Serum vitamin-D level and major depressive disorder in Upper Egypt

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Background
There is an increasing evidence of an association between low vitamin-D levels and depression. Consequently, the present study aimed to investigate the serum levels of vitamin D in cases with major depressive disorder in Sohag Governorate in Upper Egypt. Also, we studied the correlation between serum vitamin-D level and different demographic and clinical variables in these patients. This study included 60 patients who attended our outpatient psychiatric clinic at Sohag University Hospital, who were diagnosed as major depressive disorder (group I) and a similar number (60) of age-matched and sex-matched controls (group II). The diagnosis was based on *Diagnostic and statistical manual of mental disorders*, 5th ed. criteria and verified by application of Quick Inventory of Depressive Symptomatology. A blood sample was taken from all participants for assessment of the levels of serum vitamin D.
Results
Patients with major depressive disorder have significantly lower serum vitamin-D levels than controls (mean±SD was 17.2±12.3 for patients and 33.4±24.2 for controls, P=0.001). About 58.33% of patients had deficient vitamin D, while 45% of controls had deficient vitamin D (P=0.022). There is a statistically significant negative correlation between the severity of depression and serum vitamin D.
Conclusions
Serum vitamin D was significantly lower in major depression patients than controls. In addition, it is evident to have a direct correlation with severity of symptom depression.

Keywords:
major depressive disorder, Upper Egypt, vitamin D

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Background

Although vitamin D is evident to contribute to bone metabolism as well as calcium homeostasis, a growing body of data suggests that it has a substantial impact on health, particularly mood (Giovannucci, 2009; Libuda *et al.*, 2020). Deficiency of vitamin D is a prevalent health issue across the world (Holick, 2004).

There is no agreement on a specific definition of deficiency of vitamin D (Okereke and Singh, 2016). Vitamin-D deficiency is a common risk factor for poor health outcomes (PanelKaren *et al.*, 2021). During the past 25 years, a lot of research was carried out regarding the contribution of vitamin D to depression (Menon *et al.*, 2020).

There are increasing evidences for the correlation between low vitamin D and depression (Parker *et al.*, 2017). There are strong bases for the hypothesis of inclusion of low vitamin D in controlling our mood (Toffanello *et al.*, 2014).

The precise biological mediators between depression and vitamin D remain unknown. The following mechanisms may demonstrate the correlation between depression and deficiency of vitamin D: first, affection of neuronal signaling due to disturbance of the equilibrium between gamma amino butyric acid and glutamate due to disturbances in calcium homeostasis, both intracellular and extracellular (Berridge, 2017). Second, receptors of vitamin D are abundant in brain regions responsible for mood regulation, such as limbic system and prefrontal region (Eyles *et al.*, 2005). Third, vitamin D contributes to modulation of the hypothalamo–pituitary–adrenal axis that controls monoamine neurotransmitter production (dopamine, norepinephrine, and epinephrine) in the adrenal cortex (Muscogiuri *et al.*, 2015; Wierzbicka *et al.*, 2016). Fourth, vitamin D modulates immune-inflammatory pathways that have been found to be relevant to the pathophysiology of depression (Kaufmann *et al.*, 2017).

Last, vitamin D might regulate tyrosine hydroxylase synthesis genes that are responsible for synthesis of catecholamines (Garcion *et al.*, 2002).

Vitamin D refers to a cohort of secosteroid hormones that are significantly correlated (Holick, 2007). Vitamin D can present in multiple forms, for example, vitamin D3 or D2 in supplements and food, or like vitamin D3 (cholecalciferol) through converting 7-dehydrocholesterol in skin by ultraviolet rays (Norman, 2008). Metabolites of vitamin D can pass the blood–brain barrier (Diesel *et al.*, 2005).

Aim

Our aim in this study was to investigate the serum levels of vitamin D in cases with major depressive disorder in Sohag Governorate in Upper Egypt and its correlation with different demographic and clinical factors.

Patients and methods

The present cross-sectional study was conducted in the interval from November 2019 to November 2020 on 60 participants diagnosed as major depressive disorder (group I) who attended our outpatient psychiatric clinic at Sohag University Hospital. In total, 60 age-matched and sex-matched volunteers were enrolled as controls (group II). The local ethical committee authorized the study. Patients were informed about the study and its aims, and subsequently, they were recruited. All participants signed a written informed consent for this study. Individuals who did not complete the interview or did not provide consent were excluded.

