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# Calciferol Deficiency and Supplementation influence on Lipid Profile Variables in Diyala Governorate


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**Abstract**

**Background:** vitamin D deficiency is a global health problem associated with rickets and growth retardation in children, and osteoporosis and osteomalacia in adults. In addition, in recent years, there has been increasing evidence to demonstrate the extraskeletal role of vitamin D. Vitamin D deficiency has also been linked to many acute and chronic illnesses including some cancers, autoimmune diseases, cardiovascular disease, type 1 and type 2 diabetes mellitus, infectious diseases, and neurocognitive dysfunction, among others

**Objective and methods::** This study was conducted to determine the association between serum level of vitamin D and lipid profiles, including serum concentrations of cholesterol, triglyceride (TG), HDL, and LDL in healthy subjects and predict the risk of dyslipidemia with changes in vitamin D status. .. A prospective, randomized open-label trial was carried out in apparently healthy men and women from diyala governorate (20–55 years) who were divided into two groups, in which one group received vitamin D supplements (Received oral cholecalciferol 6000 IU/day for 3 months ) and the other group received placebo.venous blood sample was withdrawn 8 ml after fasting. Serum levels of 25(OH) D (25, hydroxy vitamin D3) were measured . The levels of total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) were measured before and after intervention.

**Results:** Mean age in the total mixed population was 35.5 ± 20.5 years. Subjects were 40% male and 58% female**.** Significant increase in 25OHD concentrations was seen in intervention group. Mean 25(OH) D in the total population before and after intervention were 23.74 ± 5.09 ng/ml and 43.20 ± 15.94* ng/ml respectively. After using vitamin D supplementation for 3 months , lipid profile variables did not change significantly except increased level of HDL-C.

*Represents significant differences from baseline; Level of significance is at $P < 0.05$.

**Conclusions:** after this research found Vitamin D Supplementation in deficient patients has been found to lower the levels of total cholesterol, triglycerides, and LDL cholesterol and increase the levels of HDL cholesterol. Vitamin D deficiency increases vascular cell adhesion molecules and E-selectin, with a potential role in the formation of atheroma plaque. It also influences the vascular tone by modifying endothelial nitric oxide production. Deficiency can lead to oxidative stress, increased inflammation, and expression of immune cells, i.e., monocytes and macrophages, that play a pivotal role in atherosclerosis of the intima. Another pathway by which vitamin D is involved in atherogenesis is through inhibition of vascular smooth muscle cell proliferation. Furthermore, studies have shown that vitamin D deficiency is associated with cardiovascular events, such as myocardial infarction, STEMI, NSTEMI, unstable angina, ischemic stroke, cardiovascular death, and increased mortality, after the acute stroke.

## Introduction

Vitamin D, a lipid-soluble cholesterol-based molecule, is synthetized in adequate amounts in people with sufficient sun exposure or, in lesser amounts, taken up through diet. If deficient, the intake can be supplemented with oral formulations [1]. Although presently uncommon in developed countries, vitamin D severe deficiency can cause rickets and osteomalacia in children and adults, respectively[2]. Not withstanding, less severe subclinical deficiency levels encompassing osteoporosis are more prevalent and associated with the risk of fractures . Although the effects on bone turnover and calcium-phosphate homeostasis are its most widely recognized functions, this molecule acts as a hormone, exerting immunomodulatory actions , controlling cellular proliferation and differentiation, and is directly associated with lower risk of obesity, diabetes mellitus, metabolic syndrome, and cardiovascular disease and has neuroprotective and antiaging effects There is great interest in extra-skeletal effects of vitamin D[13] [11].. Epidemiological studies have shown a link between vitamin D deficiency and lipid profile changes ..[6]. Other studies have also shown that vitamin D deficiency is associated with increased risk of cardiovascular disease . [2],[3].Levels of serum cholesterol are a strong predictor of cardiovascular risk. Observational studies have demonstrated that high levels of vitamin D are associated with a favorable lipid profile, whereas low levels of vitamin D are associated with an atherogenic lipid profile.[7],[8].However, intervention studies show contradictory results[5] . Therefore, further studies are needed to confirm or refute these possible effects. In the present study, we investigated the effect on lipid profile of vitamin D supplementation with vitamin D deficiency. [4],[5],[6].

