



Prevalence and Deficiency of Vitamin D among Children in Gharyan City: A Descriptive Study

Amal Abdussalam A. Hmaid ^{1*}, Amani Abdussalam A. Hmaid ², Abdulmutalib Mohammed Alarbi ³, Hana Dhaw A. Awn ⁴, Aya Nooreddin Nassr ⁵, Haadil Jumaa M. Idaab ⁶

^{1,4,5,6} Department of Zoology, Faculty of Science, Gharyan, University of Gharyan, Libya

² Department of Environment & Natural Resources, Faculty of Science, University of Gharyan, Gharyan, Libya

³ Department of Statistics, Faculty of Science, University of Gharyan, Gharyan, Libya

تقييم انتشار ونقص فيتامين (د) لدى الأطفال في مدينة غريان: دراسة وصفية

أمال عبدالسلام على احمد ^{1*}، أماني عبدالسلام على احمد ²، عبدالمطلب محمد العربي ³، هناء ضو علي ⁴، آية نور الدين نصر ⁵، هديل جمعة دعاب ⁶

^{1,4,5,6} قسم علم الحيوان، كلية العلوم، جامعة غريان، غريان، ليبيا

² قسم البيئة والموارد الطبيعية، كلية العلوم، جامعة غريان، غريان، ليبيا

³ قسم الاحصاء، كلية العلوم، جامعة غريان، غريان، ليبيا

*Corresponding author: amal.hmaid@gu.edu.ly

Received: August 28, 2024

Accepted: October 08, 2024

Published: October 15, 2024

Abstract:

Vitamin D deficiency is a prevalent health issue among children, with potential consequences for bone health and overall well-being. This study aimed to investigate the prevalence of vitamin D deficiency in a pediatric population and identify associated factors. A cross-sectional study was conducted on 400 children (aged 1-10 years) recruited from medical laboratories in Gharyan City, Libya, between January 2022 and June 2024. Participants were categorized based on their vitamin D levels (deficient, insufficient, adequate, or optimal). Demographic data (age, gender) and vitamin D levels were collected and analyzed using descriptive statistics and two-way ANOVA. Approximately half of the study participants (49.75%) exhibited vitamin D deficiency. Females had a slightly higher prevalence of deficiency (27.5%) compared to males (22.25%). Significant differences in vitamin D levels were observed across age groups. Infants under 12 months had higher levels compared to older children (36-72 months). While gender was not a significant predictor of vitamin D deficiency in our study, previous research has suggested potential gender-related disparities. The findings of this study highlight the concerning prevalence of vitamin D deficiency among children in the region. Age appears to be a significant factor influencing vitamin D status, with younger children being more susceptible to deficiency. While gender may not be a major determinant in this population. The high prevalence of vitamin D deficiency in our study underscores the importance of promoting sun exposure, dietary intake of vitamin D-rich foods, and supplementation strategies to address this public health issue. Further research is needed to explore the underlying factors contributing to vitamin D deficiency in children

Keywords: vitamin D, vitamin D deficiency, infants and children, supplementation VD.

الملخص

نقص فيتامين د هي مشكلة صحية شائعة بين الأطفال، وقد تؤدي إلى عواقب محتملة على صحة العظام والرفاهية العامة. هدفت هذه الدراسة إلى التحقيق في انتشار نقص فيتامين د بين الأطفال وتحديد العوامل المرتبطة به. أجريت دراسة على 400 طفل (من عمر 1 إلى 10 سنوات) تم تجميع بياناتهم من عدد من المختبرات الطبية في مدينة غريان، ليبيا، بين يناير 2022 ويونيو 2024. تم تصنيف المشاركين بناءً على مستويات فيتامين د لديهم (ناقص، غير كافٍ، كافٍ، أو مثالي). وتم جمع البيانات الديموغرافية (العمر، الجنس) ومستويات فيتامين د وتحليلها باستخدام الإحصائيات الوصفية وتحليل التباين التثلاثي (ANOVA). أظهر حوالي نصف المشاركين في الدراسة (49.75%) نقصاً في فيتامين د. كانت نسبة النقص أعلى لدى الإناث (27.5%) مقارنة بالذكور (22.25%). كما لوحظ وجود اختلافات كبيرة في مستويات فيتامين د بين الفئات العمرية. كان لدى الرضع دون سن 12 شهراً مستويات أعلى مقارنة بالأطفال الأكبر سناً (36-72 شهراً). على الرغم من أن الجنس لم يكن عاملاً مؤثراً كبيراً في نقص فيتامين د في دراستنا، فقد أشارت

