Evaluation of vitamin D supplementation intake among children; cross-sectional observational study [version 1; peer review: 1 approved with reservations]

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Abstract
Background: The purpose of this study was to review the vitamin D supplementation intake status among children in the general public, determine the vitamin D supplements practices, and the barriers that parents and children face with supplementation.

Methods: A cross-sectional observational questionnaire-based survey study design was used. A convenience sampling technique was used to collect the data. An online Rao soft sample size calculator was applied to determine the sample size of 319. The response rate of participants was expected to be 63%, the margin of error was 5% and the level of confidence was 95%.

Results: A total of 248 parents (89.1% mothers (n =203)) and 15.7% fathers (n=39) with a mean ± SD age of 35.4 ± 7.04 years, completed the study (77.7% response rate). Parents reported that the supplements used the most by children were vitamin D supplements (21.85%) and multivitamins (21.8%) followed by calcium supplements (5.6%). However, 27.8% of children in this study did not take any supplements. Of all the parents, 65% (162) of them reported sending their child outside to play while 34.67% (86) of parents had reported no outdoor activity. Approximately 184 (74.2%) parents reported the child's diet to contain multiple natural sources of vitamin D. However, 69 (27.8%) parents reported giving none of the natural sources of vitamin D to their children through the diet. Parents with higher education about 62.9% (n=156) had a higher frequency of providing vitamin D supplements to their children. Children in high-income families (43.63%) were more likely to take vitamin D supplements than those in middle- or low-income families.

Open Peer Review

Approval Status

1

version 1

08 Dec 2022

1. Tauqeer Hussain Mallhi1, Jouf University, Al-Jouf, Saudi Arabia

Any reports and responses or comments on the article can be found at the end of the article.
Conclusion: The study concluded that challenges like the educational and financial background of parents, family-income level, and health insurance status could help aid in addressing the overall burden of vitamin D deficiency among young children.

Keywords
Vitamin D, deficiency, frequency, supplementation, dietary sources, sunlight exposure, challenges
Introduction
Vitamin D is known among the critical minerals to play an important role in maintaining normal body functions.\(^1\) It allows bone mineralization and avoids hypocalcemic tetany (such as involuntary muscle contraction, cramps, spasms, etc).\(^2\) It is also known for aiding osteoblasts and osteoclasts in developing and remodeling the bone preventing it from being brittle.\(^3\) Other functions of vitamin D in the body include inflammation reduction and regulation of cell growth, neuromuscular and immune function, and glucose metabolism.\(^4\) Vitamin D also affects the expression of several genes that code for proteins that govern cell proliferation, differentiation, and apoptosis. Vitamin D receptors can be found in many tissues, and some of them transform 25(OH) D to 1,25 (OH) D.\(^5\)

Maintaining optimum levels of calcium and vitamin D during childhood and adolescence is critical for bone growth.\(^6\) Vitamin D is said to lower the risk of cancer, prevent viral infections, alleviate musculoskeletal pain, and calm mood disorders including depression, according to some claims. There has also been a surge in scientific interest in studying vitamin D at both the basic and clinical levels to address these and other claims.\(^7\) Children with vitamin D deficiency develop a disease known as rickets, which is characterized by a frame and fragile bone, making the legs appear bent.\(^8\) Vitamin D has been shown to reduce the risk of premature birth in pregnant women.\(^9\)

A child’s vitamin D deficiency can start as early as birth, which can damage not just their bone metabolism but also their immunological system, making them more susceptible to illnesses early in life.\(^10\) For the treatment of vitamin D deficiency rickets, the American Academy of Pediatrics (AAP) recommends an initial two- to three-month regimen of “high-dose” vitamin D therapy of 1000 units daily in neonates, 1000 to 5000 units daily in infants one to 12 months old, and 5000 units daily in patients over 12 months old.\(^11\)

Epidemiologic studies, at least in adults, apart from the risk of osteomalacia and osteoporosis, have associated hypovitaminosis D with an increased risk of several cancers, autoimmune diseases (type 1 diabetes, multiple sclerosis, rheumatoid arthritis, and Crohn’s disease), heart disease, hypertension, metabolic syndrome, asthma, upper respiratory tract infections, muscle weakness, and falling.\(^12\) The pleiotropic action of vitamin D was already revealed on molecular, cellular, tissue, and organ levels.\(^13\) These observations modified the current knowledge about vitamin D metabolism and methods of diagnosis of vitamin D deficiency states.\(^14\)

