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Correlation between Vitamin D3 Supplementation and Lipidemia in Women of Maysan Province, Iraq with Uncontrolled Type 2 Diabetes

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ABSTRACT

A total of 130 overweight Iraqi women with uncontrolled type 2 diabetes, the ages of the women (28 to 60) years, were divided into groups, group 5000 IU (65 women) as group **A** and control (65 women) as group **B**. were participants from The Specialized Center for Diabetes in Maysan Province and its related areas in the countryside and the city for this double-blind, randomized control trial (Maysan Province, Iraq). A placebo and 5000 IU of D3 daily were given to the participants for four months. Laboratory tests were conducted at baseline and four months to analyze serum levels. After four months of treatment, positive changes in **total cholesterol, D3** levels, and **LDL** cholesterol. There was no statistically meaningful change in **HDL** and **TG** concentration, and there were no significant differences in age and place of residence. According to this study, vitamin D may help type 2 diabetics lower their total cholesterol and **LDL** concentrations.

1. Introduction

According to the reviewed literature, D3 and dyslipidemia are still debatable. Low levels of serum D3, Furthermore have been linked to poor lipid profiles in observational studies, and D3 can influence serum lipid levels in a variety of ways (Kendrick, et al., 2009; Wang, et al., 2012). As a result, vitamin D enhances intestinal calcium absorption, which affects fat absorption in the gut. In this model, a calcium-fatty acid soap is manufactured by reacting calcium with fatty acids and bile acids and then expelled in feces (Boon, et al., 2007). It reduces fat absorption from the intestinal tract, lowering both total cholesterol and LDL cholesterol, as well as triglycerides levels in the blood (Grundy & Denke, 1990; Zittermann, et al., 2009) Vitamin D may also help prevent dyslipidemia by raising serum parathyroid hormone concentrations (Jorde & Grimnes, 2011). The presence of the parathyroid hormone concentration in the blood has been related to an increased risk of obesity, and in vitro, lipolysis has been reported to be inhibited by PTH (Jorde, et al., 2005; Kamycheva, et al., 2004; Hagstrom, et al., 2009). Consequently, D3 is thought to lower serum lipid levels by decreasing parathyroid hormone production by the parathyroid glands (Zemel, et al., 2000).

This study aimed to examine if supplementing with vitamin D improves dyslipidemia indicators in Iraqi females with poorly managed type 2 diabetes (Maysan Province, Iraq).

2. Materials and Methods

2.1. Materials and Reagents

All the reagents used in the research were supplied from (Roche Diagnostics, Germany), Vitamin D total 25-hydroxyvitamin D immunoassay kit, Cholesterol Gen. 2 colorimetric assay kit, Triglycerides enzymatic colorimetric assay kit, HDL-Cholesterol plus 3rd generation enzymatic colorimetric assay kit and LDL-Cholesterol plus 2nd generation enzymatic colorimetric assay kit. Use deionized

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water (Local store, Iraq), distilled water (Local store, Iraq), Sterile Gloves (Local store, Iraq), Microcrystalline cellulose placebo (German), and 5000 IU vitamin D3 (German).

2.2. Vitamin D Concentration Measurement

Vitamin D binding protein (V.D.B.P.) was utilized as a capture protein for D3 and D2 in the Roche Cobas e 411 analyzer to measure the total of D3 in the plasma of blood. Using PreciControl Varia, the control interval was established with a lower threshold of 13.179- 20.619 ng/ml and a higher threshold of 24.200- 37.700 ng/ml. Prior research compared this vitamin D assessment method with others and found that it had a good level of concordance (Abdel-Wareth, et al., 2013). According to the Endocrine Society's classification, the deficiency of Vitamin D is determined by the serum levels (Holick, 2004; Holick, et al., 2011; Holick & Chen, 2008).

2.3. Lipid Concentration Measurement

In this investigation, total cholesterol,high-density lipoprotein (HDL), triglycerides (TG), and low-density lipoprotein (LDL) were measured via an enzymatic technique (TC). The Roche enzymatic colorimetric test system was used to quantify HDL and LDL. The lower limit control threshold for HDL was established at 23.6–32.6 mg/dL using PreciControl ClinChem Multi 1. The upper limit control threshold was 53.2–73.6 mg/dL using PreciControl ClinChem Multi 2. Using PreciControl Multi 1 & 2, the control threshold for LDL was set at 44.5–61.3 mg/dL for a lower threshold and 80.3–110.7 mg/dL for a higher threshold.

