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Knowledge, attitude, and practice of Libyan medical students about vitamin D deficiency

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Abstract: The prevalence rate of vitamin D deficiency over the last decades has grown up rapidly worldwide among young adults. Therefore, the aim of this study is to explore the knowledge, attitude, and practice of Libyan medical students of Sebha University regarding vitamin D deficiency. Out of a total of 200 questionnaires, 148 completed questionnaires were returned (74.0% response rate). The majority of respondents did not measure their vitamin D levels (62.1%). Participants who indicated they were exposed to sunlight for less than 15 min were 47.2% while 74.9% were exposed to less than 30 min with a highly significant gender difference (p<0.001). All the males did not use sunscreen creams compared with females (43.5%). Nearly two-thirds of the participants (61.4%) denied drinking milk almost daily with significant differences based on gender (p<0.005) while 56.0 % of the participants reported eating fish, 60.8% of the students denied eating fast food and 74.3% eating eggs daily or weekly. However, 49.3% of the students usually drink tea and coffee after meals, and do not usually practice exercise (53.3%), however, disagreed that their food has a low amount of calcium (30.4%). Most of the students agreed with the benefits of vitamin D (72.0%). Based on the assessment of awareness of the participants about vitamin D information, the average of correct answers percentage of the respondents was 47.1%. The most frequent sources of vitamin D information were the internet which accounted for 49.3%, followed by relatives and friends (31.7%). Some of the respondents (58.7%) reported that unawareness is the main cause of vitamin D deficiency. This study highlights the lack of awareness about the importance of vitamin D among medical students. This finding provides the institutions of medical education in Libya with an evidence base for a deficit of knowledge regarding young health which could be utilized to draw a strategy to correct the health behaviors of students and the community through medical education programs.

Introduction

Vitamin D is essential for intestinal calcium absorption and it plays a central role in maintaining calcium homeostasis and skeletal integrity [1]. Vitamin D is unique because it can be made in the skin from exposure to sunlight [2]. Deficiency of vitamin D, or hypovitaminosis most commonly occurs in people when they have inadequate sunlight exposure (particular sunlight with adequate ultraviolet B rays, UVB, and reduction in taking of foods rich in vitamin D [3, 4]. Vitamin D deficiency has several complications which they associate



with increases in mortality and adverse effects such as cardiovascular diseases, type 2 diabetes mellitus, obesity, metabolic syndrome, immune disorders and various types of cancer and mortality [5-7]. Individuals such as the elderly may have a high risk of vitamin D deficiency since they have concurrent other factors related to vitamin D deficiency, including decreased sunlight exposure, reduced intake of vitamin D in the diet and decreased vitamin D absorption from sunlight due to decrease in their skin thickness [8]. However, the prevalence rate of hypovitaminosis D is not restricted to the elderly and hospitalized population. Modernization has also brought changes in the lifestyle and food habits of the young generation which may contribute to low dietary intake of vitamin D. The prevalence rate of vitamin D deficiency has grown up rapidly worldwide in adults during the past decades [9, 10]. In addition, some studies have reported a high prevalence rate of vitamin D deficiency among healthy, young adults [9-11]. Thus, in a Boston study, nearly two-thirds of healthy, young adults were found to be vitamin D insufficient at the end of winter [11].

In Libya due to modernization and the sudden rise in temperature, the number of hours spent outdoors has decreased and the sedentary way of working is most appreciated among urban people. Among Libyan population including young students may have a high risk of vitamin D deficiency. Recently, Alaasswad and others examined vitamin D status among pharmacy students of Sebha University which was conducted concurrent with this study and some participants were involved in this study [12]. The majority of pharmacy students in male and female blood donors have low vitamin D levels which represent 87.0% [12]. Inadequate awareness regarding vitamin D deficiency or non-adherence to the daily practice of the acquired knowledge or inappropriate exposure to the sun may also be the influential causes of deficiency of vitamin D. Therefore, this study was undertaken to explore awareness, knowledge, attitude and practice of healthy medical students toward vitamin D deficiency in Libya.

Materials and methods

This is a cross-sectional study designed to determine vitamin D status among healthy young medical students at Sebha University, Sebha, Libya. It was carried out between January and April 2020. All the medical students attending Sebha Medical School were asked to participate voluntarily in the study (n=200). The questionnaire was based on previous studies [13-15]. The survey contained 34 item questions that required varied response types. Most of the questions required specific categorical answers but some questions included another box to allow for more expressive answers. The questionnaire was translated to Arabic language form in order to clearly express for the participants. A verbal and written explanation of the study was provided when needed to the students for more detailed expression. All the students were informed about the study and were required to read an informative brochure to explain the purpose of the survey and the research. The investigator requested the participant's verbal and written consent. They have also been informed that the questionnaire was anonymous and should be deposited in a box located in front of the classroom, in order to guarantee confidentiality. An ethics approval action for the study was obtained from the Sebha University Research Ethics Committee (2/2020).