Inclusion criteria included participants diagnosed with major depressive disorder according to the diagnostic criteria of the fifth edition of the *Diagnostic and statistical manual of mental disorders*, 5th ed. with age range from 18 to 65 years.

Exclusion criteria were diagnosis of other psychiatric disorders, substance-use disorder, intellectual disability, or a chronic medical illness that may affect vitamin-D levels like renal, hepatic, endocrine, or metabolic diseases. Patients who were taking vitamin-D supplements were excluded. Patients who refused to give written consent were also excluded. Controls were free from psychiatric disorders or chronic medical disorders that may affect vitamin-D levels like renal, hepatic, endocrine, or metabolic diseases, and were not using vitamin-D supplements.

We enrolled all patients with major depression attending our outpatient psychiatric clinic on a daily basis who conformed with our inclusion and exclusion criteria.

Tools

Clinical individualized interview with each patient by the researchers using a preformed sheet for collection of demographic (age, sex, residency, marital status, socioeconomic status, and educational level) and clinical data (age at onset, duration of symptoms, number of depressive episodes, and antidepressants used) from patients.

Structured Clinical Interview for DSM-IV-Clinician Version (SCID-CV) (First *et al.*, 1997), we used the Arabic version (El Missiry *et al.*, 2004) to exclude other psychiatric disorders.

Family socioeconomic status scale was prepared by Abd El-Tawab (2012) to assess the socioeconomic status of the participants. It includes four items: family income, level of education of parents, job of parents, and lifestyles. It gives total score and separate score for each item. The three classes of the total score are low, moderate, and high.

Quick Inventory of Depressive Symptomatology Self-Report (QIDS-SR) (Rush *et al.*, 2003) is an abbreviated version of the scale (16-item). It appears to be sensitive to evaluate depressive symptoms and only takes 5–10 min. Scoring: each item on the scale is assigned a score that ranges from 0 to 3. The range of total score: 0–27. Criteria of score: 0–5 normal; 6–10 mild; 11–15 moderate; 16–20 severe; more than or equal to 21 very severe.

Serum vitamin-D level: after fasting overnight, blood samples for 25(OH) vitamin-D assay in serum were collected in the morning. We classified serum vitamin-D levels into three types: deficient ($\leq$20 ng/ml), normal ($\geq$30 ng/ml), and insufficient (20–30 ng/ml) according to Motsinger *et al.* (2012).

Statistical analysis

SPSS Inc. Released 2007. SPSS for Windows, Version 16.0. Chicago, USA was utilized for data analysis. Quantitative data were presented in the form of means and SDs. Qualitative data were presented in the form of frequencies and percentages. The comparison of mean values was performed utilizing unpaired *t* tests. Comparison between categorical variables was done by χ^2 test. Correlation coefficients were utilized to calculate the correlations

between different variables. *P* value less than 0.05 is considered statistically significant.

Results

Table 1 shows no significant difference between group I and group II regarding age, sex, educational level, residency, marital status, or socioeconomic status.

Table 2 shows that the age at onset of depressive symptoms in patients' group is 29.2±6.4 years (mean ±SD), duration of depressive symptoms is 1.5±1.2 years (mean±SD), number of depressive episodes is 1.7±0.8 (mean±SD), 81.66% of the patients were drug-naive, and 18.33% were on selective serotonin-reuptake inhibitors.

Table 3 demonstrates that the number of major depression patients who have deficient vitamin D (≤20 ng/ml) was significantly higher than the number of controls who have deficient vitamin D (58.33%, *N*=35 vs. 45%, *N*=27, respectively). The number of participants who have a normal serum vitamin-D level (≥30 ng/ml) was significantly higher among the control group (21.66%, *N*=13) than patients' group (11.66%, *N*=7). Vitamin-D level was insufficient (20–30 ng/ml) in 18 (30%) participants of the control group and 20 (33.33%) participants of patients' group with no significant differences between the two groups.