Unfortunately, vitamin D is found rare in food.\(^15\) Vitamin D is found in only a few foods. Fish liver oils and the meat of fatty fish (such as trout, salmon, tuna, and mackerel) are among the greatest sources. The amount of vitamin D in a human’s tissue is influenced by its food. Vitamin D is also found in modest levels in beef liver, egg yolks, and cheese, mostly in the form of vitamin D3 and its metabolite 25(OH)D3.\(^16\) Vitamin D2 is found in varying levels in mushrooms. Some commercially available mushrooms have been exposed to UV radiation to boost their vitamin D2 levels. In addition, the FDA has approved UV-treated mushroom powder as a food additive for use as a vitamin D2 source in food items.\(^17\)

Furthermore, vitamin D is added to milk, many ready-to-eat bowls of cereal, and some yogurt and orange juice brands. It is found in modest concentrations in cheese and some margarine.\(^18\)

In the U.A.E., the consistent predominant hot weather, inadequate exposure to sunlight, and low nutritional intake of vitamin D result in low serum concentrations of circulating 25(OH) D, a condition known as hypovitaminosis D.\(^19\) Furthermore, recent lifestyles involving using cars for transport over walking, and children indulging in electronics and staying indoors have also influenced low vitamin levels. Low dietary intake of vitamin D and calcium, and other factors, including obesity and low social status, are all associated with low serum levels of vitamin D.\(^20–22\)

Further research is needed to be conducted on the production of high-potency–food-based vitamin D supplements, the move to mandatory fortification of cereal grain staples, and the development of natural food sources with higher vitamin D content are all potentially safe and efficient pathways for overcoming the barriers to optimal vitamin D status. Although various studies suggest a high prevalence of vitamin D deficiency among adults and children, no randomized controlled trials have been fully performed on vitamin D deficiency and supplementation among children in the UAE. When compared to the expense of providing therapies for many chronic diseases closely linked to vitamin D deficiency, taking vitamin D supplements is a much better alternative.

The purpose of this study was to review the vitamin D supplementation intake status among children in the general public, to evaluate the vitamin D supplements practices, the natural sources of vitamin D from their diet, and the barriers that parents and children face with supplementation.
Methods

Study design and setting
A cross-sectional observational questionnaire-based survey study design was used in this study. The survey was conducted in public places in the U.A.E. The data was collected over seven months from October 2021 to April 2022.

Research tool
The questionnaire was adapted from the literature and evaluated for content validation.

Part one of the questionnaire consists of demographic information (e.g. age, nationality, gender, etc.)

The second part collected information about supplementation intake and natural sources of vitamin D intake (e.g., if the child has milk, yogurt, etc. in his diet).

The last part consists of the outdoor activity level of the child (e.g., hours the child spends playing outdoors).

All the parts of the data were collected based on yes or no or multiple response questions.

Variables
Vitamin D deficiency, education level of parents, outdoor activity hours of children, health insurance status of parents, income level of the families.

Primary outcome
- The primary outcome of this study was to observe the vitamin D supplementation intake status.
- The possible reasons for vitamin D deficiency among children. Parents may have difficulties in supplementing their children's diets due to their financial level, health insurance status, and level of literacy.

Participants and sampling method
A convenient sampling technique was used to collect data from approximately 248 participants from public places in Ajman, U.A.E. An online Rao soft sample size calculator was applied to determine the sample size, which was 319. The response rate of parents was expected to be 63%, the margin of error was 5% and the level of confidence was 95%. Around 319 participants were expected and 248 responded and actively participated in the study, 77.7% was the response rate of the study participants.

Missing data
This study has no missing data.

Inclusion criteria
Participants who had at least one child between 4-15 years of age and who agreed to participate.

Exclusion criteria
Children with minor illnesses that are common in the general population and those suspected clinically of having rickets. Children with cognitive and behavioral disorders were excluded from the study.

Ethical issues
Ethics approvals have been obtained for the study. This is the ethics approval number IRB/COP/STD/74/Oct-2021 from GMU.

