

# Association Between Serum Vitamin D Level And Lipid Profile In a Jordanian Adult Cohort

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## ABSTRACT

**Aim:** The main aim of our study was to investigate the association between vitamin D levels and lipid profiles in a Jordanian adult cohort.

**Methods:** This retrospective study was conducted during the period from January 2017 to February 2018 on 762 patients who attended the internal medicine clinics at King Hussein Medical Centre in Amman. Blood samples were analysed at the Department of Chemistry of the Princess Iman Centre for Research and Laboratory Sciences using Cobas e411 analyser to determine serum 25hydroxyvitamin D<sub>3</sub> (25[OH] D<sub>3</sub>) levels, and Cobas 501 for lipid profile analysis (triglycerides, total cholesterol, low-density lipoprotein cholesterol and high-density lipoprotein cholesterol levels). Data were analysed using the statistical software SPSS version 20.0. The observed differences in values were analysed for statistical significance and a p-value of <0.05 was considered significant.

**Results:** Of the 762 subjects, 300 (39.37%) were vitamin D deficient, 416 (54.59%) were insufficient and 46 (6.04%) had sufficient levels. We found a positive significant correlation between 25(OH)D<sub>3</sub> and triglycerides ( $\beta$  coefficient = 0.258,  $p = 0.000$ ), total cholesterol ( $\beta$  coefficient = 0.194,  $p = 0.000$ ), low-density lipoprotein cholesterol ( $\beta$  coefficient = 0.279,  $p = 0.000$ ) and high-density lipoprotein cholesterol ( $\beta$  coefficient = 0.149,  $p = 0.000$ ).

**Conclusion:** Our present study showed a direct positive association between vitamin D level and triglycerides, cholesterol, low-density lipoprotein and high-density lipoprotein.

**Keywords:** Vitamin D deficiency, 25(OH) D<sub>3</sub>, dyslipidemia, lipid profile.

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## Introduction

Vitamin D is a fat-soluble vitamin that comprises a family of compounds essential for mineral homeostasis, and it plays a pivotal role in the proper formation and growth of teeth and bones [1].

The human body has two main sources of vitamin D; the major one is endogenous production through the cholesterol metabolism pathway. This occurs in the skin, where 7dehydrocholesterol is transformed [2]. the second source is exogenous, through ingestion of the diet and supplements. Dietary sources are mainly fatty fish, egg yolk and fortified milk [3]. Vitamin D<sub>2</sub> (ergocalciferol) is found in sun-exposed mushrooms and can be synthesised by the UV irradiation of yeast ergosterol. Since both sources need the exposure to UVB for activation, vitamin D has long been known as the 'sunshine vitamin' [4].

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After entering the body, vitamin D is rapidly converted to the major circulating form, 25-hydroxyvitamin D (25[OH] D) in the liver.

Then it is converted in the kidneys to the active hormone 1,25dihydroxyvitamin D (1, 25[OH]<sub>2</sub>D) by a second hydroxylation step influenced by parathyroid hormone [5]. The vitamins D<sub>2</sub> and D<sub>3</sub> are equally effective in the early improvement of serum 25(OH) D levels after administering loading doses. As for long-term sustenance, vitamin D<sub>3</sub> was found to be more appropriate [6]. The serum level of 25(OH)D<sub>3</sub>, rather than 1,25(OH)<sub>2</sub>D<sub>3</sub>, is commonly measured in serum to assess the individual's vitamin D status despite its being an inactive precursor that needs modification by further hydroxylation before function. This choice was based on its stability and longer half-life (about 3 weeks vs. 8 hours) and its higher blood concentration (>100 times greater) compared to the active form, 1,25(OH)<sub>2</sub>D<sub>3</sub> [7].

The main role of vitamin D is to regulate blood levels of minerals such as calcium, phosphorus, and, to a lesser extent, magnesium. Thus, vitamin D is vital for bone health and growth, and its deficiency leads to two well-known skeletal disorders: rickets in children and osteomalacia in adults [8].

Besides this important physiological role, vitamin D plays a complex role in numerous biological processes that regulate the immune system, inflammatory pathways and many vital cellular processes [9].

An insufficient vitamin D level has been identified as a worldwide health problem, especially in Middle Eastern countries [10, 11]. Risk factors include advanced age (especially if institutionalised), African American race, obesity, limited sun exposure, diabetes and chronic illnesses [12, 13]. Recent evidence has linked vitamin D deficiency with many adverse health outcomes such as hypertension, type II diabetes, cancer [14] and many autoimmune diseases (e.g. type I diabetes in children and multiple sclerosis) [15].