Table 4 shows that serum vitamin D was significantly lower in patients with severe and very severe depression than patients with mild and moderate depression.

Table 5 shows that there is a statistically significant negative correlation between the severity of depression

Table 1 Sociodemographic data of group I (patients) and group II (controls)

	Group I (*N*=60)	Group II (*N*=60)	*P* value
Age (mean±SD)	37±6	35±7	0.07
	n (%)	*n* (%)	
Sex			
Male	21 (35)	23 (38.33)	0.12
Female	39 (65)	37 (61.67)	
Educational level			
Less than high school	15 (25)	14 (23.33)	0.08
High school	27 (45)	28 (46.66)	
College	18 (30)	18 (30)	
Residency			
Rural	25 (41.66)	23 (38.33)	0.47
Urban	35 (58.33)	37 (61.66)	
Marital status			
Single	15 (25)	16 (26.66)	0.073
Married	26 (43.33)	27 (45)	
Divorced	11 (18.33)	11 (18.33)	
Widow	8 (13.33)	6 (10)	
Socioeconomic status			
Low class	27 (45)	26 (43.33)	0.15
Middle class	22 (36.66)	23 (38.33)	
High class	11 (18.33)	11 (18.33)	

P value less than 0.05 is considered statistically significant.

Table 2 Clinical characteristics of major depression group

Clinical characteristic	Major depression group (*N*=60)
Age at onset in years (mean±SD)	29.2±6.4
Duration of symptoms in years (mean±SD)	1.5±1.2
Number of episodes (mean±SD)	1.7±0.8
Treatment [*n* (%)]	
SSRIs	11 (18.33)
No treatment	49 (81.66)

SSRI, selective serotonin-reuptake inhibitor.

Table 3 Serum vitamin-D level in patients' group (group I) and control group (group II)

Serum vitamin D	Group I (*N*=60) [*n* (%)]	Group II (*N*=60) [*n* (%)]	*P* value
Serum vitamin D (mean±SD)	17.2±12.3	33.4±24.2	0.001
Normal (≥30 ng/ml) [*n* (%)]	7 (11.66)	13 (21.66)	0.001
Insufficient (20–30 ng/ml) [*n* (%)]	18 (30)	20 (33.33)	0.069
Deficient (≤20 ng/ml) [*n* (%)]	35 (58.33)	27 (45)	0.022

P value less than 0.05 is considered statistically significant.

Table 4 Serum vitamin D in different degrees of severity of depression

Depression severity	*n* (%)	Serum vitamin-D level (mean±SD)	*P* value
Mild	6 (10)	21±6	
Moderate	11 (18.33)	18±4	0.032
Severe	22 (36.66)	15±3	
Very severe	21 (35)	7±2	

P value less than 0.05 is considered statistically significant.

Table 5 Association between serum vitamin D and different demographic and clinical variables in patients and controls

Demographic and clinical variables	Patients (*N*=60) *r*	*P*	Controls (*N*=60) *r*	*P*
Age	–0.183	0.226	–0.215	0.115
Sex	1.322	0.117	1.427	0.287
Duration of depression	–0.163	0.236		
Number of episodes	–0.112	0.542		
Severity of depression	–0.372	0.032		

P value less than 0.05 is considered statistically significant. *r* is correlation coefficient.

and serum vitamin-D levels (the more the severity of depression, the less is the level of serum vitamin D). There is negative but statistically insignificant correlation between serum vitamin D and age of the patients, duration of depressive symptoms, and number of depressive episodes (the more the age of the patient, duration of depression, or number of episodes, the less is the level of vitamin).

Discussion

In this study, we found that the patients with major depressive disorder have significantly lower serum vitamin-D level than controls (17.2±12.3 for patients and 33.4±24.2 for controls, *P*=0.001). About 58.33% of patients had deficient vitamin D, while 45% of controls had deficient vitamin-D level (*P*=0.022). There is statistically significant negative correlation between the severity of depression and serum vitamin-D level (when the severity of depressive symptoms increases, serum levels of vitamin D decrease). There was no statistically significant association between serum vitamin-D level and age, sex, duration of symptoms, or number of episodes in patients' group.