Statistical analysis: All analyses were carried out by using Microsoft Office Excel 2013 and the SPSS statistical package the generated data presented as percentage, variant increases and decreases, and mean and standard deviations were calculated. Paired *t*-test was used to compare between the individual groups. A probability value of less than 0.05 was considered as a level of significance difference.

Results

In this study, the questionnaires were handed to all the students who attended the first years of pharmacy, medicine and dentistry faculties. The returned questionnaires were 148 out of 200 which represents a response



rate of 74.0% with notably more females than males, 83.7%, and 16.3%, respectively. The majority of participants were female and aged between 18- and 20-years old accounting for 96.6%. Most of the participants denied having diabetes mellitus (97.2%). A great proportion of the participants reported that bone weakness is their family history (males: 29.1% and females: 45.1%). 62.1% did not measure their vitamin D levels compared with 35.1% who declared did. Only 02.7% did not answer the question. An equal rate of male and female students who reported did not measure their vitamin D levels, 62.5% and 62.4%, respectively.

Table 1:	Data about responses of	f the medical stu	dents for fact	ors related	to vitamin D	
		Drinking of milk			Chi-square	
	Yes	No		Total	P - value	
Male	12 (50.0%)	12 (50.0%)	0	024	0.209	
Female	45 (36.2%)	79 (63.7%)	0	124		
Total	57 (38.5%)	91 (61.4%)	0	148		
	Usi	ing sunscreen cre	am			
Male	00 (00.0%)	24 (100%)	0	024		
Female	54 (43.5%)	70 (56.4%)	0	124	0.000	
Total	54 (36.4%)	94 (63.5%)	0	148		
	Eating fast foods					
Male	11 (45.8%)	13 (54.1%)	00 (00.0%)	024	0.327	
Female	45 (36.2%)	77 (62.0%)	02 (01.6%)	124		
Total	56 (37.8%)	90 (60.8%)	02 (01.3%)	148		
		Eating fish				
Male	16 (66.6%)	07 (29.1%)	1	024	0.459	
Female	67 (54.0%)	05 (04.0%)	0	124		
Total	83 (56.0%)	64 (43.2%)	1	148		
		ng eggs daily or w	eekly			
Male	22 (91.6%)	02 (08.3%)	00 (00.0%)	024		
Female	88 (70.9%)	34 (27.4%)	02 (01.6%)	124	0.035	
Total	110 (74.3%)	36 (24.3%)	02 (01.3%)	148		
		tea and coffee af		-		
Male	16 (66.6%)	08 (33.3%)	0	024	0.060	
Female	57 (45.9%)	67 (54.0%)	0	124		
Total	73 (49.3%)	75 (50.6%)	0	148		
	· · · · · · · · · · · · · · · · · · ·	ing physical exer	cise			
Male	18 (75.0%)	06 (25.0%)	00 (00.0%)	024	0.001	
Female	48 (38.7%)	73 (58.8%)	03 (02.4%)	124		
Total	66 (44.5%)	79 (53.3%)	03 (02.4%)	148		
Total	` '	Diabetes mellitus		140		
Male	01 (04.1%)	023 (95.8%)	0	024	0.099	
Female	01 (00.8%)	121 (97.5%)	0	124		
Total	02 (02.7%)	144 (97.2%)	0	148		
Total	\ /	of food with calciu	Ů	140		
Male	05 (20.8%)	13 (54.1%)	06 (25.0%)	024		
Female	71 (57.2%)	32 (25.8%)	21 (16.9%)	124	0.009	
Total	76 (51.3%)	45 (30.4%)	27 (18.2%)	148		
Total	· · · · · · · · · · · · · · · · · · ·	history of bone v		1+0	 	
Male	07 (29.1%)	16 (66.6%)	01 (04.1%)	024		
Female	56 (45.1%)	54 (43.5%)	14 (11.2%)	124	0.542	
			, ,		J.542	
Total	63 (42.5%)	70 (47.2%)	15 (10.1%)	148		
24.1	<u>*</u>	tory of vitamin D		00.4		
Male	11 (45.8%)	09 (37.5%)	04 (16.6%)	024	0.471	
Female	70 (56.4%)	35 (28.2%)	19 (15.3%)	124		
Total	81 (54.7%)	44 (29.7%)	23 (15.5%)	148		



