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Effect Of Vitamin D Correction in Depressed Patients with Metabolic Syndrome and Reflection of This on General Health

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Abstract

Background: A person who has metabolic syndrome is more likely to experience diabetes, heart disease, and strokes. Vitamin D is a fat-soluble vitamin that is essential for maintaining healthy bones, immune system strength, and the control of insulin and glucose metabolism, among other physiological processes. Decreased vitamin D levels have been linked to an elevated likelihood of depression because vitamin D is crucial for healthy brain functioning. Aim: The current study's objective was to evaluate vitamin D levels in people with metabolic syndrome and depression and determine how their health would improve if their levels were raised. Method:100 depressed individuals with metabolic syndrome and vitamin D deficiency participated in the study, which was divided into two groups: 50 depressed patients with metabolic syndrome and vitamin D deficiency were placed in Group 1 and given antidepressants, diet control, and vitamin D replacement therapy. Group 2: 50 individuals suffering from depression who also had metabolic syndrome and a vitamin D deficiency underwent diet control and antidepressant treatment. Blood pressure, physical activities, and food habits were among the sociodemographic and clinical variables that were collected. The following laboratory tests were performed: liver functioning, renal functioning, fasting plasma glucose, lipid profile, vitamin D, and HbA1c. The cutoff point for vitamin D deficiency was <20 ng/mL. The clinical characteristics of vitamin D deficiency have been assessed. To evaluate depression, the Arabic version of the Beck Depression Inventory-II (BDI-II-ARABIC) was utilized. Results: The average age was 50.8 ± 6.6 years and 52.4 ± 6 years, with BMIs of 32.4 ± 2.4 kg/m2 and 32.7 ± 1.7 kg/m2, correspondingly, in the vitamin D as well as control groups. The baseline mean score of the BDI-II scale was 19.55 ± 6.18 for the control group and 18.99 ± 5.95 for the vitamin D group with no significant differences between the groups (p=0.058). After 6 months of intervention, the mean score for the control group was 18.19 ± 4.17 and 16.77 ± 2.77 for the vitamin D group with a significant difference between the groups (p=0.039). By using the ANCOVA test for in-between groups comparison, there was a

statistically significant difference (p=0.029). Following six months, there was a great significant difference between the control and vitamin D group according to weight loss, DM, HTN, dyslipidemia, and depression (p<0.001). There was a significant variation between the two groups in the mean increase of 25(OH) D serum levels (16.8 ± 5.8 ng/ml for the vitamin D group vs. 0.8 ± 4.4 for the control group, p-value <0.001). The relationship between vitamin D deficiency and metabolic syndrome and hypertension stayed significant after controlling for physical activity and eating patterns. Conclusion: Although the extent, nature, and implications of this association are uncertain, vitamin D insufficiency has been associated with higher blood pressure, depression, and the metabolic syndrome, in particular.

Keywords

Vitamin D, Hypertension, Metabolic Syndrome, Depression, General Health.

An individual who has metabolic syndrome is more likely to experience stroke, heart disease, and diabetes[1]. Vitamin D is a fat-soluble vitamin that is essential for maintaining healthy bones, immune system strength, and the control of glucose and insulin metabolism, among other physiological processes[2].

Investigations have revealed that those who have metabolic syndrome typically have decreased vitamin D levels and that lower levels of vitamin D are linked to a greater chance of acquiring metabolic syndrome[3, 4]. Additionally, metabolic syndrome components, including insulin resistance, hypertension, and dyslipidemia, can be made worse by a vitamin D deficit[5, 6].

Furthermore, vitamin D may help with the metabolic syndrome by lowering inflammation, strengthening endothelial functioning, and increasing insulin sensitivity[1]. As a result, preserving sufficient amounts of vitamin D could be crucial for controlling and managing the metabolic syndrome. To fully comprehend the effect of vitamin D on metabolic syndrome and its possible therapeutic advantages, more study is necessary[7].

According to studies, there is a link between vitamin D and depressive symptoms. Insufficient amounts of vitamin D have been linked to an elevated likelihood of depression because vitamin D is crucial for healthy brain functioning[8, 9].

Lower vitamin D concentrations have been linked to depression, according to studies, and supplementing with vitamin D could, in some situations, lessen depressive symptoms[10, 11]. A single study discovered that vitamin D treatment reduced depressive symptoms in those with vitamin D deficiency more effectively than a placebo[12, 13].

Sustaining optimal quantities of vitamin D through food, exposure to sunlight, or supplements could be crucial in avoiding and controlling the symptoms of depression, even though additional study is required to completely understand the connection between vitamin D and depression[14].

There is a strong correlation between vitamin D and general health. Among other physiological functions, the fat-soluble vitamin D is crucial for maintaining bone health, immune system performance, and managing glucose and insulin metabolism[15, 16].

