

KNOWLEDGE AND AWARENESS OF VITAMIN D DEFICIENCY AMONG THE GENERAL POPULATION IN SAUDI ARABIA

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Abstract

Background: Vitamin D deficiency is a common problem worldwide, during the past decade, Vitamin D status has been a major concern. Numerous variables, including inadequate dietary vitamin D, malabsorption, and poor utilization, as well as increased needs, increased excretion, and catabolism, can contribute to vitamin D insufficiency. In addition, there are a variety of diseases that impair the bioavailability of vitamin D, such as gastrointestinal issues that restrict absorption and liver and kidney issues that can prevent the activation of parenteral vitamin D or interfere with its conversion to active metabolites. Lack of vitamin D is linked to autoimmune conditions like multiple sclerosis and rheumatoid arthritis. **Objectives:** the study aimed to assess the level of knowledge and awareness level of vitamin D deficiency among the general population of Saudi Arabia. **Methodology:** A cross-sectional study design was employed. A self-administered questionnaire was administered to an adult sample of 384 participants seeking information on their knowledge about vitamin D. Data was subsequently transmitted to the SPSS, version 20 (IBM SPSS Statistics for Windows, Version 20.0, Armonk, NY: IBM Corp.). **Results:** the total sample size is 375 individuals 189 males, 186 females. As regard knowledge and awareness score, 32.8% demonstrated a low level of knowledge about vitamin D deficiency. Conversely, 143 participants, comprising 38.1% of the sample, exhibited a moderate level of knowledge, while 29.1% of the respondents showed a high level of awareness. Comparison of knowledge scores among sociodemographic groups revealed significant differences in knowledge scores for age while no significant relation to nationality, education level, gender, family income and

marital status. **Conclusion:** The study highlighted a fair level of knowledge regarding vitamin D deficiency among study participants. There is a significant association between level of knowledge and age. More campaigns need to be held to educate people sufficiently regarding the dietary sources and established health benefits of vitamin D for bones, muscles, and immune system. Nongovernment organizations and social workers may work together with government health-care organizations to teach parents and children about the uses and benefits of vitamin D.

Keywords: vitamin D deficiency, vitamin D, awareness, Saudi Arabia, knowledge.

Introduction:

Vitamin D3 and vitamin D2 are two physiologically inactive precursors of vitamin D. To create active 1, 25-dihydroxyvitamin D (calcitriol), both precursors from diet and sunshine exposure undergo two hydroxylation's: one in the liver and the other in the kidney [1]. Vitamin D also known as the sunshine vitamin has a great importance in increasing intestinal absorption of calcium, magnesium, phosphate, and zinc & maintaining good healthy bones. Sun is the main source for this vitamin and there are few foods that contain it, for example milk and egg. The normal range of vitamin D is defined as a 25(OH)D Concentration greater than 30 ng/mL (75 nmol/L) and deficiency is less than 20 ng/mL (50 nmol/L) [2]. Vitamin D deficiency is currently recognized as a major health problem worldwide, affecting both sexes and all age groups. Severe vitamin D deficiency may result in rickets in infants and children, osteomalacia in adults, and subclinical vitamin D deficiency, which is more prevalent and is linked to osteoporosis. In addition, vitamin D deficiency is associated with non-skeletal diseases such as cancers, diabetes mellitus & cardiovascular disease [3]. Low levels of knowledge about Vitamin D deficiency and low supplement intake were reported to be causal factors for the high prevalence of Vitamin D deficiency among Saudi adults [4]. Low dietary vitamin D levels, limited sun exposure, obesity, restricted mobility, geographic latitude, and genetic susceptibility all contribute to vitamin D insufficiency [5].