Almost half of the participants (47.2%) have exposure to sunlight less than 15 min per day and 74.9% have exposure to less than 30 min. On the contrary, 24.9% reported to exposed to light for more than 30 min. Thus, an analysis by Chi-square test revealed a high significant difference between males and females in exposure to sunlight (p<0.01). Half of the females declared to usually expose to sunlight (52.4%) for less than 15 minutes compared with males (20.8%). 36.4% of the total participants used sunscreen products. However, all the male students did not use sunscreen creams compared with 43.5% of female students who declared using sunscreen products (**Table 1**). In **Table 1**, 61.4% denied drinking milk every day. Female students have a higher rate of drinking milk than males, 63.7% and 50.0%, respectively. Females who denied drinking almost every day were as double as the males with no significant difference. 60.8% denied eating fast food. Female students were less likely to eat fast foods compared with males. In the same way, 45.8% of the males declared eating fast foods compared with females (37.8%). 56.0% eat fish and males eat more than females, 66.6% and 54.0%, respectively. The majority of male and female students usually eat eggs whether daily or weekly (74.3%). This habit was more dominant in males (91.6%) than females (70.9%) with a significant difference of p<0.035. About half of the students (49.3%) usually drink tea and coffee after meals but 66.6% of the males reported yes and half of the females denied doing that regularly (54.0%).

In **Figure 1**, male students (54.1%) denied their food has a poor quantity of calcium compared with 25.1% of females. 30.4% disagreed that their food has a low amount of calcium. This difference is significant between genders (p<0.01). **Table 1** shows that three quarters of male students do regular exercise. Thus, students do not usually practice physical exercise (53.3%) with a highly significant difference (p<0.001). A family history of vitamin D deficiency was found to be 54.7%. Females were more likely to have a family deficiency of vitamin D than males (56.4% and 45.8%, respectively). Most of the students' answers agreed that vitamin D is used for the treatment of bone disorders and rickets (71.6%) and only 02.7% disagreed, but 25.6% did not know in their answers.

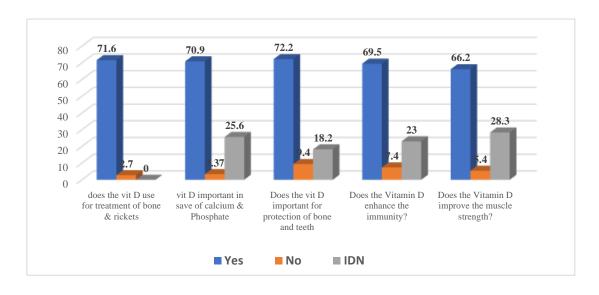


Figure 1: Libyan Medical participant's responses to benefits of vitamin D

Figure 1 shows the respondents agree that vitamin D is important in saving the level of calcium and phosphate. However, only 03.37% disagreed and all of them were solitary females. Three quarters of the respondents agreed that vitamin D can protect the bones and teeth compared with 09.4% who disagreed (female students). 69.5% agreed that vitamin D can enhance the body's immunity. 70.9% of females slightly agreed with the statement compared with 62.5% of males with 23.0% could not answer this question. Also, in **Figure 1**, 66.2% agreed that vitamin D can improve muscle strength compared to those who disagreed (05.4%) and 28.3% could not answer this question