Consent form
The questionnaire content was described before giving it to the parents and the written consent form was taken from each participant. The consent form was as follows:

"Your participation in this survey is voluntary. You may choose not to participate. If you decide to participate in this survey, you may withdraw at any time. If you decide not to participate in this study, or if you withdraw from participating at any time you will not be penalized. Filling out this form means that you accept to participate in this research."
Statistical analysis
The data analysis was done using the SPSS statistical package for social sciences software. A Chi-square analysis was done. Mean, standard deviation, and mean comparison was utilized for continuous data. Both a tabular and graphic version of the data was used to show it. A 5% degree of confidence and a 0.5 margin of error were chosen.

Bias
There is no bias in any trend in the collection, analysis, interpretation, or review of the data that can lead to conclusions that are different from the truth.

Results
The study reported no missing data. A total of 248 parents (89.1% mothers (n=203)) and 15.7% fathers (n=39) with a mean±SD age of 35.4±7.042 years, completed the study. About 62.9% (n=156) parent were holding a university degree, while 26.2% (n=65) of the participants completed a secondary school, 9.7% (n=24) completed primary school and 1.2% (n=3) of parent were uneducated. Moreover, almost 61.7% (n=153) of mothers were unemployed, while a smaller number of mothers 27% (n=67), and 11.3% (n=28) were employed and employed with medical background. For fathers the 70.2% (n=174) were employed and 21% (n=52), 4.8% (n=12) and 4% (n=10) were self-employed, employed with a medical background and unemployed, respectively. Approximately 42.7% (n=106) participants had income level of more than 10,000, while 35.5% (n=88), 10.1 (n=25) and 4.8 (n=12) had income level of 5,000-10,000, 2,000-5,000 and less than 2,000, respectively. More than half of the participants has insurance and only a few participants 28.6% (n=71) had no insurance (Table 1).
This research has participants from different countries (total=23). The majority (67%) of participants are from five countries (India, Iran, Pakistan, Syria, and Emirates). The completed data has been presented in Figure 1.

A higher proportion of children received supplements whose parents were educated to the level of secondary school and above. Table 2 shows the literacy level of parents and supplementation.

The data on outdoor activity levels included the average frequency of outdoor activity per day. Of all the parents, 65% (162) of them reported sending their child outside to play while 34.67% (86) had no outdoor activity. The mean hours of outdoor activity for the children were 2.046\pm1.61. It was found that on average, children spent 0.15-6 hours playing outside in the sun therefore exposed to sunlight (Table 3).

Parents reported that supplements used the most by children were Vitamin D supplements (21.85%) and multivitamins (21.8%) followed by calcium supplements (5.6%). However, 27.8% of children in this study did not take any supplements. While other parents reported mixed intake of supplements (for example some children took vitamin D plus calcium supplements while others took vitamin D and multivitamins (Figure 2).

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>N(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Mother</td>
<td>203(81.9)</td>
</tr>
<tr>
<td>Father</td>
<td>39(15.7)</td>
</tr>
<tr>
<td>Others*</td>
<td>6(2.4)</td>
</tr>
<tr>
<td>Age (mean±S.D.)</td>
<td>35.4±7.042</td>
</tr>
<tr>
<td>Education Level</td>
<td></td>
</tr>
<tr>
<td>Not educated</td>
<td>3(1.2)</td>
</tr>
<tr>
<td>Primary School</td>
<td>24(9.7)</td>
</tr>
<tr>
<td>Secondary School</td>
<td>65(26.2)</td>
</tr>
<tr>
<td>University</td>
<td>156(62.9)</td>
</tr>
<tr>
<td>Father Employment</td>
<td></td>
</tr>
<tr>
<td>Employed</td>
<td>174(70.2)</td>
</tr>
<tr>
<td>Unemployed</td>
<td>10(4.0)</td>
</tr>
<tr>
<td>Self-employed</td>
<td>52(21)</td>
</tr>
<tr>
<td>Employed with Medical Background</td>
<td>12(4.8)</td>
</tr>
<tr>
<td>Mother Employment</td>
<td></td>
</tr>
<tr>
<td>Employed</td>
<td>67(27)</td>
</tr>
<tr>
<td>Unemployed</td>
<td>153(61.7)</td>
</tr>
<tr>
<td>Employed with Medical Background</td>
<td>28(11.3)</td>
</tr>
<tr>
<td>Income</td>
<td></td>
</tr>
<tr>
<td>Level Less than 2,000</td>
<td>12(4.8)</td>
</tr>
<tr>
<td>2,000-5,000</td>
<td>25(10.1)</td>
</tr>
<tr>
<td>5,000-10,000</td>
<td>88(35.5)</td>
</tr>
<tr>
<td>More than 10,000</td>
<td>106(42.7)</td>
</tr>
<tr>
<td>Insurance</td>
<td></td>
</tr>
<tr>
<td>Government</td>
<td>51(20.6)</td>
</tr>
<tr>
<td>Private</td>
<td>126(50.8)</td>
</tr>
<tr>
<td>None</td>
<td>71(28.6)</td>
</tr>
</tbody>
</table>

