



## TENDENCY OF VITAMIN D SUPPLEMENTATION AMONGST THE POPULATION IN HAIL REGION OF SAUDI ARABIA

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### ABSTRACT

Vitamin D, which is either produced in the skin upon sunlight exposure or acquired through diet, plays an important role in calcium hemostasis and bone remodeling. Vitamin D deficiency is a global issue and awareness about its importance has brought a tendency to use its supplements worldwide. The present study was aimed to assess the use of vitamin D supplementation among the general population in Hail region of Saudi Arabia. The data from 377 subjects was analyzed. The study revealed that 40.31% of participants used supplements. Importantly, 18.42% individuals were using supplementation without knowing the vitamin D level. On the other hand, several participants with low level were not using supplements, while some with normal or even high level reported using supplements. A significant difference was observed for knowing vitamin D level in supplement consumers versus others at  $p$  value  $<0.05$ . Excessive supplementation is risk for development of side effects. There is a need to be cautious with artificial supplements as their long-term effects are not fully known. Thus, dietary sources and basking in sunlight should be preferred unless there is a strong clinical indication to start supplementation.

**Keywords:** Diet, hypercalcemia, renal stones, sunlight, vitamin D supplements

### INTRODUCTION

The minerals and vitamins are essential for body maintenance; and people mostly rely on the external dietary sources for these owing to the inability or inadequacy in their production by body system (Godswill *et al.*, 2020). Micronutrients are to be supplemented continuously because of their role in various body functions like tissue formation (in bone and teeth), maintenance of healthy tissues, and role in various enzyme systems (Gernand *et al.*, 2016; Tucker, 2016). Although their requirements are minute, yet they are essential (Awuchi, 2019). There are 9 water soluble vitamins which include 8 B vitamins and vitamin C, and 4 fat soluble vitamins i.e. vitamin D, A, K and E (Godswill *et al.*, 2020).

Human beings depend on external dietary sources for vitamin supplementation and various factors like food variety, food processing, cooking and human gut health affect vitamin availability to the body. For example, the medical conditions resulting in disturbance in nutrient absorption from gut can lead to a state of deficiency (Maqbool and Stallings, 2008). Likewise, lack of enough quantities in food can result in low levels of vitamins. A detailed study conducted between 2003 and 2006 in USA has reported low levels of vitamins in as many as 9 out of 10 individuals (Bailey *et al.*, 2012). Overall, vitamin deficiencies are divided into two main categories i.e., primary, and secondary. The former is due to lack of sufficient quantity from dietary sources, while the latter is linked to another factor like alcoholism, smoking or a disease such as malabsorption syndrome (Godswill *et al.*, 2020).

Vitamin D, a fat-soluble vitamin, is involved in many vital functions in human body through direct and indirect mechanisms. Vitamin D<sub>2</sub> and D<sub>3</sub> are the two forms of vitamin D normally dealt (Jäpelt and Jakobsen, 2013). Human skin keratinocytes have the necessary enzymes for producing 1,25 dihydroxy vitamin D [1,25(OH)<sub>2</sub>D]; and multiple factors such as pigmentation level of skin, age, use of sun protection and exposure level to sunlight, influence the vitamin D production in skin (Webb, 2006). Skin diseases like inflammatory diseases also lead to vitamin D deficiency (Bikle, 2018). Vitamin D is generally known for its role in calcium metabolism and bone mineralization. It has role as a hormone in human body system affecting extra-skeletal tissues (Bouillon *et al.*, 2019). Vitamin D also plays role in energy metabolism at genetic level as well as in immune-stem regulatory mechanisms (Tsukasaki and Takayanagi, 2019). In fact, vitamin D is recognized for huge range of functional contribution in human body system. This makes it not only a hormone in endocrine system but also an autocrine and paracrine molecule too (Saponaro *et al.*, 2020).

In most populations the use of vitamin D without any physician's prescription is very common practice. No proper data is available from Saudi Arabia about their use in populations who self-administer such medicines to obtain health benefits. This is usually done under influence from advertisements claiming health benefits related to such supplements and over the counter availability. All claimed benefits of supplementation are not evidence-backed medicine. The excessive use can result in side effects or even toxicity, which should be prevented. Thus, there is a need to develop clear guidelines for using such supplements. The cross sectional study was aimed to assess the use of vitamin D supplements in general population residing in Hail region of Saudi Arabia with focus on assessing the rate of supplement use, the correlation between vitamin D level and supplements usage, correlation between demographics of supplement users versus others, and accordingly present recommendations for fair use of vitamin D. An important focus of the study was to investigate the use of vitamin D supplements in general population without even knowing if they are deficient in it.

