)	
Highschool	160 (28.5)	99 (61.9)	61 (38.1)	
University	72 (13)	49 (68)	23 (32)	
Working status of mother				
Unepmloyed	504 (90)	311 (61.7)	193 (38.3)	.15
Employed	56 (10)	40 (71.4)	16 (28.6)	

However, when the data were analyzed using logistic regression analysis, only visits to family physicians seem to be a statistically significant independent variable in increasing supplementation (p<.05; Table 3).

Table 3. Assessment of Factors Influencing Vitamin D Administration to the Infants by Logistic Regression Analysis

Factors	OR	%95 CI	P
Monthly in come			
<1400 tl	1.20	0.73- 1.98	
1400tl-1999tl	1.39	0.83- 2.31	.59

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2000tl-2999 tl	1.06	0.50- 2.22	
≥3000 tl	1.00		
Visits to Family Physicians			
No	**2.71**	1.15-6.38	**.02**
Yes	1.00		
Maternal Education Status			
Highschool graduate	1.19	0.63-2.24	.74
Primary or secondary school graduate	1.16	0.62-2.17	
Illiterate	0.73	0.24- 2.17	
University graduate	1.00		
Maternal Employment Status			
Employed	0.74	0.38 -1.43	.37
Unemployed	1.00		

Vitamin D was not administered to 209 (%37,3) infants. Compared with family refusal, the rate of discontinuation by the healthcare providers was higher after the first year of life. The rates of discontinuation by healthcare providers believing that the duration of supplementation was sufficient after the first year of life was significantly higher when compared with the fontanel closure and other reasons. Other reasons for discontinuation were kidney stones and the adequate vitamin D status of the infants. Due to the belief insufficient duration of supplementation after the first year of life, nurses' discontinuation rates were high (p <.05; Table 4).

Table 4. Reasons for discontinuation of vitamin D supplementation

	Age		
	n %	1-12 months n %	13 to 24 months n%	P
Reasons to stop supplement (n: 209)				
Parents Refused	99 (47.4)	39 (39.4)	60 (60.6)	
Stopped by a Healthcare Staff	110 (52.6)	21 (19)	89 (81)	**<.001**
Reasons of discontinuation by healthcare staff (n: 110)				
Sufficient duration	84 (76.3)	10 (11.9)	74 (88.1)	
Fontanel closure	21 (19)	8 (38)	13 (62)	**.004**
Other	5 (4.7)	3 (60)	2 (40)	
Reasons of discontinuation by physician (n: 31)				
Sufficient duration	19 (61.3)	4 (21)	15 (79)	.10
Fontanel closure	7 (22.5)	2 (28.6)	5 (71.4)	

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Other	5 (16.2)	3 (60)	2 (40)	
Reasons of discontinuation by nurse (n: 79)				
Sufficient duration	65 (82.3)	6 (9.3)	59 (90.7)	**<.001**
Fontanel closure	14 (17.7)	6 (42.8)	8 (57.2)	

4. Discussion

Vitamin D insufficiency and deficiency affect infants and children more than adults. Turkish Ministry of Health started distributing free-of-charge vitamin D bottles to all family health centers in 2005 at a dose of 400 IU/day for infants up to 1 year of age and recommended continuation for 3 years [12] . As a result, the prevalence of rickets was reduced from 6% in 1998 to 0.1% in 2008 in the eastern parts of Turkey [17] . Nevertheless, vitamin D insufficiency/deficiency remains a critical health problem in Turkey [11,13-16] . For this reason, this study covered infants from 1 to 24 months of life which the consequences of rickets are so severe that vitamin D supplementation is recommended routinely.

Studies from Saudi Arabia, Switzerland, and the USA reported that vitamin D supplementation rates were 38,3%, 64%, and 58% up to the first year of life, respectively [18-20] . A study from Turkey reported that among mothers of infants aged 1-24 months, 75% administered vitamin D [21] , while in another study 82.7 % of infants received vitamin D in the first year of life [22] . Similarly, 62.6% of the infants were administered vitamin D during the first 2 years of life in the present study. This figure reflects the success of the project in some parts of Turkey.

To find out the impact of national recommendations regarding vitamin D supplementation, the European Society for Pediatric Endocrinology (ESPE) conducted a study with member countries and reported 79% of them recommended vitamin D for all infants in the first year of life whether they are breastfed or not. Good adherence to vitamin D supplementation was reported by 59% of the countries including Turkey and report demonstrate that the prevalence of supplementation is 80% in Turkey [9] ; consistently, 83% of the infants received vitamin D during the first year of life in our study.