Additionally, studies in Jeddah, Saudi Arabia, found that 67.5% of Saudi teenage females had low vitamin D levels (50 nmol/L), making them more susceptible to developing conditions like osteoporosis that are linked to low vitamin D levels [6]. Around the world, 50% of the population suffers from vitamin-D insufficiency, with an estimated 1 billion people suffering from vitamin-D deficiency [7]. Numerous variables, including inadequate dietary vitamin D, malabsorption, and poor utilization, as well as increased needs, increased excretion, and catabolism, can contribute to vitamin D insufficiency. In addition, there are a variety of diseases that impair the bioavailability of vitamin D, such as gastrointestinal issues that restrict absorption and liver and kidney issues that can prevent the activation of parenteral vitamin D or interfere with its conversion to active metabolites. Lack of vitamin D is linked to autoimmune conditions like multiple sclerosis and rheumatoid arthritis. Vitamin D insufficiency and the likelihood of developing chronic diseases are strongly correlated. A 30%–50% higher risk of colon, prostate, and breast cancers, as well as other cancers, has been associated with vitamin D levels under 20 ng/mL [8]. Lack of knowledge about the significance of vitamin D, its health advantages, and ways to prevent deficiency states in populations has been one of the main factors contributing to the global spread of this nutritional condition [9]. There is insignificant number related to our topic, especially in

Saudi Arabia. Thus, we conduct this research.

Objectives:

This study aimed to assess the level of knowledge and awareness level of vitamin D deficiency among the general population of Saudi Arabia.

Materials and Methods:

Study design: This is an observational cross-sectional study that was conducted among the general population of Saudi Arabia from July 2023 to April 2024.

Study setting: Participants, recruitment, and sampling procedure:

The study's population consisted of Saudi adult over the age of 18, participants were recruited during 2023-2024 from people receiving the questionnaire.

Inclusion and Exclusion criteria:

Male and female adults over 18 years of age from all social classes were included. Saudi adults under 18 years of age, Individuals on vitamin D supplements were excluded.

Sample size:

The sample size was calculated by (Raosoft, Inc., Seattle, WA, USA)(22) at 384 individuals using the following formula, and applying means and standard deviation. Considering standard deviation (=1.96) for 95% confidence interval and the maximum acceptable marginal error (=0.05). Therefore, the calculated minimum sample size required for this study is $n = (1.96)^2 \times 0.50 \times 0.50 / (0.05)^2 = 384$ participants.

$$n = \frac{Z^2 p(1-p)}{d^2}$$

Method for data collection and instrument (*Data collection Technique and tools*):

A 25-item questionnaire was developed after performing thorough literature review and influences were drawn from some of the research published earlier. The questionnaire was originally developed in English and later was translated into Arabic using the WHO protocol for translation of a questionnaire [11]

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After doing a thorough literature study, a 25-item questionnaire was created, with some of the preceding research's influences used. The questionnaire was initially created in English and afterwards translated into Arabic in accordance with the WHO protocol for questionnaire translation. [10].

Scoring system:

Overall, fifteen sentences were used to describe the level of knowledge and awareness of vitamin D deficiency among the general population in Saudi Arabia. One point is given for correct answers and zero points for incorrect answers, or I don't know. The scoring system was divided as follows. More than or equal to 14 is considered a high level of knowledge, less than 14 and more than 10 or equal is considered a medium level of knowledge, less than 10 is considered a low level of knowledge

Analyzes and entry method: Using the "Microsoft Office Excel Software" software (2021) for Windows, data was entered into the computer, in order to do statistical analysis, data was subsequently transmitted to the SPSS application, version 20 (IBM SPSS Statistics for Windows, Version 20.0, Armonk, NY: IBM Corp.).

Results:

Table (1) provides a comprehensive overview of the participants' profiles, highlighting key parameters such as age, gender, nationality, education level, marital status, family income, sun exposure, and sunscreen usage rate. The data, derived from a sample size of 375 individuals, reveals a diverse representation across various demographics. Notably, the majority of participants fell within the age range of 18 to 30 years old, with a fairly balanced distribution between males and females. The high proportion of Saudi nationals in the study reflects the local context, while the educational attainment varied from primary school to postgraduate levels. Furthermore, the data sheds light on factors such as marital status, family income brackets, sun exposure durations, and sunscreen usage patterns among the participants. This detailed breakdown of sociodemographic characteristics provides a valuable foundation for understanding the prevalence of vitamin D deficiency and devising targeted interventions to enhance awareness and knowledge within the Saudi Arabian population.