*Caregivers.
Figure 3 summarizes and describes that out of the 248 participants, 184 (74.2%) parents reported their child’s diet to contain multiple natural sources of vitamin D (for example some children had milk plus cheese in their diet while others had yogurt plus cheese plus vitamin D fortified orange juice). However, 69 (27.8%) parents reported giving none of the natural sources of vitamin D to their children through the diet.

Children in high-income families (43.63%) were more likely to receive vitamin D supplements than those in middle- or low-income families (Table 4).

Parents with private health insurance 51.85% were more likely to give vitamin D supplements to their children compared to those with government health insurance 25.92% and no health care insurance 22.22% (Table 5).
The study included participants from 23 various nationalities. The top five countries with the most participants were India, Pakistan, Syria, and the U.A.E. Out of 34 participants from India, only 11 (32.35%) reported the use of vitamin D supplementation by their children, four (11.76%) reported using calcium supplements, six (17.64%) reported using multivitamins and the other 6 of them (17.64%) reported giving multiple sources of vitamins to their children.

**Table 4. Participant’s income level and supplementation practices.**

<table>
<thead>
<tr>
<th>Income level</th>
<th>Supplements taken</th>
<th>Vitamin D</th>
<th>Calcium supplements</th>
<th>Multivitamins</th>
<th>Multiple sources</th>
<th>None</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N(%)</td>
<td>N(%)</td>
<td>N(%)</td>
<td>N(%)</td>
<td>N(%)</td>
<td>N(%)</td>
</tr>
<tr>
<td>Less than 2,000</td>
<td>5(9.09)</td>
<td>0</td>
<td>6(11.11)</td>
<td>1(1.78)</td>
<td>2(2.89)</td>
<td></td>
</tr>
<tr>
<td>2,000-5,000</td>
<td>8(14.54)</td>
<td>0</td>
<td>8(14.81)</td>
<td>6(10.71)</td>
<td>8(11.59)</td>
<td></td>
</tr>
<tr>
<td>5,000-10,000</td>
<td>18(32.72)</td>
<td>7(50)</td>
<td>17(31.48)</td>
<td>21(37.5)</td>
<td>30(43.47)</td>
<td></td>
</tr>
<tr>
<td>More than 10,000</td>
<td>24(43.63)</td>
<td>7(50)</td>
<td>23(42.59)</td>
<td>28(50)</td>
<td>29(42.02)</td>
<td></td>
</tr>
</tbody>
</table>

The study included participants from 23 various nationalities. The top five countries with the most participants were India, Pakistan, Syria, and the U.A.E. Out of 34 participants from India, only 11 (32.35%) reported the use of vitamin D supplementation by their children, four (11.76%) reported using calcium supplements, six (17.64%) reported using multivitamins and the other 6 of them (17.64%) reported giving multiple sources of vitamins to their children.

