

## Vitamin D deficiency and its association with depression in Saudi female students at Taibah University

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### Abstract

Recent studies on vitamin D levels and depressive symptoms have indicated that a deficiency of vitamin D in the blood may associate with depression. However, further investigations are warranted to unravel the link between depression and Vitamin D. Therefore, the current work aims to indicate and evaluate the association between vitamin D deficiency and depression in female students of Taibah University. A cross-sectional study was performed to determine depressive outcomes for participants with deficiency in vitamin D compared with those with normal levels of vitamin D. The 100 female students were recruited in current study. Data was processed using the software package of SPSS 20. Independent t-test was applied as far as mean  $\pm$  SD concerned. The  $P$ -value  $\leq 0.05$ ,  $\leq 0.001$  was considered as statistically significant. It was found that 14% of patients had severe score of depression correlating with severe deficiency of vitamin D (DD) and 17% of mediatory depression patients had DD. However, normal female subgroup had insufficient and normal levels of vitamin D (42% and 9%, respectively) according to HAM-D scores. Furthermore, patients with severe depression and mediator depression had significantly lower levels of vitamin D when compared with patients without depressive disorders ( $P < 0.05$ ). Current study provides a strong evidence about the relationship between vitamin D deficiency and depression in female students at Taibah university.

**Keywords:** Depression, Deficiency of vitamin D, Vitamin D, HAM-D rating scale.

### 1. Introduction

In Saudi Arabia (SA) and the Gulf region in general, there are many public health issues related to vitamin D deficiency that need to be addressed (Bertone et al., 2012; Anglin et al., 2013). Saudi Arabians are more vulnerable to vitamin D deficiency because of certain risk factors predisposing them to this disorder. These include diet comprising of energy-rich food and drink, lack of exercise and other physical activities, cultural habits, avoiding exposure to sun due to excessive heat (Bertone et al., 2012; Anglin et al., 2013). Recent studies have advocated that up to 50% of adults and children worldwide are vitamin D deficient (Dean et al., 2011; Dennis et al., 2012). Vitamin D has a crucial role in the development and maintenance of bones and teeth. In addition, researchers are now noticing that vitamin D may have an impact on several other arenas of health. For example, the receptors for vitamin D are located in many parts of the brain, implying its role in the brain (Eyles et al., 2005). Some studies have suggested association

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of vitamin D receptors with development of depression and other mental health issues but the exact mechanism of action of vitamin D in the brain is not clear. One notion is that vitamin D may enhance the number of monoamines, such as serotonin, which may relieve depression (Hollis, 2004; Holick et al., 2011). There has been a surge in the number of studies on the vitamin D levels and depression. A deficiency of vitamin D in the blood has been linked with development of depression and a vitamin D supplement has been found to prevent depression (Kinuta et al., 2000; Jorde et al., 2008). Whether vitamin D was the cause or effect of depression has not been demonstrated; therefore, there is no evidence whether intake of vitamin D supplements is effective at treating depression or preventing it (Kjærgaard et al., 2012). Another study from Norway discovered that low level of vitamin D in the blood correlated with more depressive symptoms (Knekt et al., 2015). This investigation also highlighted that vitamin D supplements can improve these symptoms of depression. Another study on a large group of women who were on a very low dosage of vitamin D, 400 IU per day, suggested that the amount of vitamin D may have effects on the depressive symptoms (Merhi et al., 2012; Milaneschi et al., 2014). However, a calcium supplement was also taken by these participants which may have impacted the results. The researchers concluded that vitamin D together with calcium, rather than vitamin D alone, may have affected depression. Conversely, a study conducted in 2012 (Merhi et al., 2012) indicated that intake of vitamin D supplements had no effect in alleviating depression in women. Analysis of blood samples revealed no relation between the depressive symptoms and vitamin D receptors on the cells. However, observational studies have indicated increased risk of depression coinciding with vitamin D deficiency (Milaneschi et al., 2014; Nasser et al., 2016). Therefore, more studies are extremely encouraged to define the relationship between the vitamin D levels and depressive symptoms especially in Saudi Arabian females, wherein studies are limited. Based on previous studies, we aim in this study is to evaluate the vitamin D levels in Saudi female (especially students at University) with depression and the potential role of vitamin D on depression symptoms.