Table (1): Sociodemographic characteristics of participants (n=375)

Parameter		No.	Percent (%)
Age	18 to 30 years old	143	38.1
	31 to 50 years old	128	34.1
	more than 50 years old	104	27.7
Gender	Male	189	50.4
	Female	186	49.6
Nationality	Saudi	345	92.0
	Non-Saudi	30	8.0
Education level	Primary school	2	.5
	Middle school	6	1.6
	High school	49	13.1
	Diploma	27	7.2
	Bachelor's degree	245	65.3
	Postgraduate	46	12.3
Marital status	Single	124	33.1
	Married	237	63.2
	Divorced	9	2.4
	Widowed	5	1.3
Family income	<10000	104	27.7
	10000-15000	81	21.6
	16000-20000	60	16.0
	>20000	130	34.7
Sun exposure per day (in minutes)	Less than 5	95	25.3
	5 to 10	123	32.8
	20 to 25	66	17.6
	30 or more	91	24.3
Sunscreen usage rate	Always	64	17.1
	Sometimes	80	21.3
	Never	231	61.6

In figure (1), it is evident that there is a notable disparity in the frequency of sunscreen application among the surveyed individuals. The figure indicates that a significant portion of the respondents, specifically 231 individuals, reported never using sunscreen. This finding raises concerns about the potential risks and consequences associated with inadequate sun protection, such as an increased susceptibility to skin damage and a higher risk of developing skin cancer. On the other hand, it is encouraging to see that a considerable number of individuals, 80 in this case, reported using sunscreen

sometimes, demonstrating a level of awareness and willingness to protect their skin from harmful UV rays. However, the most striking observation is that only 64 respondents reported always using sunscreen.