الأبحاث السابقة إلى احتمالية وجود اختلافات مرتبطة بالجنس. تسلط نتائج هذه الدراسة الضوء على الانتشار المقلق لنقص فيتامين د بين الأطفال في المنطقة. يبدو أن العمر هو عامل مؤثر كبير على حالة فيتامين د، حيث يكون الأطفال الأصغر سناً أكثر عرضة للنقص. بينما قد لا يكون الجنس عاملاً رئيسياً في هذا المجتمع، تشير الدراسات السابقة إلى احتمالية وجود اختلافات مرتبطة بالجنس. أيضاً يشدد ارتفاع انتشار نقص فيتامين د في دراستنا على أهمية تعزيز التعرض لأشعة الشمس، وتناول الأطعمة الغنية بفيتامين د، واستراتيجيات المكملات الغذائية لمعالجة هذه المشكلة الصحية العامة. يلزم إجراء المزيد من الأبحاث لاستكشاف العوامل الكامنة وراء نقص فيتامين د لدى الأطفال.

الكلمات المفتاحية: فيتامين د، نقص فيتامين د، حديثي الولادة والأطفال، المكملات.

Introduction

Vitamins are necessary nutrients for the best possible growth and function of the body. Water-soluble and fat-soluble vitamins are the two primary types of vitamins. Vitamins that are fat-soluble, including A, D, E, and K, are essential for numerous physiological functions. Many health issues can arise from a vitamin deficiency. These vitamins have different suggested daily intakes; vitamin D, for example, usually needs higher quantities (8000–5000 micrograms/day) because of its involvement in bone health and calcium absorption [1]. The liver transforms vitamin D—whether it comes from oral supplements or is produced by exposure to UV radiation—into 25-hydroxyvitamin D [25(OH)D]. Vitamin D₂ (ergocalciferol) and vitamin D₃ (cholecalciferol) are the two main forms of vitamin D. The human body's metabolic pathways for these two types are nearly the same, despite the minor structural variations in their side chains [2,3]. Vitamin D levels are determined by measuring this metabolite. Vitamin D has antioxidant qualities in addition to controlling calcium and phosphorus. It also encourages bone mineralization, boosts phosphate reabsorption, and stimulates cell proliferation [4, 5, 6]. Through its ability to suppress the creation of blood vessels around tumors and so cut off the supply of nutrients needed for tumor growth; vitamin D also lowers the risk of cancer. In addition, it lowers the risk of cardiovascular illnesses by blocking the blood pressure-regulating renin-angiotensin system. It also lowers the chance of respiratory infections including COVID-19 and influenza, as well as type 1 and type 2 diabetes [7]. Low levels of vitamin D cause the intestines to absorb calcium less well, which lowers blood calcium levels. As a result, several various disorders are caused by vitamin D insufficiency (VDD) [8]. Restricted fetal growth has also been linked to VDD in pregnant women [9]. Furthermore, this deficit can result in low birth weight, high incidence of cesarean sections, gestational diabetes, and other health issues for both the mother and the child. [10, 11, 12], VDD can have grave repercussions. may result in rickets in children, which is characterized by weak and malformed bones. Adults with a vitamin D deficit may develop osteomalacia (softening of the bones), osteoporosis, or persistent muscle soreness. Furthermore, vitamin D is essential for the growth of the lungs, teeth, bones, and nervous system in fetuses [13, 14, 15]. Numerous unfavorable health consequences for the pregnancy and the baby have been linked to VDD. Hypocalcemia in neonates and heightened vulnerability to respiratory infections have been associated with intrauterine vitamin D insufficiency [16, 17]. Moreover, vitamin D insufficiency has been linked to poor growth, type 1 diabetes, asthma, delayed heart growth in infants, and an elevated risk of HIV transmission [18]. Numerous non-skeletal illnesses, such as neurological conditions, cardiovascular conditions, autoimmune diseases, and even some forms of cancer, have been closely associated with VDD [19]. Newborns with VDD have been common, particularly those whose moms did not take vitamin D supplements or get enough sun exposure [20]. The prevalence of vitamin D deficiency (VDD) in infants who are exclusively breastfed without supplementation varies greatly, with values ranging from 0.6% in Nepalese children at seven months of age [22] to as high as 83% in Qatari newborns at one month of age [23]. This variation can be attributed to the low quantities of vitamin D found in breast milk [21]. Numerous factors, such as geographical location (latitude and season), skin pigmentation, dress behaviors, and methodological discrepancies, are probably responsible for these disparities [24, 25]. Although vitamin D deficiency (VDD) has been associated with a number of health issues, vitamin D supplementation has demonstrated potential to improve a number of health outcomes, including positive effects on total T4 and TSH levels in patients with type 2 diabetes who also have thyroid abnormalities. Additionally, taking vitamin D supplements is a safe, affordable way to improve general health [26, 27]. A 25(OH)D level less than 20 ng/mL is considered very low disease (VDD), according to the National Academy of Sciences (NAS) and the Recommended Dietary Allowance (RDA). On the other hand, vitamin D deficiency was classified as less than 12 ng/mL, insufficiency as 12–20 ng/mL, and sufficient as 50 nmol/L (20 ng/mL) in the 2016 Global Consensus Guidelines [25, 28]. Regular sun exposure is essential for maintaining proper amounts of vitamin D because it allows the body to produce the nutrient. For humans, sunlight is the main source of vitamin D, accounting for about 80% of our daily requirements. The amount of vitamin D generated in the skin is influenced by the sun's angle, which is influenced by latitude, season, and time of day [29, 30]. Maintaining a balanced diet full of foods high in vitamin D, such as eggs, dairy products with added vitamin D, and fatty fish, is also crucial [31]. Liver and kidney disorders may cause VDD. Enzymes necessary for the synthesis and activation of vitamin D are present in both organs. Vitamin D levels can be reduced as a result of these processes being disrupted by impaired liver or kidney function, such as cirrhosis or renal failure [32]. An additional important risk factor for VDD is