Hypovitaminosis D has also been linked to respiratory problems (e.g. higher frequency of asthma exacerbations and tuberculosis reactivation) [16]. It may even have an influence on certain neonatal conditions such as the risk of small for gestational age births and neonatal hypocalcaemia [17].

Vitamin D may affect different biological mechanisms, including insulin sensitivity, the renin-angiotensin-aldosterone system (and consequently, blood pressure), inflammatory cytokines, and vascular muscle contractility and response to injury [18]. In the recent literature, studies investigating the effects of the vitamin D level on the fasting lipid profile have given conflicting results.

In this retrospective study, we investigated the relationship between 25(OH) D<sub>3</sub> levels and fasting serum lipid profile parameters in Jordanian adults.

## Methods

Our study was approved by the ethics committee of the Royal Medical Services, Amman, Jordan.

This study was carried out on 762 patients. All were attending the internal medicine clinics at King Hussein Medical Centre during the period from 1 January 2017 to 1 February 2018. In the Royal Medical Services, patients at the age of 14 years are no longer treated at the pediatric clinic. They are treated in adult clinics instead. This is why we included patients starting from the age of 14 year in this adult cohort.

After an overnight fast of 10–12 hours, a single venous blood sample was collected from each patient into gel separator yellow top tubes between 8:00 and 10:00 am. The samples were allowed to clot for 15–30 minutes at room temperature, then were centrifuged at 4000 g for 10 minutes and immediately analyzed for lipid profile parameters and 25(OH) D<sub>3</sub> levels. The fully automated analysis for all the parameters in our study was carried out in the clinical chemistry laboratory at the Princess Iman Centre for Research and Laboratory Sciences. Serum 25(OH) D<sub>3</sub> levels were measured using a Cobas e411 auto-analyzer (Roche Diagnostics GmbH, Mannheim, Germany). Although 1,25(OH)<sub>2</sub>D<sub>3</sub> is the most potent form, 25(OH)D<sub>3</sub> levels are not influenced by parathyroid hormone and therefore reflect vitamin D status more accurately. The triglycerides (TG), total cholesterol, low-density lipoprotein (LDL) cholesterol and high-density lipoprotein

(HDL) cholesterol levels were measured using a Cobas 501 auto-analyzer (Roche Diagnostics GmbH, Mannheim, Germany). In our center, the reference ranges for the lipid profile parameters are: total cholesterol, 150–200 mg/dL; TGs, 50–200 mg/dL; HDL cholesterol, 35–65 mg/dL; and LDL cholesterol, 50–150 mg/dL. There is a slight variation from universal values. Recently, the National Lipid Association and the National Cholesterol Education Program defined desirable levels as total cholesterol < 200 mg/dL, TGs < 150 mg/dL, LDL < 100 mg/dL (with the range between 100 and 129 mg/dL termed above desirable) and HDL > 40 mg/dL for females and >50 mg/dL for males.

## Statistical analysis

Based on the serum lipid levels (total cholesterol, triglycerides, HDL cholesterol and LDL cholesterol), subjects were divided into two groups: those with normal levels, and those with high levels. With regard to the serum 25(OH) D3 level, the subjects were divided into three groups: the vitamin D deficiency group [25(OH)D<sub>3</sub> < 20 ng/mL], the insufficiency group [25(OH)D<sub>3</sub> 20–30 ng/mL] and the sufficiency group [25(OH)D<sub>3</sub> > 30 ng/mL]. The management and statistical analysis of the data were performed using the software SPSS 20.0 for Windows (SPSS Inc., Chicago, IL, USA) and the Microsoft Excel 2007 program. All variables were presented as means and standard deviation (SD), and a P-value < 0.05 was considered to be statistically significant.

## Results

The study included 762 patients with a mean age of 48.85 years (range, 14–92 years) and a female predominance: 473 (62%) were female and 289 (38%) were male. We divided our study subjects into three groups according to their 25(OH) D3 levels, as shown in (Table I).

**Table I:** 25(OH) D3 levels in all 762 subjects

25(OH)D <sub>3</sub> level	Frequency	Gender distribution	Percentage
Deficient (<20 ng/mL)	300	Male: 126 Female: 174	39.4
Insufficient (20–30 ng/mL)	416	Male: 151 Female: 265	54.6
Sufficient (>30 ng/mL)	46	Male: 12 Female: 34	6.0
Total	762	Male: 289 Female: 473	100.0

The first group was vitamin D deficient, with 25(OH) D3 levels <20 ng/mL (39.4%). The second group was vitamin D insufficient, with 25(OH) D3 levels between 20 ng/mL and 30 ng/mL (54.6%). The third group was vitamin D sufficient, with 25(OH) D3 levels >30 ng/mL (6.0%). The 25(OH) D3 level was set as a reference, and the results showed significant differences in lipid profiles among the three groups. We found a significant positive correlation between 25(OH) D3 level and triglycerides ( $\beta$  coefficient = 0.258,  $p = 0.000$ ). A high triglyceride level was found in 304 subjects; 69 of them had 25(OH) D3 deficiency, 211 had 25(OH)