For the body to preserve healthy levels of calcium and phosphorus, which are essential for keeping teeth and bones healthy, vitamin D plays a role[17]. Vitamin D deficiency can cause rickets in children and osteomalacia in adults, a weakening of the bones[18].

An abnormality in the blood's lipid or cholesterol concentrations is referred to as dyslipidemia, which is a predictor of acquiring cardiovascular disease. There is evidence from investigations indicating vitamin D and dyslipidemia are related[19].

According to research, dyslipidemia is more likely to occur in people who have low vitamin D levels, and vitamin D supplements can contribute to reduced blood levels of lipids and cholesterol[20]. Additionally, studies have revealed that a lack of vitamin D is linked to a rise in triglycerides and a drop in high-density lipoprotein (HDL), known as the "good" cholesterol[21].

There is proof that vitamin D intake and weight loss are related. According to several investigations, obesity and weight gain could be linked with lower levels of vitamin D, and taking vitamin D supplements may help people lose weight[22].

Vitamin D plays a crucial role in controlling diabetes mellitus (DM) through several mechanisms:

Improving insulin sensitivity: Vitamin D helps maintain healthy blood sugar levels and improves insulin sensitivity by promoting the transport of glucose into cells[23].

Vitamin D aids in the reduction of inflammation, which is linked to the emergence of insulin resistance and the development of diabetes[24].

Enhancing beta-cell function: Vitamin D helps regulate insulin secretion by enhancing the function of pancreatic beta cells[25].

Blood pressure control: Blood pressure, an indicator for type 2 diabetes, can be controlled by vitamin D as well[26].

Immune system support: Vitamin D strengthens the immune system and aids in the prevention of infections, which can have a detrimental impact on blood sugar levels in diabetics[27].

Considering its numerous effects on the cardiovascular system, vitamin D is crucial in regulating hypertension (high blood pressure), including:

Regulating the renin-angiotensin-aldosterone system (RAAS): Vitamin D helps regulate the activity of the RAAS, which is a system involved in regulating blood pressure[28]. Reducing inflammation: Vitamin D helps decrease inflammation in the blood vessels, which can improve blood flow and reduce blood pressure[29]. Improving endothelial function: Vitamin D enhances endothelial function, which is the ability of blood vessels to dilate or constrict as needed[30]. Lowering insulin resistance: Vitamin D helps lower insulin resistance, which can contribute to hypertension by promoting sodium retention[31]. Reducing sympathetic nervous system activity: Vitamin D may help decrease the activity of the sympathetic nervous system, which is involved in regulating blood pressure[32].

Patients

Study Design

Between May 2022 and April 2023, participants with metabolic syndrome and mild to moderate depression were referred to the Internal Medicine and Psychiatric Department's outpatient clinics at Al-Azhar University Hospitals. The participants had no other psychiatric diseases.

Sample Size

In accordance with earlier research, a sample size of 100 patients was determined by taking into account an effect size of 0.75 and a power of 80%[33].50 patients were randomly allocated to each group using the following formula with straightforward randomization methods:

$$n = \left[\frac{2\left(z_1 - \frac{a}{2} + z_\beta\right)^2 SD^2}{\left(\mu_1 - \mu_0\right)^2} \right]$$

The study included 100 depressed patients with metabolic syndrome and vitamin D deficiency and was subdivided into two groups:

Group 1:(50) depressed patients with metabolic syndrome and vitamin D deficiency were subjected to vitamin D replacement with diet control and anti-depressants. We followed them up after 6 months.

Group 2:(50) Depressed patients with metabolic syndrome and vitamin D deficiency were subjected to diet control and anti-depressants. We followed them up after 6 months.

Inclusion Criteria

We enlisted both incidental and old cases of depression in patients with ages 18 to 60, written consent, metabolic syndrome, vitamin D deficiency, and mild to moderate depression without any psychiatric disorder, as certified by the psychiatrist.

Exclusion Criteria

Presenceof other psychiatric disorders, pregnancy or breast-feeding, chronic kidney disease, nephritic syndrome, weight-lowering drugs, patients diagnosed with thyroid disorders, liver diseases, and conditions causing intestinal mal-absorption or present use of medications that affect the metabolism of vitamin D, such as phenobarbital, phenytoin, carbamazepine, isoniazid, theophylline, and rifampin. Individuals with a history of heart attacks, angina pectoris, strokes, vitamin D consumption from two months before the intervention, reluctance to keep participating in the trial, and non-compliance with the interventional program.

Ethical Consideration

The investigation was carried out in conformity with the ethical standards outlined in the 1975 Helsinki Declaration as updated in 1983 and its subsequent additions because it was permitted and accepted by the organizational research ethical committee at Al-Azhar University Hospitals.