obesity. Adipose tissue stores vitamin D since it is a fat-soluble vitamin. Because vitamin D is sequestered in fat cells, those with a body mass index higher than 30 kg/m² may have reduced vitamin D distribution. Children who are overweight or obese, particularly those who have morbid obesity, are more likely to develop VDD [33, 34, 35, 36]. Vitamin D metabolism can be accelerated by several medicines. Cytochrome P450 enzymes, for instance, are involved in the breakdown of vitamin D. Drugs that cause these enzymes can raise the metabolism of vitamin D, which lowers blood levels of the vitamin [37, 38]. It is possible for someone with mild or moderate VDD to not show any obvious symptoms. Severe deficiency, however, can result in a number of health issues, such as exhaustion, hair loss, and other issues [39, 40]. Particularly for youngsters, the threshold for classifying vitamin D deficiency (VDD) based on serum 25-hydroxyvitamin D levels is still debatable. This is because there is insufficient solid clinical data to back up particular cutoff numbers. Because of its lengthy half-life, generally constant blood levels, and limited sensitivity to variations in parathyroid hormone (PTH), 25-hydroxyvitamin D is frequently employed to evaluate vitamin D status [41, 42, 43, 44].

VDD is associated with an increased risk of several diseases, making it a well-known public health concern. Numerous studies have been done by scientists worldwide to solve this issue. The purpose of this study is to determine the underlying causes of vitamin D deficiency and to measure the levels of vitamin D in a sample of children in Gharyan. The possible influence of gender on vitamin D status will be examined in this study. The study will also look at the connection between age and vitamin D levels.

Material and methods

The study sample comprised 400 children, equally divided by gender and age (1-10 years), recruited from medical laboratories in Gharyan city (Al-Daka Laboratory, Al-Thiqa Laboratory, and Al-Safaa Clinic Laboratory) between January 2022 and June 2024. Participants were categorized as vitamin D deficient, Insufficient, Adequate and optimum. Data collected included age, and gender, All the subjects were divided into subgroups according to their age (< 12 months, 12-36 months, 36-72 months, ≥ 72 months) and vitamin D levels, measured using standard laboratory protocols.

Statistical methods used in the study:

A descriptive approach was employed by calculating frequencies and percentages of the study sample's responses to all questionnaire items. Two-way ANOVA was used, along with post hoc comparisons for hypotheses with significant differences. Study hypotheses:

1. There is no statistically significant difference in mean vitamin D levels between males and females.
2. There is no statistically significant difference in mean vitamin D levels between different age groups.
3. There is no statistically significant interaction effect between gender and age on mean vitamin D levels.

Results and discussion

Table (1) Analysis of Descriptive Statistics.