There is not sufficient vitamin D breast milk (12-60 IU / L) for an infant's daily need, which is the same in foods [12] . Infants who received 400 IU / day of vitamin D, had sufficient vitamin D levels, but it was lower in infants who were only breastfed [23] . In a study, the rate of supplementation for exclusively breastfed infants was 15.9% and 44.6% of their parents stated that they administer vitamin D to their babies because their pediatrician recommended it. Parents who did not administer vitamin D believed that breast milk supplies all needed nutrition [24] . In another study, 20% of physicians who do not recommend supplementation stated that breast milk had adequate amounts of vitamin D [25] . The latest study from the US for evaluating adherence to supplementation guidelines underlined that nonbreastfeeding infants were more likely to meet guidelines than breastfeeding infants [26] . A Canadian study reported that none of the parents of formula-fed newborns started supplementation because they did not

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receive advice to do so [10] . A study conducted by pediatricians and pediatric residents showed that 85.2% of them recommended vitamin D to all infants irrespective of the type of nutrition, 13.4% to exclusively breastfed infants and 1.4% to exclusively formula-fed infants [27] . Between family physicians, 15.3% and 14.2% recommended vitamin D to infants who were only breastfed and only formula-fed respectively and 54% recommended it for all infants regardless of nutrition type [28] . In a European study, it was emphasized that factors significantly associated with good adherence were universal supplementation independent of the mode of feeding and providing information on supplementation at discharge from hospital after birth [9] .

Nearly half of the mothers (49.8%) breastfed their infants in our study, but the significantly higher rate of supplementation among exclusively formula-fed infants (81%) compared to only breast-fed infants (%58) highlights that mothers embrace the importance of breastfeeding but they have a misperception that breastfed infants do not need vitamin D supplementation. Turkish Ministry of Health has been conducting a project called 'Baby-friendly Hospital' in hospitals since 2003 to communicate the importance of breastfeeding. Given the lower rate of supplementation among breastfed babies, we believe that healthcare providers should also deliver information on vitamin D while educating mothers on the importance of breastfeeding and these efforts may possibly be integrated with the 'Baby-friendly hospital' project and the 'Project for Prevention of Vitamin D Insufficiency and Protection of Bone Health'.

Studies from the US, Saudi Arabia, and Turkey reported that vitamin D was recommended by 52.3%, 60%, and 54% of the family physicians for infants, respectively [29,30] . It is reported that receiving advice from healthcare providers is a positive determinant of supplementation practice [10] . In our study, 95.7% of the families regularly visited family physicians and 63.8% of the administered vitamin D to their infants. Also, the families who did not visit family physicians were 2.71 times less likely to supplement vitamin D compared to those who did. Therefore, regular visits to the family physician provide a valuable opportunity for healthcare providers to explain the importance of vitamin D, and advice for supplementation should be given in all well-baby visits.

Several studies reported that higher maternal education status provides higher rates of supplementation [10,21-22] . In contrast, other studies stated that maternal education status did not have an impact [19,31] . There was no relationship between maternal education and supplementation in our study. We believe that irrespective of maternal education, adherence to supplementation would be high if the mothers were informed about vitamin D.

Despite recommendations for continued supplementation in children up to the first 3 years of life in Turkey, regular use was reported only during the first year. It was reported that while 77% of infants supplemented in the first 3 months of life, it decreased to 57% and 35% at the end of the first and second years respectively, and the decline in supplementation rate related to the termination of free-of-charge vitamin D distribution [21] . In another study rate of supplementation was found 82.7 % in the first year but only 26.9% after 12 months [22] . Also, vitamin D deficiency was found

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significantly higher 13-24 months of age compared to the first year of life and emphasized that free-of-charge vitamin D supplementation might be given to infants beyond 1 year of age [32] .

In our study, the percentage of infants receiving vitamin D during the first year of life was 83% but only 28% between 13 to 24 months of life. Reasons for not administering in all age groups were parental refusal (47.4%) and discontinuation with the advice of healthcare providers (52.6%). The most common reason for discontinuation in the first year of life was family refusal (65%). As an assumption when an infant thrives and gets older parents may neglect administering vitamin D to their infants. Thus, education of families on supplementation for their infants up to 1 year of age has a key role in preventing vitamin D deficiency.