Methods

All the studied cases were subjected to the following after oral and written consent:

Full history taking: Personal history: patient demographics [patient age, residence, education, employment, etc.], symptoms of diabetes [polyuria, poly-dyspepsia], symptoms of hypertension, symptoms of depression, and any type of treatment received.

Clinical Examination

Each patient underwent a rigorous clinical evaluation to identify any related conditions. First,

a general examination was performed, and anthropometric measurements were documented [e.g., patient height, weight, waist size, hip size, and waist/hip ratio]. Digital scales were used to weigh people while they were wearing the bare minimum of clothing, and the results were tracked. Having the shoulders positioned properly and standing with no shoes, height was measured.The hip circumference has been determined as the largest circumference at the symphysis pubis level and the waist circumference as the smallest circumference at the umbilicus level using an upstretched tape measure without exerting pressure to the body surface. Weight (kg) divided by height square (m^2) was used to compute the body mass index (BMI).

After 5 minutes of rest, blood pressure was then taken and noted. The mean of the last 2 readings was then used for analysis. We measured and recorded the pulses. The complexion was then inspected and recorded.Last but not least, all systems were thoroughly examined using the methods of examination, palpation, percussion, and auscultation. Any abnormalities were then recorded.

The metabolic syndrome was recognized using the modified ATP III for Korean definitions (three or more of the ensuing five parameters). Abdominal obesity is defined as having a waist circumference of over 90 cm for men and 85 cm for women[34];FPG more than 100 mg/dL (5.6 mmol/L) or medication for elevated blood sugar levels and blood pressure ≥ 130/85 mm Hg or medication for elevated blood pressure, men's serum HDL cholesterol should be below 40 mg/dL (1 mmol/L) and women's should be below 50 mg/dL (1.3 mmol/L), while serum triglycerides should be ≥150 mg/dL (1.7 mmol/L) or treated with medication if they are high.

Outcomes And Measurements

Primary Outcome: Assessment Of Depression

The Bdi-Ii

The BDI-II Arabic version was approved in the current study[35]. The twenty-one elements on the BDI-II are individually assessed on a 4-point Likert scale, with 0 denoting "minimal depression" and 3 denoting "severe depression," determining a wide range of depressive symptoms experienced over the previous two weeks. Overall scores range from 0 to 63. The following classification was made based on the findings that higher scores indicated greater severity of depression: Scores between 14 and 19 suggest mild depression, 20 to 28 imply moderate depression, while 29 or more imply severe depression [36]. For diagnosing depression in adult instances, scores below the age of 18 have been demonstrated to achieve the greatest sensitivity and specificity, while in teenage samples, a cut score of 16 produced a sensitivity rate of 84% and a false-positive rate of 18%[37].

Applying the DSM-5 Semi-structured Clinical Interview SCID-I, individuals who met the DSM-5 criteria for a major depressive episode (MDE) underwent interviews. The degree of depression was evaluated at baseline and six months after the treatment was completed.

Secondary Outcomes: Anthropometric Factors

Anthropometric measurements, blood pressure readings, fasting blood sugar, hemoglobin A1C, serum insulin, triglyceride, high-density lipoprotein (HDL), and low-density lipoprotein (LDL) values were the secondary outcomes. At the start and end of the experiment, venous blood samples from the participants were collected after a 12- to 14-hour fast. Prior to treatment, the anthropometric measurements were performed following permitted protocols. The BMI was computed by dividing weight in kilograms by height in meters squared.

Laboratory Assessment:

Al-Azhar University, clinical pathology department; the blood samples were collected after a 10- to 12-hour overnight fast and centrifuged within 30 to 45 minutes of the gathering.

Everyone who participated had 6mL of peripheral venous blood collected from them in tight sterility in accordance with global safety standards for biosecurity. After a 10- to 12-hour fast, blood samples were obtained in the early hours of the day and separated into two aliquots. The first 3 mL of blood were transferred into EDTA anticoagulation vacutainers for the HbA1c assay and complete blood counts; which were determined by the cell counter Cell Dyne Ruby (Germany) using kits from Abbott (Germany), while the HbA1c assay was done using the turbidimetric method using Cobas C 311 (Germany), Roche Diagnostics kits (Germany).

The remaining blood was put in an isolating polymeric serum gel tube with a clot activator (Kremsmьnster, Upper Austria, Greiner Bio-One GmbH, Australia), and allowed to coagulate for fifteen minutes at room temperature (24 °C), followed by a 10-minute 10,000Чg, 4 °C centrifugation step. They were divided up into Eppendorf tubes for the sera testing.

Following the manufacturer's guidance, serum insulin was evaluated using an ELISA kit (DRG International Inc., USA), with the use of AS 1851

Das, Italy (reader), and 16041412 Bio Tek, USA (washer).