L.V.D	Gender	Frequency	Percentage
Deficient	m	89	22.25%
	f	110	27.5%
Insufficient	m	86	21.5%
	f	66	16.5%
Adequate	m	21	5.25%
	f	17	4.255%
Optimum	m	3	0.75%
	f	8	2%
Total		400	100.0%

The table reveals that L.V.D deficiency is more prevalent among females (27.5%) than males (22.25%). Additionally, L.V.D insufficiency is more common in males (21.5%) compared to females (16.5%). Both genders exhibit low levels of sufficient (5.25% for males, 4.25% for females) and optimal (0.75% for males, 2% for females) L.V.D.

Approximately half of our study participants (49.75%) reported vitamin D deficiency. Notably, this prevalence is similar to the 45.5% rate reported in Saudi Arabia (960/2110)[45] However, a study in the United States of America (USA) found a lower prevalence of vitamin D deficiency among healthy infants and toddlers, reaching 40% (146/365) [46]. Furthermore, the prevalence of vitamin D deficiency and rickets remains unacceptably

high in regions such as Asia, Africa, and the Middle East [47]. Another study in China, involving 6008 children aged 1 to 16 years, observed a lower prevalence of vitamin D deficiency compared to vitamin D insufficiency.[48]

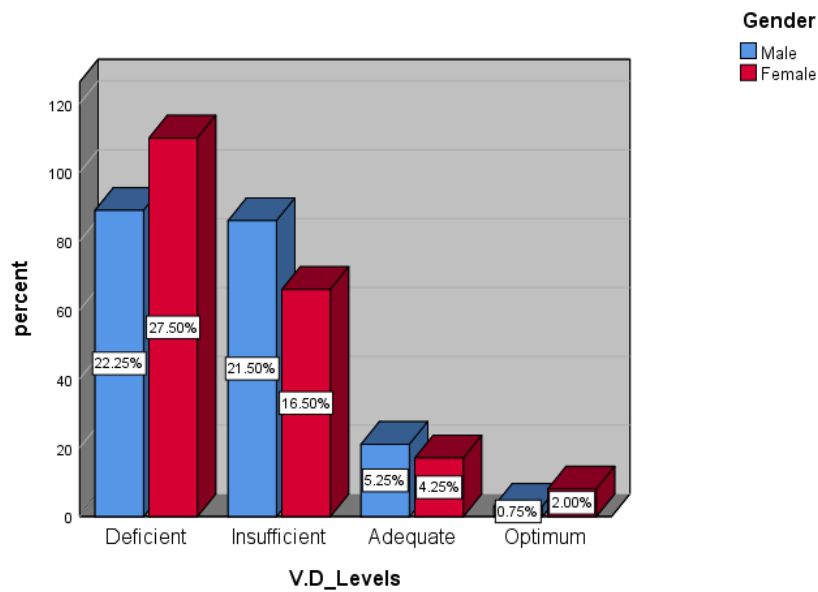


Figure 1 Vitamin D levels according to the gender variable.

These findings suggest that among the study participants, gender had no discernible effect on the existence or absence of vitamin D insufficiency. Our results conflict with those of a study by [49], which found a statistically significant difference in the levels of vitamin D deficiency in children, male and female. This difference could be explained by the fact that our sample of children was not as likely as the male youngsters in their study to be overweight. However, these results are consistent with a prior study [50] that found gender does not appear to be a significant determinant in vitamin D deficiency.

Table (2): Two-Way ANOVA

Tests of Between-Subjects Effects						
Dependent Variable: V.D Levels						
Source	Type III Sum of Squares	Df	Mean Square	F	Sig.	Partial Eta Squared
Gender	.274	1	.274	.483	.487	.001
Age	9.716	3	3.239	5.720	.001	.042
Gender * Age1	.577	3	.192	.340	.797	.003
Error	221.968	392	.566			
Total	1325.000	400				
Corrected Total	232.697	399				

Analysis of Results:

Gender: The relationship between gender and vitamin D levels was not statistically significant (Sig = 0.487). With a very small partial eta squared value (0.001), gender was shown to explain very little of the variation in vitamin D levels.

Age: It was discovered that age had a statistically significant impact on vitamin D levels (Sig = 0.001). The partial eta squared value of 0.042 indicates a mild to moderate effect, meaning that age explained 4.2% of the variation in vitamin D levels.

