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Vitamin D Deficiency for Patients with Depression (case control study)

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Abstract: Background: Depression is considered to be a leading cause of disability worldwide and is a major contributor to the overall global burden of disease. Changes in sleep are a common problem for patients with depression; in fact, in many cases, it is the chief complaint.

Aim of the Study: The objective of this study is to assess the vitamin D deficiency as a risk factor for depression

Patients and method: A case control study conducted in Diwanyia teaching hospital from 1st February to 1st May 2023. the study enrolled depression patients as cases and healthy person visiting hospital for any causes or relative to patients.

Results: one hundred sixty participants enrolled in this study with mean age 33.9±8.2 years. Mean age for healthy control was 34.2±13.7 years and for cases was a 33.1±15.6 year. Vitamin D deficiency was seen 71.8% of total sample and insufficiency in 20%. There was significant difference between cases and controls with p=0.01 regarding vitamin D level, cases group reveal more prevalent vitamin D deficiency than control 72.5% and 51.3% respectively.

Conclusion: The present study provides additional evidence for the hypothesis that low vitamin D serum concentration is associated with depression, and highlights the need for further research to find out whether this association is causal.

Key words: Vitamin D, depression.

Introduction

Depression is considered to be a leading cause of disability worldwide and is a major contributor to the overall global burden of disease. Changes in sleep are a common problem for patients with depression; in fact, in many cases, it is the chief complaint[(1)].

Depression leads a persisting impairment of social functioning and living conditions can be replicated to some extent from the point of view of the patients themselves. Depression often leads to weight changes as appetite may increase or decrease. For some, overeating or comfort eating may occur and lead to weight gain[(2)]. The tendency in this population to carry excess weight may be exacerbated by a preference for higher-calorie liquids and/or convenience foods as well as a sedentary lifestyle. Other individuals with depressive disorders may under eat due to feelings such as not being worthy enough to eat, lacking motivation or energy to prepare foods, or somatic delusions of not being able to eat. Reduced food intake leads to nutrient inadequacies and weight loss[(3)].

Majority of people are not aware of the relation between nutrition and depression. Nutrition can play a key role in the onset as well as severity and duration of depression. Many of the easily noticeable food patterns that precede depression are the same as those that occur during depression. These may include poor appetite, skipping meals, and a dominant desire for sweet foods[(4)]. A notable feature of the diets of patients suffering from mental disorders is the severity of deficiency in these nutrients. Study has showed that daily supplements of vital nutrients are often effective in reducing patients' symptoms of depression[(5)].

Vitamin D is also known as a secosteroid hormone known for its vital role in maintaining the normal function of bones. Research regarding the specific role of vitamin D in the immune system has been discovered[(6)].

Vitamin D can influence more than 200 genes in various tissues, showing its credibility among the fat-soluble vitamins[(7)].

Vitamin D deficiency is directly proportional to primary clinical conditions such as cardiovascular diseases, diabetes, malignancy and multiple types of scleroses. Therefore, clinicians recommend large intake of vitamin D in the Diet so as to prevent these significant clinical conditions[(8)].

Vitamin D deficiency exists throughout the world in various populations, including children, adults, both male and female (pregnant and lactating), and those who often avoid sunlight exposure. It is worth mentioning that individuals who have darkly pigmented skin are more prone to vitamin D deficiency[(9)].

Food is a limited source of vitamin D. Hence, overcoming the deficiency of vitamin D through food will not be sufficient. However, vitamin D supplements could be used to control its deficiency, but their efficacy is inconsistent and variable.

It has been noticed that vitamin D level is low in those individuals who have a mood disorder, and its mechanism of action has been noticed in causing depression. Vitamin D synthesis in the fair skin is enormously fast and significant even after a few minutes of exposure to sunlight [(10)].

Incidental sun exposure is the major and prominent source of circulating vitamin D. Upon exposure to sunlight in the summer season, Fair Skin can produce about 20,000 IU of vitamin D in less than 30 min[(11)]. A study conducted in the US in 89 different geographical locations on a large population

suggested that the incidence of depression is greater in those people who have deficient vitamin D levels instead in those who have normal vitamin D levels[12]

Vitamin D has a key role in preventing rickets in children and reduces the risks of cancer, multiple sclerosis, and bacterial infections . Vitamin D deficiency leads to diabetes mellitus; its deficiency causes a decrease in microglial inflammatory function leading to increased brain infections[13].