We employed the chemiluminescence approach (Cobas E411 system "Germany" with Roche kits"Germany") to measure serum vitamin D, serum TSH, serum-free T3, and serum-free T4. The 25-OH Concentrations of vitamin D greater than or equal to 30 ng/ml were regarded as normal; those between 20 and 29.9 were regarded as insufficient; and those below 20 ng/ml were regarded as deficient. The reference ranges of thyroid function are (0.5−5.0 mU/l) for TSH, (1.2−4.4 pg/ml) for T3, and (0.8−2.0 ng/dl) for T4[38].

An auto analyzer (Cobas C 311 system "Germany" with Roche kits "Germany") was used to assess the lipid profile and fasting serum glucose,2 h postprandial serum glucose, serum calcium, liver, and renal function tests.

The formula shown below was used for assessing insulin resistance (HOMA-IR):

HOMA-IR = fasting blood sugar (mmol/L) x fasting serum insulin (μUI/ml) ч22.5 [39].

Employing a manual sphygmomanometer, individuals' systolic and diastolic blood pressures were assessed while they were seated.The upcoming laboratory tests have been concluded.

Statistical Analysis

The two- independent t-test or Mann-Whitney U-test had to be used to compare socioeconomic and clinical data in relation to the prevalence of vitamin D deficiency. After adjusting for physical activity and diet, we used logistic regression analysis to find the link between low serum vitamin D levels and metabolic syndrome. IBM Corp., Armonk, New York, USA, provided SPSS for Windows version 26.0 for use in the statistical analysis. All two-sided testing methods were statistically significant at the 0.05 level.

Results

Baseline

Table 1 lists the demographic information and initial traits of each person who was randomly assigned to the research investigation. Regarding general, anthropometric, and laboratory factors, the groups were homogeneous (p-value >0.05). The average age was 50.8 ± 6.6 years and 52.4 ± 6 years, with BMIs of 32.4 ± 2.4 kg/m^2 and 32.7 ± 1.7 kg/m^2, correspondingly, in the vitamin D as well as control groups. However, there was no distinction between the two cohorts in terms of predicted average FBS or total cholesterol (p-value >0.05). Vitamin D deficiency was evident in both groups based on average 25(OH) serum D levels (serum 25(OH) D <20 ng/ml). Serum TSH, T3, and T4 were within the normal range in both groups without significant differences.Metformin was taken by 40% of the control group and 38% of the vitamin D group. At baseline, insulin resistance was high in both groups (2.6 ± 0.96 in the control group and 2.8 ± 0.155 among the vitamin D supplement group), with no significant difference between the two groups (p=0.856).

Table (1): Patients' initial characteristics

	Control (n=50)	Vitamin D supplement group (n = 50)	P-value
Sex, n (%)			0.8
Female	13 (26)	12 (24)	
Male	37 (74)	38 (76)	
Age, (year)	52.4 ± 6	50.8 ± 6.6	0.3
Educational level, n (%)			0.4
University/college	36 (72)	36 (72)	
Secondary	5 (10)	13 (26)	
Not-educated/Primary-	9 (4.5)	1 (2)	
Employed, n (%)			0.9
No	23 (46)	22 (44)	
Yes	27 (54)	28 (56)	
Marital status, n (%)			0.8
Divorced/widow	4 (8)	5 (10)	
Married	42 (84)	41 (82)	
Single	4 (8)	4 (8)	
Smoking habit, n (%)			0.8
Ever	2 (4)	0 (0)	
Current	8 (16)	8 (16)	
Never	40 (80)	42 (84)	
WHR	0.89 ± 0.07	0.89 ± 0.06	0.4
BMI (kg/m^2)	32.7 ± 1.7	32.4 ± 2.4	0.7
Body weight (kg)	77.4 ± 10.5	79.8 ± 15.2	0.5

Height (cm)	167.1 ± 7.8	170.0 ± 11.8	0.3
Metformin use, n (%)			0.5
No	30 (60)	31 (62)	
Yes	20 (40)	19 (38)	
PA (MET/mint/week)	17.9 ± 10.9	17.0 ± 13.3	0.8
DBP(mmHg)	86.2 ± 10.9	82.9 ± 8.2	0.2
SBP (mmHg)	128.9 ± 14.4	127.8 ± 9.6	0.4
Serum 25(OH)D (ng/ml)	14.7 ± 12.5	16.6 ± 8.9	0.9
Total cholesterol (mg/dl)	206.5 ± 50.5	190.5 ± 49.5	0.2
LDL (mg/dl)	94.7 ± 35.7	99.2 ± 36.4	0.7
HDL (mg/dl)	46.6 ± 11.9	44.2 ± 13.3	0.4
TG (mg/dl)	180.7 ± 84.6	183.6 ± 70.9	0.9
Serum insulin (mU/L)	11.8 ± 4.4	11.5 ± 5.6	0.9
HbA1c (%)	6.8 ± 1.2	6.7 ± 1.2	0.4
FBS(mg/dl)	187.2 ± 54.5	178.7 ± 44.7	0.5
Serum T4 (ng/dl)	1.60 ± 0.41	1.71 ± 0.11	0.245
Serum T3 (pg/ml)	2.83 ± 1.12	2.77 ± 1.68	0.651
Serum TSH (mU/L)	3.77 ± 1.71	3.69 ± 2.01	0.378
HOMA IR	2.6 ± 0.96	2.8 ± 0.155	0.856

For means distinctions, an independent t-test was used. For categorical variables, chi-square and Fisher exact tests were used. Categorical characteristics are expressed as frequencies (percentages), and quantitative variables are shown as mean ± SD.