Figure (1): illustrates sunscreen usage rate among participants

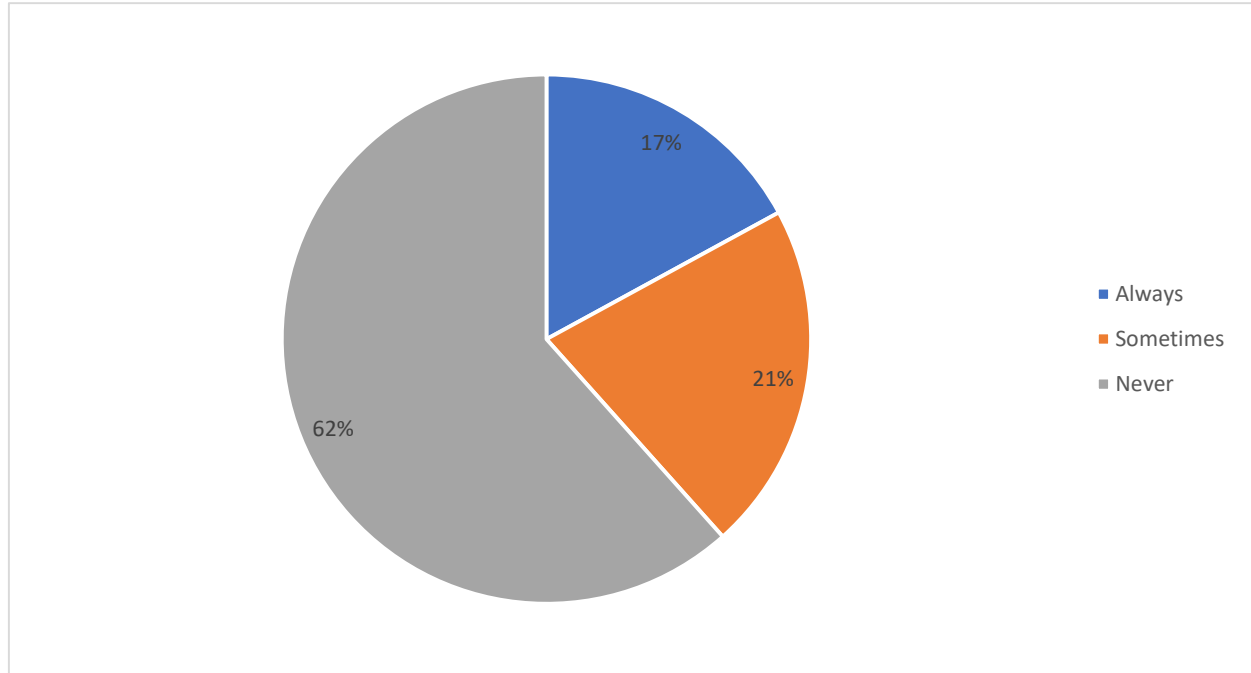


Table (2) reveals significant findings, such as the percentage of individuals who have been tested for vitamin D, the prevalence of vitamin D deficiency among the participants, and the usage of multivitamins, vitamin D supplements, and calcium supplements. Additionally, the table delves into the presence of diseases causing vitamin D deficiency among the participants, the use of drugs that may lead to vitamin D deficiency, and the presence of conditions or habits affecting the body's absorption of vitamin D. These findings provide valuable insights into the current level of knowledge and awareness regarding vitamin D deficiency among the general population in Saudi Arabia.

Table (2): Participants' knowledge and awareness of vitamin D deficiency among the general population in Saudi Arabia (n=375).

<i>Parameter</i>	<i>Yes</i>	<i>No</i>	<i>I don't know</i>
<i>Tested for vitamin d</i>	266 (70.9%)	109 (29.1%)	-
<i>Vitamin d deficient</i>	262 (69.9%)	113 (30.1%)	-
<i>Using multivitamins</i>	242 (64.5%)	133 (35.5%)	-
<i>Using vitamin D supplements</i>	247	128	-

	(65.9%)	(34.1%)	
<i>Using calcium supplements</i>	166 (44.3%)	209 (55.7%)	-
<i>Do you have any disease-causing Vitamin D deficiency?</i>	- Cystic disease 1 (.3%) - Celiac disease 3 (.8%) - Other 16 (4.3%)	355 (94.7%)	-
<i>Do you use any drug causing Vitamin D deficiency?</i>	- Steroid (prednisone) 1 (.3%) - Cholesterol lowering drugs (cholestyramine and colestipol) 27 (7.2%) - Rifampin (a tuberculosis drug) 1 (.3%) - Other 6 (1.6%)	340 (90.7%)	-
<i>Do you suffer from diseases that affect the body's absorption of vitamin D?</i>	17 (4.5%)	221 (58.9%)	137 (36.5%)
<i>Do you suffer from bad habits that reduce vitamin D absorption?</i>	61 (16.3%)	140 (37.3%)	174 (46.4%)

Table (3) reveals the participants' rates of consumption of various vitamin D sources, including eggs, fish, liver, and milk. It is evident from the data that there is a significant disparity in the frequency of consumption across different food categories. For instance, while a substantial portion of participants reported consuming eggs once a week, the consumption of fish, liver, and milk on a daily basis was notably lower. These findings shed light on potential gaps in dietary habits that may contribute to vitamin D deficiency within the Saudi Arabian population.

Table (3): Participants' rate of consumption of vitamin d rich food (n=375).