TG was determined using a Roche method. Using PreciControl ClinChem Multi 1 for the lower limit and PreciControl ClinChem Multi 2 for the higher limit, a sample size of 2µl was employed, with control intervals of 92–112 mg/dL for a lower threshold and 183–223 mg/dL for a higher threshold. A Roche test was used to determine total cholesterol (TC). Cobas c 111 analyzer is used to determine the rise in absorbance. PreciControl ClinChem Multi 1 was used to sample a volume of 2µl of serum, with control intervals of 73.1–90.49 mg/dL for a lower threshold and 154–190 mg/dL for a higher threshold. The American Heart Association's desired low, borderline high, high, and high cutoff limits for lipid readings (Robinson & Stone, 2015; Forouhi & Wareham, 2010). To evaluate if D3 had a significant effect on lipid levels, these cutoffs were utilized to compare lipid levels before and after the intervention. The (ADA) established guidelines on optimum lipid levels for diabetes patients in 2019, including a low HDL cutoff point (Karandish, 2014).

3. Results and Discussion

3.1. High-Density Lipoprotein (HDL)

Table 1 shows the changes in individuals' average HDL compared in both groups A and B (the tests after four months minus baseline tests) reveal no statistically significant difference in HDL concentrations between the before four months and after four-month groups.

Table 1
Comparison of HDL (mg/dl) concentrations before and after four months

Group	Before four months (Tests)	After four months (Tests)	Change in the mean (the tests after four months minus baseline tests)	b p-value
	Mean ±SD			
A	48.21 ±9.63	46.70 ±10.93	-1.50 ±6.60	0.183
B	47.74 ±9.65	45.18 ±10.45	-0.55 ±6.87	0.622

Figure 1 shows the mean HDL difference between baseline and after four months and the differences between the two groups. However, it revealed that HDL levels did not differ substantially between the A and B groups (F (2, 125) = 0.469, p = 0.629). Using mixed ANOVA, there was no found significant interaction between time, group A and B. (F (2,124) = 572, p = 0.564).

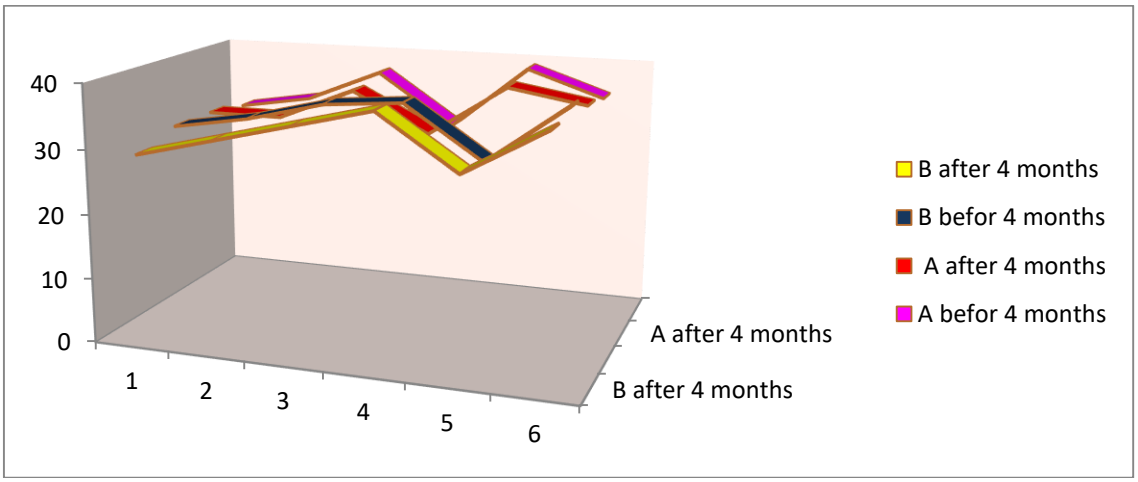

Fig. 1. Comparison of the two groups' mean HDL (mg/dl) with time (baseline and after four months)