Santi et al.'s study [33] reported that supplementation is advised by 97% of pediatricians during the first year of life, by 72% during the 2 to 3 years of life, and by 3.2% after 3 years of life. This decline is explained by poor awareness and fear of toxicity. Elitok et al.'s study [27] reported that supplementation is advised by 44.7% of pediatricians during the first year of life, by 36.8% during the 2 years of life, and by 7% during the 3 years of life, and pediatricians were inclined to prescribe vitamin D to children with chronic diseases after the first year of life. Between family physicians, while 39% recommended vitamin D during the first year of life, only %1 for 36 months did. Physicians believed that there was sufficient vitamin D in foods and thought that sun exposure produced sufficient vitamin D [28] . In another study, only 67% of the infants received vitamin D and in 48% supplementation was terminated on the physician's recommendation [34] . In the latest study from the US, 40% of infants met guidelines, and this low rate was associated with reasons such as lack of physician awareness or disagreement with guidelines, inadequate physician communication to caregivers, or failure to adhere to physician recommendations by caregivers [26] .

In our study, in 14,8% of infants who were not supplemented this was related to family physicians. The primary reason for vitamin D discontinuation among family physicians was the belief of sufficient duration of supplementation (61.3%) and the rate of withdrawal, for this reason, was higher among infants aged between 13-24 months (79%) when compared to 1-12 months (21%). Other reasons were fontanel closure in seven patients and kidney stones in three patients. Similarly to our study, pediatricians reported that 20% of them discontinued vitamin D upon fontanel closure [35] . In the case of vitamin D deficiency, the closing of fontanelles is delayed, but normal or even high doses of vitamin D are not related to the early closure or smallness of fontanelles [36] . Vitamin D supplementation was shown not to be associated with an increased risk of kidney stones [37,38] .

These findings suggest that some family physicians do not have adequate information on the sufficient duration and indications for discontinuation of vitamin D supplementation, so their education on this matter is important to maintain continuity of supplementation among infants especially after the first year of life. For the reasons mentioned above, education towards vitamin D must be a part of all family medicine residency programs.

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In a study including several European countries with supplementation programs, it was recommended that monitoring administration of vitamin D during child health surveillance visits increases adherence [9] . In the project for vitamin D supplementation in Turkey, it was stated that an additional program is not necessary for monitoring and it is sufficient to question administration during scheduled vaccinations of the infants [39] . In our study in 37,8% of infants who were not supplemented, this was caused by at a significantly higher rate by nurses than family physicians. The primary reason for vitamin D discontinuation among nurses was the belief of sufficient duration of supplementation (82,3%) and the rate of withdrawal, for this reason, was higher among infants aged between 13-24 months (90,7%) when compared to 1-12 months (9,3%). This might be the consequence of nurses' lack of information about vitamin D. Thus education about vitamin D supplementation can be implemented in nursing school programs to avoid high discontinuation rates.

To be a 'Baby-friendly Family Medicine Unit', family physicians and nurses working there receive training, take an exam and consequently receive a certificate and they get inspected on this subject regularly. However, this training is on breastfeeding and supplementary foods and does not contain information about vitamin D supplementation. We believe that including education on supplementation in this certificate program would increase the awareness of healthcare providers and it would be practical to add new subjects to an ongoing education rather than start a new program. Thus, healthcare providers can explain the aim and benefits of vitamin D to parents, reminding parents to give their children vitamin D supplements at each visit.

5. Conclusions

Since vitamin D supplementation rates were higher in families who visited their family physicians regularly, they must be encouraged to visit their family physician for well-baby visits at every opportunity. The newborn unit can be an ideal place to start a program that educates breastfeeding families about the need for supplements, as only breastfeeding infants receive less vitamin D. Healthcare providers has the most important role in supplementation practices, so they must participate in education programs on initiation and continuation of vitamin D supplements within the strategy of preventing vitamin D deficiency.

The limitation of this study is that it reflects regional results, so further studies at a national scale are required regarding supplementation practices. The low continuation rates of supplementation in our study, because of advice by healthcare providers, revealed the need for other studies to assess the knowledge and attitudes family of physicians and nurses directly by asking them.