4.3. Post-Intervention

Bdi-Ii Score

Table 2 illustrated the assessment of BDI-II score before and after intervention in both vitamin D and control groups. The baseline mean score of the BDI-II scale was 19.55 ± 6.18 for the control group and 18.99 ± 5.95 for the vitamin D group with no significant differences between the groups (p=0.058). After 6 months of intervention, the mean score for the control group was 18.19 ± 4.17 and 16.77 ± 2.77 for the vitamin D group with a significant difference between the groups (p=0.039). By using the ANCOVA test for in-between groups comparison, there was a statistically significant difference (p=0.029).

Table (2): BDI-II assessment score before and after intervention

Group	Control (n=50)	Vitamin D supplement group (n = 50)	P	P*
Baseline	19.55 ± 6.18	18.99 ± 5.95	0.58	0.029
After 6 months of intervention	18.19 ± 4.17	16.77 ± 2.77	0.039	
Change	-1.36 ± 4.07	-2.22 ± 4.27	0.044	
p-value within group*	0.09	0.02		

*By ANCOVA for between-groups comparison. P significant if <0.05.

Vitamin D Correction And Laboratory Outcome

The contrasting results of the average variation in weight loss as well as laboratory variables at the start and completion of the intervention are shown in Table 3. Following six months, there was a great significant difference between the control and vitamin D group according to weight loss (p<0.001). There was a significant variation between the two groups in the mean increase of 25(OH) D serum levels (16.8 ± 5.8 ng/ml for the vitamin D group vs. 0.8 ± 4.4 for the control group, p-value <0.001). In comparison to the control group, the group receiving vitamin D experienced a greater reduction in HbA1c and serum levels of insulin (p-values = 0.03 and 0.008, respectively). The same findings were obtained for TG levels, where the average shift was considerably greater in the vitamin D group as opposed to the control group (p-value = 0.004). The results showed a statistically significant variance in the average change of FBS, HDL, LDL, or total cholesterol levels between the group receiving vitamin D and controls (p-value <0.05), while there was a little variation in the average shift of DBP among both groups (p-value = 0.057). After intervention, insulin resistence decreased among vitamin D supplemet group (1.88 ± 0.612) than in control group (2.711 ± 0.411) with a highly significant difference between the two groups (p<0.001). This highlighted

the role of vitamin D in lowering insulin resistence, LDL level, total cholestrole, TG, serum insulin and organizing DBP and SBP; however, it increased HDL level (Figures 1-10).