In that study, there was no association between consuming D3 and changes in HDL concentrations. This was added to the findings that taking D3 had no effect on HDL levels (Jorde & Figenschau, 2009; Al-Sofiani, et al., 2015). Researchers employed a randomized double-blind control design in a 2015 trial to provide 87 D3-deficient obese type 2 diabetics with 6000 IU of D3 daily for three months, followed by a direct 3000 IU daily, and their HDL levels stayed stable (Sadiya, et al., 2015). Three months of taking 5000 IU of vitamin D a day did not make a big difference in the amount of HDL in the blood (Al-Sofiani, et al., 2015). Even with a higher number of samples and a high dose concentration, such as in research in which 100 type 2 diabetics were given 50,000 IU of D3 weekly for eight weeks, there was no significant change in HDL Cho concentration in serum (Talaei, et al., 2013). As far as the researcher knows, there have only been two trials from the Middle East showing an improvement in HDL resulting from vitamin D supplementation (Rad, et al., 2014; Mohamad, et al., 2016).

A study conducted two-month randomized controlled experiments that involved 59 type2 of diabetics, the majority of whom were women, who were provided with 4000 IU/day. While the study had a limited sample size and was short in duration, The use of D3 resulted in increases in HDL concentrations (Rad, et al., 2014). It is not known what caused this. In a study of 100 type2 of diabetics taking 4500 IU of D3 daily for 60 days, the sufficient D3 concentration in serum (higher than 61 ng/ml) after supplementation resulted in better HDL cholesterol concentration (Mohamad, et al., 2016). This shows that more research into vitamin D's dosage response is needed, and those blood D3 values higher than 61 ng/ml will result in considerable changes in HDL.

3.2. Low-Density Lipoprotein (LDL)

Table 2 shows the changes in individuals' average LDL compared to groups A and B (the tests after four months minus baseline tests).

Table 2
Comparison of LDL (mg/dl) concentrations before and after four months.

Group	Before four months (Tests)	After four months (Tests)	Change in the mean (the tests after four months minus baseline tests)	b p-value
	Mean ±SD			
A	105.90 ±34.20	100.43 ±25.40	-5.47 ±32.05	0.282
B	102.79±32.52	115.29 ±36.36	12.50 ±30.17	0.014

Figure 2 depicts the difference in average LDL between the tests after four months minus baseline tests and the differences between the A and B groups. Despite the small effect size (eta squared = 0.056), the findings demonstrated a significant difference in mean LDL between the two groups (F (2, 124) = 3.685, p = 0.027). Using mixed ANOVA, the interaction between time and the two groups was considerable (F (2,126) = 3.343, p = 0.038). According to the one-way ANOVA results (baseline and four-month), There was no considerable difference in average LDL between the A and B groups; after four months, using the test to compare pairs of individuals.

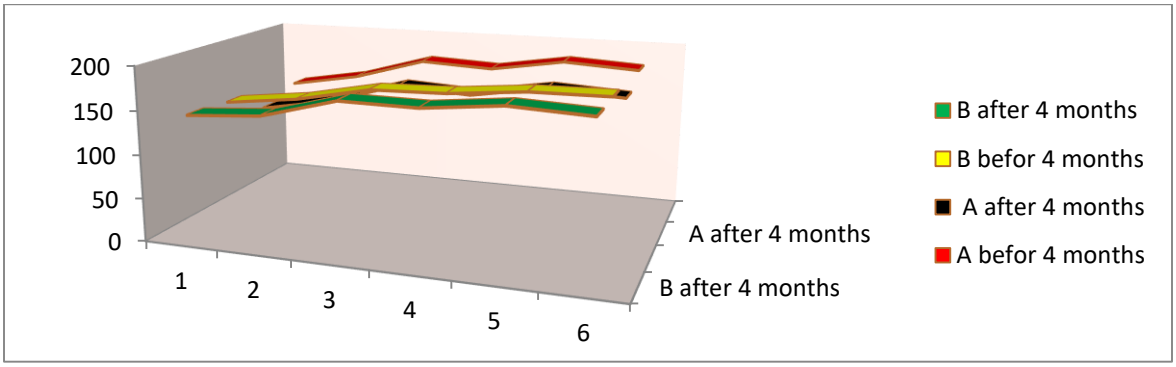

Fig. 2. Comparison of the two groups' mean LDL (mg/dl) with time (baseline and after four months)

Table 3 reveals that the average LDL of group A was considerably lower than that of group B (average change = -14.86, p = 0.043).