The aim of this study is to evaluate calciferol (Vitamin D) deficiency and supplementation impact on lipid profile variables in diyala governorate by dividing volunteers into two groups one of them is control group who receive placebo and other group receive oral cholecalciferol 6000 IU/day for 3 months

## Methods

### Subjects

This study was performed among men and women from diyala governorate (20–55 years). Convenient method was used to enroll participants to the study. The following inclusion criteria was used to select participants: 20–55 years males and females, nonsmoking, no history of diabetes, no hyperthyroids and hypothyroids, normal serum creatinine, normal blood urea nitrogen levels, regular menstrual cycle, and no pregnancy . Furthermore, we excluded studies in which vitamin intake was mixed with other dietary treatments or drugs. We excluded studies that focused on the patients with non-cardiovascular diseases, such as chronic kidney disease, hemodialysis states and rheumatoid arthritis for the reason that these diseases have remarkable impact on lipids profile and might confused the effects of vitamin D supplement on lipids. The general questionnaire included information about demographic characteristics such as location, education level, marital status, drug history and the number of pregnancy and children. In addition, we asked other questions about physical activity, the duration and times of sleep, sunlight exposure, consumption of supplements, and being on a special of diet. After giving general overview about this study, all individuals provided informed written consent.

### Study design

The aim of this study is to evaluate calciferol (Vitamin D) deficiency and supplementation impact on lipid profile variables in diyala governorate by dividing volunteers into two groups one of them is control group who receive placebo and other group receive oral cholecalciferol 6000 IU/day for 3 months. The participants continued their usual diet during the study. The intervention follow-up was 6 weeks that began from november , 2022 to january 28, 2023. At the first visit, we gave them 6 pearls of vitamin D supplements to intervention group and 6 pearls of placebo to the controls and we asked them to eat one per day. The dozens of supplements were 6000 IU and placebo had the same shape, color, and packaging with given supplement. In addition, at the first meeting, food record has been explained to the individuals and they were asked to prepare it for 3 days including one weekend and 2 week days. Furthermore, the individuals were asked to report their physical activity during one selected week. In addition, participants recorded their daily amount of sun exposure from sunrise till sunset. The levels of total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-c), high-density lipoprotein cholesterol (HDL-c) and vitamin D were measured at two different occasions

**Biochemical analysis**

Blood samples were taken in a sitting position following (12_16 hr) of fasting before and after the intervention. lipid profiles were measured by biochemical autoanalyzer A15 with Biosystem kit (made by Spain). Serum levels of 25(OH) D (25, hydroxy vitamin D3) were measured using the enzyme-linked immunosorbent assay (ELISA).

**Biochemical estimations**

A venous blood sample (8 ml) was collected between 8a.m. and 11 a.m. from each individual after an overnight fast for more than 12 h using Vacutainers (BD, Franklin Lakes, NJ, USA). Serum was separated after centrifugation at 2500 rpm for 15 min at room temperature within 2 h of collection. Serum level of 25(OH) D (25, hydroxy vitamin D3) were measured by ELISA .. High-density lipoprotein cholesterol (HDL-C), total cholesterol (TC), and triglycerides (TG) were measured enzymatically. LDL-C and very LDL-C concentrations were calculated using Friedewald equation.

**Results**

At the end of 3 months , 66 and 60 individuals completed the study in control and cholecalciferol group, respectively. The individuals who completed the study showed 95% compliance to the regimen and were similar in both intervention groups. There was no intolerance or adverse reaction to cholecalciferol supplements or placebo in any subjects. Remaining individuals discontinued intervention prematurely as they were not interested in continuing the intervention.

At baseline, there were no significant differences in age and lipid parameters between the two groups. Mean serum levels of 25(OH) D (25, hydroxy vitamin D3) concentrations in the control group were higher.[Table 1]

**Table 1:** Important baseline parameters in two groups

| | Control Group | Cholecalciferol Group |
|---|---|---|
| **Age (Years)** | 35.5 ± 20.5 | 35 ± 20.5 |
| **25(OH)-Vitamin D (nmol\L)** | 32.5 ± 10.5 | 15± 6.5 |
| **Total Cholesterol (mmol\L)** | 4.3 ± 0.8 | 4.9 ± 1.2 |
| **HDL-Cholesterol (mmol\L)** | 1 ± 0.33 | 0.7± 0.2 |
| **LDL-Cholesterol (mmol\L)** | 2.0± 0.5 | 2.6 ± 0.8 |
| **Triglyceride (mmol\L)** | 1.30 ± 0.3 | 1.50 ± 0.6 |

After 3 months intervention, a significant increase in 25(OH) D concentrations was observed in the cholecalciferol group. The increase of 25(OH) D concentrations in cholecalciferol supplemented group was significantly higher than in control group. Those in cholecalciferol supplemented group also showed a significant increase in HDL-C concentrations.[Table 2]