<i>Parameter</i>	Daily	4–5 times a week	2–3 times a week	Once a week
Egg	43 (11.5%)	42 (11.2%)	152 (40.5%)	138 (36.8%)
Fish	8 (2.1%)	3 (0.8%)	24 (6.4%)	340 (90.7%)
Liver	7 (1.9%)	1 (0.3%)	18 (4.8%)	349 (93.1%)
Milk	61 (16.3%)	26 (6.9%)	113 (30.1%)	175 (46.7%)

As illustrated in table (4), It is evident from the data that a significant percentage of participants recognize the role of vitamin D in strengthening immunity, with 66.7% acknowledging this fact. Moreover, a substantial proportion, 73.6%, understand the link between vitamin D deficiency and depression. Interestingly, when it comes to the sources of vitamin D, 54.9% of participants believe that all of the above options, including sunlight exposure, food supplements, and certain foods, are viable sources. Additionally, the data reveals varying levels of awareness regarding the symptoms and complications of vitamin D deficiency among the participants. Overall, the findings highlight the importance of enhancing knowledge and awareness regarding vitamin D among the general population in Saudi Arabia to promote better health outcomes and disease prevention.

Table (4): Parameters related to Specific questions to assess the knowledge and awareness level of participants (n=375).

Parameter		No.	Percent (%)
<i>Vitamin D helps strengthen immunity?</i>	Yes	250	66.7
	No	13	3.5
	I don't know	112	29.9
<i>Vitamin D deficiency linked with depression?</i>	Yes	276	73.6
	No	13	3.5
	I don't know	86	22.9
<i>vitamin D is higher in animal meat than vegetables and fruits?</i>	Yes	89	23.7
	No	81	21.6
	I don't know	205	54.7
<i>Choose the symptoms of vitamin D deficiency, that you know **</i>	Overweight	0	0
	Mood swings	0	0
	High blood pressure	0	0
	Digestive problems	81	21.6
	Dry skin	143	38.13
	Fatigue	329	87.73
	Immune impairment	156	41.6
	Joint pain	241	64.27
<i>vitamin D is important in maintaining calcium and phosphate?</i>	Yes	190	50.7
	No	8	2.1
	I don't know	177	47.2
<i>Do you think that vitamin D deficiency is related to other diseases like: cardiovascular, diabetes, depression, hypercholesterolemia, cancer, and multiple sclerosis?</i>	Yes	240	64.0
	No	15	4.0
	I don't know	120	32.0
<i>If yes, state the diseases associated with vitamin D deficiency (n=254) **</i>	Cardiovascular diseases	86	33.68
	Diabetes	60	23.62

	Depression	205	80.71
	Hypercholesterolemia	91	35.83
	Cancer	35	13.78
	Multiple sclerosis	66	25.98
<i>Do you know normal range of vit d?</i>	Between 10 and 20 ng/mL	18	4.8
	Between 15 and 25 ng/mL	24	6.4
	Between 20 and 40 ng/mL	58	15.5
	Above 40	98	26.1
	Don't know	177	47.2
<i>What are the best Sources of Vitamin D?</i>	Sunlight Exposure	162	43.2
	Food supplements (multivitamins)	4	1.1
	Certain Foods	3	.8
	All of the above	206	54.9
<i>Do you know the Complications of vitamin D deficiency? (You can choose more than one answer) **</i>	Osteoporosis	281	74.93
	Depression	286	76.27
	Hair loss	242	64.53
	Eczema	42	11.2
	Peptic ulcer	42	11.2
	Blindness	19	5.1

Results may overlap**

Figure (2) provides a breakdown of responses regarding the best sources of Vitamin D. It appears that a significant majority of individuals, totalling 206 respondents, believe that all the options listed - sunlight exposure, food supplements (multivitamins), and certain foods - are essential sources of Vitamin D. This suggests a comprehensive understanding among the participants of the diverse ways in which Vitamin D can be obtained. Sunlight exposure emerges as the most popular choice, with 162 individuals recognizing its importance. This aligns with the well-known fact that the human body can naturally synthesize Vitamin D when exposed to sunlight. Only a small number of respondents, 4 and 3 respectively, identified food supplements and certain foods as primary sources of this vital nutrient. This disparity in responses may indicate varying levels of awareness or perhaps differing opinions on the efficacy of these sources in meeting Vitamin D requirements.