As demonstrated in Table 2, the only significant variation in LDL between baseline and four months was for group B (average change = 12.50, p = 0.014).

Table 3
LDL (mg/dl) differences between the A and B groups after four months.

Time	Group	Group	Change in the mean	b p-value
after four months -test	A	B	-14.86	0.043

The study found that the D3-treated group showed an important reduction in LDL Cho. surprisingly, after four months, the placebo group's LDL cholesterol levels climbed. Similar Middle Eastern research found that vitamin D treatment in varied doses and durations resulted in an important improvement in LDL Cho (Al-Daghri, et al., 2012; Eftekhari, et al., 2014; Mohamad, et al., 2016). In another study, despite the fact improvements in LDL Cho, it's difficult to draw firm conclusions from this study (Eftekhari, et al., 2014) used lower D3 (2000 IU daily) than the previous two trials and the current study, and neither tested serum D3 concentrations. A study of 92 Saudi type2 diabetics taking 2000 IU/day for 72 weeks found an important reduction in LDL, which was more pronounced in women than in men when serum D3 concentrations also increased an important (Al-Daghri, et al., 2012).

Another study found a substantial reduction in LDL in patients who had more than double the necessary serum concentration of D3 (higher than 61 ng/ml) after supplementation compared to those who had lower serum concentrations (Mohamad, et al., 2016). This shows that higher serum D3 levels may be necessary to obtain positive lipid benefits. This backs up the current investigation's results., which indicated that following supplementation, 70% of people in the A and A1 group had adequate serum D3 concentrations.In contrast, the majority of research undertaken to date in the rest of the world appears to imply that vitamin D has no substantial function in lowering LDL (Patel, et al., 2010; Breslavsky, et al., 2013; Talaei, et al., 2013; Yiu, et al., 2013; Kampmann, et al., 2014; Ryu, et al., 2014; Sadiya, et al., 2015; Al-Sofiani, et al., 2015; Rad, et al., 2014). This is explained in part by the fact that the sample sizes used in previous studies were all significantly lower than those used in this one were. The findings' discrepancy can be explained to some extent by the short research time; just three studies citation had a study times equal to or greater than the current one (Breslavsky, et al., 2013; Ryu, et al., 2014; Sadiya, et al., 2015).

Because serum vitamin D concentrations were not high enough after supplementation (higher than 30 ng/ml), a large number of studies showed no link between D3 taking and lower LDL concentrations did so. In addition, two trials came really close to the 61 ng/ml serum level that was determined to be the most effective for decreasing LDL cholesterol levels. Given that, the other study was a single-blinded study; its credibility may be questioned. Similarly, the results of the other study were not replicated in the Iraqi population, raising doubts about their reproducibility (Talaei, et al., 2013; Yiu, et al., 2013; Mohamad, et al., 2016). According to studies, taking at least 2000 IU of D3 daily can result in considerable improvements in LDL concentrations in Countries in the Middle East. The studies with serum D3 levels of more than 60 ng/ml showed the greatest reduction in LDL cholesterol.

3.3. Triglycerides

Table 4 shows the changes in individuals' average TG compared to groups A and B (the tests after four months minus baseline tests).

Table 4
Comparison **of TG (mg/dl) concentrations before and after four months.**

Group	Before four months (Tests)	After four months (Tests)	Change in the mean (the tests after four months minus baseline tests)	b p-value
	Mean ±SD			
A	126.77 ±80.34	123.09 ±53.88	-3.67 ±54.42	0.713
B	142.91 ±64.54	151.22 ±96.28	8.32 ±70.96	0.405

According to the data, the A and B groups' mean TG did not considerably differ (F (2, 123) 1.067, p = 0.346). When mixed ANOVA was used, there was no considerable interaction between the A group, the B group, and time (F (2, 123) = 0.530, p = 0.588).). Figure 3 depicts the difference in average TG between the tests after four months minus baseline tests and the differences between the A and B groups. As shown in Table 4, there was no statistically considerable difference in TG values before and after four months in each group.