## 2. Subjects and methods

This was a cross-sectional study comprising of 100 female students from Taibah University Medical Center who were assessed using a Hamilton Depression Rating Scale (HAM-D), was established by Williams in 2001. Saudi students who study at Taibah University and aged  $\geq 18$  years and gave their consent to take part in this study be eligible for inclusion. The exclusion criteria of the study included females taking supplementary vitamin D or on medication for systematic disease.

### 2.1. Collection of clinical data

Age, medication history, depressive symptoms, and complications of each students were investigated from their records and files at Taibah University Medical Center in female department. Then, the research subjects were chosen according to the inclusion and exclusion criteria.

### 2.2. Routine laboratory investigations

3 ml of the venous blood of every research subject was collected and levels of thyroid hormones, glucose and parathyroid hormone were detected in the clinical laboratory. Meanwhile, 2 mL of residual blood samples were collected and the serum was kept in the refrigerator at  $-20^{\circ}\text{C}$  to carry out the investigation for vitamin D which was carried out in the Maternity and Children Hospital, Al Madinah, Saudi Arabia.

### 2.3. Assay of vitamin D

Vitamin D in serum was detected by measurement in the Cobas b 311 immunoassay analyzer (Roch Diagnostics, GmbH, German) in the Maternity and Children Hospital. Normal, insufficient and deficient vitamin D status were defined as 25 (OH) D serum concentration of 75.00 nmol/L, 25.00-75.00 nmol/L, and less than 25.00 nmol/L, respectively according to Endocrine Society Clinical Practice Guideline of vitamin D deficiency (Holick et al., 2011).

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### 2.4. Statistical Analysis

Data was processed using the software package of SPSS 20. Independent t-test was applied as far as mean  $\pm$  SD concerned. Pearson correlation coefficients were used to examine the relationship between different parameters and depression. The P-value  $\leq 0.05$ ,  $\leq 0.001$  was considered as statistically significant.

### 3. Results

Characteristics of female students by randomization group are presented in Table 1. Both Vitamin D levels and other laboratory parameters are shown as mean  $\pm$  standard deviation. Another parameter such as HAM-D Scale is expressed as scores (0-4).

To determine the association between Depression level and vitamin D levels in females, we divided the cases into subgroups based on vitamin D levels. It is found that 14% of patients had severe score of depression with severe deficiency of vitamin D (DD) while 17% of mediatory depression patients have deficiency of vitamin D (DD). However, normal female subgroup according to HAM-D, had insufficient and normal levels of vitamin D (42% and 9%, respectively, Table 2).

**TABLE 1: BASELINE CHARACTERISTICS OF ALL PARTICIPANTS. DATA PRESENTS AS MEAN $\pm$  SD**

<b>Parameter</b>	<b>PRECIPITATES N==100</b>
Age (years)	<b>22<math>\pm</math>2.53</b>
FBG (mmol/L)	<b>4.97<math>\pm</math>1.22</b>
PTH (ng/L)	<b>72<math>\pm</math>29.54</b>
Vit D (nmol/L)	<b>38.45<math>\pm</math>22.04</b>
T4 (mmol/L)	<b>12.7<math>\pm</math>2.68</b>
TSH (mmol/L)	<b>2.95<math>\pm</math>1.05</b>
<b>HAM-D (0-4)</b>	
0 (normal)	<b>51%</b>
1	<b>10%</b>
2	<b>8%</b>
3	<b>17%</b>
4(severe)	<b>14%</b>

**TABLE 2: THE PERCENTAGE OF PARTICIPANTS ACCORDING TO VITAMIN D LEVEL AND HAM-D.**

HAM-D (0-4)	Severe DD	Insufficient DD	NORMAL D
0 (normal)		42%	<b>9%</b>
1	7%	3%	
2	8%		
3	17%		
4 (severe )	14%		

Compared with non-depressed persons, depressed persons were significantly ( $P < 0.001$ ) had lower vitamin D and PTH levels (Table 3). Whereas no significant difference was indicated in T4 or TSH between two groups.