## **MATERIALS AND METHODS**

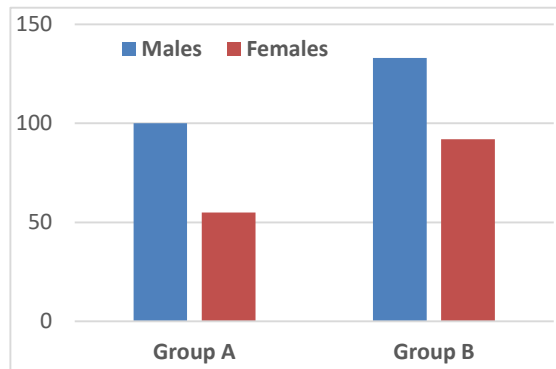
The ethical approval for this cross sectional study was obtained from the Research Ethics Committee (REC) of the University of Hail vide their No. 20455/5/42. The study was conducted in the Hail region of Saudi Arabia. The study is based on data collection using an online google form. A total of 527 individuals (both genders) filled in the online survey-based questionnaire. The demographic inquiries included gender, age, marital status, nationality, education level and occupation. In general, the survey targeted multiple aspects related to health such as detailed personal demographics as mentioned above, presence of health conditions such as diabetes and use of vitamin D.

The candidates who answered the questions related to use of vitamin D supplementation were selected for this part of study (429 participants) and the rest candidates were excluded. The details of questions related to vitamin D are presented in Table 2. Out of these 429 participants, 160 individuals reported taking supplementation (categorized as group A for current study) and 269 reported not taking vitamin D supplements (categorized as group B).

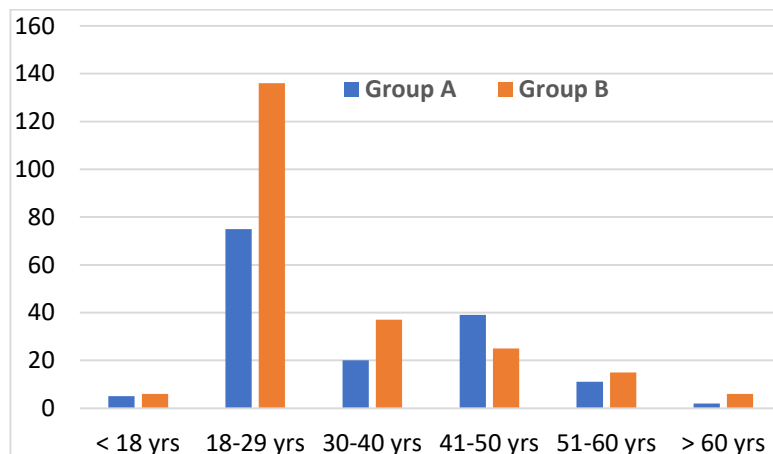
The data of candidates using the supplements (i.e., group A with 160 candidates) was cross checked and eight more candidates were excluded due to the lack of response or inconsistent responses. Finally, data from 152 individuals of "group A" was analysed. The data of participants who were not using the supplements (i.e. group B with 269 individuals) was further evaluated and forty-four individuals were excluded due to the lack of information related to gender, ethnicity, and other missing/unclear information. Finally, the data from 225 individuals of "group B" was further analysed. The comparison of various values was done by comparing the percentage values. In addition to this, *p* values were calculated using online available Chi square calculator for 2 x 2 and 5 x 5 tools (<https://www.socscistatistics.com/>).

## RESULTS AND DISCUSSION

The data from 377 individuals (152 from group A and 225 from group B) was analysed and comparison of various demographic information of both the groups was made. In total 232 males (99 from group A and 133 from group B) and 145 females (53 from group A and 92 from group B) participated in this study. Gender, age, marital status, nationality, and occupation of the participants from both the groups were compared and their statistical significance determined. Gender-wise no



**Fig. 1: Gender-based comparison between the vitamin D user (A) and non-user groups (B)**



**Fig. 2: Age-wise comparison of between vitamin D user (A) and non-user (B) groups. Collectively, the difference is significant at  $p < 0.05$**

sectors require needs further investigations.