Table 2: Knowledge of the Libyan participants about vitamin D deficiency						
Questions	Yes	No	IDN			
Do you agree that the incidence of vitamin D deficiency in Libya more than other countries	42 (28.3%)	21 (14.1%)	85 (57.4%)			
Does the sun is the main source of vitamin D	130 (87.8%)	09 (06.0%)	09 (06.0%)			
Does the Osteoporosis is one of the symptoms of vitamin D deficiency?	111 (75.0%)	13 (08.7%)	24 (16.2%)			
Can vitamin D deficiency be replenished by eating dairy products?	52 (35.1%)	41 (27.7%)	55 (37.1%)			
Does the vitamin D deficiency cause depression?	86 (58.1%)	11 (07.4%)	51 (34.4%)			
Dose the level of vitamin D in the body differ by change in time and seasons?	64 (43.2%)	08 (05.4%)	76 (51.3%)			
Does the vitamin D sources are found in animals but not in Vegetables and fruits?	15 (10.1%)	83 (56.0%)	50 (33.8%)			
Are the people who live in cloudy areas more susceptible to vitamin D deficiency?	87 (58.7%)	13 (08.7%)	48 (32.4%)			
Does frequent exposure to the sun not lead to vitamin D toxicity?	27 (18.2%)	43 (29.0%)	78 (52.7%)			
Could the use of sunscreen be a cause of vitamin D deficiency?	34 (22.9%)	41 (27.7%)	73 (49.3%)			
Could a fat-free diet be a cause of vitamin D deficiency?	46 (31.0%)	31 (20.9%)	71 (47.9%)			
Dark skin more susceptible to vitamin D deficiency than light skin?	18 (12.1%)	54 (36.4%)	76 (51.3%)			
Can vitamin D toxicity cause hypercalcemia?	29 (19.5%)	17 (11.4%)	102 (68.9%)			
In the case of vitamin D deficiency, taking pharmaceutical preparations containing vitamin D is more effective compared to foods, diet and exposure to sunlight.	75 (50.6%)	37 (25.0%)	36 (24.3%)			
Taking vitamin D supplements (medications) is wrong unless prescribed by a doctor.	107 (72.2%)	20 (13.5%)	21 (14.1%)			
Taking vitamin D supplements is necessary to treat vitamin D deficiency, but not to prevent it.	90 (60.8%)	19 (12.8%)	39 (26.3%)			
Average percentage of correct answers of the	e respondents is	47.1%.				

In **Table 2**, 57.4% did not know the incidence of vitamin D deficiency in Libya more than in other countries while 28.3% agreed with this statement compared with 14.1% who disagreed. 87.8% believed that the sun is the main source of vitamin D compared with 06.0% in each of those who disagreed with the statement and those who could not answer the question. Also, in **Table 2**, the majority agreed that osteoporosis is one of the symptoms of vitamin D deficiency compared to only 08.7% who disagreed. However, 16.2% chose they do not know. Furthermore, 35.1% agreed with the statement that vitamin D can be replenished by eating dairy products compared with 27.7% who disagreed. 58.1% agreed with the statement vitamin D deficiency can cause depression compared with only 07.4% who disagreed. Over half of the respondents could not answer the question that levels of vitamin D differ by time and season changes. 05.4% disagreed with the statement. 10.1% agreed with the statement that vitamin D is found in animal sources rather than vegetable or fruit sources while 56.0% contradicted this statement, but 33.8% could not answer the question. 58.7% agreed with the statement that people who live in cloudy areas are more susceptible to vitamin D deficiency compared with 08.7% who disagreed and 32.4% could not answer this question. Only 12.1% agreed with the statement that dark skin is more susceptible to vitamin D deficiency than light skin compared with 36.4% who disagreed with the same statement and 36.4% could not answer this question. As shown in **Table 2**, 50.6% agreed with



the question that taking pharmaceutical preparation is more effective than foods, diet and exposure to sunlight and they represent as double as respondents (25.0%) who disagreed with this statement with 24.3% could not answer this question. Furthermore, 72.2% agreed with the statement that vitamin D supplements are wrong unless prescribed by a physician while a minority of respondents disagreed and could not answer the question represented by 13.5% and 14.1%, respectively. 60.8% agreed that a vitamin D supplement is necessary to treat vitamin D deficiency rather than to prevent it. 76.3% knew the disease of vitamin D deficiency while 16.2% did not have knowledge about this disease. Females (77.4%) were more declared that have knowledge about the disease than males (70.8%) and 07.4% were unable to answer this question. The highest rate of source of information among respondents was the Internet which accounted for 49.3% followed by relatives and friends (31.7%). To less extent, respondents chose medical providers and media by 16.2% and 10.1%, respectively. 12.1% would not receive information about vitamin D compared with 82.4% who would like to get this information. Also, in Figure 2, respondents disagreed with males more than females (25.0% and 09.6%, respectively). The highest rate of causes reported by respondents (58.7%) was unawareness of the risk of vitamin D deficiency followed by medication (53.3%). To a lesser extent, imbalance in nutrition was represented by 34.4%. Thus, Figure 2 shows respondents reported a lifestyle and less exposure to sun rays, concomitant disease and others reported by 11.5%, 07.4% and 10.1%, respectively.