**Table 2:** Effect of intervention (cholecalciferol supplementation) on mean Vitamin D and lipid profile compared to control group

| | Control Group | Cholecalciferol Group |
|---|---|---|
| **Age (Years)** | 35.5 ±20.5 | 30± 20.5 |
| **25(OH)-Vitamin D (nmol\L)** | 32. ± 10.6 | 57 ± 8.8 |
| **Total Cholesterol (mmol\L)** | 4.5± 0.8 | 4.9 ± 0.9 |
| **HDL-Cholesterol (mmol\L)** | 0.9 ± 0.31 | 1.5 ± 0.3 |
| **LDL-Cholesterol (mmol\L)** | 2.3 ± 0.58 | 2.65 ± 0.9 |
| **Triglyceride (mmol\L)** | 1.30 ± 0.3 | 1.59 ± 0.5 |

## Discussion

In the current study, vitamin $D_3$ supplementation at 6000 IU/day significantly reduced total cholesterol, and triglycerides in a sample of iraqi people with vitamin D insufficiency and lipid levels variable. However, the significance was lost after adjusting for confounders.[8],[9].

In fact, vitamin D insufficiency is related to other cardiovascular risk factors such as obesity, smoking, and unhealthy diet . Regarding the strong association between obesity and vitamin D insufficiency, it has been hypothesized that vitamin D is stored in the fat tissue and is not bioavailable in obese participants resulting in low levels of serum vitamin D despite sufficient intake .In this context, if obesity is corrected we may see improvements in both serum vitamin D levels and lipid profile. Our results support this hypothesis. [9],[10],[11],[12].

## Limitations

The short duration of the study is our limitation.and there is no help or guidance from hospital or medical lab also from people it self .

## Conclusion

Our study demonstrates that orally administered Vitamin D significantly increase HDL-C concentration. Our observations have implications for public health advice on improving Vitamin D status and lipid profile of the population.

Vitamin D has lately been found to modify the mechanisms of atherosclerosis. Supplementation in deficient patients has been found to lower the levels of total cholesterol, triglycerides, and LDL cholesterol and increase the levels of HDL cholesterol. Vitamin D deficiency increases vascular cell adhesion molecules and E-selectin, with a potential role in the formation of atheroma plaque. It also influences the vascular tone by modifying endothelial nitric oxide production. Deficiency can lead to oxidative stress, increased inflammation, and expression of immune cells, i.e., monocytes and macrophages, that play a pivotal role in atherosclerosis of the intima. Another pathway by which vitamin D is involved in atherogenesis is through inhibition of vascular smooth muscle cell proliferation. Furthermore, studies have shown that vitamin D deficiency is associated with cardiovascular events, such as myocardial infarction, STEMI, NSTEMI, unstable angina, ischemic stroke, cardiovascular death, and increased mortality, after the acute stroke.

## Future Directions

To date, vitamin D, a highly important hormone in the homeostasis and metabolism of calcium bone, has lately been found to produce effects on other physiological and pathological processes, including the cardiovascular system. [1],[2],[12],[14].

While lower baseline vitamin D levels have been found to corelate with atherogenic blood lipid profiles, 25(OH)D supplementation has been found to influence the levels of serum lipids in that it lowers the levels of total cholesterol, triglycerides, and LDL cholesterol and increases the levels of HDL cholesterol. [6].

To detect whether a true association between vitamin D and atherosclerosis exists, future interventional studies should be designed with sufficient sample size, long follow-up duration, higher vitamin D doses, restriction of lipid-lowering drug use, and potentially control for confounders of atherosclerosis (such as metabolic and endocrine diseases). [7],[8],[11].

Vitamin D is also involved in the development of atherosclerosis at the site of the blood vessels. Deficiency of this vitamin has been found to lead to an increase of adhesion molecules or endothelial activation and at the same time supplementation is linked to the lowering presence of adhesion surrogates. Vitamin D also influences the vascular tone by increasing endothelial nitric oxide production as seen in supplementation studies. A better understanding of these queries might have significant implications for the potential use of vitamin D analogues in the prevention of atherosclerosis. [10],[15],[16].

Vitamin D deficiency is consistently associated with cardiovascular events, such as myocardial infarction, STEMI, NSTEMI, unstable angina, ischemic stroke, cardiovascular death, and increased mortality after the acute faze of stroke. Conversely, vitamin D supplementation does not seem to produce beneficial effects in cohorts with all intermediate baseline levels of vitamin D. [7],[17],[18].

Future work is needed to ascertain whether vitamin D therapy is effective in reducing mortality through reducing the incidence of acute coronary syndromes.[20].. Vitamin D might be deficient in patients who smoke, have high blood lipids, diabetes, or other specific risk factors.[19],[20].

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