Table 2 presents the data related to the questions asked to all participants related to vitamin D. The participants were asked about the dosage of vitamin D tablets and consumption of milk, but the data linked to these questions was not clear and not answered by many candidates, thus it was not possible to analysed it. The participants were asked a direct question, whether they know their vitamin D level if it was tested. The options included low, normal, and high levels or “I don’t know”. In general, serum level of vitamin D below  $30 \text{ nmol L}^{-1}$  ( $12 \text{ ng mL}^{-1}$ ) is considered as severe deficiency, between  $30\text{-}50 \text{ nmol L}^{-1}$  ( $12\text{-}20 \text{ ng mL}^{-1}$ ) is insufficient/deficient, and levels  $> 50 \text{ nmol L}^{-1}$  ( $20 \text{ ng dL}^{-1}$ ) are considered sufficient. Importantly, the individuals having levels  $> 75 \text{ nmol L}^{-1}$  ( $30 \text{ ng mL}^{-1}$ ) do not have any additional benefit (Kahwati *et al.*, 2018; Salas-Salvadó *et al.*, 2008). The overall comparison of vitamin D level between both group participants was not significant. Even normal versus low level too depicted insignificant results at a  $p$  value  $< 0.05$ . From group A (152 individuals), 42 individuals reported normal while 77 reported low level of vitamin D supplementation. In group

significant difference was observed between both the groups (Fig. 1). Likewise, the differences were insignificant for various age groups, except for 41-50 years age category (Fig. 2). This revealed more supplement use in middle-aged individuals. Interestingly, vitamin D supplementation was more common in unmarried (52.03%) than married (23.71%) participants (Table 1). Future studies need to be focussed on to explore the factors related to the over-use of vitamin D supplements amongst singles. The nationality of participants showed insignificant difference with respect to vitamin D use. Two occupational sectors i.e., office

workers and educational field participants showed significant difference in comparison to the participants from other groups. In group A only 3% were office workers as compared to 10% in group B, indicating low tendency of vitamin D supplements for this occupation. Education level of individuals showed almost similar pattern with 13% in group A and 22% in group B revealing vitamin D usage. The reason for low tendency or usage in these

**Table 1: Demographic comparison of individuals consuming (A group) or not consuming (B group) vitamin D supplements**

Parameters	Categories	Group A (No.)	Group B (No.)	p value	Significance
Age (years)	< 18	5	5	0.52701	Not significant
	18-29	75	134	0.05033	Not significant
	30-40	21	37	0.48773	Not significant
	41-50	39	25	0.00022	Significant
	51-60	10	14	0.88932	Not significant
	> 60	2	6	0.37198	Not significant
Gender	Males	99	133	0.23854	Not significant
	Females	53	92		
Marital status	Married	37	119	< 0.00001	Significant
	Single	115	106		
Nationality	Saudi	143	214	0.66094	Not significant
	Expatriate	9	11		
Occupation*	Office work	5	24	0.00837	Significant
	Health care worker	6	11	0.66563	Not significant
	Military personnel	12	15	0.65010	Not significant
	Manual work	7	5	0.19603	Not significant
	Education sector	21	51	0.03198	Significant
	Student	64	78	0.14369	Not significant
	Unemployed	21	25	0.43125	Not significant

\*16 individuals from each group did not select any occupation

B (225 individuals), 21 reported normal level of vitamin D while 65 reported a low level. The analysis showed insignificant difference in both populations at  $p < 0.05$ , thereby indicating vitamin D deficiency in general population.