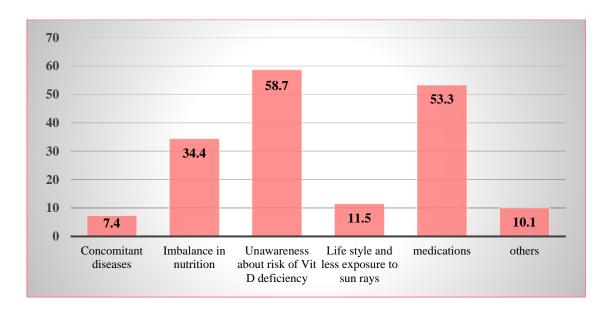


Figure 2: Causes of prevalence of vitamin D deficiency among Libyan participants

Discussion

Vitamin D can be made in the skin from exposure to sunlight [16]. The major source of vitamin D is to synthesis of vitamin D from skin exposure to ultraviolet B radiation which leads to the conversion of 7-dehydrocholesterol to pre-vitamin D3 and rapidly converted to vitamin D3 [17]. Regarding its role, it suggests a low prevalence of vitamin D deficiency in Mediterranean Sea countries. This study reports that medical students have exposure to sunlight for less than 30 minutes. Males had a higher average compared with females exposing themselves to sunlight. In a Chinese study, 62.3% declared that they did not like going in the sun [15]. Exposure to peripherals such as legs and arms for 15 min twice a week was reported to be enough for adequate sun-induced cutaneous vitamin D synthesis in adolescents [17]. In veiled Arab women, vitamin D deficiency is a result of a combination of limitations in sunlight exposure and low oral intake of vitamin D [18]. The current evidence showed wearing concealing clothes is associated with vitamin D deficiency irrespective of race or strength of solar radiation [18, 19]. The influence of clothing style on vitamin D status



was the subject of several previous studies [20-22]. All Libyan females wearing hijabs. Thus, covering most of the body when women get outdoor activities, can decrease the skin opportunity for exposure to direct sunlight. Hypovitaminosis of vitamin D is less prevalent among individuals who stay indoors for more time, wearing clothes covering a wide area of the skin and their skin pigmentation is darker [23]. In Sudan, onethird of female medical students used sunscreen [24]. Using of sunscreens could result in vitamin D deficiency since they have a protective effect against ultraviolet B. Using sunscreen with a sun protection factor of 30 reduces vitamin D synthesis in the skin [3, 25]. This differs from China's study which reveals 85.0% of the participants used some sun protection and 33.0% of males used sunscreen compared with females [26]. The reason behind this variation could be related to the difference in geographical, socioeconomic and educational factors. A finding of a study of medical students in Pakistan was in accord with our study, in which the female students have a greater proportion of using sunscreen than males [14]. This could be elucidated that males believe that sunscreen is not for masculine and it is a product intended for feminine since they are not as highly concerned with skincare as remarkable with females [12]. Healthy young adults may develop vitamin D deficiency when vitamin D intake is below the recommended intake [28]. The intake of a diet rich in vitamin D is important for maintaining body vitamin D hemostasis. Dietary supplements are useful to prevent and treat this deficiency [29, 30]. The present study revealed the participants' consumption frequency of some foods rich in vitamin D was low and participants denied usually drink milk. The UK retail study showed vitamin D3 and 25(OH)D3 concentrations of eggs were significantly different depending on egg production systems [31]. Evidence demonstrated that vitamin D in eggs is increased in birds exposed to ultraviolet radiation [31]. Performing physical activity in the outdoor environment with sun exposure would provide benefits from the physical work itself and from vitamin D synthesis and action in the body [32]. This finding is slightly higher in a Libyan study in which reported that 44% of adults do not get sufficient exercise [18]. Women are inclined to follow a sedentary lifestyle compared with men where they spend much time at home [33]. Physical inactivity among other factors such as obesity, and low vitamin D dietary and supplement intake are major modifiable predictors of low vitamin D status [34].