Figure (2): illustrates the best sources of vitamin D among participants.

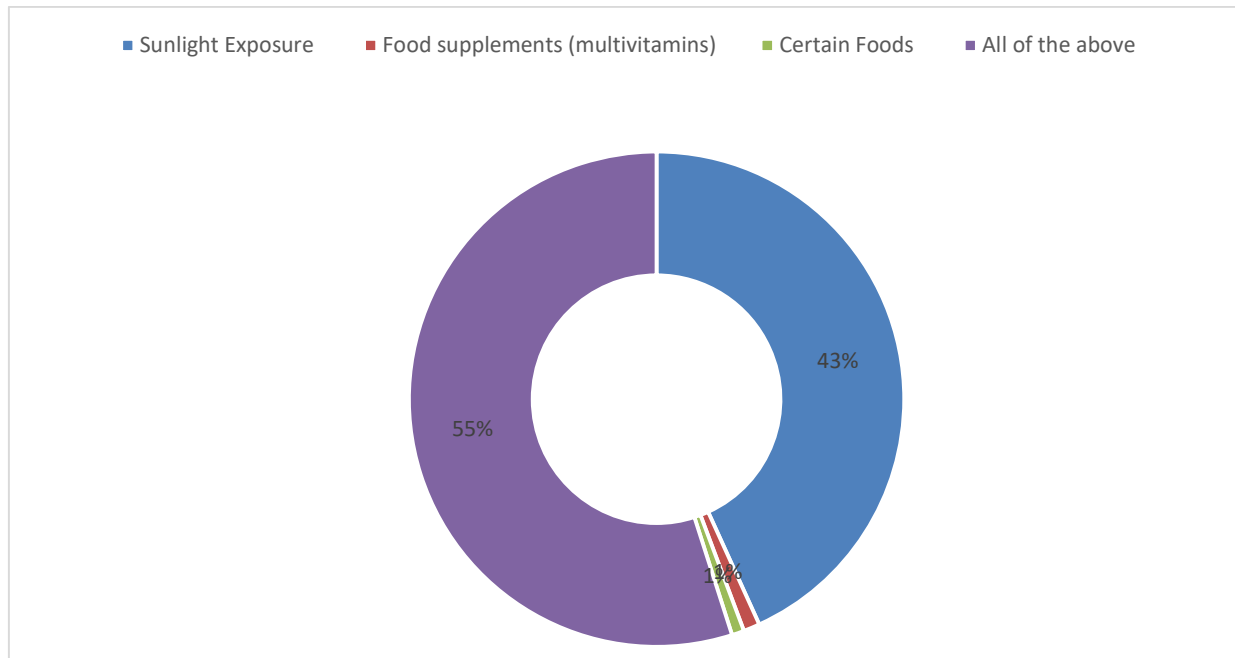


Table (5) presents a comprehensive overview of the knowledge and awareness of vitamin D deficiency among the general population in Saudi Arabia, as indicated by the score results. The data is segmented into three categories: high level, moderate level, and low level of knowledge. It is evident from the table that a significant portion of the population falls under the moderate level category, with 143 individuals accounting for 38.1% of the total sample size. The high level of knowledge group comprises 109 individuals, representing 29.1% of the respondents. Conversely, the low level of knowledge group consists of 123 individuals, making up 32.8% of the total sample. These findings suggest a varied distribution of awareness levels regarding vitamin D deficiency among the Saudi Arabian population. The data underscores the importance of targeted educational initiatives to enhance public knowledge and awareness of this critical health issue.

Table (5): Shows knowledge and awareness of vitamin D deficiency among the general population in Saudi Arabia score results.

	Frequency	Percent
High level	109	29.1
Moderate level	143	38.1
Low level of knowledge	123	32.8
Total	375	100.0

As illustrated in table (6), It is evident that the level of knowledge of vitamin D supplements shows statistically significant relation to gender (p value=0.0001). It also shows statistically insignificant relation to age, nationality, and family income.