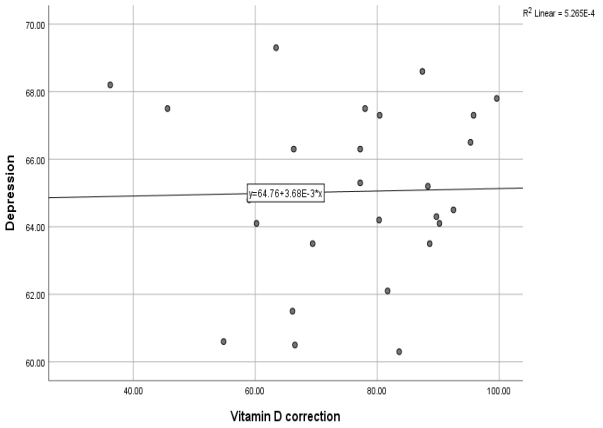

Figure (1): Correlation between vitamin D correction and depression improvement

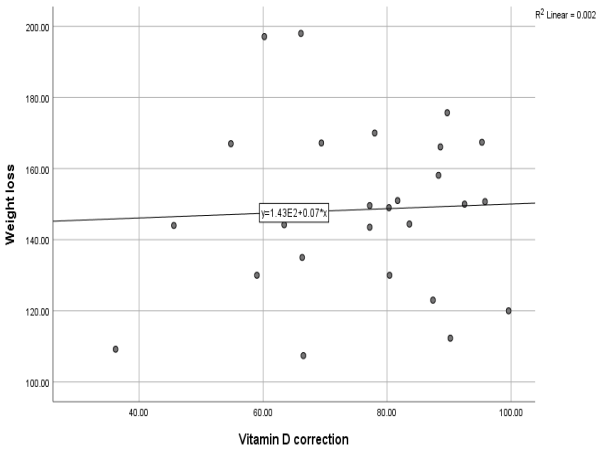

Figure (2): Correlation between vitamin D correction and weight loss improvement

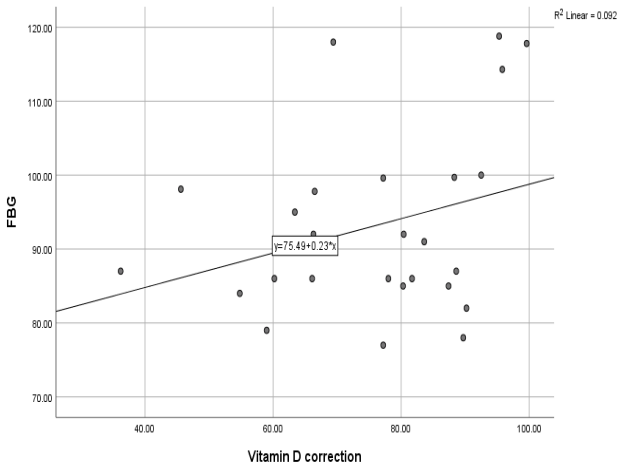

Figure (3): Correlation between vitamin D correction and FBG

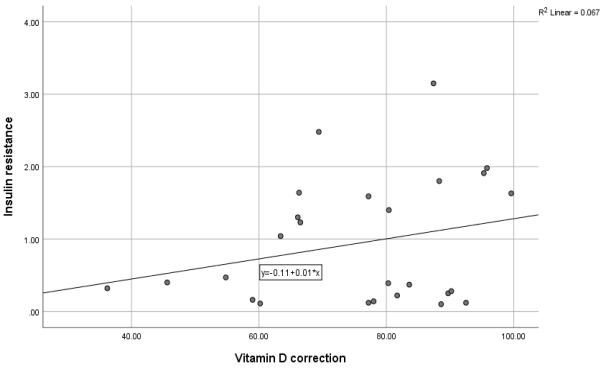

Figure (4): Correlation between vitamin D correction and insulin resistance

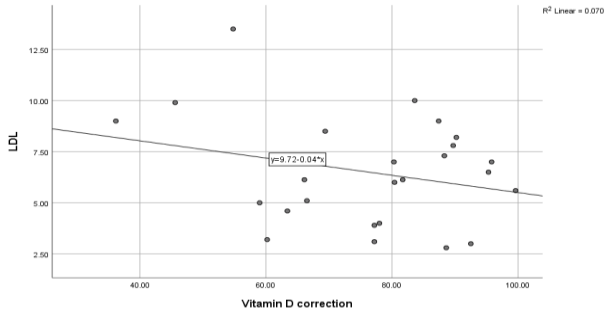

Figure (5): Correlation between vitamin D correction and LDL

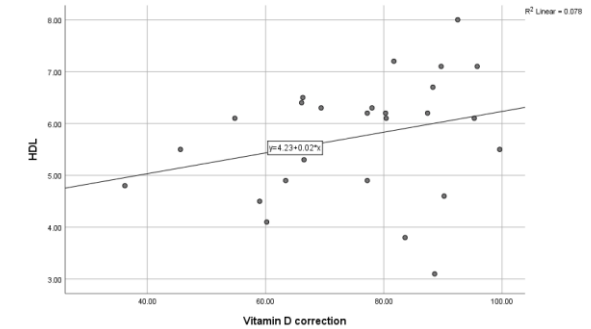

Figure (6): Correlation between vitamin D correction and HDL

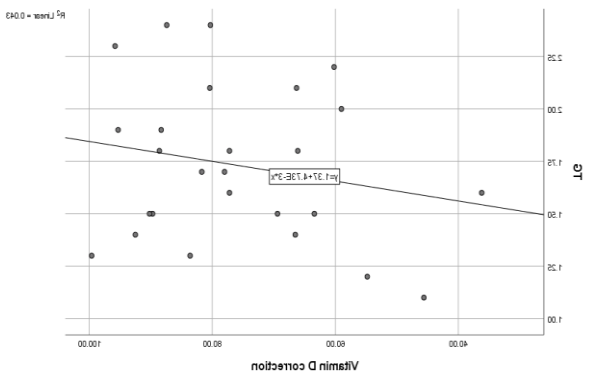

Figure (7): Correlation between vitamin D correction and TG

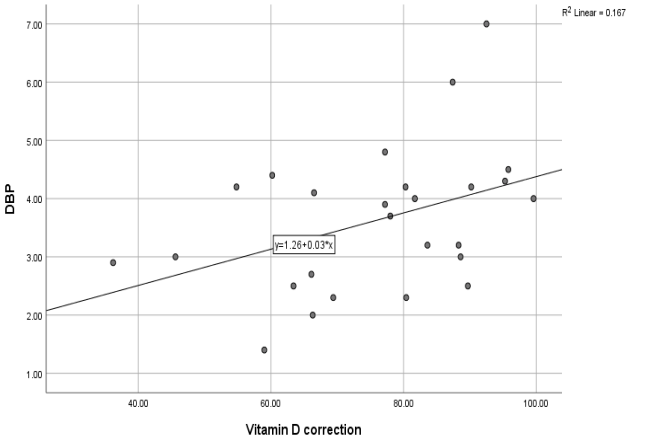

Figure (8): Correlation between vitamin D correction and DBP

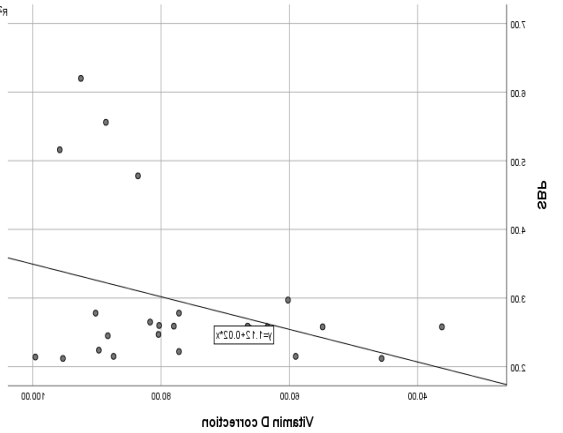

Figure (9): Correlation between vitamin D correction and SBP

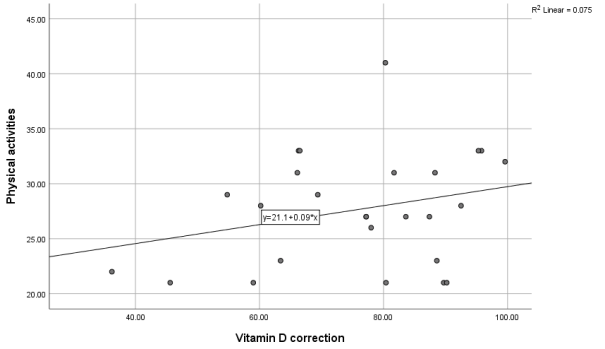

Figure (10): Correlation between vitamin D correction and physical activities improvement

Table (3): Following 6 months of treatment assessment of the average shifts invitamin D and each laboratory outcome between the vitamin D supplementing and the control group*.

	Control group (n = 50)	Vitamin D supplement group (n = 50)	p-value
	Mean ± SD	Mean ± SD	
Weight (Kg)	0.06 ± 1.1	-1.7 ± 1.4	<0.001