Gender and Age Interaction: There was no statistically significant interaction impact on vitamin D levels between gender and age (Sig = 0.797). The extremely low partial eta squared value (0.003) suggests that the variation in vitamin D levels was only marginally explained by this interaction.

Overall, we discover that there was no statistically significant difference between gender and vitamin D levels. Vitamin D levels were statistically significantly impacted by age, with a small to moderate effect size. Between gender and age, there was no statistically significant interaction.

Table (3): Multiple Comparisons						
Dependent Variable: Level_V.D						
Scheffe						
(I) Age	(J) Age	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
< 12 months	12-36 months	-.0895-	.19533	.976	-.6379-	.4589
	36-72 months	.5035	.18800	.068	-.0244-	1.0313
	> 72months	.2884	.18003	.464	-.2170-	.7939
12-36 months	< 12 months	.0895	.19533	.976	-.4589-	.6379
	36-72 months	.5930*	.17062	.008	.1140	1.0720
	> 72months	.3780	.16179	.143	-.0763-	.8322
36-72 months	< 12 months	-.5035-	.18800	.068	-1.0313-	.0244
	12-36 months	-.5930-*	.17062	.008	-1.0720-	-.1140-
	> 72months	-.2150-	.15287	.577	-.6442-	.2142
> 72months	< 12 months	-.2884-	.18003	.464	-.7939-	.2170
	12-36 months	-.3780-	.16179	.143	-.8322-	.0763
	36-72 months	.2150	.15287	.577	-.2142-	.6442

The table (3) presents the results of post hoc comparisons using the Scheffé method to determine statistically significant differences in mean vitamin D levels across different age groups. Results indicate a statistically significant difference in mean vitamin D levels between infants under 12 months and children aged 36-72 months, with the younger group having higher levels. Similarly, there was a statistically significant difference between children aged 12-36 months and those aged 36-72 months, with the 12-36-month age group having higher levels. No other significant differences were found between the remaining age groups. These findings suggest that variations in age between the research populations affect whether vitamin D insufficiency is present or not. This discovery is predicted, given dietary choices and daily activities vary across different age groups, which might contribute to vitamin D insufficiency. Contributing reasons could include moms' neglect, not giving kids vitamin D supplements, and kids' dread of the sun and outside activities. This is confirmed by [23,51, 52,53] which reported that just 25.6% of newborns in their London-based study were exposed to sunshine by their mothers, compared to 65.1% who were not. [54] also discovered a link between low sun exposure and a higher risk of vitamin D insufficiency, nutritional rickets, and rickets in the US. The relationship between gender and vitamin D levels was not statistically significant. With a small to moderate effect size, age had a statistically significant impact on vitamin D levels. Age and gender did not interact in a way that was statistically significant. Research to date backs up the safety and efficacy of pulse therapy, often known as "stoss therapy," in treating childhood vitamin D deficiency, even if the majority of current recommendations are based on expert opinion. [55]

Table 4: Vitamin D Dosing for Children's Nutritional Vitamin D Deficiency Prevention and Treatment with Vitamin D Supplementation (Cholecalciferol).

Vitamin D Supplementation (Cholecalciferol)	
Prevention	400 IU/day
Treatment	< 1 month: 1000 IU/day orally for × 2-3 months
	1-12 months: 1000-5000 IU/day orally for × 2-3 months
	> 12 months: 5000 IU/day orally for × 2-3 months

IU; International Unit

Conclusion

The study highlights the alarming rate of vitamin D deficiency in the region, especially among younger children. Age appears to be a significant factor, but gender may also play a role, as suggested by previous research. To address this public health issue, promoting sun exposure, incorporating vitamin D-rich foods into diets, and implementing supplementation strategies are crucial. Further research is necessary to delve into the underlying causes of vitamin D deficiency in children and develop effective interventions. Despite its preventability, vitamin D deficiency continues to be a persistent health concern among children.