**Figure 2. Supplementation intake among the study participants.**

**Figure 3. Children’s intake of natural sources containing vitamin D.**
However, out of the 34 participants from India, seven (20.58%) did not use any vitamin supplements at all. While out of 28 participants from Iran, only 6 participants, (21.41%) reported the use of vitamin D supplementation by their children, three (10.71%) reported using calcium supplements, ten (35.71%) reported using multivitamins and the other eight of them (28.57%) reported giving multi-sources of vitamins to their children. Among the 34 participants from Pakistan, the lowest amount of vitamin D supplements intake, only four (11.76%) participants reported giving supplements to their children and three (8.82%) reported using calcium supplements, only one (2.94%) parent reported using multivitamins and the other 12 of them (34.29%) reported giving multi-sources of vitamins to their children. Out of 27 participants from Emirates, few participants which are five (18.51%) of them reported the use of vitamin D supplementation by their children, two (7.4%) reported using calcium supplements, seven (25.94%) reported using multivitamins and the rest 11 (40.74%) reported giving multi-sources of vitamins to their children. The participants from Syria reported the highest vitamin D intake among the countries, out of 40 participants from India, only 12 (30.76%) reported the use of vitamin D supplementation by their children, one (2.56%) reported using calcium supplements, nine (23.07%) reported using multivitamins and the other 10 (25.64%) reported giving multiple sources of vitamins to their children.

### Table 5. Health insurance status of study participants and vitamin D supplementation intake.

<table>
<thead>
<tr>
<th>Supplements taken</th>
<th>Vitamin D</th>
<th>Calcium supplements</th>
<th>Multivitamins</th>
<th>Multiple sources</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N(%)</td>
<td>N(%)</td>
<td>N(%)</td>
<td>N(%)</td>
</tr>
<tr>
<td>Insurance</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Governmental</td>
<td>14(25.92)</td>
<td>0</td>
<td>14(25.92)</td>
<td>5(8.92)</td>
</tr>
<tr>
<td>Private</td>
<td>28(51.85)</td>
<td>14(100)</td>
<td>20(37.03)</td>
<td>38(67.85)</td>
</tr>
<tr>
<td>No insurance</td>
<td>12(22.22)</td>
<td>0</td>
<td>20(37.03)</td>
<td>13(23.21)</td>
</tr>
</tbody>
</table>

### Table 6. Nationality of study participants [top 5=163 (67%)] and vitamin supplements.

<table>
<thead>
<tr>
<th>Supplements taken</th>
<th>Vitamin D</th>
<th>Calcium supplements</th>
<th>Multivitamins</th>
<th>Multiple sources</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N(%)</td>
<td>N(%)</td>
<td>N(%)</td>
<td>N(%)</td>
</tr>
<tr>
<td>India (N=34)</td>
<td>11(32.35)</td>
<td>4(11.76)</td>
<td>6(17.64)</td>
<td>7(20.58)</td>
</tr>
<tr>
<td>Iran (N=28)</td>
<td>6(21.42)</td>
<td>3(10.71)</td>
<td>10(35.71)</td>
<td>8(28.57)</td>
</tr>
<tr>
<td>Pakistan (N=34)</td>
<td>4(11.76)</td>
<td>3(8.82)</td>
<td>1(2.94)</td>
<td>14(41.17)</td>
</tr>
<tr>
<td>Syria (N=40)</td>
<td>12(30.76)</td>
<td>1(2.56)</td>
<td>9(23.07)</td>
<td>7(17.94)</td>
</tr>
<tr>
<td>Emirates (N=27)</td>
<td>5(18.51)</td>
<td>2(7.4)</td>
<td>7(25.92)</td>
<td>2(7.4)</td>
</tr>
</tbody>
</table>

However, out of the 34 participants from India, seven (20.58%) did not use any vitamin supplements at all. While out of 28 participants from Iran, only 6 participants, (21.41%) reported the use of vitamin D supplementation by their children, three (10.71%) reported using calcium supplements, ten (35.71%) reported using multivitamins and the other eight of them (28.57%) reported giving multi-sources of vitamins to their children. Among the 34 participants from Pakistan, the lowest amount of vitamin D supplements intake, only four (11.76%) participants reported giving supplements to their children and three (8.82%) reported using calcium supplements, only one (2.94%) parent reported using multivitamins and the other 12 of them (34.29%) reported giving multi-sources of vitamins to their children. Out of 27 participants from Emirates, few participants which are five (18.51%) of them reported the use of vitamin D supplementation by their children, two (7.4%) reported using calcium supplements, seven (25.94%) reported using multivitamins and the rest 11 (40.74%) reported giving multi-sources of vitamins to their children. The participants from Syria reported the highest vitamin D intake among the countries, out of 40 participants from India, only 12 (30.76%) reported the use of vitamin D supplementation by their children, one (2.56%) reported using calcium supplements, nine (23.07%) reported using multivitamins and the other 10 (25.64%) reported giving multiple sources of vitamins to their children.