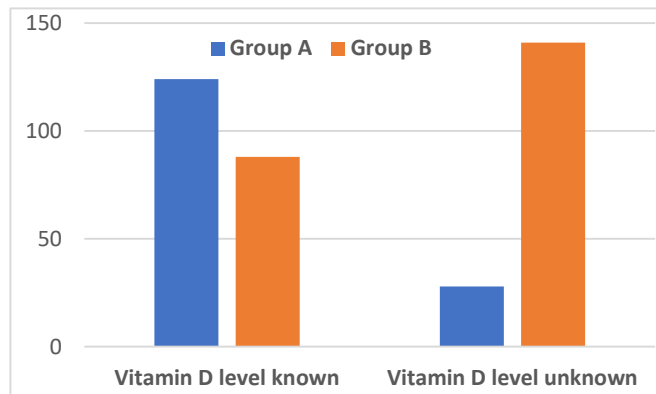
A comparison was made to assess the knowledge level of participants about vitamin D. In group A 124 (81.58%) knew about the level (42 normal, 77 low and 5 high) of vitamin D. On the other hand, of the 225 individuals who were not using the supplements (group B), 88 (39.1%) knew the level (21 normal, 65 low and 2 high) of their vitamin D use. The remaining 137 (60.88%) did not know. The results

**Table 2: Vitamin D related questionnaire and data comparison between consuming (group A) and non-consuming (B group) groups**

Questions	Group A (No.)	Group B (No.)	p value	Significance at $p < 0.05$
Do you take vitamin D tablet supplements or calcium with vitamin D?	Yes (152 participants)	No (225 participants)	-	-
What is the vitamin D level when you tested last time?	Normal	21	0.193863	Non-significant
	Low	77		
	High	5		
	Level unknown	28		
On average, how much sun exposure you have per week?	< 5 min	40	0.541956	Non-significant
	5-15 min	26	0.688569	Non-significant
	15-30 min	29	0.437548	Non-significant
	> 30 min	31	0.758226	Non-significant

Note: 26 participants from group A and 58 from group B did not respond to question related to sun exposure time.

showed significance differences at  $p < 0.05$  (Fig. 3). This indicates that more people who know their level of vitamin D belong to the category of consumers of vitamin D supplements. On the other hand, 65 individuals from group B did not take any supplementation despite having low levels of vitamin D. This category is important as they might need supplementation, yet they are not using it, or they might not be able to use it due to some reason. Recent literature has reported that around 7% people globally are expected to suffer from vitamin D deficiency, who do not use vitamin D supplements or are unable to use them (Bouillon *et al.*, 2022).



**Fig. 3: Comparison between vitamin D consuming group (A) and non-consuming group (B) to check if the participant knew the level of vitamin D. The difference is significant at level of  $p < 0.05$**

Collectively, 152 (40.3%) reported vitamin D usage. The increased vitamin supplement use may be attributed to the awareness about their role in body and easy availability from medical stores without formal prescription. People believe that vitamin D use is safe and beneficial, even if it may not be effective. In fact, if we consider the effects of vitamin supplements over an extended period, we are not really sure of their consequences (Hamishehkar *et al.*, 2016). A report from USA shows vitamin D use in more than 50% adults (Bailey *et al.*, 2010). Other studies have reported similar results (Bolland *et al.*, 2018; Bouillon *et al.*, 2019).

In group A 28 (18.42%) individuals were using supplementation without knowing their vitamin D level. Such individuals might not only be using supplements while they do not need them but also putting themselves at risk of side effects from excessive use. A total of 212 participants (out of 377) from both group A and B knew their level of vitamin D (low, normal, or high). In total 142 candidates (67%) reported of having a low level of vitamin D. This indicates with presence of vitamin D deficiency in general population in Hail region of Saudi Arabia. The studies from USA, Canada and Europe have reported vitamin D deficiency in significant chunk of populations i.e. 5.9, 7.4 and 13.0%, respectively (Sarafin *et al.*, 2015; Cashman *et al.*, 2016; Schleicher *et al.*, 2016). About one in three individuals suffer from low vitamin D level (Bouillon, 2020). The low vitamin D is usually due to the lack of sun exposure and deficient dietary consumption. Sun exposure can produce nearly 100% required vitamin D for body (Kimlin, 2008). The role of sunlight in various skin conditions including skin cancers has enhanced the use of sun protection factor (SPF) containing creams. If properly applied, these creams block the complete synthesis of vitamin D. Skin synthesis of vitamin D also reduces in older population (Holick, 2008).

Five individuals with high vitamin D level reported of using vitamin supplements as well. For such candidates, it appears that they either have a strong clinical indication to keep using vitamin D or lack guidance and information regarding the risk of developing side effects. Similarly, 42 individuals having normal level of vitamin D have also reported of taking vitamin D supplementation. This may be linked either with maintenance dose for those who were diagnosed with deficiency or lack of guidance and information or taking it due to temptation from the claimed benefits of such supplementation.