Vitamin D has a crucial role in developing a normal brain, while its deficiency is associated with morphological changes, such as enlarged ventricles and decreased cortical thickness.

For about 30 years, a complicated interaction has been described between neuroinflammation, immune activation and modifications in brain circuits associated to depression and anxiety[14].

Therefore, vitamin D is known for regulation of innate immunity, both as a transcription and growth factor by interrelating with surface receptors in diverse immune cells[1]. Vitamin D is, therefore, associated with its ability to regulate both immune responses of peripheral and central nervous systems[15].

The antimicrobial properties of vitamin D has been described as its first immune-related properties, but it is also involved in the modulation of both innate and adaptive immune reactions. In this perspective, depression and anxiety are often related with a low-grade inflammatory significance and peripheral increase in acute-phase proteins and inflammatory cytokines[16].

It is observed that vitamin D regulates the gene expression for one of the essential enzymes Tyrosine Hydroxylase, which is involved in synthesizing dopamine and norepinephrine. These neurotransmitters are famous for their role in depression and mood disorders[17].

Vitamin D maintains physiological functions, such as calcium homeostasis, membrane permeability and axonal conduction, and neurotransmission[18] .

Vitamin D stimulates the receptors in those regions of the brain concerned with the regulation of emotion and behavior, such as the limbic system, cortex, and cerebellum. It also stimulates the release of neurotrophin, which has an important role in the regulation of neuronal development [19].

The role of vitamin D in depression has also received increasing research focus. Currently, there are at least three lines of evidence to support this association: first, an increased region-specific expression of vitamin D receptors (VDRs) in brain areas (such as prefrontal and cingulate cortices) known to play a key role in mood regulation; second, the modulatory role proposed for vitamin D in the association between depression and inflammation (through a possible immune-modulatory

mechanism); last, the emerging insights about the neuroprotective properties of vitamin D (by virtue of its anti-inflammatory effects) [18].

Aim of the Study:

The objective of this study is to assess the vitamin D deficiency as a risk factor for depression

Patients and method

Study design : a case control study conducted in Diwanyia teaching hospital from 1st February to 1st May 2023. the study enrolled depression patients as cases and healthy person visiting hospital for any causes or relative to patients.

Sample size:- the number of cases and controls were calculated by following formula

$$n\ (each\ group) = \frac{(p_0 q_0 + p_1 q_1)(z_{1-\alpha/2} + z_{1-\beta})^2}{(p_1 - p_0)^2}$$

- The value of alpha
- The value of beta
- Proportion of controls with exposure (p0) = 17%
- Proportion of cases with exposure (p1) = 30%
- Ratio of cases to controls, suppose 1:1

Conventionally, alpha (two-sided) = 0.05 (or 5%) and beta = 0.20 (or 20%).

$z_{(1-\alpha/2)}$ = 1.96

$z_{(1-\beta)}$ = 0.84

Total participants are 160
Cases were 80 patients with depression
Control were 80 person without depression

Inclusion criteria

Patients with depression selected as cases, while healthy person without diseases as control.

Exclusion criteria

Study participants with chronic diseases such as liver and renal diseases, mal absorption syndrome, and other diseases that can affect the level of vitamin D were excluded from the study.

Data collection

Patients were selected from psychiatric clinic in teaching hospital with age range from 20-60 years. Patients were appropriately estimated on PHQ2 criteria and senior diagnosis. Healthy individual enrolled after written consent and blood sample was taken for investigated vitamin D level.

Each participant completed a questionnaire to provide socio-demographic characteristics (age, marital status, smoking status, alcohol consumption and occupation), medical history, and medications. Bodyweight and height were measured for the participants for the calculation of body mass index (BMI).

Collection of blood samples

Blood samples (3 mL) were collected from subjects, labelled, and stored in vials at 4°C. The tubes were centrifuged (Megafuge 1.0, Heraeus Sepatech) at 5000 rpm for 10 min. The blood serum was analysed for vitamin D level.

Determination of vitamin D level

For vitamin D determination, serum was separated. The serum level of vitamin D is monitored in Architect Plus, Abbott. The recorded data was noted automatically and further processed on the instrument CI 4100, where vitamin D level was determined and reported in ng/mL. from the study.