### Discussion

This cross-sectional study demonstrates that inadequacy of vitamin D remains a risk in the U.A.E due to its geographical location being at the equator leading to the hot harsh climate throughout the year limiting the children’s exposure to sunlight. Depending on the effectiveness of UVB photons to promote vitamin D production, the amount of sun exposure necessary for the creation of ultraviolet B-induced vitamin D in the skin impacts cutaneous synthesis. This study also identifies the association between socioeconomic and demographic barriers with vitamin D supplementation among children. Children in high-income families (43.63%) were more likely to take vitamin D supplements than those in middle- or low-income families.

Parents with private health insurance (51.85%) were more likely to provide vitamin D supplements to their children compared to those with government health insurance (25.92%) and no health insurance (22.22%).

Furthermore, it was found in this study that parents’ education and literacy level largely determines children receiving vitamin D supplementation. Parents in this study with a lower literacy rate who did not complete primary school were less likely to give vitamin D supplements to their children. However, evidence of gender differentials in vitamin D supplementation was not found in this study.
In U.A.E., since there is no law requiring the fortification of vital foods with vitamin D, there are few vitamin D-fortified products on the market. Among the participants of the study, 184 (74.2%) reported the child’s diet to contain multiple natural sources of vitamin D (for example some children had milk plus cheese in their diet while others had yogurt plus cheese plus vitamin D fortified orange juice) and most parents reported that their child has milk in their diet. Moreover, 69 parents (27.8%) reported giving none of the natural sources of vitamin D to their children through the diet. As a result, individual vitamin D dietary intake is strongly influenced by dietary preferences as well as the country’s fortification plan. Without supplementation, however, vitamin D status is heavily on endogenous vitamin D synthesis, which is influenced by genetic determinants and lifestyle.

Vitamin D aids calcium absorption in the intestine by facilitating active calcium transport across the mucosa. Vitamin D insufficiency is usually caused by a lack of calcium in the diet and leads to bone deterioration or osteoporosis. The results of this study are generalizable since it has been done on general population and multiple ethnicities in the U.A.E, it reflects that this study is generalizable to different parts of the world.

Limitations of the study
However, this study had potential limitations. From a methodological point of view, the weakness of the study is that it is based on a cross-sectional design. The inherent problem of a cross-sectional design is that the outcome (vitamin D supplementation status) and the exposure (in this case, socioeconomic characteristics and a State’s social and economic development status) are collected simultaneously, thereby preventing conclusions regarding causality. The data was mostly collected from mothers. The present literature lacks data on the vitamin D level of children, thus a comparison between outdoor level activity of the children and the vitamin D level of children was presented in this study.

Conclusion
The findings of the study concluded that the educational and financial background of parents and health insurance status could aid in addressing the challenges parents face with providing vitamin D supplements to their children as well as nutritional assessment for early natural supplement treatment.

Data availability

This project contains the following data:

- The purpose of this study was to review the vitamin D supplementation intake status among children in the general public, determine the vitamin D supplements practices, and the barriers that parents and children face with supplementation.

References

Publisher Full Text


24. Reference Source


Open Peer Review

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Tauqeer Hussain Mallhi
Department of Clinical Pharmacy, College of Pharmacy, Jouf University, Al-Jouf, Saudi Arabia

Thank you for the invitation to review this study. The authors made a good effort to explore the use of vitamin D supplementation among children in UAE. I have a few comments on this manuscript.

1. The sample size estimation can be omitted from the abstract section.

2. Please provide a few references that aid in the development of data collection form.

3. Please provide information on the validation and reliability of the data collection form.

4. Please clarify that the data was collected through interviews or self-administration techniques.

5. The quality of figure 1 can be improved.

6. Convenient sampling is also the limitation of this study that precludes the generatability of the findings.

7. There is a need to provide some information on the barriers of vitamin D supplementation in children.

8. The manuscript will require some corrections in syntax at some places.

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Yes
Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
Yes

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Yes

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** Pharmacy Practice, Clinical Pharmacy, Pharmacotherapy

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

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