Table (6): Relation between knowledge level of vitamin D and sociodemographic characteristics.

	Level of knowledge		Total (N=375)	P value*
	High or moderate	Low		

Gender	Male	100	89	189	0.0001
		39.7%	72.4%	50.4%	
	Female	152	34	186	
		60.3%	27.6%	49.6%	
Age	18 to 30 years old	100	43	143	0.153
		39.7%	35.0%	38.1%	
	31 to 50 years old	90	38	128	
		35.7%	30.9%	34.1%	
	more than 50 years old	62	42	104	
		24.6%	34.1%	27.7%	
Nationality	Saudi	234	111	345	0.381
		92.9%	90.2%	92.0%	
	Non-Saudi	18	12	30	
		7.1%	9.8%	8.0%	
Family income	<10000	70	34	104	0.850
		27.8%	27.6%	27.7%	
	10000-15000	57	24	81	
		22.6%	19.5%	21.6%	
	16000-20000	41	19	60	
		16.3%	15.4%	16.0%	
	>20000	84	46	130	
		33.3%	37.4%	34.7%	
Education level	Primary school	2	0	2	N/A
		0.8%	0.0%	0.5%	
	Middle school	4	2	6	
		1.6%	1.6%	1.6%	
	High school	23	26	49	
		9.1%	21.1%	13.1%	
	Diploma	16	11	27	
		6.3%	8.9%	7.2%	
	Bachelor's degree	179	66	245	
		71.0%	53.7%	65.3%	
Marital status	Single	88	36	124	N/A
		34.9%	29.3%	33.1%	
	Married	153	84	237	
		60.7%	68.3%	63.2%	
	Separated	9	0	9	
		3.6%	0.0%	2.4%	

	Widowed	2	3	5	
		0.8%	2.4%	1.3%	

**P value was considered significant if ≤ 0.05 .*

Discussion:

During the last decade, there has been major concern about vitamin D status in the health and biomedical fields, and many studies have been conducted examining its benefits, use, and deficiency [11]. Internationally, vitamin D deficiency is a global health problem in both children and adults and is considered an epidemic. The Middle East and North African region which includes Saudi Arabia has a very high rate of vitamin D deficiency which reaches 81% among various age groups [12]. Vitamin D has two biologically inert precursors: vitamin D3 and vitamin D2. Both precursors which come from sunlight exposure and diet are converted by two hydroxylation's: one in the liver and the other in the kidney to form active 1, 25-dihydroxyvitamin D (calcitriol) [13]. Metabolism of vitamin D also takes place in other tissues where the 1, 25(OH)₂D produced serves a paracrine/autocrine function [14]. Vitamin D deficiency can be attributed to many different factors, including insufficient vitamin D in the diet, malabsorption, and poor usage also increased demands, increased excretion, and catabolism. Besides that, there are numerous conditions that influence vitamin D bioavailability, such as gastrointestinal problems that limit absorption; The problems of the kidneys and liver can inhibit the activation of parenteral vitamin D or affect its conversion to active metabolites [15]. Vitamin D deficiency is correlated to rheumatoid arthritis and other autoimmune diseases such as multiple sclerosis. There is a substantial link between vitamin D deficiency and the chance of suffering chronic diseases. Vitamin D levels below 20 ng/mL have been linked to a 30%-50% greater risk of colon, prostate, and breast cancers, as well as a higher mortality rate from these malignancies, according to another research. Lately, vitamin D deficiency has been connected to the severity of COVID-19-related symptoms [16]. The role of vitamin D in calcium and phosphorus homeostasis and bone metabolism has been well recognized. The presence of vitamin D receptors in many cell types indicates that it has other physiologic functions. In children, it is associated with nutritional rickets, impaired growth, developmental delays, lethargy, and hypocalcemic seizures [17]. Lack of knowledge and awareness of vitamin D deficiency can be potential risk factors for the condition. Many studies show that there is lack of awareness and knowledge of vitamin D role and sources in several countries, including Hong Kong, Saudi Arabia, USA, and India [18,19,20,21]. Thus, our study aim was to assess the level of knowledge and awareness level of vitamin D deficiency among the general population of Saudi Arabia.