We have selected patients with severe depression and mediator depression (as defined by HAM-D) and compared them with those without it. Patients with severe depression and mediator depression had significantly lower levels of vitamin D when compared with patients without it ( $P < 0.05$ ) as shown in

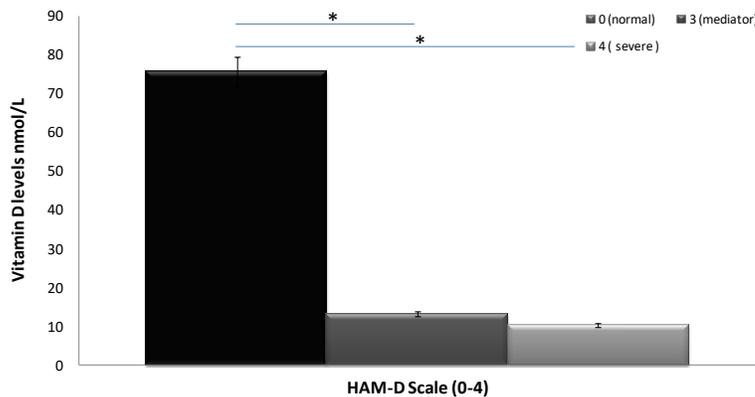


Figure 1: Patients with severe depression and mediator depression had low levels of vitamin D. The Pearson correlation coefficient between serum 25(OH)D and severe group was  $-6.30$  ( $P < 0.001$ ) and mediator group was  $-4.7$  ( $P < 0.05$ ). Our results reveal an inverse association between 25(OH)D levels and depression. Whereas, no association between depression different groups and the level of PTH (Table 4).

#### 4. Discussion

The putative impact of vitamin D on depression has received significant attention, especially in the Gulf region. However, various research studies have found conflicting results regarding the role vitamin D plays in depression. The key reason why Saudi Arabia is almost vitamin D deficient is due to the risk factors that predispose individuals living in the gulf region such as diet, cultural habits which involves covering of the head, face and body,

**TABLE 3: COMPARING BETWEEN THE LEVELS OF VITAMIN D AND HORMONES IN WOMEN WITH AND WITHOUT DEPRESSION.**

Parameter	Women without depression, N=51	Women with depression, N=49	P-VALUE
PTH (ng/L)	47.5±13.7	10.5±5.3	<b>0.03*</b>
Vit D (nmol/L)	25.5±10.6	8.5±2.21	<b>0.004**</b>
T4 (mmol/L)	12.5±0.44	12.4±0.52	<b>0.08</b>
TSH (mmol/L)	5.8±1.05	5.5±1.25	<b>0.07</b>

**DATA PRESENTS AS MEAN ± SD, T-TEST WAS USED TO ANALYZE THE DATA BETWEEN TWO GROUPS , STATICALLY SIGNIFICANT AT  $P \leq 0.05$ \* OR  $\leq 0.001$ \*\*.**

**TABLE 4: CORRELATION BETWEEN DEPRESSION CATEGORIES AND VITAMIN D AND PTH LEVELS.**

Parameters	Normal		Mediator		SEVER	
	r	P	r	P	r	P
Vit D	0.2	>0.05	<b>-4.7</b>	<b>0.03*</b>	<b>-6.3</b>	<b>0.002**</b>
PTH	0.12	>0.05	1.2	>0.05	1.7	<b>&gt;0.05</b>

**\*\*CORRELATION IS SIGNIFICANT AT THE 0.001 LEVEL (2-TAILED), \*CORRELATION IS SIGNIFICANT AT THE 0.05 LEVEL (2-TAILED).**

lack of exercise, and most importantly, evading sun exposure due to excessive heat in the region. Thus, most people in the region are vitamin D deficient and this increases their risk of depression. Although it has been noted that vitamin D is associated with depression (Yang et al., 2015), the evidence to support this claim is limited. Therefore, this research aims to determine the relation between vitamin D and depression among females residing in Saudi Arabia.