Statistical analysis

Data was collected and included in a data based system and analyzed by statistical package of social sciences ((SPSS, Inc., Chicago, IL, USA)) version 23.

Parametric data were expressed as mean ± standard deviation (SD). It was analyzed statistically using student t-test while non-parametric data were expressed as percentages and were analyzed using chi square. Receiver operating characteristics (ROC) analysis was used to identify the optimal threshold values of 25 OH vitamin D. Sensitivity and specificity, values of 25 (OH) vitamin D were profiled by curves. A *P*-value of <0.05 was considered to be statistically significant.

Result

One hundred sixty participants enrolled in this study with mean age 33.9±8.2 years. Mean age for healthy control was 34.2±13.7 years and for cases was a 33.1±15.6 year. Female constituent about 51.2% and male were 48.8%. Regarding residence, 68.7% of them were live in urban area and 31.2% resident in rural area as in table 1.

Table 1:

Variables		**Cases**	**Control**	**Total**	**p-value**
Age group	**20-39 years**	**39**	**43**	**82**	**0.6**
	40-60 years	**41**	**37**	**78**	
Mean age					**0.5**
Gender	**Male**	**42**	**36**	**78(48.8%)**	**0.4**
	Female	**38**	**44**	**82 (51.2%)**	

Mean BMI					**0.3**
BMI	**Under weight**	**12**	**9**	**21**	**0.8**
	Normal	**32**	**31**	**63**	
	Over weight	**28**	**29**	**57**	
	Obese	**8**	**11**	**19**	
Residence	**Urban**	**57**	**53**	**110**	**0.6**
	Rural	**23**	**27**	**50**	

Table two show, 16 patients had private worker and 24controls, more employment regarding patients than controls, these differences not statistical significant. In according to education, there was no significant difference between patients and controls.

Table 2: presented occupation and education characters of sample.

		Cases	Control	Total	P-Value
Occupation	Worker	16	24	40	0.2
	Employment	37	30	67	
	Non worker	27	26	53	
Education	Illiterate	13	12	25	0.7
	Primary and secondary	48	54	102	
	Bachelors and above	19	14	33	

Vitamin D deficiency was seen 71.8% of total sample and insufficiency in 20% as in table 3. There was significant difference between cases and controls with p=0.01 regarding vitamin D level, cases group reveal more prevalent vitamin D deficiency than control 72.5% and 51.3% respectively, as in table 4.

		Number	**Percent**
Vitamin D status	Normal	29	**18.2%**
	In sufficiency	32	**20%**

	Deficiency	99	**71.8%**
	Total	160	

Table 4

		Cases	**Control**	**p-value**
Vitamin D status	Normal	10(12.5%)	19(23.7%)	**0.01**
	In sufficiency	12(15%)	20(25%)	
	Deficiency	58(72.5%)	41(51.3%)	
	Total	80	80	

The variation in level of vitamin D between age and gender were in significant, in spite of older age group demonstrated higher level. In addition, the mean level between cases and control in comparison among age group and gender were insignificant also. However, female presented low mean vitamin D18.5 ± 9.1and male21.3 ± 19.1 with p-value 0.1, as in table 5 and 6.

Moreover, mean of vitamin D was significantly difference between cases and control with p-value 0.01. as in table 6.

ROC curve was done to differentiation healthy from depression patient depending on Vitamin D level and information show table 7, sensitivity 94% and cut off 11.5.

Table 5:

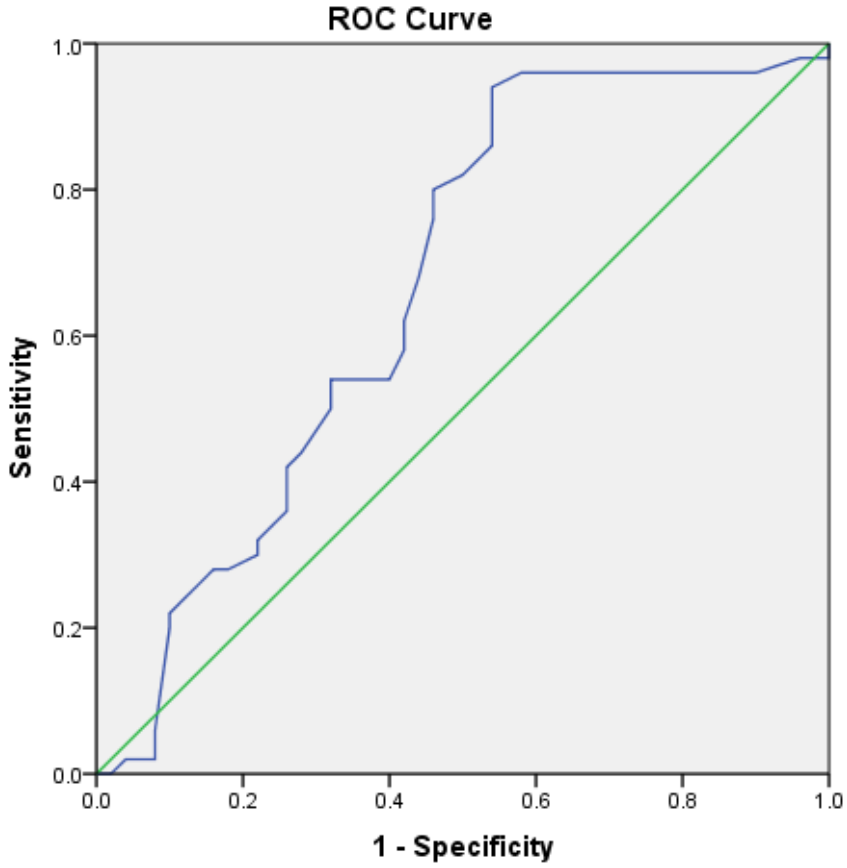
Variables		**Vitamin D Mean ±SD**	**p-value**
Age group	**20-39 years**	**23.1±11.2**	**0.6**
	40-60 years	**25.3±9.5**	
Gender	**Male**	21.3 ± 19.1	**0.18**
	Female	18.5 ± 9.1	

Table 6:

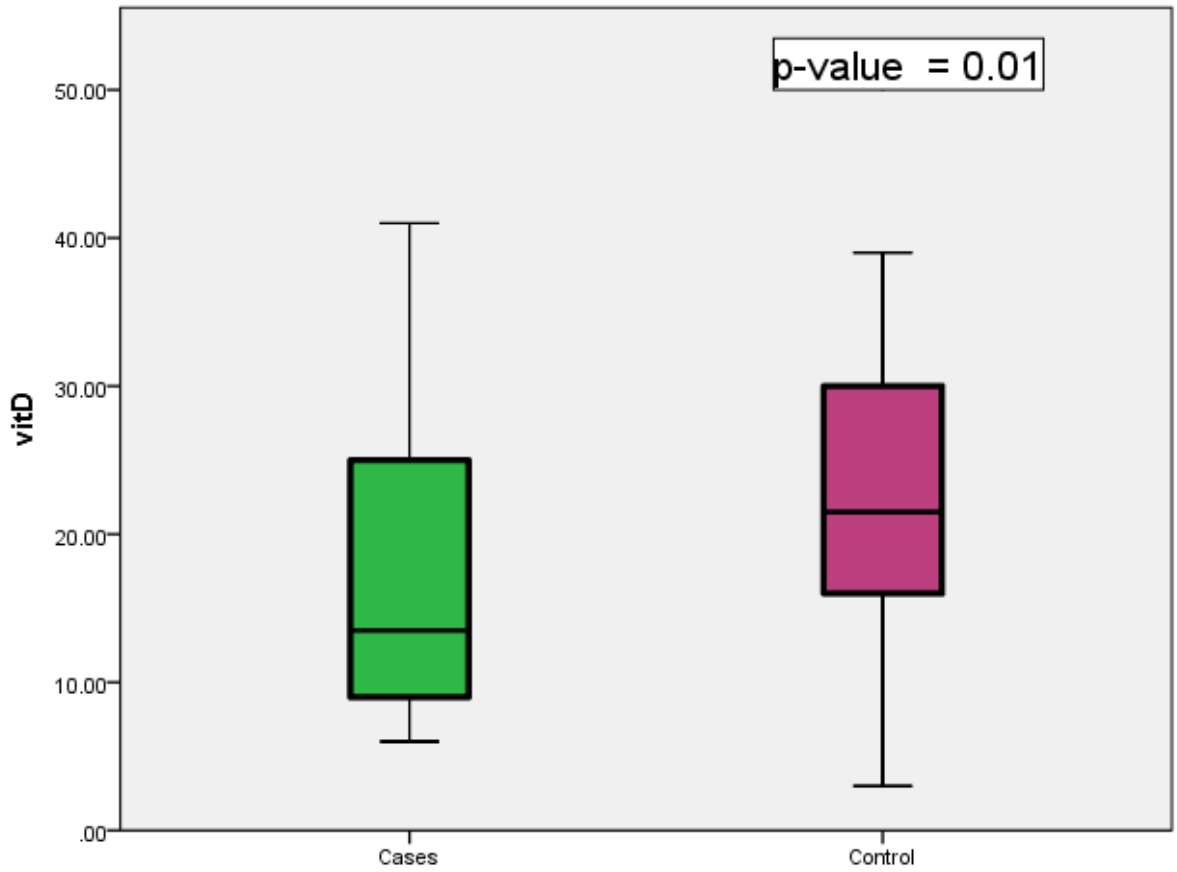
Variables		Cases Vitamin D Mean ±SD	Control Vitamin D Mean ±SD	Total	p-value
	Total	17±10	21±8		0.01
Age group	20-39 years	18±9	25±14	82	0.6
	40-60 years	23±10	28±8	78	
Gender	Male	21±15	27±12	82	0.4
	Female	17±11	22±13	78	