Author Contributions: Conceptualization, S.H.K and T.S.; methodology, T.S.; validation, S.H.K, T.S; formal analysis, S.H.K; investigation, S.H.K.; resources, T.S.; data curation, T.S.; writing—original draft preparation, S.H.K.; writing—review and editing, S.H.K, T.S.; visualization, S.H.K.; supervision, T.S.; project administration, T.S. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

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Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Ethics Committee of T.R. Health Sciences University Ankara Pediatric Hematology-Oncology Research and Training Hospital (protocol code 85 and June 2017).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. DeLuca HF. Overview of general physiologic features and functions of vitamin D. *Am J Clin Nutr*. 2004;80,1686-1689.
2. Bikle D. Nonclassic actions of vitamin D. *J Clin Endocrinol Metab*. 2009;9,26-34.
3. Hyppönen E, Läärä E, Reunanen A, Järvelin MR, Virtanen SM. Intake of vitamin D and risk of type 1 diabetes: a birth-cohort study. *Lancet*. 2001;358,1500-1503.
4. Lappe JM, Travers-Gustafson D, Davies KM, Recker RR, Heaney RP. Vitamin D and calcium supplementation reduces cancer risk: results of a randomized trial. *Am J Clin Nutr.* 2007;85,1586-1591.
5. Walker VP, Modlin RL. The vitamin D connection to pediatric infections and immune function. *Pediatr Res*. 2009;65,106-113.
6. Greenbaum LA. Rickets and Hypervitaminosis D. In: Kliegman RM. ed. Nelson Textbook of Pediatrics. 21st ed. Elsevier; 2019;200-208.
7. Greer FR. Vitamin D Deficiency - It ' S More Than Rickets. *J Pediatr*. 2003;143,422-423.
8. Munns CF, Shaw N, Kiely M, Specker BL, Thacher TD, Ozono K, Michigami T, Tiosano D, Mughal MZ, Mäkitie O, Ramos-Abad L, Ward L, DiMeglio LA, Atapattu N, Cassinelli H, Braegger C, Pettifor JM, Seth A, Idris HW, Bhatia V, Fu J, Goldberg G, Sävendahl L, Khadgawat R, Pludowski P, Maddock J, Hyppönen E, Oduwole A, Frew E, Aguiar M, Tulchinsky T, Butler G, Högler W. Global Consensus Recommendations on Prevention and Management of Nutritional Rickets. *J Clin Endocrinol Metab.* 2016;101,394-415.
9. Uday S, Kongjonaj A, Aguiar M, Tulchinsky T, Högler W. Variations in infant and childhood vitamin D supplementation programmes across Europe and factors influencing adherence. *Endocr Connect*.2017;6,667-675.
10. Gallo S, Jean-Philippe S, Rodd C, Weiler HA. Vitamin D supplementation of Canadian infants: practices of Montreal mothers *App. Physio. Nutr Metab*. 2010;35,303-309.
11. Hatun S, Ozkan B, Bereket A. Vitamin D deficiency and prevention: Turkish experience. *Acta Paediatr.* 2011;100,1195-1199.
12. Hatun S, Bereket A, Ozkan B, Coskun, Kose R, Calikoglu AS. Free vitamin D supplementation for every infant in Turkey. *Arch Dis Child*. 2007;92,373-374.
13. Özdemir A, Ercan Gündemir Y, Küçük M, Yıldıran Sarıcı D, Elgörmüş Y, Çağ Y, Bilek G. Vitamin D Deficiency in Pregnant Women and Their Infants. *J Clin Res Pediatr Endocrinol*. 2018;10,44-50.
14. Hocaoglu-Emre FS, Saribal D, Oguz O. Vitamin D deficiency and insufficiency according to the current criteria for children: Vitamin D status of elementary school children in Turkey. *J Clin Res Pediatr Endocrinol*. 2019;11,181-188.
15. Andiran N, Celik N, Akca H, Dogan G. Vitamin D deficiency in children and adolescents. *J Clin Res Pediatr Endocrinol.* 2012;4,25-29.
16. Ozcan A, Kendirci M, Kondolot M, Kardas F, Akin L. Evaluation of Vitamin D prophylaxis in 3-36-month-old infants and children. *J Pediatr Endocrino. Metab.* 2017;30,543-549.