Total cholesterol (mg/dl)	−14.3 ± 38.9	−5.4 ± 52.6	0.05
LDL (mg/dl)	−0.5 ± 27.4	−0.6 ± 33.4	0.008
HDL (mg/dl)	−2.2 ± 5.7	−2.2 ± 6.7	0.008
TG (mg/dl)	7.5 ± 49.4	−35.1 ± 62.5	0.004
Serum insulin (mU/L)	0.1 ± 1.2	−0.7 ± 1.5	0.008
HbA1c (%)	−0.08 ± 0.8	−0.6 ± 0.6	0.03
FBS(mg/dl)	−6.7 ± 43.2	−23.8 ± 33.4	0.008
DBP(mmHg)	1.5 ± 6.5	−1.5 ± 5.3	0.057
SBP(mmHg)	−0.1 ± 7.1	−1.4 ± 4.8	0.05
Serum 25(OH)D (ng/ml)	0.8 ± 4.4	16.8 ± 5.8	<0.001
HOMA IR	2.711 ± 0.411	1.88 ± 0.612	<0.001

*Using the Student's t-test, determine the average variation across groups. High-density lipoproteins are referred to as HDL and LDL, respectively. Triglycerides, haemoglobin A1c Fasting Blood Sugar (FBS), Systolic blood pressure (SBP) is higher than diastolic blood pressure.

A multiple linear regression model of the standardized predictive value was produced. The standardized residuals' distribution seems to closely resemble a standard curve. For each of the remaining independent variables and predicted values of the present depression degrees, scatterplots for the standardized residuals were created (weight loss, total cholesterol, LDL, HDL, TG, serum insulin, HbA1c, FBS, DBP, SBP, and serum 25(OH)D). There was no discernible systematic trend in the distribution of the standardized residuals for predicted values of the present degrees

of depression, suggesting that the dependent variable's variance was identical at all degrees (r^2=0.127) (Figure 11).