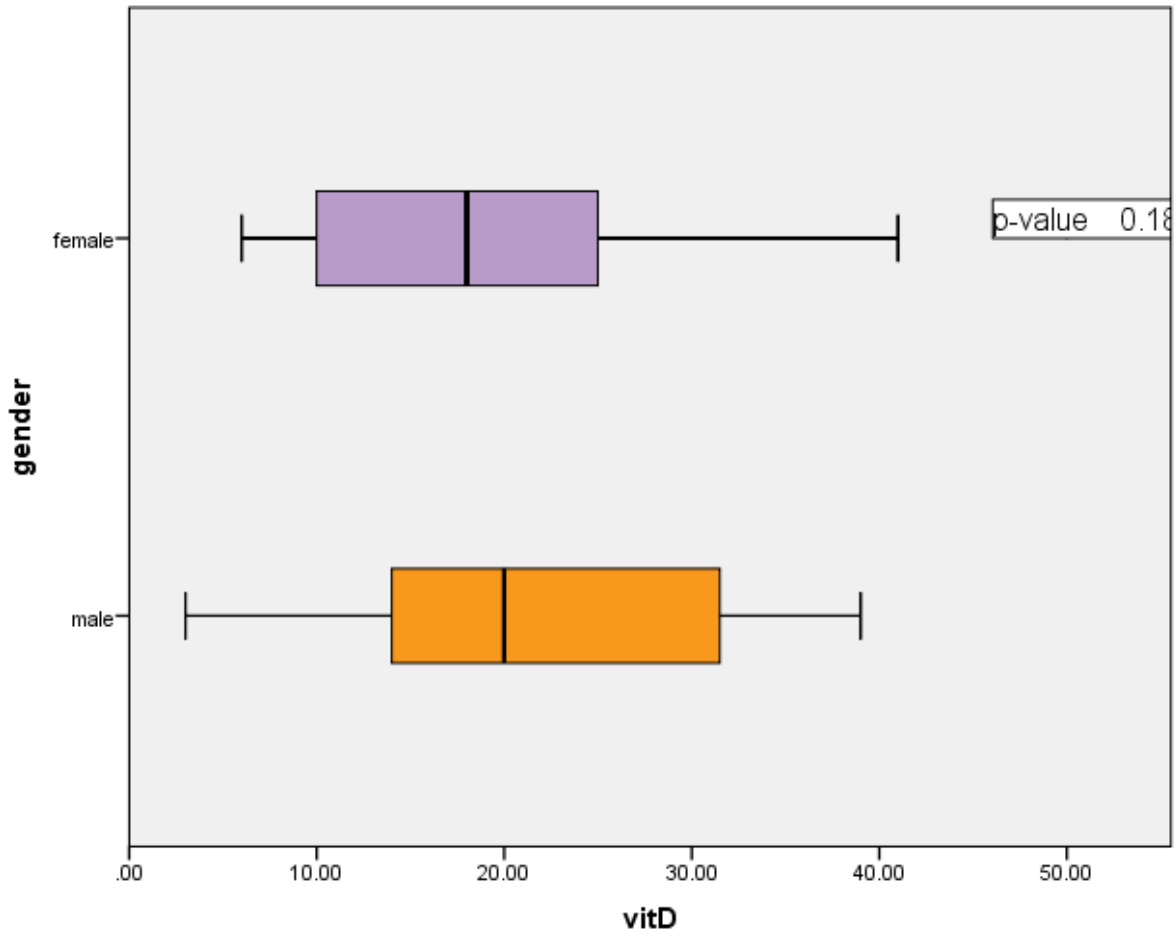
Table 7:

Variables	Cutoff	Sensitivity	Specificity	AUC(95%CI)	p-value
Vitamin D	11.5	94%	46%	0.66(0.55-0.77)	0.004



Diagonal segments are produced by ties.





Discussion

Vitamin D has been increasingly attached to mental health cognitive decline, and it has been hypothesized that hypovitaminosis D may give a share to depression [20].

Many researchers have found that receptors of Vitamin D are primarily doled out throughout the brain of human, and its lack mutates neurotransmitters which are familiar to be included in of depression's symptoms [21].

Vitamin D deficiency a worldwide problem and affecting males and females any age. The prevalence of vitamin D deficiency in this study different between males and females and this could be due to many factors such as clothes type, duration of sun exposure and this is similar to other studies worldwide [22].

In present study reveal vitamin D deficiency about 61.8% while insufficiency was 20%, it come with other community-based studies have reported that vitamin D deficiency ranges between 45-52 %. In Europe, vitamin D deficiency has been observed to range between 30-60% of Western, Southern, and Eastern European populations and >20% of populations in Northern Europe[23] .

Although sunlight is abundant in developing countries, particularly in the Middle East, vitamin D deficiency appears to be a much more prevalent, with only a minority of these populations having adequate vitamin D levels[24] . In China, Ning *et al* [25] reported that 87.1% of the Beijing population was vitamin D-deficient, and only 2.9% of the participants achieved optimal levels.

A study conducted in Qatar revealed a prevalence of 64% [26]. A meta-analysis on the prevalence of vitamin D deficiency in Saudi Arabia also revealed that 81% of the population was deficient [24]. In Kuwait, the prevalence of deficiency was found to be 83% (19) [27].

A cross-sectional study to measure the prevalence of vitamin D deficiency among females aged (12 -30) years old in Karbala city, showed that high prevalence (85.9%) of vitamin D deficiency and insufficiency of the females [28].

Another study in Iraq which had done in Sulaimani in 2017, found that over 79% among the studied group were below the standard range value for serum vitamin D level [29].

Different findings may be attributed to the differences in the study population (different races, gender, and age groups), diverse methodology and different baseline levels of serum 25(OH) D concentrations [30].

There were statistical significant differences between cases and control regarding vitamin D level, vitamin deficiency was more prevalent in cases than controls 72.5%, 51.3% respectively. These result consistent with previous studies [31,32].

Dr. Abass T. Al Joud study was concluded that depression was associated with low Vitamin D level in patients' especially old peoples[33].

Kamalzadeh et al reported the mean 25(OH) D levels were significantly different between depressed and non-depressed groups (20 ± 15 vs. 27 ± 13, $P < 0.001$). Vitamin D insufficiency/deficiency was detected in 78 and 67% of the depressed and non-depressed groups, respectively, which was significantly different ($P = 0.03$). The associations between depression and the serum 25(OH) D levels were observed regardless of gender and age [30].

This finding is supported by previous works which have revealed that there is an improvement in the state of depression after it D deficiency correction [34].

On the other hand, our finding did not agree with the study of **Kouider DA**[35].

The previous studies vary in their results as many reported that there were an association between depression and vitamin D deficiency and others reported that there were no associations between depression and vitamin D deficiency[36].

A randomized controlled trial on children and adolescents, who were both vitamin D deficient and at least mildly depressed at baseline, showed that vitamin D supplementation has no effect on self-reported depression symptoms[37].

On the other hand, vitamin D deficiency can increase the risk of developing depression, through several biological . pathways including effects on immunomodulation, regulation of intracellular calcium stores, cellular signaling, modulation of the hypothalamic-pituitary-adrenal axis, intracellular calcium homeostasis, and production of neurotransmitters[1,38]

Conclusion

The present study provides additional evidence for the hypothesis that low vitamin D serum concentration is associated with depression, and highlights the need for further research to find out whether this association is causal.

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