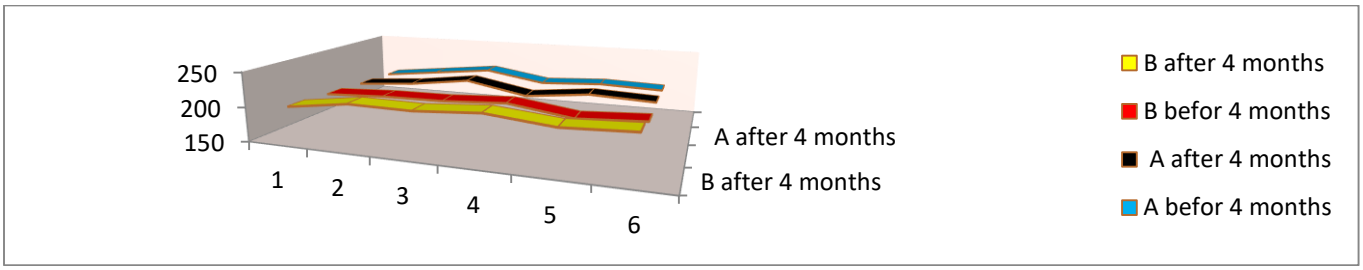

Fig. 3. Comparison of the two groups' mean TG (mg/dl) with time (baseline and after four months).

In this study, there was no link between lower serum triglycerides and higher D3 concentrations. According to current research, vitamin D3 supplementation has little effect on triglyceride levels (Jorde & Figenschau, 2009; Patel, et al., 2010; Talaei, et al., 2013; Ryu, et al., 2014; Sadiya, et al., 2015; Al-Sofiani, et al., 2015; Rad, et al., 2014).

According to the researcher's best understanding, only three investigations (in the Arab world) have revealed a significant reduction in triglyceride concentrations after vitamin D delivery (Eftekhari, et al., 2014; Mohamad, et al., 2016; Alkharfy, et al., 2013). A study of 499 volunteers taking 2000 IU daily over a period of 48 weeks is noteworthy. The large sample size and the large time of the

study are likely factors in the discovery of a substantial link between vitamin D and lower triglyceride levels (Alkharfy, et al., 2013). Case research of three D3–deficient people with type2 diabetes who got a single 300,000 IU vitamin D intramuscular injection in 1998 refuted the current findings. Triglycerides in the blood increased considerably after 12 weeks. In this scenario, too much vitamin D may have a negative impact on TG levels (Taylor & Wise, 1998). More research is needed to determine the appropriate amount of D3 supplementation for lowering TG levels over the course of a year.

3.4. Total Cholesterol

Table 5 compares the changes in each group's mean total Cho (after four months, minus baseline testing). Table 5 shows that the mean total Cho in group A was lower than essential (average change = -15.16, p = 0.010), as determined by after four-month test.

Table 5
Comparison **of total Cho. (mg/dl) concentrations before and after four months.**

Group	Before four months (Tests)	After four months (Tests)	Change in the mean (the tests after four months minus baseline tests)	b p-value
	Mean ±SD			
A	177.00 ±41.47	161.84 ±31.50	-15.16 ±40.44*	0.010
B	177.70 ±34.82	179.07 ±41.44	1.37 ±34.56	0.813

Despite the small effect size (eta squared = 0.042), the findings revealed that the mean total Cho differed substantially among the A group and B group (F (2, 124) = 2.685, p = 0.048). The differences in mean total Cho between baseline and four months for each group and the differences between the two groups are depicted in Figure 4. Using an ANOVA of mixed (F (2,124) = 4.42, p = 0.036), an essential interaction was identified between the A group, the B group, and time. According to an analysis of variance, the mean total cholesterol before and after the test was not an essential difference between the A and B groups.