References

1. Kamangar, Farin, and Ashkan Emadi. "Vitamin and mineral supplements: do we really need them?." *International journal of preventive medicine* 3.3 (2012): 221.
2. Rodríguez-Gil, Alfonso, et al. "Effect of vitamin D on graft-versus-host disease." *Biomedicines* 10.5 (2022): 987.
3. Gil, Ángel, Julio Plaza-Díaz, and María Dolores Mesa. "Vitamin D: classic and novel actions." *Annals of Nutrition and Metabolism* 72.2 (2018): 87-95.
4. Christakos, S., Dhawan, P., Verstuyf, A., Verlinden, L., & Carmeliet, G. "Vitamin D: metabolism, molecular mechanism of action, and pleiotropic effects." *Physiological reviews* 96.1 (2016): 365-408.
5. Wei, Ran, and Sylvia Christakos. "Mechanisms underlying the regulation of innate and adaptive immunity by vitamin D." *Nutrients* 7.10 (2015): 8251-8260.
6. Lee, Ji Yeon, Tsz-Yin So, and Jennifer Thackray. "A review on vitamin d deficiency treatment in pediatric patients." *The Journal of Pediatric Pharmacology and Therapeutics* 18.4 (2013): 277-291.
7. Grant, W. B., Boucher, B. J., Al Anouti, F., & Pilz, S. "Comparing the evidence from observational studies and randomized controlled trials for nonskeletal health effects of vitamin D." *Nutrients* 14.18 (2022): 3811.
8. Kowalówka, M., Główska, A. K., Karaźniewicz-Łada, M., & Kosewski, G. "Clinical significance of analysis of vitamin D status in various diseases." *Nutrients* 12.9 (2020): 2788.
9. Chen, Y. H., Liu, Z. B., Ma, L., Zhang, Z. C., Fu, L., Yu, Z., ... & Wang, H. "Gestational vitamin D deficiency causes placental insufficiency and fetal intrauterine growth restriction partially through inducing placental inflammation." *The Journal of Steroid Biochemistry and Molecular Biology* 203 (2020): 105733.
10. Poel, Y. H. M., Hummel, P., Lips, P. T. A. M., Stam, F., Van Der Ploeg, T., & Simsek, S. "Vitamin D and gestational diabetes: a systematic review and meta-analysis." *European journal of internal medicine* 23.5 (2012): 465-469.
11. Scholl, Theresa O., Xinhua Chen, and Peter Stein. "Maternal vitamin D status and delivery by cesarean." *Nutrients* 4.4 (2012): 319-330.
12. Burris, H. H., Rifas-Shiman, S. L., Camargo Jr, C. A., Litonjua, A. A., Huh, S. Y., Rich-Edwards, J. W., & Gillman, M. W. "Plasma 25-hydroxyvitamin D during pregnancy and small-for-gestational age in black and white infants." *Annals of epidemiology* 22.8 (2012): 581-586.
13. Wong, A. Y., Chan, E. W., Chui, C. S., Sutcliffe, A. G., & Wong, I. C. "The phenomenon of micronutrient deficiency among children in China: a systematic review of the literature." *Public health nutrition* 17.11 (2014): 2605-2618.
14. Bahinipati, Jyotirmayee, and Rg Asutosh Mohapatra. "Serum magnesium and vitamin D in patients presenting to the orthopedics out-patient department with chronic low back pain." *Biomedical and Pharmacology Journal* 13.1 (2020): 347-352.
15. Thacher, Tom D., and Bart L. Clarke. "Vitamin D insufficiency." *Mayo Clinic Proceedings*. Vol. 86. No. 1. Elsevier, 2011.
16. Belderbos, M. E., Houben, M. L., Wilbrink, B., Lentjes, E., Bloemen, E. M., Kimpen, J. L., ... & Bont, L. "Cord blood vitamin D deficiency is associated with respiratory syncytial virus bronchiolitis." *Pediatrics* 127.6 (2011): e1513-e1520.
17. Mehrotra, P., Marwaha, R. K., Aneja, S., Seth, A., Singla, B. M., Ashraf, G., ... & Tandon, N. "Hypo vitaminosis d and hypo calcemic seizures in infancy." *Indian pediatrics* 47 (2010): 581-586.
18. Barrett, Helen, and Aidan McElduff. "Vitamin D and pregnancy: An old problem revisited." *Best practice & research Clinical endocrinology & metabolism* 24.4 (2010): 527-539.
19. Han, A., Park, Y., Lee, Y. K., Park, S. Y., & Park, C. Y. "Position statement: vitamin D intake to prevent osteoporosis and fracture in adults." *Journal of Bone Metabolism* 29.4 (2022): 205.
20. Vierucci, F., Fusani, L., Saba, A., Minucciani, T., Belluomini, M. P., Domenici, R., ... & Federico, G. "Gestational vitamin D3 supplementation and sun exposure significantly influence cord blood vitamin D status and 3-epi-25-hydroxyvitamin D3 levels in term newborns." *Clinica Chimica Acta* 524 (2022): 59-68.
21. Højskov, C. S., Møller, U. K., Heickendorff, L., Vestergaard, P., Mosekilde, L., & Rejnmark, L. "Vitamin D content in human breast milk: a 9-mo follow-up study." *The American Journal of Clinical Nutrition* 103.1 (2016): 107-114.
22. Haugen, J., Ulak, M., Chandyo, R. K., Henjum, S., Thorne-Lyman, A. L., Ueland, P. M., ... & Strand, T. A. "Low prevalence of vitamin D insufficiency among Nepalese infants despite high prevalence of vitamin D insufficiency among their mothers." *Nutrients* 8.12 (2016): 825.
23. Salameh, K., Al-Janahi, N. S. A., Reedy, A. M., & Dawodu, A. "Prevalence and risk factors for low vitamin D status among breastfeeding mother–infant dyads in an environment with abundant sunshine." *International Journal of Women's Health* (2016): 529-535.