Vitamin D deficiency relates to diseases such as diabetes mellitus [35]. A meta-analysis study indicated the risk of developing diabetes mellitus decreases by 04.0% with each 10 nmol/L increase in 25(OH) D [36]. A nutrition examination survey reported an inverse relationship between 25(OH) D and glycated hemoglobin (HbA1c) levels aged people (35-74 years) with no history of diabetes mellitus [37]. Previous studies have revealed genetic variants related to vitamin D hemostasis and strongly depend on endogenous vitamin D production, which is influenced by genetic determinants [38]. Twin and family studies have shown high vitamin D heritability [39, 40]. Ethnic differences in the prevalence of common genetic polymorphisms are another likely explanation for low vitamin D in African Americans [41]. Among the ethnic groups in Malaysia, Malay and Indian females were six-fold times more likely to have vitamin D deficiency compared to Chinese females [38]. The majority of students agreed that vitamin D used for the treatment of bone disorders and rickets, and importance of saving the level of calcium and phosphate, protecting the bones and teeth, enhancing the body's immunity and improving muscle strength. This is in good line with Babelghaith et al. [42]. The high awareness of the benefits of vitamin D deficiency could be related to university students and particularly medical students who might pursue higher education in health subjects. Brand et al. [43] reported older age appeared to be associated with a lower perception of risk of vitamin D deficiency. Many healthcare professionals are not fully aware of the benefits of vitamin D to public health [44]. A similar trend is reported in Pakistan and Australian studies [45, 46]. This awareness about the benefits of vitamin D is important to encourage people and university students to influence their behaviors toward vitamin D practice. Over three quarters of the participants knew about vitamin D deficiency disease which is similar to a previously published study [47]. This could be elucidated that the respondents received some information but were still unsatisfied with the amount of information they had. This aligned with study conducted in Bahrein on the adult population



[48]. The majority had heard about vitamin D despite the low level of awareness of sources and the role of vitamin D [15]. This poor knowledge could be due to conflicting information available from various sources about vitamin D. In contrast, 02.0% reported that the internet is the source of their knowledge and information about calcium and vitamin D [49]. In the UK, the most common source of vitamin D information is the media followed by friends and family [50]. In Saudi Arabia, the information source was healthcare providers followed by friends [42]. It is not surprising that evidence also reported that healthcare workers lack a high knowledge of vitamin D deficiency [51]. The knowledge of medical students about some direct and simple questions generally scored as good knowledge. For example, the majority believed that the sun is the main source of vitamin D and recognized the influence of vitamin D deficiency can cause osteoporosis. This finding is in line with the Indian study conducted on female medical students in the majority of the participants correctly pointed out the effect of vitamin D on bone health [13]. The statement that vitamin D is found in animal sources but not in vegetable or fruit sources was high in our study. However, fruits were the main source of vitamin D among university students followed by vegetables participants [45]. 20.0% of pharmacy students failed to mention at least one vitamin D-rich product [49]. Over half of respondents agreed that taking pharmaceutical preparation is more effective than foods, diet and exposure to sunlight. However, participants had poor knowledge about toxicities and pharmacokinetics of vitamin D management. Over a quarter of respondents rejected the statement that exposure to the sun leads to the toxicity of vitamin D. A minority of respondents disagreed with the same statement can vitamin D toxicity causes hypercalcemia. Lack of awareness will increase this problem while adequate knowledge about vitamin D deficiency and its prevention can cause a potential decrease in the disease burden. Similarly, in Sudan, half of female medical students stated sunscreen does not interfere with vitamin D synthesis in the skin [24]. The highest rate of causes of hypovitaminosis D among the Libyan population was unawareness of people about the risk of vitamin D deficiency. This is consistency with the finding that lack of awareness about the importance of vitamin D, its health benefits and the prevention of deficient states across populations as important factors for the spread of vitamin D deficiency [52, 53]. Lack of knowledge about vitamin D and negative attitudes toward sunlight exposure is prevalent among university students [45, 54]. Ironically, in this study, a lifestyle and less exposure to sunlight can cause vitamin D deficiency which is in contrast to the fact that the worldwide pandemic of hypovitaminosis D mainly is attributed to lifestyle and environmental factors that reduce exposure to sunlight [55]. As a consequence, the sedentary lifestyle of individuals who have fewer physical activities such as female gender due to sociocultural or indoor job is liable to exposure to sunlight at a lower rate since they have limited time for outdoor activities.

Conclusion: This study presents poor practice, inadequate knowledge, and low awareness of the importance of vitamin D deficiency among medical students of the University. The majority have an adequate understanding of the benefits of vitamin D. This study provides Libyan institutions of medical education evidence for a deficit of knowledge which could be utilized as a strategy to correct health behaviors through medical education programs.

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Author contributions: All the authors substantially contributed to the conception, compilation of data, checking and approving the final version of the manuscript and agreed to be accountable for its content.

Author declarations: The authors confirm that all relevant ethical guidelines have been followed and any necessary IRB and/or ethics committee approvals have been obtained.

Conflict of interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Data availability statement: The raw data that support the findings of this article are available from the corresponding author upon reasonable request.

Ethical issues: Including plagiarism, informed consent, data fabrication or falsification and double publication or submission were completely observed by the authors.



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