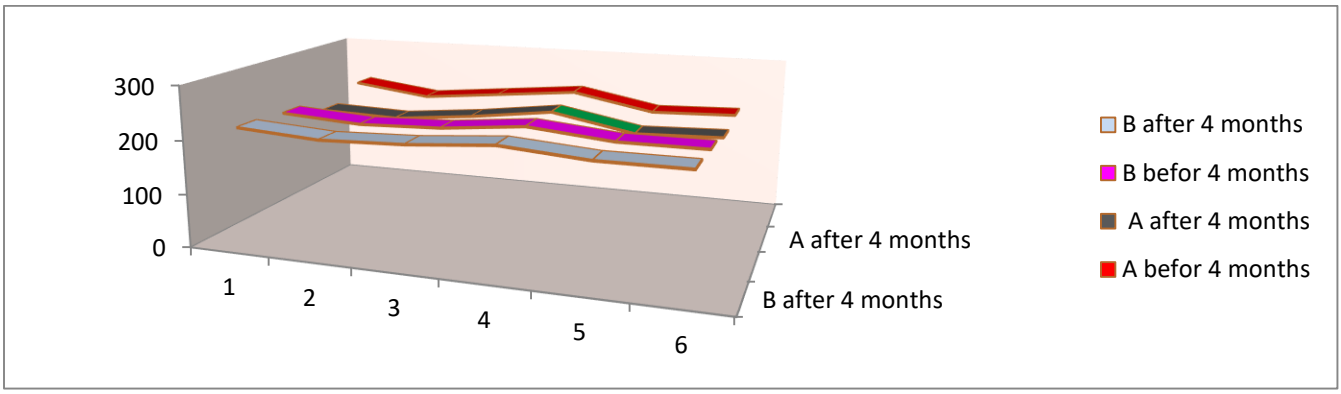

Fig. 4. Comparison of the two groups' mean total Cho. (mg/dl) with time (baseline and after four months)

After four months, a paired comparison test revealed an important difference in total Cho concentration between groups A and B (average change =-14.86, p = 0.046). In group A, the average total Cho was considerably lower than the average total Cho in group B (See Table 6).

Table 6
Total Cho (mg/dl) differences between the A and B groups after four months.

The time	The group	The group	The change in the mean	b p-value
after four months -tests	A	B	-14.86	0.046

In this research, the vitamin D-treated group saw a considerable reduction in total Cho. After four months, the control groups experienced a substantial increase in total cholesterol. Because total Cho is the sum of blood LDL, HDL, and TG concentrations, the decline in LDL may help show these findings.In similar trials undertaken in the Middle East, D3 treatment resulted in considerable decreases in blood total Cho (Al-Daghri, et al., 2012; Eftekhari, et al., 2014; Alkharfy, et al., 2013). D3's influence on total cholesterol, on the contrary,, is still contested in the literature, with numerous research findings finding no link between the two (Jorde & Figenschau, 2009; Patel, et al., 2010; Talaei, et al., 2013; Ryu, et al., 2014; Sadiya, et al., 2015; Al-Sofiani, et al., 2015; Rad, et al., 2014). This could be justified by ethnicity, sample size, and the three-month duration of the research. It has been proposed that research with Countries in the Arab world can make big changes in total cholesterol with at least 70 volunteers and 12 weeks study (Alkharfy, et al., 2013).

4. Conclusion

There is no proof of a connection between blood HDL and triglyceride levels and vitamin D intake of 5000 IU daily. D3 supplementation resulted in a considerable decreases in blood LDL (p = 0.027) and total cholesterol (p = 0.048). More interventional trials, including D3 supplementation at greater levels, are undoubtedly required to arrive at blood values of (> 60 ng/ml) and repeat these promising results in type2 diabetics' lipid profiles. It is worth mentioning that the vast of the participants were women. The study's volunteers were taking statins already when they signed up, so many of them started with a lipid profile that was within normal limits.

In another investigation, statins were discovered to have a considerable anti-inflammatory impact, which may have obscured vitamin D's anti-inflammatory effect. Alternatively, the level of inflammation in type 2 diabetics may be already so high that 16 weeks of D3 administration had no impact (Taylor & Wise, 1998). To the researcher's knowledge, There has been no research on the effects of D3 supplementation on the lipid profiles of type 2 diabetes patients who are not taking statins. More research into the effects of D3 in type 2 diabetics with an uncontrollable profile lipid is needed, as evidenced by this finding.

Competing Interests

The authors have declared that no competing interests exist.

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