As regard knowledge and awareness score of vitamin D deficiency among the general population in Saudi Arabia, the total sample size is 375 individuals 189 males, 186 females. As regard knowledge and awareness score, 32.8% demonstrated a low level of knowledge about vitamin D deficiency. Conversely, 143 participants, comprising 38.1% of the sample, exhibited a moderate level of knowledge, while 29.1% of the respondents showed a high level of awareness. These findings underscore a moderate lack of understanding among the Saudi Arabian population regarding the importance of vitamin D and the risks associated with its deficiency. This result is in concurrence with two Egyptian studies done on mothers in the Delta region, both studies reported the poor knowledge level among Egyptian mothers regarding vitamin D and its deficiency [22,23]. The congruity in the

results could be related to the similarity in culture and background in the two neighboring countries. While Conner et al., in their population-based study in England, found that more than half of their study sample was having a good level of knowledge about vitamin D [24]. This finding is better than the recent findings. The discrepancy between both outcomes may be caused by the dissimilarities in the cultural aspects and health care systems - between the two study settings. Consistently with our results, a study conducted in United Kingdom revealed that more than two-thirds of participants had a low level of knowledge about the commonest symptoms of vitamin D deficiency [25]. Another study in India study showed that more than half of participants had a low level of knowledge about vitamin D deficiency in antenatal mothers [26] and another study reported in Saudi Arabia revealed that 40% of the mothers attending primary health centers in Al-Ahsa had a low level of knowledge about vitamin D supplementation to their infants [27]. In contrast, a study conducted by Nahla Kambal et.al, (2023) revealed that almost half of the participants in the study exhibited an overall high level of knowledge toward vitamin D and its role in health [28].

As regard awareness of vitamin D sources, we have found that 54.9% of participants believe that sunlight exposure, food supplements, and certain foods, are viable sources. Similarly, Al-Agha's study showed a good level of knowledge about sun exposure and dietary intake as vitamin D sources, but many people had poor knowledge about the safe times for sun exposure and many did not have time due to their working lifestyle [29]. Similar results were found in a French study where 72% of participants reported sun exposure as the main source of vitamin D and 50–60% of participants reported the right food sources like fatty fish [30].

Comparison of knowledge scores among sociodemographic groups revealed significant differences in knowledge scores for age while in an Australian study, the authors reported that being female, older, and having a higher educational degree were indicators for having a higher level of knowledge [31]. Similar findings were reported in a French study that included a higher monthly income as a predictor [32]. While in Al-Agha's study, the low level of knowledge was not associated with education level [33], and in a United Kingdom study, older people showed a low level of knowledge [34].

Conclusion:

The current study detected a moderate level of knowledge about vitamin D deficiency among general population in Saudi Arabia. The public should be educated to improve their knowledge, awareness, and attitudes regarding vitamin D deficiency and its sources. This information should be provided in conjunction with messages on preventative measures to ensure people do not increase their risk of skin cancer in an attempt to improve their vitamin D levels through excessive sun exposure. We strongly recommend that these findings are used in health policy-making. Non-government organizations and social workers may collaborate with the government to educate parents and children regarding the uses and benefits of vitamin D. This will help to improve overall health among the Saudi population.

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Ethics approval consideration:

Institutional research ethics board approval was acquired before conducting any study-related

procedures. Ethical approval was obtained from Research Ethics Committee of Ministry of Health in Jeddah with the IRB approval number (A017944).

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Conflict of interests

The authors declare that there are no conflicts of interest.

Informed consent:

Written informed consent was obtained from all individual participants included in the study.

Data and materials availability

All data associated with this study are present in the paper.

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