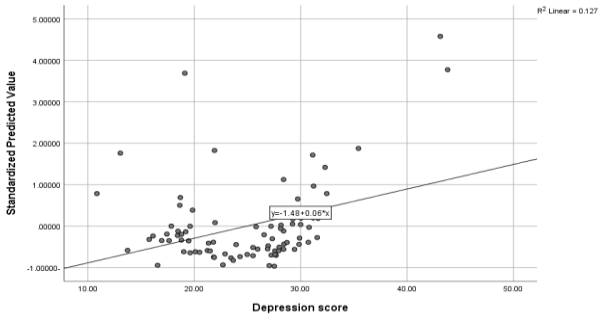

Figure (11): Multiple linear regression model between the score of depression and other study variables.

Discussion

The findings of the present investigation demonstrated that vitamin D administration is useful in reducing mild to moderate depression symptoms in metabolic disorder patients. In individuals with metabolic disorders who were vitamin D deficient, therapy with vitamin D supplements not only considerably reduced HbA1c, insulin, and TG levels but also significantly alleviated symptoms of depression. According to the current study, the baseline mean score of the BDI-II scale was 19.55 ± 6.18 for the control group and 18.99 ± 5.95 for the vitamin D group with no significant differences between the groups (p=0.058). After 6 months of intervention, the mean score for the control group was 18.19 ± 4.17 and 16.77 ± 2.77 for the vitamin D group with a significant difference between the groups (p=0.039). Metformin was taken by 40% in the control group and 38% in the vitamin D group. The reason for weight loss observed among patients with vitamin D supplements that vitamin D inhanced insulin resistance and physical activity, consequently, it improved loss of weight.As a result, vitamin D enhanced quality of life through eliminating fatigue, improving daily physical activities and decreasing muscle pain or ache.Our findings agree with those of other researchers. Following three months of treatment, Mozaffari-Khosravi et al.'s clinical study participants who obtained supplement of vitamin D showed a significant improvement in their depression-related mood. Another clinical research by Penckofer et al. [40] revealed that vitamin D treatment significantly reduced depressive symptoms in women with metabolic disorders. Additionally, strong data suggested that vitamin D supplements work well as an additional therapy to antidepressant medications for managing depression in those with the major depressive disorder[41]. While no such relationships were found in other investigations[42, 43], numerous cross-sectional investigations have revealed a connection between lower serum levels of 25-hydroxyvitamin D and depressive symptoms[44, 45].

Depression medications such as tricyclics and paroxetine, however, may result in increased body weight and elevated insulin levels[46, 47], furthering metabolic disruption. Antidepressant medications may successfully decrease depressive mood and its accompanying symptoms in individuals with metabolic disorders [48].

Although there are various theories, the processes by which vitamin D affects mood are not entirely known. Various parts of the brain have vitamin D receptors, and vitamin D can cross the blood-brain barrier[49-51]. It has been shown that vitamin D is capable of regulating serotonin synthesis. Among the main neurotransmitters associated with mood regulation is serotonin[52]. Additionally, an alteration in brain functioning and an imbalance between GABAergic inhibition and excitatory neurons are the two main contributors to depression. GABAergic neurons play a critical role in regulating one's mood, although function and quantity are compromised in depressed individuals. In a depressive state, glutamatergic pathway activation might result in decreased GABAergic neurons. On activation of the inositol trisphosphate cellular pathway (InsP3), elevated levels of glutamate may raise the concentration of Ca^{2+} in neurons. This rise in Ca^{2+} neuronal concentrations could help to explain why depression symptoms emerge[53-56]. Ca^{2+} neuronal concentrations may drop as a result of vitamin D's potential ability to control the expression of Ca^{2+} pumps and buffers[57, 58].

Vitamin D substantially reduced HbA1c and insulin resistance among individuals with metabolic disorders in the current investigation. It supports numerous researches that show vitamin D supplementation helped lower HbA1c and insulin resistance in people with metabolic disorders[59, 60].

One theory for this effect process is connected to the positive effects of vitamin D on insulin production. The release of insulin from beta cells is aided by vitamin D[61].

It should be noted that individuals with metabolic disorders were included in this study even though they did not meet MDD diagnostic or take antidepressants. Additionally, only metabolic disorder patients with mild to moderate depression symptoms and vitamin D insufficiency levels are applicable to our findings.

Strengths and limitations of the study

The homogeneity of the research's participants, the low amount of missing data, the double-blind, randomized, placebo-controlled design, and the use of the accurate and valid BDI-II-Arabic version depression scale are the study's strengths. Our limitation included a brief duration of follow-up.

Conclusion

In addition to improving metabolic function, this placebo-controlled, double-blind, randomized experiment demonstrated that vitamin D administration can reduce depressive symptoms among individuals with metabolic disorders. Individuals with metabolic disorders are more likely to experience depression. Individuals with depressed metabolic disorders who take vitamin D supplements may avoid developing MDD in the future.Vitamin D supplements lowered body weight compared with the control group. It also controls blood pressure, controlsdiabetes, and improves dyslipidemia.

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