24. Kasalová, E., Aufartová, J., Krčmová, L. K., Solichová, D., & Solich, P. "Recent trends in the analysis of vitamin D and its metabolites in milk—A review." *Food chemistry* 171 (2015): 177-190.
25. Munns, C. F., Shaw, N., Kiely, M., Specker, B. L., Thacher, T. D., Ozono, K., ... & Höglér, W. "Global consensus recommendations on prevention and management of nutritional rickets." *The Journal of Clinical Endocrinology & Metabolism* 101.2 (2016): 394-415.
26. Alemam, H. A., Omar, A. A., Alfaid, M. M., Alarbi, A. M., Sweidan, A. M., & Ibrahim, K. M. "Beneficial Role of Vitamin D Supplementation on Thyroid Hormone Levels among T2DM Patients with Thyroid Disorders: Statistical Evaluation."
27. Rebelos, Eleni, Nikolaos Tentolouris, and Edward Jude. "The role of vitamin D in health and disease: A narrative review on the mechanisms linking vitamin D with disease and the effects of supplementation." *Drugs* 83.8 (2023): 665-685.
28. EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA). "Dietary reference values for vitamin D." *EFSA journal* 14.10 (2016): e04547.
29. Vitamin, D. "deficiency. Holick MF." *N Engl J Med* 357 (2007): 266-281.
30. Nair, Rathish, and Arun Maseeh. "Vitamin D: The "sunshine" vitamin." *Journal of pharmacology and pharmacotherapeutics* 3.2 (2012): 118-126.
31. Cashman, K. D., & Kiely, M. (2016). Tackling inadequate vitamin D intakes within the population: fortification of dairy products with vitamin D may not be enough. *Endocrine*, 51, 38-46.
32. Elahjal, M., Elhaji, F., Rhoma, A., Elkouha, M., Ferrara, N., & Ashour, A. "Vitamin D Insufficiency and Deficiency in Chronic Kidney Disease Patients on Hemodialysis." *AlQalam Journal of Medical and Applied Sciences* (2023): 484-488.
33. Turer, Christy B., Hua Lin, and Glenn Flores. "Prevalence of vitamin D deficiency among overweight and obese US children." *Pediatrics* 131.1 (2013): e152-e161.
34. Alemzadeh, Ramin, et al. "Hypovitaminosis D in obese children and adolescents: relationship with adiposity, insulin sensitivity, ethnicity, and season." *Metabolism* 57.2 (2008): 183-191.
35. Yanoff, L. B., Parikh, S. J., Spitalnik, A., Denkinger, B., Sebring, N. G., Slaughter, P., ... & Yanovski, J. A. "The prevalence of hypovitaminosis D and secondary hyperparathyroidism in obese Black Americans." *Clinical endocrinology* 64.5 (2006): 523-529.
36. Rajakumar, K., de Las Heras, J., Chen, T. C., Lee, S., Holick, M. F., & Arslanian, S. A. "Vitamin D status, adiposity, and lipids in black American and Caucasian children." *The journal of clinical endocrinology & metabolism* 96.5 (2011): 1560-1567.
37. Luo, G., Guenther, T., Gan, L. S., & Humphreys, W. G. "CYP3A4 induction by xenobiotics: biochemistry, experimental methods and impact on drug discovery and development." *Current drug metabolism* 5.6 (2004): 483-505.
38. Zhou, Shu-Feng. "Drugs behave as substrates, inhibitors and inducers of human cytochrome P450 3A4." *Current drug metabolism* 9.4 (2008): 310-322.
39. Lazzerini, M., Barcala Coutinho do Amaral Gomez, D., Azzimonti, G., Bua, J., Brandão Neto, W., Brasili, L., ... & Mariani, I. "Vitamin D insufficiency in infants with increased risk of developing type 1 diabetes: a secondary analysis of the POInT Study." *BMJ Paediatrics Open* 8.1 (2024).
40. Rosser, F. J., Han, Y. Y., Forno, E., Bacharier, L. B., Phipatanakul, W., Guilbert, T. W., ... & Celedón, J. C. "Effect of vitamin D supplementation on total and allergen-specific IgE in children with asthma and low vitamin D levels." *Journal of Allergy and Clinical Immunology* 149.1 (2022): 440-444.
41. Holick, Michael F. "Vitamin D deficiency." *New England journal of medicine* 357.3 (2007): 266-281.
42. Chapuy, M. C., Preziosi, P., Maamer, M., Arnaud, S., Galan, P., Hercberg, S., & Meunier, P. J. Prevalence of vitamin D insufficiency in an adult normal population. *Osteoporosis international*. (1997): 7, 439-443.
43. Rahman, A., Al-Taiar, A., Shaban, L., Al-Sabah, R., & Mojiminiyi, O. "The routine chemiluminescence assay for plasma 25-hydroxyvitamin D analysis does not overestimate the prevalence of vitamin D deficiency in adolescents." *Nutrition Research* 79 (2020): 60-67.
44. Fraser, David R. "Regulation of the metabolism of vitamin D." *Physiological Reviews* 60.2 (1980): 551-613.
45. Al Shaikh, A. M., Abaalkhail, B., Soliman, A., Kaddam, I., Aseri, K., Al Saleh, Y., ... & Mukhtar, A. M. Prevalence of vitamin D deficiency and calcium homeostasis in Saudi children. *Journal of clinical research in pediatric endocrinology*, 8(4), (2016): 461.
46. Gordon CM, Feldman HA, Sinclair L, Williams AL, Kleinman P, Perez-Rossello J, et al. Prevalence of vitamin D deficiency among healthy infants and toddlers. *Arch Pediatr Adolesc Med*. 2008;162(6):505–12.
47. Bassil D, Rahme M, Hoteit M, Fuleihan Gel-H. Hypovitaminosis D in the Middle East and North Africa: Prevalence, risk factors and impact on outcomes. *Dermatoendocrinol*. 2013 Apr 1;5(2):274-98. doi: 10.4161/derm.25111. PMID: 24194968; PMCID: PMC3772916