Vitamin D supplementation is known to provide protection against fractures as per its role in bone strengthening but a meta-analysis presented in 2018 has claimed no scientific proof for such benefits in old age individuals using vitamin D and calcium supplementation (Zhao *et al.*, 2017). Similarly, there are clinically no proof of health benefits linked to vitamin D supplementation in individuals who have normal vitamin D level. The individuals deficient in vitamin D gain benefit from its supplements such as improvement in lung functions, diabetes mellitus progress and bone loss

linked to age, while no benefits like protection against cancers, diabetes, cardiac diseases, risk of falls and bone density are proven. The studies which have generally claimed that vitamin D supplementation is linked with such benefits are mainly based on subgroup or post hoc analyses, so we cannot really use their results as recommendation, rather use them as guidance for further studies (Bouillon *et al.*, 2022).

Using certain vitamins, including vitamin D, in high dosage can be detrimental to health (Hamishehkar *et al.*, 2016). Out of the 13 vitamins in our body, only vitamin A and D can cause hypervitaminosis (Godswill *et al.*, 2020). There is generally no vitamin D toxicity if the production is linked with sun exposure or the dietary intake is increased but consuming artificially manufactured supplements can put a person at risk of toxicity. There may be the development of hypercalciuria and lately hypercalcemia in such individuals (Dudenkov *et al.*, 2015). The next effect in this sequence is nephrolithiasis (Tebben *et al.*, 2016). Overall, there are various complications which can follow vitamin D toxicity such as increased calcium level in blood, increased urinary level, renal calculi, deranged renal functions and generalized weakness (Hathcock *et al.*, 2007). Hypercalcemia is a common occurrence when vitamin D is used in high doses but usually temporary and not severe (Billington *et al.*, 2020). The development of complications is dose-dependent. A study wherein the level of calcium in blood of patients was put on 1000 or 4000 IU day<sup>-1</sup> of vitamin D for 2-5 months revealed no hypercalcemia development. But the duration of supplementation would also be playing some role in hypercalcemia development (Vieth *et al.*, 2001). Another study reported that even use of 10000 IU day<sup>-1</sup> is linked with risk of hypercalcemia. This study compared between the individuals taking 600 or 10000 IU on daily basis (Aloia *et al.*, 2018).

There should be a dietary plan to get the desired quantities of vitamins, if any deficiency is suspected or diagnosed; and the use of supplements should be the second choice (Tardy *et al.*, 2020). Food fortification may be an alternative to enhance the supply of these nutrients in food. A person consuming a variety of food items in his routine diet is less likely to develop primary deficiency (Bailey *et al.*, 2012). There should be a focus on preventing vitamin D deficiency in children, pregnant women, and elderly people. Yet, usefulness of vitamin D supplementation in general needs more clinical evidences (Amrein *et al.*, 2020). The vitamin D be used only when needed (Lips *et al.*, 2020). There is a need to develop global criteria and recommendations for diagnosing vitamin D deficiency, follow remedies like basking in sunlight and dietary measures, use vitamin D supplementation based on the level of deficiency and follow up. Further, the management criteria need to be set, depending on the variables such as age, gender, comorbidities, profession and other lifestyle factors influencing vitamin D level. Since the side effects and toxicity are dose-dependent, so regulation of the over-the-counter availability of vitamin is essential. Focus should be on limiting the free availability of high dosage. There is a need to conduct long term studies to check the benefits of supplements and any long-term side effects. Although vitamin D plays an important role in many body systems but relying on supplements should be the last thing in the list of its level management. The dietary and skin sources should be focused on. The long-term consequences of vitamin supplement use are not known. Lastly, its use should be limited to those who need it, and its deficiencies should be corrected.

The study based on general information obtained from volunteers revealed that the deficiency and use of vitamin D in Hail region of Saudi Arabia is common. There have been some inconsistencies in information, so the data from many individuals was excluded and/or analysed. It is suggested to collect this type of data in presence of someone who can guide participants if they are unsure about anything. This may help in minimizing the missing data as well as multiple responses, so improve the accuracy level. As this study relied on the patient-response information, it is recommended to collect similar data along with laboratory testing of vitamin D levels and record of vitamin D dosages to explore more aspects linked with vitamin D supplementation.

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