The research included a cross sectional study of 100 participants who were assessed using the HAM-D rating scale. The participants in this study were all adult females above the age of 18 years with diagnostic criteria of depression and vitamin D deficiency. In order to determine the link between the levels of depression and vitamin D, the cases were divided into subgroups based on vitamin D levels. The results indicated that 14% of cases or patients had a severe score of depression and at the same time, those patients had a severe lack of vitamin D. Moreover, 17% of mediatory depression female patients had vitamin D deficiency. Normal patients according to HAM-D score, were found to have either insufficient or normal levels of vitamin D (42% and 9%, respectively). The study then selected female patients with severe depression and mediator depression as indicated by HAM-D and compared with those without the same. However, it was found that patients with either severe or mediator depression had considerably lower levels of vitamin D compared with patients without any symptoms of depression. This aligns well with the research by Kojima et al. (2016) wherein it was found that people with lower levels of vitamin D in their blood seemed to present more depressive symptoms than those without vitamin D deficiency. Additionally, the study by Polak et al. (2014) was almost similar to our study since it focused on a large group of women. In Polak's study, women used small dosages of vitamin D (400 IU) on a daily basis, indicating that the amount of vitamin D had effects on the symptoms of depression. Contrary to these findings, a study by Kjærgaard et al. (2012) showed that intake of vitamin D supplements had no effects on depression in women. There was no correlation between the depressive symptoms and vitamin D receptors on the cells of these patients (Al Hariri, 2016).

Nonetheless, our current study provided an evidence of a relationship between depression and vitamin D deficiency among females in Saudi Arabia. In fact, those who were found to have severe depression were also

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deficient in vitamin D, which indicated that vitamin D may play a significant role in depression. Besides, the participants without any signs of depression were found to have no deficiency of vitamin D, which further supports the assertion that vitamin D, and depression correlates.

### 5. Conclusion

Lower levels of vitamin D among student females in Saudi Arabia is a serious health problem that may risk causing depression. This study showed that deficiency in vitamin D is significantly associated with enhanced levels of depressive symptoms as the student's females with severe or mediator depression had considerably lower levels of vitamin D in their blood. Insufficient levels of vitamin D in student's females increases their susceptibility to depression especially those with severe levels of depression have significant drop in vitamin D. Considering the high prevalence of vitamin D deficiency as well as depression in Saudi Arabia, a relationship between the two conditions would have a significant public health impact with clinical implications.<sup>[23]</sup> This study provides a strong confirmation of the relation between vitamin D and depression. Since the low levels of vitamin D seem to promote depression and depressive symptoms, therefore, antidepressant effect of vitamin D supplementation is required investigation on large scale patients especially those with severe depression. Although the study shows a link between the two, it is difficult to find the exact causal factors that lead to depression in patients with insufficient levels of vitamin D. Thus, further research is needed to examine the exact causes that links vitamin D with depression.

### Ethical statement

This study was approved by Institutional Ethics Committee with reference number (CLS 201705) obtained on 12 / 03/ 2017.

### Declaration of patient consent

Patient consent statement was taken from each patient as per institutional ethics committee approval along with consent taken for participation in the study and publication of the scientific results / clinical information / image without revealing their identity, name or initials. The patient is aware that though confidentiality would be maintained anonymity cannot be guaranteed.

### Conflicts of interest

There are no conflicts of interest.

### Acknowledgement

The authors appreciate the support of the lab technicians, Miss Rania Osta and Miss Johayna Aboalkayer, in the current study.

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