Our results agree with the results of Okasha *et al.* (2020) who studied vitamin-D levels in major depression, schizophrenia, and healthy controls; they found that 75% of patients with major depressive disorder have deficient vitamin-D levels, which was significantly lower than controls. They also found no statistically significant association between serum vitamin-D level and age of the patients, sex of the patients, duration of illness, or number of depressive episodes.

In agreement with our results, Elseesy *et al.* (2020) found that 94.6% of major depression patients have vitamin-D deficiency. Opposite to our findings, they found no significant correlation between the levels of vitamin D and severity of depression according to HAM-D (Elseesy *et al.*, 2020). Studies done by Kerr *et al.* (2015) and by Sherchand *et al.* (2018) found that more than half of their samples of depressed patients have deficient vitamin-D levels, which is in agreement with our findings.

Our results are compatible with the results of Wilkins *et al.* (2006), who found a significant correlation between deficient vitamin-D level and depression. Furthermore, they found that depression is 11 times more frequent in participants with deficiency in vitamin-D level than participants who have sufficient vitamin-D levels.

Our results are in line with the findings of Rejnmark *et al.* (2017), Wong *et al.* (2018), and Li *et al.* (2019), who postulated that there are increasing evidences for a correlation between vitamin-D levels and depression. Also, similar results were obtained by Tolppanen *et al.* (2012), who found a significant negative correlation between the levels of serum vitamin D and severity of symptoms of depression.

Similar results were obtained by Parker *et al.* (2017), who mentioned that empirical studies have provided increasing evidences for a correlation between deficiency of vitamin D and depression. In addition, Föcker *et al.* (2021) demonstrated that diminished levels of vitamin D are correlated with depression. Husmann *et al.* (2017) go hand-in-hand with our results in which they postulated that the levels of serum vitamin D are correlated with symptoms of depression. In addition, this hypothesis is supported

by a study done by Marcos-Perez *et al.* (2020) who found a significant negative correlation between the severity of depressive symptoms and serum vitamin-D levels.

Against our results, Lapid *et al.* (2013) did not detect any correlation between vitamin-D level and depression. In a study done by Ikonena *et al.* (2019), they found no difference in serum vitamin-D level between patients with major depression and healthy controls. Also, van den Berg *et al.* (2021) found that serum vitamin-D levels are not correlated with symptoms of depression, neither longitudinally, prospectively, nor cross-sectionally.

Contradictions in the findings in these studies may be attributable to differences in study-sample characteristics, study design and setting, laboratory analyses, and widely different definitions of deficiency of vitamin D.

The relationship between vitamin D and depression is a multifactorial one. Eyles *et al.* (2013) illustrated that high prevalence of depression among vitamin-D-deficiency patients can be attributed to the neurotrophic impacts of vitamin D as well as its contribution to neurotransmitter synthesis. On the other hand, depression commonly has an adverse impact on lifestyle, leading to deficiency in vitamin D in depressed patients, as these patients may avoid outdoor activities, which lead to less exposure to sunlight, hence vitamin-D deficiency. Also, diminished appetite in depression leads to poor vitamin-D intake and deficiency. Also, metabolic problems in depression may increase the demands of vitamin D to maintain balanced levels of calcium (Thomas and Al-Anouti, 2018).

Strength

Based on our knowledge, the present study is the first in Upper Egypt to investigate the relationship between alternations in vitamin-D levels and depression.

Limitations

Some limitations of the current piece of work should be considered before drawing firm conclusions. The study was carried out on patients who live only in our governorate. It is a cross-sectional study that frequently lacks causality and adequate control of potential confounders. The small sample size limits generalization of the results to all patients with major depressive disorder. Some patients were on selective serotonin-reuptake inhibitors, which may affect serum vitamin-D levels.

Recommendations

Clinicians should monitor and manage deficiency of vitamin D in patients suffering from depression. A diet rich in vitamin D may help in prevention of depression. Further investigation is required to accurately determine the definite correlation between vitamin D and depression and its underlying mechanisms.

Conclusions

Our study suggests that patients with major depressive disorder have significantly lower levels of serum vitamin D than controls with no depression. There is a significant negative correlation between the vitamin-D level and severity of symptoms of depression.

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Conflicts of interest

There are no conflicts of interest.

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