D3 insufficiency and 24 had sufficient vitamin D<sub>3</sub>. We also found a significant positive correlation between 25(OH) D3 and total cholesterol ( $\beta$  coefficient = 0.194, p= 0.000). A high cholesterol level was found in 194 subjects; 44 of them had 25(OH) D3 deficiency, 133 had 25(OH) D3 insufficiency and 17 had sufficient vitamin D<sub>3</sub>. Regarding LDL cholesterol, a significant positive correlation was found with 25(OH) D3 ( $\beta$  coefficient = 0.279, p= 0.000). Of the 289 subjects with a high LDL level, 65 were found with 25(OH) D3 deficiency, 195 with 25(OH) D3 insufficiency and 29 with sufficient vitamin D<sub>3</sub>. Our results also showed a significant positive correlation between 25(OH) D3 and HDL cholesterol ( $\beta$  coefficient = 0.149, p= 0.000). We found 129 subjects with high HDL levels; 26 had 25(OH) D3 deficiency, 95 had 25(OH) D3 insufficiency and 8 had sufficient vitamin D<sub>3</sub>. (Table II).

**Table II:** Lipid profile parameters in the three 25(OH) D3 groups

Lipid profile parameter		25(OH)D3 level			Total number (percentage)
		<20 ng/mL	20-30 ng/mL	>30 ng/mL	
<b>Cholesterol:</b>	Normal	256	283	29	568 (74.5)
	High	44	133	17	194 (25.5)
<b>TG:</b>	Normal	231	205	22	458 (60.1)
	High	69	211	24	304 (39.9)
<b>LDL:</b>	Normal	235	221	17	473 (62.1)
	High	65	195	29	289 (37.9)
<b>HDL:</b>	Normal	274	321	38	633 (83.1)
	High	26	95	8	129 (16.9)

## Discussion

In the present study, serum vitamin D level was positively correlated with all lipid profile parameters which is partly beneficial in terms of higher HDL levels, and partly harmful in terms of higher total cholesterol, LDL and TGs. Wang et al. and Jorde et al. have shown the same effect of vitamin D on total cholesterol and LDL in women [33, 34]. In our study, however, no significant differences were found between men and women. A pilot study conducted on Hispanic/Latino adults suggested a positive association between vitamin D and lipids (results similar to our study), although the sample size of their study was small [42]. Glueck et al. found in a group of hyperlipidemia patients that serum vitamin D level was a significant independent positive determinant of HDL, but a negative one for the other lipid parameters [41]. Studies in the literature vary in their results; some found no clinical impact of vitamin D deficiency on lipids in older women and no effect on TGs in patients with type II diabetes [32, 43]. Others even found an inverse correlation. Jorde and Grimnes observed that serum 25(OH) D was positively associated with a favorable lipid profile [30]. Vitamin D was inversely related to TG levels in Saudi postmenopausal women and in Iranian type 2 diabetic patients, in addition to LDL in another Japanese study [31, 39, and 40].

Aside from observational studies and reviews, some interventional studies failed to support a protective effect of vitamin D supplementation on cardiovascular health [35–37]. Heikkinen et al. even demonstrated adverse effects on the lipid profile [38]. This supports our findings regarding total cholesterol, LDL and TGs.

One of the limitations of this study was its retrospective nature. It was difficult to determine the subjects' past medical history and their medication history. It was limited to a correlation between laboratory figures only; more clinical laboratory correlation is needed to better assess the association between dyslipidaemia and vitamin D deficiency. Well-designed prospective, placebo-controlled randomised interventional studies are needed to determine the effects of vitamin D supplementation. Case-control studies could be performed to include variables such as season of the year, smoking status, medication use, vitamin D intake, calcium intake, visceral fat area and cardiorespiratory fitness.

### Conclusion:

Our present study showed a direct positive association between 25(OH) D<sub>3</sub> level and total cholesterol, TGs, LDL and HDL. This raises the question as to whether hypovitaminosis D presents a potential risk factor for cardiovascular disease by reducing HDL or a beneficial effect by lowering total cholesterol, TGs and LDL.

### Abbreviations:

1,25(OH) <sub>2</sub> D <sub>3</sub>	1,25-dihydroxyvitamin D <sub>3</sub>
25(OH)D <sub>3</sub>	25-hydroxyvitamin D <sub>3</sub>
HDL	High-density lipoprotein
LDL	Low-density lipoprotein
TGs	Triglycerides

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