48. Zhu Z, Zhan J, Shao J, Chen W, Chen L, Li W, et al. High prevalence of vitamin D deficiency among children aged 1 month to 16 years in Hangzhou, China. *BMC Public Health*. 2012;12:126.
49. هدي، م. ا، الصيد، ع. ز، عبدالمنعم، م. ا. (2018)، علاقة السمنة بنقص فيتامين د عند الاطفال في مدينة طرابلس، المجلة العربية للغذاء و التغذية، الاصدار vol.18 No.41
50. Vierucci, F., Del Pistoia, M., Fanos, M., Gori, M., Carlone, G., Erba, P., ... & Saggese, G. Vitamin D status and predictors of hypovitaminosis D in Italian children and adolescents: a cross-sectional study. *European journal of pediatrics*. (2013): 172, 1607-1617.
51. Tolppanen, A. M., Fraser, A., Fraser, W. D., & Lawlor, D. A. "Risk factors for variation in 25-hydroxyvitamin D3 and D2 concentrations and vitamin D deficiency in children." *The Journal of Clinical Endocrinology & Metabolism* 97.4 (2012): 1202-1210.
52. Saadon, Hanan. "Vitamin D Deficiency in Childhood: A Review." *University of Thi-Qar Journal of Science* 11.1 (2024): 175-183.
53. Weserman, E., & Gromish, D., 1981. Survey of clinical Pediatrics , Seventh ed ., Mc Graw- Hill international book Company, London , 325- 359.
54. Rawe, P., 2001. Why is rickets vesurqent in the USA? : lancet , Vol , 357 issue 9262, P., 1100.
55. - Hochberg Z, Bereket A, Davenport M, et al. Consensus development for the supplementation of vitamin D in childhood and adolescence. *Horm Res*. 2002;58(1):39-51