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17. Ozkan B, Doneray H, Karacan M, Vancelik S, Yıldırım K, Ozkan A, Kosan C, Aydın K. Prevalence of vitamin D deficiency rickets in the eastern part of Turkey. *Eur J Pediatr.* 2009;168,95-100.
18. Alramdhan AM, El-Zubair AG. Poor vitamin D supplementation in infants: Cross-sectional study of maternal practices and awareness of vitamin D supplementation in infants in Al-Ahsa, Eastern Saudi Arabia. *Saudi Med J.* 2014;35,67-71.
19. Dratva J, Merten S, Ackermann-Liebrich U. Vitamin D supplementation in Swiss infants. *Swiss Med Wkly*. 2016;136,473-481.
20. Perrine CG, Sharma AJ, Jefferds MED, Serdula MK, Scanlon KS. Adherence to Vitamin D Recommendations Among US Infants. *Pediatrics*. 2010;125,627-632.
21. Koc F, Halicioglu O, Asik Akman S, Aksit S.Vitamin D supplementation during the first two years of life in Izmir, Turkey. *Minerva Pediatr*. 2014;66,141-146.
22. Elitok GK, Bulbul L, Bulbul A, Cigerli S, Uslu S. Vitamin D levels of 12-24-month-old healthy children in Turkey who received Vitamin D supplementation until the age of one year. *Arch Argent Pediatr.* 2020;118,95-101.
23. Østergård M, Arnberg K, Michaelsen KF, Madsen AL, Krarup H, Trolle E, Mølgaard C. Vitamin D status in infants: Relation to nutrition and season. *Eur J Clin Nutr.* 2011;65,657-660.
24. Taylor JA, Geyer LJ, Feldman KW. Use of Supplemental Vitamin D Among Infants Breastfed for Prolonged Periods. *Pediatrics.* 2010;125,105-111.
25. Sherman EM, Svec RV. Barriers to Vitamin D Supplementation Among Military Physicians. *Mil Med.* 2009;174,302-307.
26. Simon AE, Ahrens KA. Adherence to Vitamin D Intake Guidelines in the United States. Pediatrics. 2020;145: e2019357
27. Kara Elitok G, Bulbul L, Zubarioglu U, et al. How should we give Vitamin D supplementation? evaluation of the pediatricians' knowledge in Turkey. *Ital J Pediatr.* 2017;43,95.
28. Gedikbası D, Hatun S. D vitamini yetersizligi ve D vitamini destegi konusunda pratisyen hekimlerin tutumları. *Surekli Tıp Egit Derg*. 2004;13,16-18.
29. Silk H, Thiede S, Trojian T. Counseling about vitamin D supplementation for infants: Results of a survey of pediatric and family medicine physicians in Connecticut. *Conn Med*. 2007;71,133-137.
30. Babli A, AlDawood KM, Khamis AH. Knowledge, attitude, and practice of general practitioners in Dammam, Saudi Arabia towards Vitamin D supplementation to infants. *J Fam Community Med*. 2015;22,135-139.
31. Catakli T, Tasar S, Ogulluk M, Bilge Y Knowledge and practice of mothers regarding vitamin D supplementation admitted to an hospital. *Ege J Med* 2014; 53,135-40.
32. Gulez P, Korkmaz HA, Ozkok D, Can D, Ozkan B. Factors influencing serum vitamin D concentration in Turkish children residing in İzmir: A single-center experience. *J Clin Res Pediatr Endocrinol*. 2015;7,294-300.
33. Santi M, Janner M, Simonetti GD, Lava SAG. Prescription of vitamin D among Swiss pediatricians. E*ur J Pediatr.* 2019;178,1119-1123.
34. Turkiye'de 6–17 Aylık Çocuklarda ve Annelerinde Hemoglobin Ferritin D Vitamini Duzeyi ve Demir Eksikliği Anemisi Durum Belirleme Yurutulen Programların Değerlendirilmesi Araştırması.Ankara: Sağlık Bakanlığı Yayınları, 2011: 79–88.
35. Seymen Karabulut G, Hatun S, Bideci A, Hasanoglu E. Attitudes of Pediatricians Regarding Prevention and Treatment of Vitamin D Deficiency. *J Clin Res Pediatr Endocrinol*. 2016;8,368-71.
36. Yesiltepe Mutlu G, Hatun S. Use of Vitamin D in Children and Adults: Frequently Asked Questions. *J Clin Res Pediatr Endocrinol.* 2018;10,301-306.

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 19 April 2021 doi:10.20944/preprints202104.0487.v1

37. Ferraro PM, Taylor EN, Gambaro G, Curhan G. Vitamin D Intake and the Risk of Incident Kidney Stones. *J Urol.* 2017;197,405-410.
38. Malihi Z, Wu Z, Stewart AW, Lawes CM, Scragg R. Hypercalcemia, hypercalciuria, and kidney stones in long-term studies of Vitamin D supplementation: A systematic review and meta-analysis. *Am J Clin Nutr.* 2016;104,1039-1051.
39. Coskun T, Hatun S, Bereket A, Cesur Y, Ozkan B. D vitamini yetersizliğinin önlenmesi ve kemik sağlığının korunması projesi rehberi. *Surekli Tıp Egit Derg*. 2005;14:5.